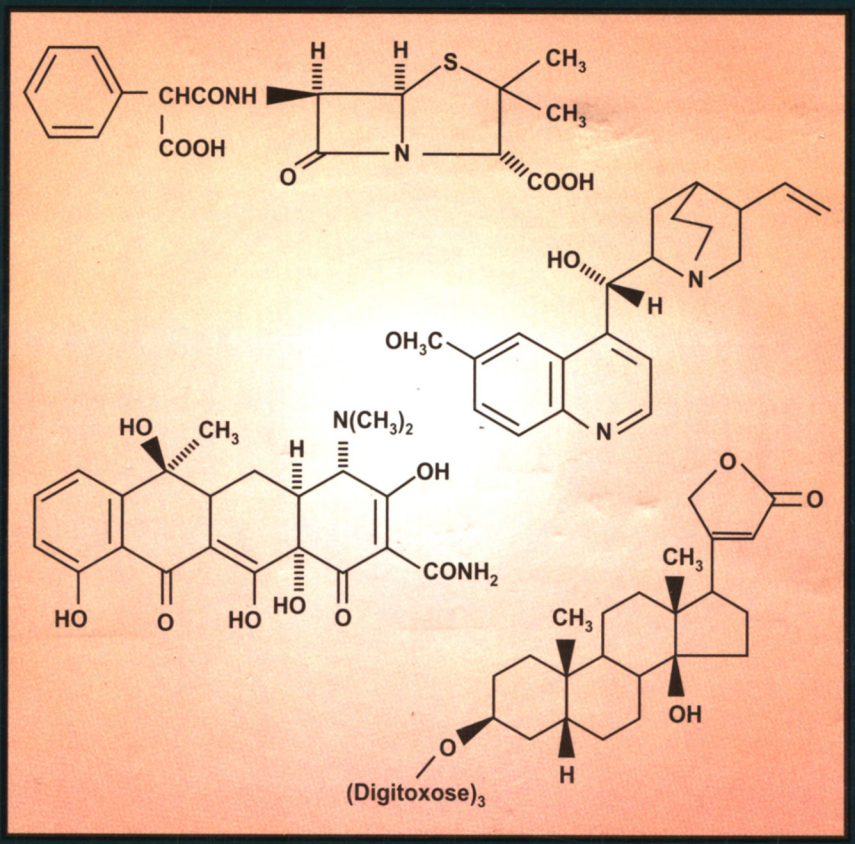
Text Book of Pharmaceutical Organic Chemistry

According to new syllabus as prescribed by P.C.I. in Education Regulation-1991, implemented in the year 1993



MOHAMMED ALI

Text Book of Pharmaceutical Organic Chemistry

This Page is Intentionally Left Blank

Text Book of Pharmaceutical Organic Chemistry

(According to new syllabus as prescribed by P.C.I. in Education Regulation-1991, implemented in the year-1993)

By

Dr. Mohammed Ali

Faculty of Pharmacy
Jamia Hamdard (Hamdard University)
Hamdard Nagar, New Delhi-110062



CBS Publishers & Distributors Pvt. Ltd.

New Delhi • Bengaluru • Chennai • Kochi • Kolkata • Mumbai
Hyderabad • Nagpur • Patna • Pune • Vijayawada

Disclaimer

Science and technology are constantly changing fields. New research and experience broaden the scope of information and knowledge. The authors have tried their best in giving information available to them while preparing the material for this book. Although, all efforts have been made to ensure optimum accuracy of the material, yet it is quite possible some errors might have been left uncorrected. The publisher, the printer and the authors will not be held responsible for any inadvertent errors, omissions or inaccuracies.

eISBN: 978-93-883-2775-6

Copyright © Authors and Publisher

First eBook Edition: 2018

All rights reserved. No part of this eBook may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or any information storage and retrieval system without permission, in writing, from the authors and the publisher.

Published by Satish Kumar Jain and produced by Varun Jain for
CBS Publishers & Distributors Pvt. Ltd.

Corporate Office: 204 FIE, Industrial Area, Patparganj, New Delhi-110092
Ph: +91-11-49344934; Fax: +91-11-49344935; Website: www.cbspd.com; www.eduport-global.com;
E-mail: eresources@cbspd.com; marketing@eduport-global.com

Head Office: CBS PLAZA, 4819/XI Prahlad Street, 24 Ansari Road, Daryaganj, New Delhi-110002, India.
Ph: +91-11-23289259, 23266861, 23266867; Fax: 011-23243014; Website: www.cbspd.com;
E-mail: publishing@cbspd.com; eduportglobal@gmail.com.

Branches

- **Bengaluru:** Seema House 2975, 17th Cross, K.R. Road, Banasankari 2nd Stage, Bengaluru - 560070, Karnataka Ph: +91-80-26771678/79; Fax: +91-80-26771680; E-mail: bangalore@cbspd.com
- **Chennai:** No.7, Subbaraya Street Shenoy Nagar Chennai - 600030, Tamil Nadu
  Ph: +91-44-26680620, 26681266; E-mail: chennai@cbspd.com
- **Kochi:** 36/14 Kalluvilakam, Lissie Hospital Road, Kochi - 682018, Kerala
  Ph: +91-484-4059061-65; Fax: +91-484-4059065; E-mail: kochi@cbspd.com
- **Mumbai:** 83-C, 1st floor, Dr. E. Moses Road, Worli, Mumbai - 400018, Maharashtra
  Ph: +91-22-24902340 - 41; Fax: +91-22-24902342; E-mail: mumbai@cbspd.com
- **Kolkata:** No. 6/B, Ground Floor, Rameswar Shaw Road, Kolkata - 700014
  Ph: +91-33-22891126 - 28; E-mail: kolkata@cbspd.com

Representatives

- **Hyderabad**
- **Pune**
- **Nagpur**
- **Manipal**
- **Vijayawada**
- **Patna**

PREFACE

Pharmaceutical organic chemistry is concerned with the chemistry, properties and uses of drugs of carbon compounds. In the ever expanding knowledge of the chemistry of drugs it is very difficult on the part of single individual to go through the various bigger volumes of text books, monographs and pharmacopoeias.

This book has primarily been written with the aim of meeting the needs and interests of under graduate students of pharmacy course according to the Education Regulation 1991 of the Pharmacy Council of India. The book is a concise form and will help the readers to a great extent. Organic chemistry students are often overwhelmed by the number of compounds and reactions, and they wonder whether they can learn all this material in a single year. But most of the Organic Chemistry consists of a few basic principles and a large number of extensions and applications of those principles. Relatively little memorization is required if the students grasp each major concept and develops flexibility in applying that concept. How much a student learns depends on himself.

The arrangement of the subject matter is based on medicinal properties. IUPAC nomenclature of drugs is stressed throughout the book and a separate chapter on common nomenclature is included to develop the student's familiarity. Following the nomenclature, brand names, chemical structure, properties, uses, adverse effects and official preparations of each drug are discussed. Synthetic procedures of important drugs are mentioned. Storage conditions of each compound are described and a chapter concerning stability is presented.

Learning the medicinal terms can be a formidable task. At the end of the book, a complete glossary summarizes and defines medicinal terms included in the book. Examination question papers of some universities and Boards of Technical

Education are provided to help the students in learning the subject. The writing style has been clear, simple and uniform, avoiding stilted language and long, complex sentences.

It is impossible to express my indebtedness to those authors of monographs, and articles from which I have gained so much information for writing the book. Without the encouragement, courtesy and full co-operation of Shri Satish Kumar Jain and Vinod Kumar Jain, CBS Publishers & Distributors, this work might not have reached beyond the talking stage. Much of the book's final form and appearance are due to tireless and exacting efforts of Mr. Sunil Kumar Dhir, Super Computers who has typeset it on a laser printer and Mr, Jitendra Kumar who has drawn structural formulae. I wish to recall my sincerest gratitude to my colleagues who ignored and spared me from the departmental activities and much of my time was utilized for compiling the manuscript. My greatest depth of gratitude is due to Dr. Miss Nirmal Sharma, College of Pharmacy, Pushp Vihar, New Delhi, for assisting me constantly throughout in checking the proofs. I also feel pleasure in expressing my sincere thanks to Mr. Amar Singh, Maharaja Surajmal College of Pharmacy, Bharatpur, Mr. Shamim Ahmed, Dehat Vikas College of Pharmacy, Taigaon, Faridabad, Mr. P.N. Raju, College of Pharmacy, New Delhi, Mrs. Neerja Suman, Maharaja Surajmal Institute of Pharmacy and Technology, New Delhi, Mr. S.S. Bajaj, Department of Pharmacy, Government Women's Politechnic, Chandigarh, Mr. N.K. Alawadi, Department of Pharmacy, Maharshi Dayanand University, Rohtak and to my colleagues Mr. Shahid Husain Ansari and Dr. Mohd. Amir for arranging examination question papers of their respective institutions and other relevent matter used for compiling the book. The contribution that I have received by sustained cooperation of my wife cann't be ignored.

The author always keeps an open eye for suggestions or comments for improving future editions of the book.

Dr. Mohammed Ali

CONTENTS

	Preface	*v*
1.	Introduction	1
2.	Classification and Nomenclature	4
3.	Stability and Storage Conditions	12
4.	Antiseptics and Disinfectants	19
5.	Sulphonamides	34
6.	Antileprotic Drugs	46
7.	Anti-tubercular Drugs	52
8.	Antiamoebic and Anthelmintic Drugs	66
9.	Antibiotics	81
10.	Antifungal Agents	126
11.	Antimalarial Drugs	134
12.	Tranquillizers	150
13.	Hypnotics	165
14.	General Anaesthetics	178
15.	Local Anaesthetics	187
16.	Antidepressant Drugs.	195
17.	Analeptics	202
18.	Adrenergic Drugs	208
19.	Adrenergic Antagonists	218
20.	Cholinergic Drugs.	221
21.	Cholinergic Antagonists	229

22. Diuretic Drugs 237
23. Cardiovascular Drugs 245
24. Hypoglycemic Agents 252
25. Coagulants and Anti-coagulants 261
26. Histamine and Anti-Histaminic Agents 269
27. Analgesics and Antipyretics 280
28. Nonsteroidal Anti-inflammatory Agents 294
29. Thyroxine and Antithyroids 299
30. Diagnostic Agents 305
31. Anticonvulsant Drugs 314
32. Cardiac Glycosides 329
33. Anti-arrhythmic Drugs 337
34. Anti-hypertensive Agents 341
35. Vitamins 350
36. Steroidal Drugs. 372
37. Antineoplastic Agents 387

Glossary of Medical terms 399
Examination Question Papers 427
Index 469

Text Book of Pharmaceutical Organic Chemistry

This Page is Intentionally Left Blank

1

INTRODUCTION

Pharmaceutical chemistry is the chemistry of substances used as drugs. The term 'organic' means plant or animal organisms. Organic chemistry is the chemistry of hydrocarbons and their derivatives or more widely the chemistry of compounds of carbon. Pharmaceutical organic chemistry is concerned with the selected aspects of medicines of organic nature.

The organic medicines can be obtained from natural sources and by synthetic processes. The natural soures are of four types:

1. **Plant kingdom :** Several alkaloids, glycosides, and antibiotics are obtained from plants.
2. **Animal kingdom :** Vitamins and hormones are derived from animals.
3. **Mineral kingdom :** Coal and petroleum are two most important substances obtained from mineral kingdom. These substances are the source of 90% of the synthetic drugs.
4. **Fungi and micro-organism :** These are responsible for production of drugs by fermentation processes and for the antibiotics.

Most of the drugs are obtained by synthetic or semi-synthetic means. By altering the structures of the natural drugs and following leads, many new analgesics, local anaesthetics, sympathomimetics and antispasmodics have been obtained. The drugs like barbiturates, antihistamines, some antihypertensives, diuretics, antimalarials, sulphonamides, disinfectants and antiseptics are the synthetic compounds.

Organic compounds are mostly nonionic and are readily differentiated by physical properties from typical inorganic compounds. They are usually liquids or low-melting solids which can be distilled or crystallized. They are not readily soluble in water, except their salts, but are soluble in organic solvents. The tetracovalency of carbon and its unique property of forming long open and closed carbon chains give a wide range of organic compounds. Organic compounds have been classifed into many classes on the basis of functional groups or pharmacological properties. Many organic compounds have large molecules involving thousands of atom as in case of proteins. Some organic compounds contain one or more asymmetric carbons and represent different stereoisomers. Only a particular isomeric form shows biological activity and is used as drug. Reactions of organic compounds are non-ionic and reversible and, therefore, proceed slowly. On slight modification of conditions, the reactions of organic compounds change their course giving rise side-reaction products.

Pharmaceutical organic chemistry involves various methods of isolation, purification and characterization of drugs from natural sources; various synthetic procedures of medicinal agents which could not be obtained from natural sources or the synthetic duplication due to reasons of economy, purity or adequate supply of substances obtained from natural sources. The branch includes conversion of natural substances into products with more favourable therapeutic properties and formation of derivatives which show optimum medicinal activity. It involves determination of chemical and biological incompatibilities among various ingredients of a preparation and helps to establish safe and more active practical standards with respect to both dosages and quality. It helps in the improvement and promotion of uses of chemical agents for treatment of diseases.

Pharmacopoeia

A pharmacopoeia is a book of standards applicable to drug substances and their dosage forms of common usage in a country or region, which accepts it as such.

Each country has legislation on pharmaceutical preparations which contains standards and quality indices used in the manufactures or drugs. These regulations are published in the form of a book called pharmacopoeia (Greek : pharmakon meaning a drug or medicine, poieo means to make).

The first British Pharmacopoeia (B.P) was published in 1864 which was quickly followed by a second in 1867. It included monographs on benzoic acid, gallic acid, tannic acid, tarnnic acid, camphor, lactose, sucrose and seven alkaloids. The first United States Pharmacopoeia (U.S.P.) was released in 1820. The first edition of the Indian Pharmacopoeia (I.P.) was published in 1955 followed by supplements in 1960, 1966 and 1975. It contained a large number of crude drugs and their preparations. Third editions of I.P. appeared in 1985 and addendum was published in 1989.

A pharmacopoeia includes introductory sections which summarizes the changes in the current edition and provides a useful pointer to pharmaceutical progress and the general notice; monographs of official drugs, preparations, and substances; and appendixes. The monographs give information about titles, chemical formulae, descriptions, solubilities, identification, tests for purity, methods of assay, methods of storage and labelling, preparation, action, uses and doses. Appendixes give details of general tests and methods of quantitative analysis, biological assays and other processes to which reference is made in the monographs of the main text, and prescribing standards, for materials and solutions employed in tests or quantitative determinations.

2

CLASSIFICATION AND NOMENCLATURE

Broadly drugs are classified on the basis of chemical structures and therapeutic actions.

1. **Drugs based on chemical structures :** According to this classification drugs are arranged as hydrocarbons, alcohols, acids, amines, amino acids, nitro compounds, phenols, quinones, sulphonamides, sulphones, urea, ureides, urethanes, etc. The chemical structures of drugs with different structures give little knowledge about their activity.
2. **Drugs based on therapeutic actions :** Drugs showing a particular activity are placed in one category. The drugs are first divided according to their therapeutic actions and sub-divided according to their chemical structures. On the basis of therapeutic action the drugs are classified as :
   (a) **CNS Agents :** Drugs acting on central nervous system include anti-depressant, anti-psychotics, anxilytics and psychomimetics, all of which affect mental functions. These drugs include anti-convulsants used for the treatment of epilepsy, sedative-hypnotics which are used in sleep disorders, analgesics for the control of pain and anti-parkinsonian agents, cholinergic and anticholinergic agents, histamine and antihistamine agents, local anaesthetics and adrenergic agents.
   (b) **Pharmacodynamic Agents :** These drugs affect the normal dynamic processes of the body and include anti-arrhythmics, antianginals, vasodilators, cardiotonic, anti-hypertensives, hypocholestermic agents, anti-

thrombotics, anti-allergic agents and the drugs used to treat gastro-intestinal disorders and renal diseases.

(c) **Chemotherapeutic Agents :** These compounds inhibit the life processes or destroy the microorganisms and include antibiotics, antineoplastics, antivirals, antifungals, anthelmintics, antimalarials, antiseptics, antineoplastic agents, antiprotozoal agents, antibacterial agents, etc.

(e) **Metabolic Diseases and Endocrine Function Affecting Agents :** Drugs of this category are used to treat inflammation, rheumatoid arthritis, diabetes, disorders of lipid metabolisms, atherosclerosis, sex hormones and peptide hormones.

(f) **Vitamins :** These compounds are used to maintain the normal growth of life. Their deficiency produces various types of disorders. There are about 25 vitamins and broadly classified as water soluble (vitamins B and C) and fat soluble (vitamins A,D,E and K) vitamins.

(g) **Hormones :** Hormones are produced by endocrine glands and added directly into the blood stream. They catalyze and control a variety of metabolic processes and are highly specific. Some of important hormones are insulin, testosterone, estrogen, progesterone, cortisone, adrenaline and pituitary hormones.

NOMENCLATURE

According to IUPAC (International Union of Pure and Applied Chemistry) the various groups are named as :

1. Hydrocarbons

Methyl	CH_3—
Ethyl	C_2H_5—
n-Propyl	$CH_3CH_2CH_2$—
n-Butyl	$CH_3(CH_2)_3$—
tert-Butyl	$(CH_3)_3C$—
Iso-pentyl-	$(CH_3)_2CH\ CH_2CH_2$—
Phenyl-	C_6H_5—
Allyl	CH_2=CH CH_2—
Ethynyl	CH≡C—
1-Methylbutyl	$CH_3CH_2CH_2CH(CH_3)$—

Phenethyl	$C_6H_5CH_2CH_2$—
Iso-propyl	$(CH_3)_2CH$—
sec-Butyl	$CH_3CH_2CH\ (CH_3)$—
Iso-butyl	$(CH_3)_2CH\ CH_2$—
Vinyl	CH_2=CH—
Benzyl-	$C_6H_5CH_2$—
Cyclohexyl	C_6H_{11}—
Benzhydryl	$(C_6H_5)_2CH$—

2. Alcohols

Methoxy	CH_3O—
Benzhydryloxy	$(C_6H_5)_2CHO$—
Hydroxymethyl	$HOCH_2$—
Propoxy	$CH_3CH_2CH_2O$—
Allyloxy	CH_2=$CHCH_2O$—
Butoxy	$CH_3CH_2CH_2CH_2O$—
Ethoxy	CH_3CH_2O—
2-Hydroxyethyl	$HOCH_2CH_2$—
Hydroxymercuri	HOHg
Phenoxy	C_6H_5O—
2-Phenoxyethyl	$C_6H_5OCH_2CH_2$—
Phenoxymethyl	$C_6H_5OCH_2$—

3. Carbonyl Compounds

Acetyl	CH_3CO—
Benzoyl	C_6H_5CO—
Butyryl	$CH_3CH_2CH_2CO$—
Propionyl	CH_3CH_2CO—
Formyl	OHC—
Oxo	O=
Acryloyl	CH_2=CHCO—

4. Amides

Acetamido	CH_3CONH—
Benzamido	C_6H_5CONH—
Butyramido	$CH_3(CH_2)_2CONH$—

Phenylacetamido	$C_6H_5CH_2CONH$—
Diethylcarbamoyl	$(C_2H_5)_2NCO$—
Carbamoyl	H_2NCO—

5. Others

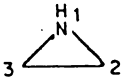
Acetoxy	CH_3COO—
Amidino	$H_2NC(=NH)$—
Amino	H_2N—
Anilino	C_6H_5NH—
Benzoyloxy	C_6H_5COO—
Carboxyl	HOOC—
Bromo	B_2—
Chloro	Cl—
Cyano	NC—
Diethylamino	$(C_2H_5)_2$ N—
Fluoro	F—
Hydroxy	HO—
Iodo	I—
Mercapto	HS—
Methylamino	CH_3NH—
Methylsulphonyl	CH_3SO_2—
Nitro	NO_2—
Sulphamoyl	H_2NSO_2
Sulphanilamido	p-$NH_2C_6H_4SO_2NH$—
Bis (2-chloroethyl) amino	$(ClCH_2CH_2)_2$ N—
Butylamino	$CH_3CH_2CH_2CH_2NH$—
Carbamoyloxy	H_2 N COO—
Diethylaminoethyl	$(C_2H_5)_2NC_2H_2$—
Diethylaminomethyl	$(C_2H_5)_2$ N CH_2—
Dimethylamino	$(CH_3)_2$ N—
2-Dimethylaminoethyl	$(CH_3)_2$ NC_2H_5—
Dimethylcarbamoyloxy	$(CH_3)_2NCOO$—
Ethoxycarbonyl	CH_3CH_2OCO—
Glycyl	H_2 NCH_2 CO—

Guanidino	$H_2NC(=N)NH$—
Methylthio	CH_3S—
Propoxy	CH_3CH_2COO—
Tosyl	p-$CH_3C_6H_4SO_2$—

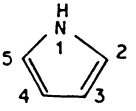
Most of the drugs are heterocyclic compounds. The common hetero atoms are nitrogen, oxygen and sulphur. The heterocyclic systems may be fused or bridged with carboxylic systems and they may be saturated or unsaturated. Many alkaloids (e.g. morphine, quinine, reserpine, vinblastine), xanthines (caffeine, theophylline), cardiac glycosides (digitoxin, digoxin), vitamins (thiamine, riboflavine, pyridoxine, nicotinamide) and antibiotics (penicillin) are heterocyclic compounds.

In one- and two-ringed heterocyclic nuclei, the heteroatoms are numbered as 1. In compounds containing more than one heteroatom, the numbering is done in such a direction that many heteroatoms are given the lowest possible numbers. If different heteroatoms are present, sulphur is given a lower number than nitrogen, and oxygen lower than either.

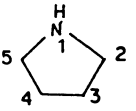
MONOCYCLIC HETEROCYCLIC SYSTEMS



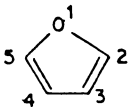
Aziridine
(Thiotepa)



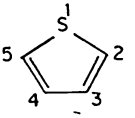
Pyrrole
(Viprynium)



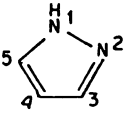
Pyrrolidine
(Pentolinium, Poldine, Triprolidine)



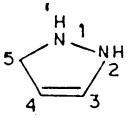
Furan
(Nitrofurantoin, Frusemide)



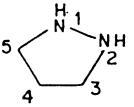
Thiophene
(Cephalothin, Cephaloridine)



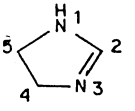
Pyrazole
(Sulphaphenazole)



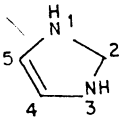
3-Pyrazoline
(Analgin, Phenazone)



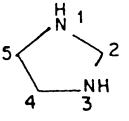
Pyrazolidine
(Phenylbutazone, Oxyphenbutazone)



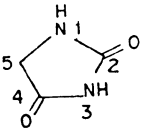
2-Imidazoline
(Antazoline, Naphazoline Phentolamine)



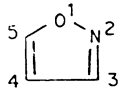
4-Imidazoline
(Carbimazole)



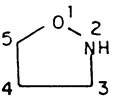
Imidazolidine
(Clonidine)



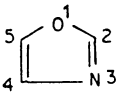
Hydantoin
(Phenytoin, Nitrofurantoin)



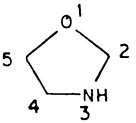
Isoxazole
(Cloxacillin,
Sulphamethoxazole,
Sulphafurazol)



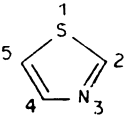
Isoxazolidine
(Cycloserine)



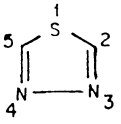
Oxazole



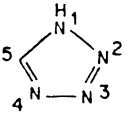
Oxazolidine
(Furazolidone,
Troxidone)



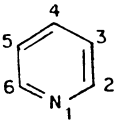
Thiazole
(Sulphathiazole,
Thiamine, Thiabendazole)



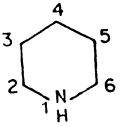
1,3, 4- Thiadiazole
(Sulphamethizole,
Acetazolamide)



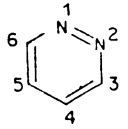
Tetrazole
(Leptazole,
Pentetrazole)



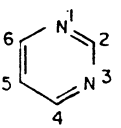
Pyridine
(Isoniazid, Nikethamide,
Nicotinamide)



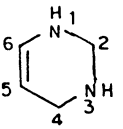
Piperidine
(Haloperidol,
Benzhexol, Pethidine)



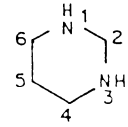
Pyridazine
(Sulphamethoxy-
pyridazine)



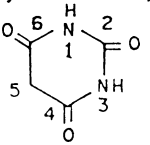
Pyrimidine
Sulphadiazine, Thiamine,
Pyrimethamine)



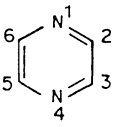
1, 2, 3, 4-Tetrahydro-
pyrimidine (Propyl-
thiourea, Idoxuridine)



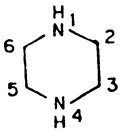
Perhydropyrimidine
(Primidone)



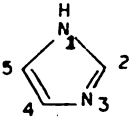
Barbituric acid
(Phenobarbitone,
Amylobarbitone,
Quinalbarbitone)



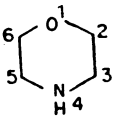
Pyrazine
(Amiloride, Pyrazinamide)



Piperazine
(Cyclizine, Fluphenazine, Diethylcarbamazine)

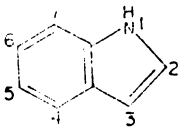


Imidazole
(Azothioprine, Metronidazole, Pilocarpine)

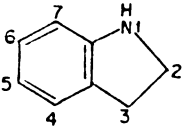


Pholcodine
(Pholcodine)

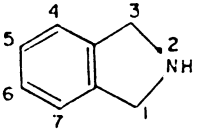
FUSED HETEROCYCLIC SYSTEM



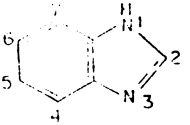
Indole
(Indomethacin)



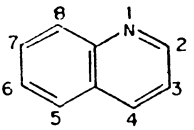
Indoline
(Methisazone, Indigo Carmine)



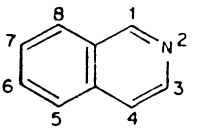
Isoindoline
(Chlorthalidone)



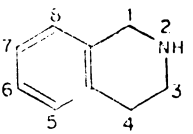
Benzimidazole
(Thiabendazole)



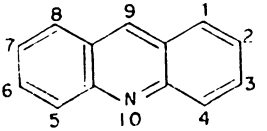
Quinoline
(Quinine, Chloroquine, Quinodochlor)



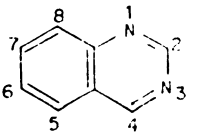
Isoquinoline
(Papaverine)



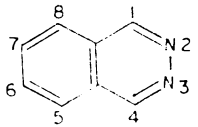
1,2,3,4,-Tetra-hydroisoquinoline
(Tubocurarine, Debrisoquine)



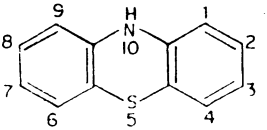
Acridine
(Mepacrine, Proflavine)



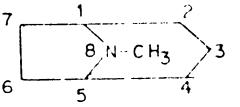
Quinazoline
(Methaqualone)



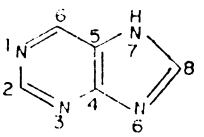
Phthalazine
(Hydralazine)



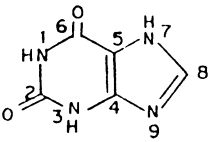
Phenothiazine
(Methylene Blue, Promethazine, Chlorpromazine)



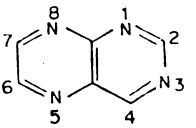
Tropane
(Atropine, Cocaine, Hyoscine)



Purine
(Azathioprine,
Mercaptopurine)

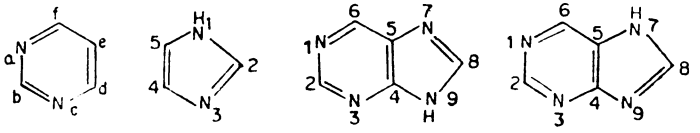


Xanthine
(Theobromine,
Theophylline,
Caffeine)



Pteridine
(Folic acid,
Methotrexate,
Triamterene)

Purine has pyrimidine and imidazole heterocyclic rings fused together. They possess the same number and kind of hetero atoms. Pyrimidine is larger than imidazole ring and is considered as the base component. The fusion of imidazole has been through the peripheral side 4, 5. In order to distinguish, the peripheral sides of pyrimidine have been marked as a,b,c,d,e and f. It is the d side of pyrimidine which has been involved in fusion with imidazole to form purine. So systematic name for purine has been imidazo [4,5-d] pyrimidine.



Purines

I Pyrimidine

II Imidazole

The structures I and II of purine are different in location of hydrogen atoms. The name is modified with the location of hydrogen, followed by italics capital for the hydrogen atom. So, I has been designated as 9H- imidazo-[4,5-d] pyrimidine; and II as 7H imidazo- [4,5-d] pyrimidine.

3

STABILITY AND STORAGE CONDITIONS

Stability of a pharmaceutical preparation is defined as the capability of a particular formulation, in a specific container, to remain within its physical, chemical, microbiological, therapeutic and toxocological specification. Assurance that the packaged product will be stable for its anticipitated shelf life come from an accumulation of valid data on the drug in its commercial package. The stability data on any drug include selected parameters, which taken together, from the stability profile. This stability profile is the basis for assigning the storage conditions and shelf life to a pharmaceutical product.

Storage conditions affect the stability of every drug. If a drug is not stored properly, its deterioration takes place due to which its all types of properties are changed. These changes may affect the therapeutic values of a medicament or increase its toxicity, thus harming the patients. Environmental conditions such as temperature, atmospheric gases, humidity, light and microorganisms are the worst enemy of drugs. Certain chemical reactions always take place inside the drug molecules whether it is in tablet, powder, syrup or liquid form. Chemical reactions tend to take place more rapidly in liquid system than in the dry state. Therefore, solutions are less stable than suspensions which in turn are less stable than solid dosage forms. Most of the drugs have a tendency to deteriorate, therefore, all the drugs should bear date of expiry of potency. For drugs specified in 'Schedule P' and their preparations including combinations with other drugs should bear on the label, the date of

manufacturing and the date of expiry of potency which should not exceed more than that specified in 'Schedule P' under the conditions of storage specified. All other drugs which are not included in 'Schedule P', shall also bear date of expiry which should not exceed sixty months from the date of manufacturing.

Effect of light : The most common decomposition reactions in medical products are oxidation and phytochemical reactions proceed by absorption of light by the molecule. Atmospheric oxygen, absolutely necessary for all living beings, can initiate oxidation of a medicament even present in low concentration. Such reactions are catalyzed by traces of metals and ultra-violet radiations from light sources. Vitamin D_2 has an extensive series of reactions, phytochemical and thermal reactions. Crystalline vitamin D_2 is light, air and heat sensitive and yields about five products of unknown structures; probably peroxides are formed. The vitamin is completely decomposed to a yellow powder after six months on exposure to room temperature and fluorescent light in air.

Crystalline esters of vitamin A are more stable than vitamin A itself. But they are decomposed by both polymerization and oxidation pathways. In tonics the presence of metallic salts, even in traces, catalyzes its oxidation. When vitamin A is exposed to air at room temperature, it forms at least five ketones on TLC plates. It becomes a gummy yellow solid after five months on exposure to room temperature, light and air.

Vitamin C, like vitamins A and D, is an important pharmaceutical product. This vitamin degrades during storage thus affecting public health. It gradually darkens on exposure to light and decomposes into dehydroascorbic, diketogluconic and oxalic acids. Vitamin C should not be formulated with sodium salicylate, sodium nitrite and methenamine since these substances accelerate its decomposition. Vitamin E, tocopherols and their acetates, is stable in air for reasonable period of time, but oxidizes slowly by air. Upon long standing of anaesthetic ether in contact with air, peroxides of ether are formed. Their formation is favoured by ultraviolet light and sunlight. In well-filled containers, the peroxides will form in about 6 months and remain for about one year. In old samples, the content of peroxides decreases and aldelydes are formed from the alcohol present. These peroxides are non-volatile and remain as a residue when such an ether is evaporated. In such cases, they explode with terrific force when heated to about 100° and constitute a real danger. Diphenylhydantoin sodium on exposure

to air absorbs carbon dioxide with the liberation of phenytoin. Vitamin K_5, codeine phosphate, warfarin sodium, manadione and sulfacetamide are affected with light. Formaldehyde and paracetaldehyde are oxidized to formic and acetic acids, respectively. Above 40° aqueous solutions of p-aminosalicylic and its salts are readily decarboxylated to form brown solutions consisting mainly of *m*-aminophenol. Ethionamide darkens on exposure to light with a slight sulphur like odour. Emetine and imipramine hydrochlorides turn to yellow, physostigmine salicylate to red, isoproterenol to pink, adrenaline to red and promethazine hydrochloride to blue colour under the influence of light. Riboflavine deteriorates under alkaline conditions, the decomposition being accelerated by light. Diphenhydramine, homatropine, chlopromazine, proguanil hydrochloride, cephaloridine, metronidazole, iodochlorohydroxyquin, sulfadiazine and sulfaguanidine darken on exposure to light. Chlordiazepoxide hydrochloride undergoes the nitrone rearrangement to produce 4, 5-epoxide in light. Aqueous solutions of triclofos slowly decompose liberating chloride and phosphate ions. Cyclopropane forms an explosive mixture with air. Procaine molecule is oxidized at the aromatic amine portion. Atropine sulphate effloresces in air while ethyl nitrite decomposes to an acid and oxide of nitrogen. Cyanocobalamine is very hygroscopic and highly sensitive to light.

The photoxidation of tablet coatings is particularly important to the pharmaceutical industries since reduction of shelf life of discoloured tablets takes place rapidly. The dye erythrosine is more readily oxidized than other dyes. Reserpine decolourizes when exposed to light, however, the loss of potency is usually small.

Effect of Water

Hydrolysis of drugs with water vapour is an important reaction in the pharmaceutical industry. Aspirin is hydrolyzed into salicylic and acetic acids in the presence of moisture. As the humidity increases, the rate of reaction in accelerated. The hydrolyzed product, salicylic acid, is used externally as an antiseptic and antifungal agent for various skin disorders. Thus the therapeutic properties of the original medicine are entirely changed due to water vapour. Excipients, antacids or granulating agents accelerate the decomposition of aspirin. Hydrolysis of nitrazepam, diazepam, diamorphin, digoxin, laevodopa, prilocain,

procaine, atropine, chloramphenicol, chloral hydrate, etc. leads to the formation of different undesirable products under the influence of moisture.

Penicillins are very sensitive to moisture losing half of its activity in five days at room temperature due to hydrolysis. Refrigeration at 5° reduces the loss of activity to about 20 per cent in the same period. Solutions prepared for parenteral use may be kept for 24 hour if refrigerated. It is extremely sensitive to acid, a pH of 2 causing a 50 per cent loss in activity in 20 minutes. Some of the crystalline salts of penicillins are hygroscopic, making it necessary to store them in sealed containers. The stability of thiamine hydrochloride in aqueous solution decreases, as the pH is increased above 5. It is oxidized readily by air to give thiochrome. Aqueous solutions of sodium acetrizoate are sensitive to light. Erythromycin is extremely unstable at a pH of 4 or lower. Aqueous solutions of tetracycline hydrochloride become turbid on standing due to hydrolysis and their potency is reduced below pH 2. Its concentrated aqueous solution at neutral pH hydrolyzes on standing and deposits crystals of oxytetracycline and the solution becomes turbid. Similarly aqueous solutions of phenolphthalein, thiophene and benzocaine hydrochloride are unstable. Aqueous solutions of biotin are very susceptible to mold growth.

Tetracycline antibiotics dehydrate in both the solid state and in solution. In aqueous solutions tetracycline degrades into 4-epitetracycline, anhydrotetracycline, 4-epianhydrotetracycline and other products. The major degradation product, 4-epitetracycline, has a very low antimicrobial activity, 4-epianhydrotetracycline is thought to be responsible for the renal dysfunction. In aqueous solution, apomorphine is oxidized to various derivatives of quinolinedione which are devoid of emetic properties.

Crystallization Effect

In solids the reactions are very sensitive to crystal packing. The crystal form of a drug is particularly important since it can alter the dissolution rate, bioavailability and stability. Oxyphenarisine antibiotic is crystallized in different forms. The amorphous form is much more reactive than the crystalline forms. The former form decomposes in few days in the absence of air, while the latter one is stable for three to six months under similar conditions. Overdrying of cephalosphorin antibiotic can lead to

an amorphous form which is extremely unstable. Similar observations have also been made for some steroidal drugs. Drugs often precipitate as amorphous solids which are sometimes hygroscopic and are often more reactive than crystalline forms. However, in some cases, i.e., nabilone and novapiocin, the amorphous form is the pharmaceutically desirable form since the crystalline structures are soluble. Polymorphic transformations can also affect the properties of creams. If the wrong polymorph is used, a phase transformation can occur, resulting in crystal growth of the new phase. The creams then become gritty and cosmetically unacceptable.

A large number of drugs and biologically important compounds crystallize with solvent of crystallization. Crystals of many drugs effervesce and rapidly dehydrate at room temperature. The loss of solvent of crystallization can change the dissolution rate, bioavailability and stability of crystals of pharmaceuticals.

An interesting property of the tetracyclines is their ability to undergo epimerization at carbon atom 4 in solutions of intermediate pH range. These isomers are called epi-tetracyclines. They exhibit much less activity than the natural isomers, thus accounting for a decrease in therapeutic value of aged solutions.

Perfect storage conditions are necessary for preservation of drugs. They must be kept in well-closed containers and protected from light. Specific storage is required for some drugs. For example, nitrofurantoin should not be kept in metal other than stainless steel or aluminium. Rifampicin is stored at a temperature not exceeding 15° in airtight containers in an atmosphere of nitrogen and protected from light. Ampicillin, cloxacillin and some other antibiotics should not be stored above 25-30° while 5° is storage temperature for carbenicillin and amphotericin.

Effect of Temperature

Drugs are to be stored under the conditions of storage specified therein. In general they are stored :

(i) in "Cool place" which means place having a temperature between 10° to 25°C.

(ii) in "Cold place" which means a place having a temperature between 2° and 8°.

(iii) at normal room temperature.

(iv) A freezer is cold place maingained between -20°, and -10°.

(v) 'Controlled room temperature' is a temperature that is maintained thermostatically between 15° and 30°.

(vi) 'Warm' is any temperature between 30° and 40°, while excessive heat is any temperature above 40°C. In case if freezing results in a loss of potency of a product, or in a destructive alteration of its dosage form, the container label should bear appropriate instructions to protect the product from freezing.

Adriamycin, ampicillin and its salts, amoxycillin trihydrate, bacitracin, cephalexin, chloramphenicol and its sodium salt, chlortetracycline hydrochloride, cloxacillin and its sodium salt, D-cycloserine, doxycycline hydrochloride and monohydrate, ethylsuccinate, estolate and stearate salts of erythromycin, gentamicin sulphate, gramicidin, griseofulvin, kanamycin acid sulphate powder, mitomycin C, oleandomycin phosphate, oxytetracycline, penicillin, procaine, penicillin G, benzathin penicillin G, potassium phenoxy methyl penicillin, polymixin B sulphate, rifampicin, spiramycin base, tetracycline, and tyrothricin are drugs which are stored in a cool place. All the vitamins are stored in well-closed containers, protected from light and in a cool place. Carbenicillin sodium, nystatin, cobra venam in solution and whole human blood are kept at a temperature not exceeding more than 5°C. Framycetin sulphate is placed in an airtight container with temperature not exceeding 30°C. Streptomycin sulphate is kept at a temperature not exceeding 20°C. Insulin and its other formulations are stored at temperature between 2° and 8°C and must not be allowed to freeze. A temperature of up to 25°C is required to store dried human plasma. Sera toxins and toxoids, tuberculin, thrombin, tetanus, various vaccines, anti-toxins, adrenaline for injection, corticotrophin, liquid extracts of ergot, liver extract, oxytocin injection, pituitary injection and vasopressin injection are placed in cold places for varying periods. Capsules should be kept in a well-closed container at temperature not exceeding 30°C. Wherever conditions of storage are not specified on the label, it may be stored under normal room temperature and it is understood that the product should be protected from moisture, freezing, and excessive heat.

Favourable storage conditions play a vital role in preserving the physical, chemical and therapeutic specifications of the

product when kept for long period. Storage assumes greater importance in case of particular dosage form. Stability considerations in dispensing practices are the responsibilities of the pharmaceutical manufacturer and the dispensing pharmacist. The product labelling of official articles provide recommended storage conditions and expiration date assigned to the specific formulation and package.

4

ANTISEPTICS AND DISINFECTANTS

Antiseptics and disinfectants are the chemical compunds which are used to destroy or inhibit the growth of pathogenic micro-organisms in the non-sporing or vegetable state. The term *antiseptic* is used to a chemical agent which destroys or inhibits micro-organisms on living tissues like skin and mucous membranes thus preventing the harmful results of infection. The term *disinfectant* is applied to a chemical agent which destroys micro-organisms, but not usually bacterial spores. It does not necessarily kill all microorganisms, but reduces them to a level which is harmful neither to health nor the perishable goods. According to their specific properties, disinfectants may be classified into *bacteriocides, sporicides, viricides* and *fungicides.*

Sterilization is the total removal or destruction of all living micro-organisms which is usually done by heat or radiation methods. *Preservatives* are used to prevent microbial spoilage of preparations. In pharmacy, presesvatives should reduce pathogenic organisms to acceptable numbers or should maintain sterility during use of the preparation.

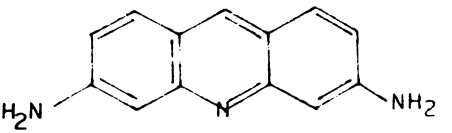
Antiseptic and disinfectant drugs are probably most widely used by the lay public. Soaps, toothpastes, creams and after-shave lotions are the pharmaceutical formulations which possess such agents. These agents may be physical, for example, heat in various forms (e.g., steam, boiling water, hot air), filtration, non-ionizing and ionizing radiation.

The main types of chemical disinfectants include alcohols (ethanol, isopropyl alcohol and methylated spirits), aldehydes

(formaldehyde, acetaldehyde), cationic surfactants (quaternary ammonium or pyridinium compounds), chlorhexidine salts (bisbiguanide), chlorine and its compounds (sodium hypochlorite, chloramine, chlorinated lime, etc), dyes [(1). acridine derivatives acriflavine, animacrine hydrochloride, and proflavine hemisulphate, (2) triphenylmethane derivatives-brilliant green, crystal violet, magenta and malachite green], mercurials (thiomersal, mercurochrome), phenols (phenol, thymol hexachlorophane), gases (propiolactone, formaldehyde) and vapours (formaldehyde).

PROFLAVINE

Nomenclature : 3, 6.-Acridinediamine; 3, 6-Diaminoacridine; 2, 8-Diaminoacridine.



It occurs as orange-red to brownish red, odourless crystals, m.p. 261°. It is soluble in water and ethanol: insoluble in benzene and ether; slightly soluble in chloroform. Solutions are brownish and show fluorescence on dilution. The aqueous solutions become turbid in which they should be discarded.

Proflavine sulphate (Brand names : Proflavine hemisulphate; neutral proflavine sulphate) occurs as an orange-red bitter crystals and is hygroscopic in nature. It is affected by light and is soluble in 300 parts of cold water and in 1 part boiling water; slightly soluble in alcohol; insoluble in ether and chloroform. It is less soluble in cold water than its corresponding dihydrochloride.

Uses : Proflavine is used as topical antiseptic. Proflavine and other acridine derivatives are slow acting antiseptics. They are used in the treatment of local infected wounds of the ear, mouth, and throat.

Their activity is not reduced by tissue fluids and serum. For the dressing of wounds or burns, a 0.1 per cent solution is used. If treatment is prolonged, weaker solutions or another antiseptic should be used, as the acridine derivatives tend to delay healing.

Stains on the skin caused by acridine derivatives may be removed by washing with a dilute solution of sulphurous acid or of hydrochloric acid.

The acridine derivatives are bacteriostatic against many gram-pasitive bacteria but less effective against gram-negative

organisms. They are ineffective against spores. Their activity is increased in alkaline solutions and is not reduced by tissue fluids. Hypersensitivity has been reported as the side effect.

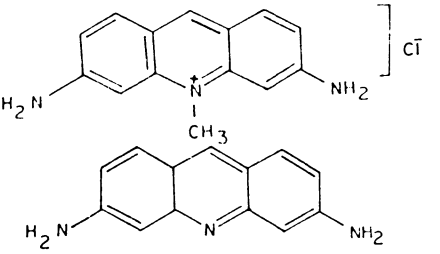
Official

Proflavine Hemisulphate, I.P.

Proflavine Cream, B.P.C.

ACRIFLAVINE

Nomenclature : 3, 6-Diamino-10-methyl acridinium chloride mixture 3,6-acridinediamine.



Brand Names : Neutral acriflavine; Euflavine; Trypaflavine; Neutroflavine; Gonacrine; Acriflavine base.

It occurs as a deep orange, odourless, granular powder. One gram dissolves in about 3 ml of water. It is sparingly soluble in alcohol; nearly insoluble in ether, chloroform and fixed oil. Aqueous solutions are reddish orange, show marked fluorescence on dilution and are sensitive to light. The compound is nearly neutral, it is less irritating to tissues than the acriflavine hydrochloride.

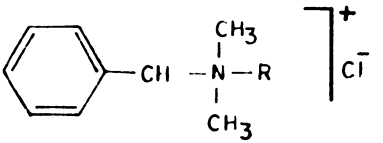
The compound is antiseptic and anti-infective. It is used locally in wounds in trichomoniasis of bulls.

Acriflavine hydrochloride (Brand Names : Acid acriflavine; Acid trypaflavine; Panflavin): It is deep reddish brown, odourless, crystalline powder; soluble in water but insoluble in ether, chloroform and petroleum ether. The aqueous solution is acidic and is more irritant than the base on mucous surfaces.

BENZALKONIUM CHLORIDE

Brand Names : Benzalkonii chloridum; Benzalkonium; Chloratum; Germinol; Osvan; Chloreto de Benzalconio; Zephirol; Zephiran chloride; Roccal, BTC; Alkyldimethyl benzyl-ammonium chloride; Benirol; Enuclen; Germitol; Drapolene; Drapolex; Cequartyl; Paralkan; Rodalon.

It is a mixture of alkyl-benzyldimethylammonium chlorides of the general formula $\{C_6H_5CH_2N(CH_3)_2R\}Cl$, in which R represents a mixture of the alkyls from C_8H_{17} to $C_{18}H_{37}$.



It occurs as a white or yellowish white powder, thick gel, or gelatinous pieces with a mild aromatic odour and bitter taste. It forms a clear molten mass on heating. It contains not more than 10% of water. It is very soluble in water, acetone and alcohol; slightly soluble in benzene; almost insoluble in ether. The anhydrous form is slightly soluble in ether. The aqueous solution is usually slightly alkaline to litmus and produces excess of foam on shaking.

It is incompatible with anionic detergents, such as soap, and with nitrates. A white precipitate is formed in a 1:3000 aqueous solution of benzalkonium chloride when nitrates are present in greater amount than the equivalent of 0.5% ammonium nitrate.

Uses : Benzalkonium chloride is a quaternary ammonium disinfectant with properties and uses identical to those of other cationic surfactants (e.g. cetrimide). Its 0.02 to 0.1% solutions are used to cleanse skin, mucous membranes and wounds as vaginal douche, as a shampoo in seborrhoeic dermititis and in higher dilutions for irrigation of the bladder and urethra. Creams containing benzalkonium chloride are used in the treatment of napkin rash. Its lozenges are used for the treatment of superficial infections of the mouth and throat. Its 0.01% solution is used as a preservative for some eye-drops. Benzalkonium chloride has also been used topically in herpes simplex infections.

When taken by mouth, benzalkonium and other quaternary ammonium compounds cause nausea and vomiting; strong solution may cause oesophageal damage and necrosis. Other side effects are depolarising muscle relaxant properties, nervous system, hypotension, coma and haemolysis.

At the concentrations used on the skin, solutions of benzalkonium and other quaternary compounds do not generally cause irritation, but some patients become hypersensitive to the drug after repeated application.

Official

Benzalkonium Chloride Solution, B.P.
Benzalkonium Lozenges, B.P.C.

CETRIMIDE

Brand Name : Cetrimidum.

Cetrimide consists chiefly of trimethyltetradecylammonium bromide together with small amounts of dodecyl-and hexadecyltrimethylammonium bromide. It may be prepared from a suitable mixture of alkyl bromide and trimethylamine.

It occurs as a white, voluminous, free-flowing powder with a faint characteristic odour and bitter soapy taste. Its 1 part is soluble in 2 parts of water; freely soluble in alcohol and chloroform and practically insoluble in ether.

Actions and Uses : Cetrimide is a quaternary ammonium disinfectant. It is a relatively non-toxic antisepitic with detergent properties. It is active against gram prositive organisms and is inactive against acid-fast bacilli and bacterial spores.

Creams and aqueous solutions are used for treating wounds and burns, for the pre-operative cleansing of the skin, and for the removal of scabs and crusts in skin diseases. Cetrimide is also used in the preparation of cetrimide emulsifying wax and for cleansing and disinfection of utensils, vessels, and apparatus (0.5-2% solution). It may be perfumed and may have colouring matter. It must be kept in a well-closed container and stored at a temperature above 15°.

When taken by mouth, cetrimide and other quaternary ammonium compounds cause nausea and vomiting. Some persons are hypersensitive to cetrimide when applied repeatedly on the skin.

Official

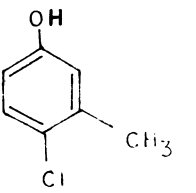
Cetrimide, B.P., I.P.

Cetrimide Cream, B.P.

Cetrimide Emulsifying Ointment, B.P.

Cetrimide Emulsifying Wax, B.P.

CHLOROCRESOL



Nomenclature : 4-Chloro-m-cresol; 4-Chloro-3-methylphenol; 3-Methyl-4-chlorophenol; Parachlorometacresol; 6-Chloro-m-cresol; 6-Chloro-3-hydroxytoluene; 2-Chloro-5-hydroxytoluene.

Chlorocresol is prepared by chlorination of *m* - cresol. It occurs as colourless or white, dimorphous crystalline powder, m.p. 63-66°. It is volatile in steam. It has characteristic phenolic odours. It is slightly soluble in water; 1g dissolves in 260 ml water at 20°; more soluble in hot water; slightly soluble in alcohol; freely soluble in ether, fatty oil, benzene, chloroform, acetone, petroleum ether, terpenes and aqueous alkaline solution. The aqueous solutions acquire a yellowish colour on exposure to light and air. It is stored in airtight containers and protected from light.

Uses : Chlorocresol is a potent disinfectant and used as a topical antiseptic. It is more active in acid than in alkaline solution. It is also used as a preservative in creams and other preparations for external use which contain water but its effectiveness is reduced if oils, fats, or nonionic surfactants are present.

When taken by mouth chlorocresol and other phenols cause, extensive local corrosion, with pain, nausea, vomiting, sweating and diarrhoea. Initially fleeting excitation may occur but it is quickly followed by unconsciousness. There is depression of the central nervous system, with circulatory and respiratory failure. Other side-effects include acidosis, haemolysis, methaemoglobinaemia with cyanosis, pulmonary oedema, and damage of liver and kidney.

Other fatal poisoning may occur from the absorption of phenolic compounds from unbroken skin or wounds. Applied to skin phenolic compounds cause blanching and corrosion.

Chlorocrosol is much less toxic than phenol. Sensitisation reactions may follow application to the skin.

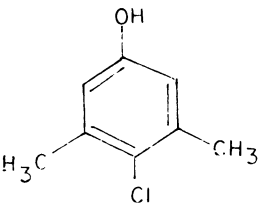
Official

Chlorocresol, B.P., I.P.

CHLOROXYLENOL

Nomenclature : 4-Chloro-3,5-dimethylphenol; p-Chloro-m-xylenol; 4-Chloro-3, 5-xylenol; Parachlorometaxylenol; 2-Chloro-m-xylenol; 2-Chloro-5-hydroxy-m-xylene; 2-Chloro-5-hydroxy-1, 3-dimethylbenzene.

Brand Names : Benzytol; Dettol.



It is prepared by treating 3,5-dimethylphenol with chlorine or SO_2Cl_2. It occurs as white or cream-coloured crystals or crystalline powder with a characteristic phenolic odour; volatiles

with steam, m.p. 115-116°. It is very slightly soluble in water, one gram dissolves in 3 litres of water at 20°; more stable in hot water; soluble one in one of alcohol (95%), ether, benzene, terpenes, fixed oils; dissolves in solutions of the alkali hydroxide. It is incompatible with nonionic surfactants and methylcellulose.

Uses : Chloroxylenol is a disinfectant, antiseptic, antibacterial and germicide. It is used chiefly in the form of chloroxylenol solution for skin and wound disinfection and for mildew prevention. It is claimed to be about 60 times as potent as phenol.

Chloroxylenol on the recommended dilutions is generally non-irritant but skin sensitivity has occurred.

Official

Chloroxylenol, B.P.

Chloroxylenol Solution, B.P.

FORMALDEHYDE

Namenclature : Methanal; Oxomethane; Oxymethylene; Methylene oxide, Formic aldehyde, Methyl aldehyde.

Brand Names : Formalin; Formol; Morbicid; HCHO.

Formaldehyde is prepared commercially by catalytic vapour phase oxidation of methanol using air as the oxidizing agent and heated silver, copper, alumina or coke as catalysts. Formaldehyde does not occur naturally in significant amounts.

Formaldehyde is usually available as a solution of about 37% by weight of formaldehyde gas in water, usually with 10-15% methanol added to prevent polymerization of the gas to solid paraformaldehyde. This solution is the full strength and also known as Formalin 100% or Formalin 40.

Formaldehyde differs from typical aliphatic aldehydes in some important reactions. When a mixture of formaldehyde and ammonia is evaporated, it forms methenamine by condensation.

$$6\ HCHO + 4NH_3 \longrightarrow (CH_2)_6N_4 + 6\ H_2O$$

Methenamine.

On treatment with an alkali under hot conditions, it yields no resin but partly undergoes the Cannizzaro reaction.

$$2H\text{-}CHO + NaOH \longrightarrow H\text{-}COONa + CH_3OH$$

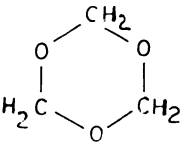
With dilute alkali it gives an aldol condensation yielding a mixture of sugars known as formose. Aldol condensation also takes place when formaldehyde is treated with other aldehydes. For example, with acetaldehyde and calcium hydroxide, it forms pentaerythritol and a formate.

$$3HCHO + CH_3CHO \longrightarrow (CH_2OH)_3\ C\text{-}CHO$$

$$(CH_2CH)_3\ C\text{-}CHO + HCHO + H_2O \longrightarrow (CH_2OH)_4\ C + HCOOH.$$

It shows a remarkable property to polymerize. Evaporation of the solution yields a white, friable mass of paraformaldehyde $(CH_2O)_n$. If a strong solution is distilled with sulphuric acid (2%) and the vapours are condensed quickly, a crystalline trimer, called trioxane or trioxymethylene, is formed.

$$3\ CH_2O \longrightarrow$$



Formaldehyde condenses with a number of other compounds. Any active hydrogen attached to carbon, nitrogen or oxygen will react with the carbonyl group to produce water. In this way, formaldehyde becomes an important synthetic agent and used to manufacture medicines, dyes, plastics, etc. Formaldehyde is added to the amino group to mark its basic character.

It is a colourless liquid with a distinct, pungent, irritating odour. On standing, especially in cold, it may become cloudy and on exposure to very low temperature a precipitate of trioxymethylene is formed. When evaporated, some formaldehyde escapes, but most of it is changed to trioxymethylene. It is a powerful reducing agent in the presence of alkali. In air it slowly oxidizes to formic and. It is miscible with water and alcohol.

Uses : Formaldehyde is used as a disinfectant for dwellings, ships, excreta, instruments, storage houses, utensils, clothes, hospitals, etc; as a germicide and fungicide for plants and vegetables; destroying flies and other insects. Phenolic resins, artificial silk and cellulose esters, dyes, organic chemicals, glass mirrors and explosives are manufactured from formaldehyde. It is also utilized for improving fastness of dyes on fabrics tanning and preserving hides; in photography for hardening gelatin plates and papers; to prevent mildew in spelt and wheat and rot in oats; to render casein, albumin and gelatin insoluble; also in chemical analysis.

When applied to the unbroken skin, formaldehyde hardens the epidermis, renders it tough and whitish, and produces a local anaesthetic effect. It has been used in tympany, diarrhoea, mastitis, pneumonia, and internal bleeding.

Formaldehyde vapours are irritant to the eyes, nose and respiratory tract, and may cause coughing, dysphagia, spasm and oedema of the larnyx, bronchitis, pneumonia and asthma.

FORAMALDEHYDE SOLUTION

Synonym : Formalin, HCHO.

Formaldehyde solution is an aqueous solution of formaldehyde containing methanol as a stabilizing agent. It contains not less than 34.0% and not more than 38.0% of HCHO.

Formaldehyde solution is a colourless liquid; odour is chracteristic, pungent and irritating. A slight white deposite may form during storage. It is miscible with water and alcohol. The solution should be kept in a well-closed container and stored at a temperature of 15° to 25°.

Treatment of dilute formaldehyde solution (1 ml) with a 1% solution of phenylhydrazine hydrochloride (2ml), dilute potassium hexacyanoferrate solution (1ml) and hydrochloric acid (5ml) forms brilliant red colour.

When formaldehyde solution is evaporated on a water bath, a white, amorphous residue is produced.

Uses : Formaldehyde solution is used in the treatment of warts.

Official

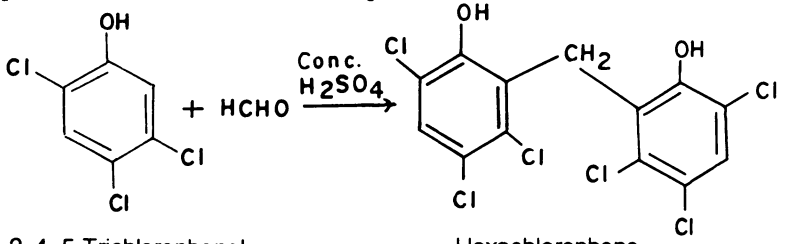
Formaldehyde Solution, B.P., I.P.

HEXACHLOROPHENE

Nomenclature : 2, 2-Dihydroxy-3, 3', 5, 5', 6, 6'-hexachlorodiphenyl methane; Bis (3, 5, 6-Trichloro-2-hydroxyphenyl) methane; 2, 2'- Methylenebis (3, 4, 6-trichlorophenol).

Brand Names : Hexachlorophane; Gamophen; Surgi- cen; pH iso Hex; Hex-O-san, Germa-Medica; G-11; AT-7; Bilevon; Dermadex; Exofene; Surofene.

Hexachlorophene is prepared by the condensation of 2 mols of 2,4,5, -trichlorophenol with 1 mol of formaldehyde in the presence of concentrated sulphuric acid as follows :



2, 4, 5-Trichlorophenol Hexachlorophene

It is a white or pale buff crystalline powder which is odourless or has a slight phenolic odour; m.p. 164-165°; practically insoluble in water; soluble in in alcohol, acetone, ether, chloroform, propylene glycol, olive oil, cottonseed oil and dilute solutions of alkalies. It is stable in air and forms salts with alkalies and alkaline earth metals. It is stored in airtight containers and protected from light.

Most bisphenolic compounds are far more effective than the monomers. The chlorine content further increases the antisepitic fertility.

Uses : It is used as anti-infective and detergent; for the manufacturing of germicidal soaps. In the form of surgical spirit, it may be applied externally. It may be used for skin preparation before injection.

Adverse effects of hexachlorophene are anorexia, nausea, vomiting, diarrhoea, abdominal pain, dehydration, shock and confusion.

Official

Hexachlorophane, B.P.

Hexachlorophene, I.P.

Hexachlorophene Liquid Soap, U.S.P.

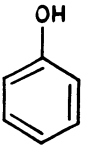
Hexachlorophane Dusting Powder, B.P.

Hexachlorophene Cleansing Emulsion, U.S.P.

PHENOL

Nomenclature : Hydroxybenzene; Phenyl hydroxide; Oxybenzene.

Brand Names : Carbolic acid; Phenic acid; Phenylic acid.



Phenol is a monohydroxybenzene obtained from coal tar by extraction with alkali in 0.7 per cent yield. The phenolates are decomposed and the phenolic fraction subjected to fractional distillation for separation and purification of the individual phenolic fractions. This source was not sufficient to meet the demand, and phenol is now synthesized on a commercial scale.

On large scale phenol is produced from benzene by sulphonation and alkali fusion in 60-75 per cent yield.

$$C_6H_6 \xrightarrow[SO_2,\ 50\text{-}70^\circ]{H_2SO_4} C_6H_5SO_3H(Na) \xrightarrow[2.\ H^+,\ 320\text{-}350^\circ]{1.\ NaOH} C_6H_5OH$$

Dow process (1928) of technical production of phenol consists in hydrolysis of chlorobenzene by a dilute aqueous solution of alkali at high temperature and pressure. Hydrolysis is conducted as a continuous process by flowing the reactants through a pipe line system at required temperature and pressure.

$$C_6H_5Cl \xrightarrow[Pressure]{NaOH,\ 300^\circ} C_6H_5ONa \xrightarrow{HCl} C_6H_5OH$$

Formation of diphenyl oxide as the side reaction product detract the efficiency of the process :

$$C_6H_5ONa + C_6H_5OH \rightleftharpoons \underset{\text{Diphenyl oxide}}{C_6H_5OC_6H_5} + NaOH$$

In the German Rasching process (1940) for production of synthetic phenol, benzene is converted through chlorobenzene into phenol by a sequence of reactions at atmospheric pressure in the presence of a catalyst. Benzene is chlorinated by halogen generated by the catalyzed oxidation of hydrogen chloride with oxygen, and on catalyic hydrolysis hydrogen chloride is regenerated (97% recovery) :

$$C_6H_6 + HCl + \tfrac{1}{2}O_2 \xrightarrow{\text{Catalyst, } 230^\circ} C_6H_5Cl + H_2O$$

$$C_6H_5Cl + H_2O \xrightarrow{\text{Catalyst, } 425^\circ} C_6H_5OH + HCl$$

Phenol occurs as colourless or faintly pink crystalline mass, becoming pink on keeping. It has characteristic phenolic odour; is proned to redden on exposure to air and light, m.p. 41-43°.

It is soluble 1:15 in water, very soluble in alcohol, chloroform, ether, glycerin, fixed and volatile oils and is sparingly soluble in petroleum ether. A saturated solution in water at 20° is clear and alkaline to methyl orange.

Phenol is the most stable member of the group of phenols. It can be stearilized by heat. It is incompatible with alkaline salts and nonionic surfactants; stored below 15° in airtight containers and protected from light.

Uses : Phenol is a general disinfectant for toilets, stables, cesspools, floors, and drains. Phenol is a protoplasmic poison and is toxic to all types of cells. The action on tissues is a toxic one, and pure phenol is corrosive to the skin, destroying much tissues.

Phenol is used in 0.1-1% concentrations as an antipruritic in phenolated calamine lotion or as an ointment or aqueous solution. Pure phenol may be used to cauterize small wounds. It is used for the manufacturing of artificial resins, medical and industrial organic compounds and dyes and as a reagent in chemical analysis.

When taken by mouth, phenol causes extensive local corrosion with pain, nausea, vomiting, sweating and diarrhoea. Other side effects are the same as described under chlorocresol.

Official

Phenol, B.P., I.P.

Phenol and Glycerol Injection, B.P.

Phenol glycerin, B.P., I.P.

Oily Phenol Injection, B.P.

LIQUIFIED PHENOL

Liquified phenol is a solution of phenol (800g) in purified water sufficient to produce 1000 g. For its preparation, phenol is warmed on a water bath until it is melted, purified water is added and mixed thoroughly. The content of phenol varies from 77 to 85 per cent.

Liquified phenol is a colourless or faintly coloured liquid; odour is characteristic and not tarry. It is soluble in water, miscible with ethanol (96%), ether and glycerol.

Chemical Tests

1. Liquified phenol (0.6 g) is dissolved in 13.3 M ammonia (2 ml) which is diluted to 100 ml with water. To the resulting solution (2 ml) sodium hypochloride solution (2 ml) is added. A blue colour is produced which becomes progressively more intense.
2. Liquified phenol gives violet colour with ferric chloride which disappears on the addition of propan-2-ol.
3. With bromine water, liquified phenol forms a white or yellowish white precipitate.

Liquified phenol should be kept in a well-closed container and protected from light. It may congeal or deposit crystals if stored at a temperature below 4°. It should be completely melted before use.

Uses : Liquified phenol is an antiseptic, antimicrobial, preservative and antipruritic.

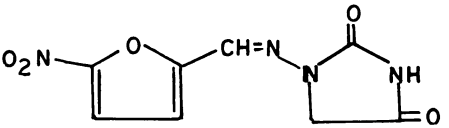
Official

Liquified Phenol, B.P., I.P.,

NITROFURANTOIN

Nomenclature : 1-[{ (5-Nitro-2-furanyl) methylene} amino] -2-4- imidazolidinedione; N-(5-Nitro-2-furfurylidene) -1-aminohydantoin; 1-(5-Nitro-2-furfurylideneamino) hydantoin.

Brand Names : Berkfurin; Berkfuran; Chemiofuran; Cyantin; Cystit; Fua-Med; Furachel; Furalan; Furadantin; Furadantine MC; Furadoine; Furadonine; Furantoin; Furobactina; Furophen; Ituran; Macrodantin; Orafuran; Parfuran; Trantoin; Urantoin; Urizept; Urodil; Urodin; Urolong; Uro-Tablinen; Welfurin; Zoofurin.



It is prepared from 1-aminohydantoin sulphate and 5-nitro-2-furaldehyde diacetate. It occurs as yellow odourless or

almost odourless crystals or fine powder with a bitter after taste, m.p. 270-272°(dec). It is discoloured by alkalis and by exposure to light. It is very slightly soluble in water and alcohol; soluble 1 in 16 of dimethylformide. It is stored at a temperature not exceeding 25° in airtight containers and avoid contact with metal other than stainless steel or aluminium; protected from light.

Nitrofurantoin is used in the treatment of uncomplicated lower urinary tract infection and for long-term suppressive therapy. It has been effective for infections that were resistant to antibiotics. Few side-effects, such as diarrhoea, pruritus or crystalluria, have been observed.

The most common side effect of nitrofurantoin is with gastro-intestinal tract causing nausea, vomiting, anorexia, and abdominal pain.

Official

Nitrofurantoin, B.P.

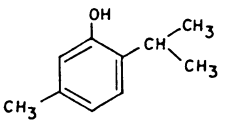
Nitrofurantoin Mixture, B.P.

Nitrofurantoin Tablets, B.P.

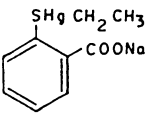
Nitrofurantoin Capsules, U.S.P.

Nitrofurantoin Oral Suspension U.S.P.

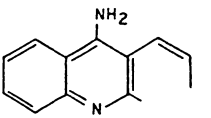
Miscellaneous Agents



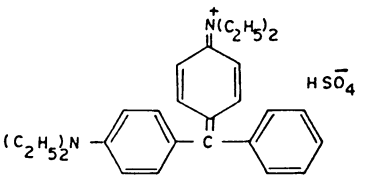
Thymol



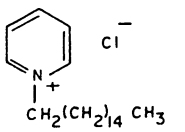
Thiomersal



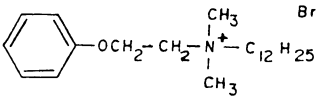
Aminacrine Hydrochloride



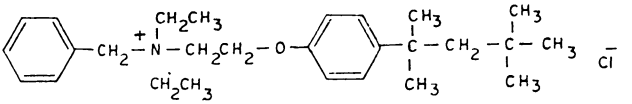
Brilliant Green



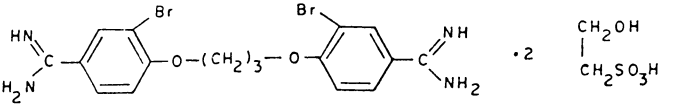
Cetylpyridinium Chloride



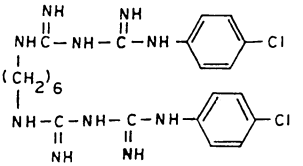
Domiphen Bromide



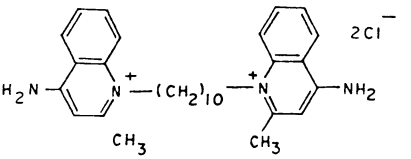
Octaphonium Chloride



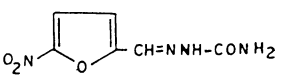
Dibromopropanidine Isethionate



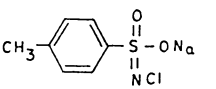
Chlorhexidine Hydrochloride



Dequalinium Chloride



Nitrofurazone



Chloramine

5

SULPHONAMIDES

Sulphonamides are synthetic chemotherapeutic agents which contain a sulphonamido (SO_2NH_2) group in their structures. These agents are active against certain gram-positive and gram-negative cocci, certain gram-negative bacilli and protozoa. The sulphonamide drugs are relatively easy to prepare, cheap and safe antibacterials.

The sulphonamides are white, crystalline powders, mildly acidic in character and relatively insoluble in water. They form salts with bases and their sodium salts are more water soluble than free sulphonamides. They are placed in well-closed containers and protected from light.

The antibacterial activity of sulphonamides depends on :

1. A free para amino group, and
2. A direct link of the sulphur atom of the sulphonamido group with the benzene ring.

Suphonamides containing free p-amino group intact or substituted by such radicals which can be converted into free amino group in the body show antibacterial activity. Substitution on the amino group exert variable effects on micro-organisms. Substitution of heterocyclic aromatic ring at 1-nitrogen yields highly potent compounds.

Sulphonamides are classified according to their therapeutic uses as :

1. those used for the treatment of systemic infections, and.
2. those used for the treatment of local gastro-intestinal infections.

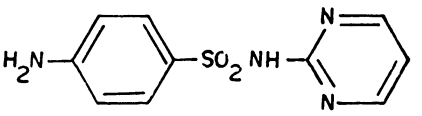
Sulphonamides of the first category are generally administered orally and include sulfadiazine, sulfadimidine, sulfacetamide, sulfafurazole, sulfasomidine, sulfomethoxine, etc. Sulfonamides used for the treatment of local gastro-intestinal infections include sulfaguanidine, phthalylsulfathiazole, succinylsulfathiazole and salicylazosulfapyridine.

All sulphonamides produce almost same kind of adverse effects which are nausea, vomiting and loss of appetite. They may cause drug fever which usually appears on 7th to 10th day and may be accompanied by headache, chill, weakness, itching and skin rashes. These conditions may occur earlier if the patient is allergic to the drug. Common allergic reactions are skin rashes, conjuctivitis, ulcer in mouth (stomatitis) and intolerance to sunlight (photosensitivity). Sometimes a person may suffer from delayed allergy in which fever, arthralgia, skin rashes, reddening of eyes, difficulty in breathing and decrease in WBC may occur. Short-acting sulphonamides may damage the kidney by forming crystals in urine leading to irritation and obstruction of urine flow. Trimethoprin is combined with sulphadiazine (co-trimazine), sulphamethoxazole (superistol), and sulfamoxazole. Available dosage forms of sulphonamides are tablets, injection, mixture, dispersible tablets, paediatric mixtures and paediatric tablets. Two tablets twice a day daily for 5 to 10 days are advised by a doctor.

SULFADIAZINE

Nomenclature : 4-Amino-N-2-pyrimidinylbenzene sulfonamide; 2-Sulfanilamidopyrimidine; N^1-2-Pyrimidinylsulfanilamide; N^1-2-Pyrimidylsulfanilamide; 2-Sulfanilylaminopyrimidine.

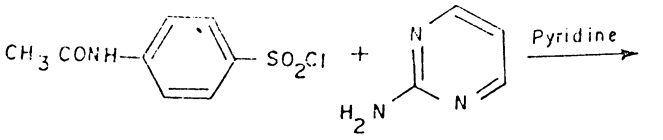
Brand Names : Sulfapyrimidine; Pyrimal; Debenal; Diazyl; Sterazine; Sulfolex; Adiazine; Ultradiazin; Eskadiazine.



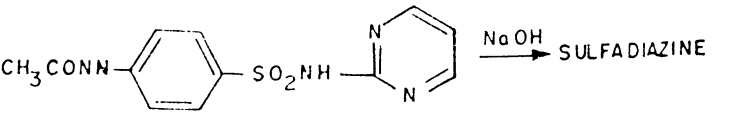
Sulfadiazine is prepared by the condensation of 2-aminopyrimidine with p-acetylsulphanilyl chloride and then hydrolyzing the product with alkali.

Sulfadiazine occurs as white or slightly yellow, odourless, crystalline powder, m.p. 252-256°, sparingly soluble in water at 37° (1 : 8, 100), alcohol and acetone. It is freely soluble in dilute mineral acids and in solutions of potassium and sodium

hydroxides and in ammonia water; insoluble in chloroform.



p-Acetylsulfanilyl chloride 2-Aminopyrimidine



It is slowly darkened on exposure to light. It is stored in well-closed containers and protected from light.

Uses : Sulfadiazine is considered a drug of choice in a number of infections, such as pneumococcal, meningococcal, Friedlanders bacillus, and influenza infections. It exhibits fewer toxic reactions than most of the other sulphonamides. It is absorbed slowly and also excreted slowly.

Nausea, vomiting and diarrhoea are relatively common following the administration of sulfadiazine and other sulfonamides. Hypersensitivity and nephrotoxic reactions may occur.

Official

Sulfadiazine, B.P., I.P.

Sulfadiazine Injection/Tablets, B.P., I.P., U.S.P.

Sulfadiazine Oral Suspension U.S.P.

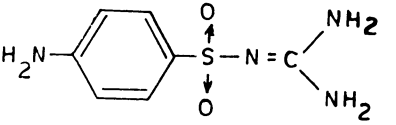
Trisulfapyrimidines Tablets, U.S.P.

Trisulfapyrimidines Oral Suspension, U.S.P.

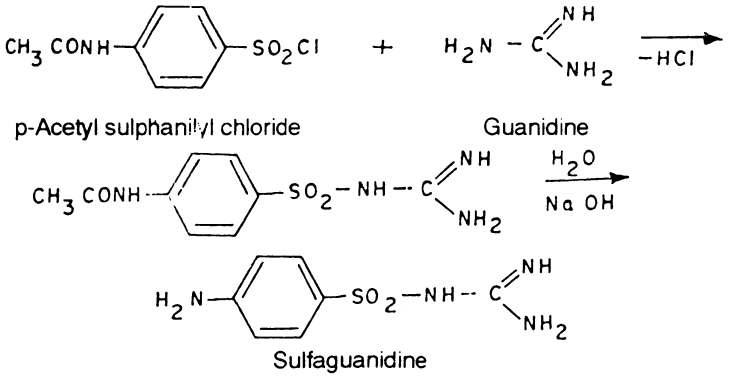
SULFAGUANIDINE

Nomenclature : 4-Amino-N-(diaminomethylene) benzenesulfonamide; 4-Amino-N-(aminoiminomethyl) benzenesulfonamide; N^1-Amidonosulfanilamide; N^1-Guanylsulfanilamide; p-Aminobenzenesulfonylguanidine; Sulfanilylguanidine;

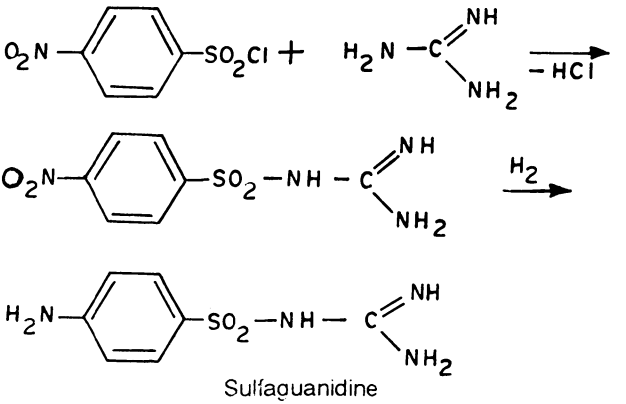
Brand Names : RP 2275; Guamide; Sulfaguine; Guanicil; Resulfon; Ruocid; Abiguanil; Diacta; Ganidan; Shigatox; Suganyl; Aterian; Sulfoguenil.



Sulfaguanidine is prepared by condensing p-acetyl-sulphanilyl chloride with guanidine followed by the hydrolysis of the acetyl group of the resulting sulfaguanidine in alkaline medium.



It may be synthesized by condensing guanidine with p-nitrobenzene sulphonyl chloride followed by the reduction of the nitro group.



Sulfaguanidine may be prepared by condensing acetylsulfanilyl chloride with guanidine nitrate in the presence of excess of sodium hydroxide in water-acetone or by fusing N^4-acetylsulfanilamide and dicyanodiamide.

The compound is a white, odourless crystalline powder: m.p. of anhydrous is 190-193°. It is soluble in water (1:1000) at 25°, sparingly soluble in alcohol or acetone, freely soluble in cold dilute mineral acids and insoluble in sodium hydroxide solutions at room temperature. Hot alkaline solutions decompose the compound to sulfanilamide with the evalution of ammonia. It slowly darkens on exposure to light.

Uses : Sulfaguanidine is used for the treatment of local intestinal infections, particularly bacillary dysentery by oral administration. It is also employed for the treatment of coccidiosis in chickens and for other veterinary purposes like enteric infections. Adverse effects are the same as for sulfadiazine.

Official

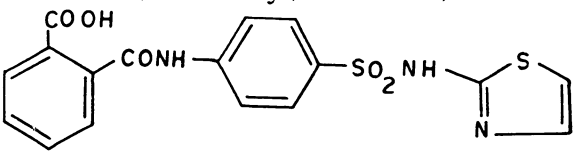
Sulfaguanidine, I.P.

Sulfaguanidine Tablets, I.P., B.P.C.

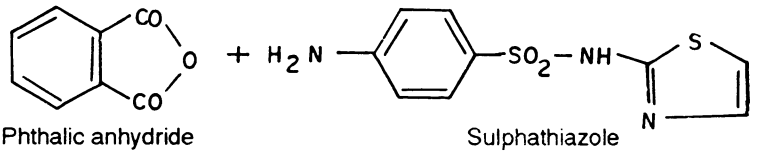
PHTHALYLSULFATHIAZOLE

Nomenclature : 2-[[[4-[(2-Thiazolylamino) sulfonyl] phenyl] amino] carbonyl] benzoic and; 4'-(2-Thiazolylsulfamyl) phthalanilic acid; 2-(N^4-Phthalylaminobenzenesulfonamido) thiazole; 2-(N^4-Phthalylaminobenzenesulfonamido) thiazole; 2-(N^4-phthalyl-sulfanilamido) thiazole; Phthalylsulfonazole; Sulfathalidine.

Brand Names : Entexidin; Entexidina; AFI-Ftalyl; Enteramida; Entero-Sulfina; Ftalazol; Intestiazol; Sulfacetil; Sulftalyl; Taleudron; Talidine; Thalistatyl; Ultratiazol; Thalazole.



It is prepared by condensing sulfathiazole with phthalic anhydride:



Phthalic anhydride Sulphathiazole

⟶ Phthalylsulfathiazole

The compound is an odourless, white, crystalline powder with slightly bitter taste. It slowly darkens on exposure to light; efferverces at 244-250° and then melts at 272°-277° (dec). It is insoluble in water and chloroform and slightly soluble in alcohol and ether; readily soluble in strong acids and alkalies and ammonia water and liberates carbon dioxide from a solution of sodium bicarbonate.

Uses : Phthalylsulfathiazole is an intestinal antibacterial agent

and is used in the treatment of bacillary dysentery and to reduce the bacterial count in the large bowel in patients undergoing surgery. Like succinylsulfathiazole, this compound is poorly absorbed from the intestinal tract. Because of its low absorption and low toxicity, compared with sulfaguanidine, it is useful in intestinal infections.

Official

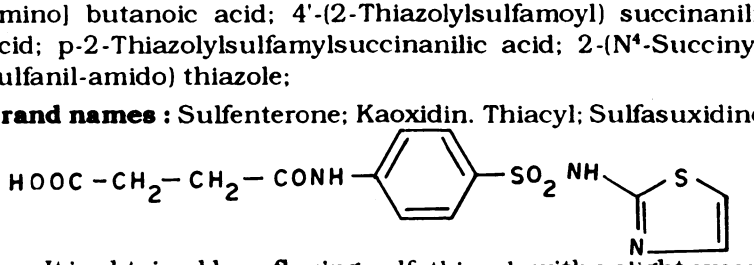
Phthalylsulfathiazole, B.P., I.P.

Phthalylsulfathiazole Tablets, B.P., I.P.

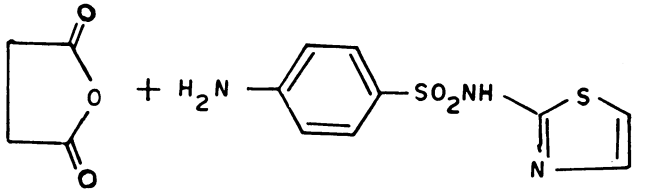
SUCCINYLSULFATHIAZOLE

Nomenclature : 4-Oxo-4-[[4-(2-thiazolylamino) sulfonyl] phenyl] amino] butanoic acid; 4'-(2-Thiazolylsulfamoyl) succinanilic acid; p-2-Thiazolylsulfamylsuccinanilic acid; 2-(N^4-Succinyl-sulfanil-amido) thiazole;

Brand names : Sulfenterone; Kaoxidin. Thiacyl; Sulfasuxidine.



It is obtained by refluxing sulfathiazole with a slight excess of succinic anhydride in alcohol or by refluxing p-succinimido benzenesulfonyl chloride with 2-aminothiazole in benzene.



Succinic anhydride Sulfathiazole

⟶ Succinylsulfathiazole

This compound occurs as a white, odourless crystalline powder with unclear m.p. (184-186°and 192-195°). It is stable in air but slowly darkens on exposure to light. It is soluble in water (1 : 4,800); sparingly soluble in alcohol and acetone and insoluble in chloroform and ether. It emits pungent fumes on heating to melting point. It is soluble in dilute acids and bases and dissolves in sodium bicarbonate solution with evolution of carbon dioxide. It is protected from light.

Uses : It is an intestinal antibacterial agent. Due to its slow absorption and low toxicity, it is useful in bacillary dysentery and cholera.

Official

Succinylsulfathiazole, B.P., I.P.

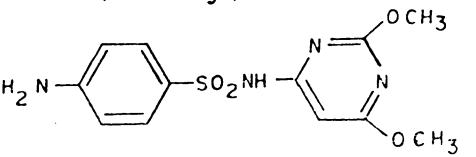
Succinylsulfathiazole Tablets, I.P.

Paediatric Succinylsulphathiazole Mixture, B.P.C.

SULFADIMETHOXINE

Nomenclature : 4-Amino-N-(2,6-dimethoxy-4-pyrimidinyl) benzenesulfonamide; N¹(2,6-Dimethoxy)-4-pyrimidinyl) sulfanilamide; 2,6-Dimethoxy-4-sulfanilamidopyrimidinyl) sulfanilamide; 2,6-Dimethoxy-4-sulfanilamidopyrimidine; 2,4,-Dimethoxy-6-sulfanilamido-1, 3-diazine; 6-Sulfanilamido-2, 4-dimethoxypyrimidine; 2,6-Dimethoxy-4-(p-aminobenzene-sulfonamido) pyrimidine.

Brand Names : Agribon; Albon; Madribon; Sulxin; Bactrovet. Dinosol; Sudine; Radonin; Dimetazina; Memcozine; Metoxidon; Neostreptal; Sulfasol; Theracanzan; Symbio; Suldixins; Diasulfa; Arnosulfan; Maxulvet; Diasulfyl; Roscosulf:



This compound is a white, odourless, crystalline powder, m.p. 201-203°, very slightly soluble in water; slightly soluble in alcohol; dissolves in dilute mineral acids and in solutions of alkali hydroxides and carbonates. It is protected from light.

Uses : Sulfadimethoxine is a long-acting sulfonamide. It is readily absorbed from the gastro-intestinal tract and the incidence of kidney damage is reported to be low.

Official

Sulfadimethoxine, B.P., I.P.

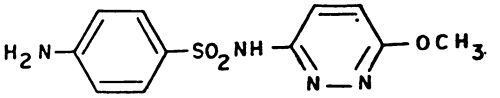
Sulfadimethoxine Tablets, B.P., I.P.

SULFAMETHOXYPYRIDAZINE

Nomenclature : 4-Amino-N-(6-methoxy-3-pyridazinyl) benzene sulfonamide; N^1-(6-Methoxy-3-pyridazinyl) sulfanilamide; 6-Methoxy-3-sulfanilamidopyridazine; 3-(p-Aminobenzene-sufamido)-6-methoxypyridazine.

Brand Names : Kynex; Lederkyn; Lentac; Midicel; Midikel; Myasul; Mylosul; Opinsul; Petrisul; Ratasulfin; Spofadazine; Sulfalex; Sulfdurazin; Sultirene; Vinces; CL 13494; RP 7522; Davosin; Depovernil; Durox;

It is prepared from 6-chloro-3-sulfanilamidopyridazine.



It is found as white or yellowish white, odourless, bitter crystalline powder, m.p. 182-183°. It is soluble in water, slightly soluble in methanol and ethanol; more soluble in acetone and dimethylformamide; freely soluble in aqueous solutions of alkali hydroxides. It is protected from light.

It is used as an antibacterial drug.

Official

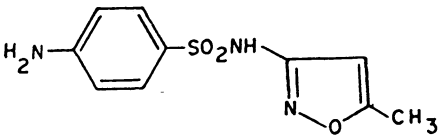
Sulfamethoxypyridazine, B.P.

Sulfamethoxypyridazine Tablets, B.P.

SULFAMETHOXAZOLE

Nomenclature : 4-Amino-N-(5-methyl-3-isoxazolyl) benzene-sulfonamide; N^1- (5-Methyl-3-isoxazolyl) sulfanilamide; 5-Methyl-3-sulfanilamido isoxazole; 3-Sulfanilamido-5-methylisoxazole; 3-(p-Aminophenylsulfonamido)-5-methylisoxazole.

Brand Names : Sulfisomezole; Sulfamethylisoxazole; Sulfamethoxizole; Gantanol; Sinomin; Sulphamethizole.



It is prepared starting with ethyl 5-methylisoxazole-3-carbamate and closely related to sulfisoxazole in chemical structure and antimicrobial activity. It occurs as a odourless, bitter, almost white, crystalline powder, m.p. 167°. It is soluble

in water (1 : 3400), alcohol (1:50) and acetone (1:3); slightly soluble in chloroform (1:1000) and in solutions of alkali hydroxides. The suspension should be stored in air-tight containers and protected from light.

Uses : The use of sulfamethoxazole and other sulfonamides has been limited by the increasing incidence of resistant organism. Their main use is in the treatment of acute, uncomplicated urinary tract infections, particularly those caused by *Escherichia coli.*

Adverse effects are the same as for sulfadiazine.

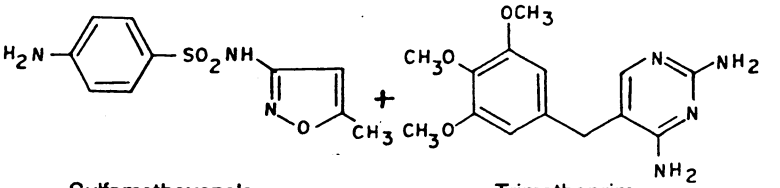
Official

Sulfamethoxazole, B.P., I.P.
Sulfamethoxazole Oral Suspension, U.S.P.
Sulfamethoxazole Tablets, U.S.P.

CO-TRIMOXAZOLE

Brand Names : Abacin; Bactramin; Bactrim, Baktar; Bactromin; Drylin, Eusaprim; Gantaprim; Gantrim; Kepinol; Momentol; Nopil; Omsat; Septra; Septrim; Sigaprim; Sulfotrim; Sulfotrimin; Sulprim; Sumetrolim; Suprim; Tacumil, Teleprim, T.M.S. 480; Trigonyl; Linaris; Eltrianyl; Microtrim; Trimesulf; Aposulfatrim; Fectrim; Trimforte; Uro-septra.

A mixture of 5 parts of sulfamethoxazole and 1 part of trimethoprim is known as co-trimoxazole.



Sulfamethoxazole Trimethoprim

The concentrate for infusion has a pH of 9.5 to 11.0 which should be protected from light.

Uses : Co-trimoxazole is used similarly to the sulfonamides (e.g. sulfamethoxazole) but in a wider variety of infections. Its indications for use include genito-urinary-tract infections, respiratory-tract infections such as bronchitis and pneumonia, and enteric infections. Trimethoprim alone may be preferred to co-trimethoxazole in urinary tract infections.

Adverse effects are the same as for sulfadiazine.

Official

Co-trimoxazole, B.P., I.P.

Co-trimoxazole Tablets, B.P.

Dispersible Co-trimoxazole Tablets, B.P.

Paediatric Co-trimoxazole Tablets, B.P.

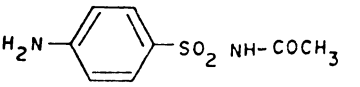
Trimethoprim and Sulfamethoxazole Tablets, I.P.

Sulfamethoxazole and Trimethoprim Tablets/Oral Suspension, U.S.P.

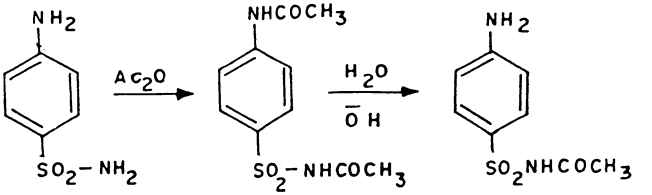
SULFACETAMIDE

Nomenclature : Acetosulfaminum; N-Sulfanilylacetamide; N^1-Acetylsulfanilamide; N-[(4-Aminophenyl) sulfonyl] acetamide; p-Aminobenzene sulfonoacetamide.

Brand Names : Acetocid; Bleph-10; Acetosulfamine; Sulfacyl; Urosulfone. Albucid; Sulamyd; Sulfacet.



Sulfacetamide, a simple acetyl derivative of sulphanilamide, was introduced for use in infections of, and injuries to, the eyes; it is used in the form of its sodium salt. It is prepared by diacetylating sulfanilamide with acetic anhydride and then removing the N^4-acetyl group by selective alkaline hydrolysis:



Sulfanilamide Sulfacetamide

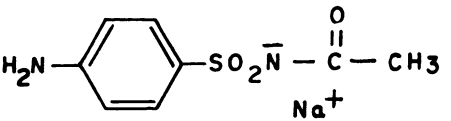
It is a white, odourless, crystalline powder, m.p. 182-184°, slightly soluble in water (1: 62.5 at 37°) and ether; soluble in alcohol; very soluble in chloroform and hot water; freely soluble in dilute mineral acids and solutions of alkali hydroxides. Its aqueous solutions are acidic to litmus and sensitive to light; they are unstable when acidic or strongly alkaline. It is stored in well-closed containers and protected from light.

Uses : Sulfacetamide is a short-acting sulfonamide which was formerly used in the treatment of bacterial infection of the urinary tract. It is absorbed readily from the gartro-intestinal tract, and the concentration in the blood is proportional to the oral dose administered. It is excreted primarily in the urine. Because of its high solubility and ready elimination, it has found considerable use in urinary tract infections, since it is possible to maintain high urinary concentration without danger of kidney damage.

Adverse effects are the same as for sulfadiazine.

SODIUM SULFACETAMIDE

Brand Names : Soluble sulfacetamide; Beocid-Isoptal; Albucid soluble, Sulamyd sodium; Supracid; Locula; Antebor; Eye-Su; Op-Sulfa.



This is obtained as the monohydrate and is white or yellowish-white, bitter, odourless crystals or crystalline powder which is very soluble in water (1:2.5). It slowly darkens on exposure to light. It is sparingly soluble in alcohol; practically insoluble in chloroform and ether. A 5% solution in water has a pH of 8.0 to 9.5. When solutions are sterilized by heat, hydrolysis occurs forming sulfanilamide which may be deposited as crystals. It is stored in air tight containers and protected from light.

Uses : Sodium sulfacetamide is used as an antibacterial mainly by local application in infections or injuries of the eyes as a 10 per cent ointment or as a 10 to 30 per cent solution every 2 to 4 hours. It is also used for skin infections and orally for urinary tract.

Official

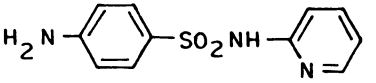
Sulfacetamide, I.P.

Sulfacetamide Sodium, B.P., I.P.

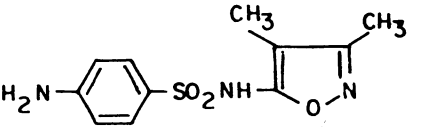
Sulfacetamide Eye Ointment, B.P., I.P.

Sulfacetamide Sodium Ophthalmic Slution/Ointment, U.S.P.

Miscellaneous Agents



Sulfapyridine



Sulfafurazole

6

ANTILEPROTIC DRUGS

Leprosy (Hansen's disease) is a disease caused by *Mycobacterium leprae* which produces characteristic lesions in the skin and the peripheral nerves. This disease is common in Burma, Bangladesh, India and other tropical and sub-tropical countries. The leprosy becteria was first discovered by Hansen in 1873. Human leprosy cannot be transmitted to animals easily. Prolonged intimate contact for several years is required to transmit leprosy in humans. It needs prolonged drug therapy.

According to their immunological response persons suffering from leprosy can be placed into 6 different categories as: polar lepromatous; sub-polar lepromatous; borderline lepromatous; borderline; borderline tuberculoid; tuberculoid. In patients with lepromatous leprosy the lepromin test is negative whereas at the tuberculoid end, it is strongly positive. An early transitory stage, called indeterminate leprosy, is also described.

All antileprotic agents currently recommended for treatment of leprosy have some bactericidal activity against *Mycobacterium leprae*. Rifampicin has the greatest bactericidal activity, ethionamide and prothionamide have intermediate bactericidal activity and dapsone and clofazimine are weakly bactericidal. Other agents that have been used in the treatment of leprosy, such as thiacetazone, thiambutosine and some sulphonamides are only bacteriostatic against *M. leprae*.

Due to its cheapness, relative nontoxicity and high activity against *Mycobacterium leprae*, dapsone has been used to treat leprosy for several decades. Since it develops resistance, therefore, dapsone should be administered in association with other antileprotic agents such as rifampicin, clofazimine, ethionamide

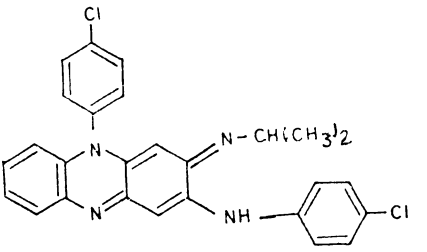
or prothionamide. Other drugs used in the treatment of leprosy are sulphonamides and thiacetazone.

CLOFAZIMINE

Nomenclature : N, 10-Bis (4-chlorophenyl)-2, 10-dihydro-2 [(10-methyl-ethyl) imino] -3-phenazinamine; 3-(p-Chloroanilino) -10-(p-chlorophenyl)-2, 10-dihydro-2-(isopropylimino) phenazine; 2-(4-Chloroanilino) - 3-isopropylimino - 5-(4-chlorophenyl) 3, 5- dihydrophenazine.

Brand Names : G 30320; B 663, Lamprene.

Clofazimine, an imino-phenazine dye, m.p. 210-212°, is a fine reddish-brown, odourless powder which is practically insoluble in water; soluble in chloroform; slightly soluble in alcohol; very slightly soluble in ether.



Uses : Clofazimine is an antileprotic agent. It is used to treat leprosy in association with other antileprotic agents to prevent the emergence of resistance.

Adverse effects to clofazimine are red to brown discolouration of skin and hair, nausea, vomiting and abdominal pain.

Official

Clofazimine, I.P., B.P.

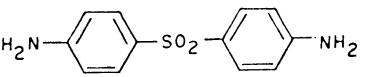
Clofazimine Capsules, B.P., I.P.

DAPSONE

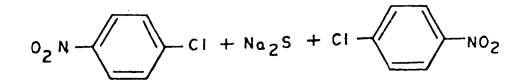
Namenclature : 4, 4'-Sulfonylbisbenzeneamine; 4,4'-sulfonyldianiline; Bis-(4-aminophenyl) sulfone; 4,4', Diaminodiphenyl sulfone;

Brand Names : Diaphenylsulfone; DADPS; 1358F; DDS; Dumitone; Avlosulphone; Sulfona-Mac; Croysulfone; Croysulphone; Disulone; Sulphadione; Avlosulfan; Eporal; Diphone; Novophone; Diphenasone; Udolac.

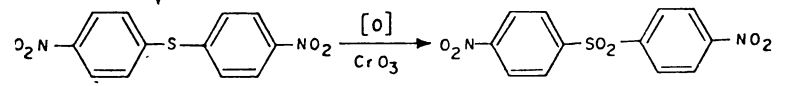
Dapsone is prepared by reduction of the corresponding dinitro-compound. The dinitro-



product cannot be preprered by nitration of diphenyl sulfone, since the $-SO_2-$ group, like $-SO_3H$, is meta-directing and, therefore, 3,3'-and not the 4,4'-dinitro-compound is obtained. Dapsone is synthesized by interaction of 4-chloronitrobenzene with sodium sulphide to give di-(4-nitrophenyl) sulphide, which is then oxidized by chromic acid to the sulphone.

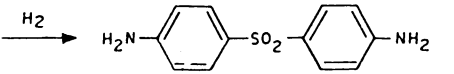


4-Chloronitro benzene



Di-(4-nitrophenyl) Sulphide

Dinitrosulphone



Dapsone

The dinitrosulphone is then reduced to give dapsone. Alternatively, the dinitrophenylsulphide is reduced to the corresponding diamino-compound, this is diacetylated to protect the amino groups, the-S-is oxidized to SO_2, and finally the acetyl groups are removed by hydrolysis.

Dapsone is a white or slightly yellowish white odourless, crystalline powder, m.p. 175-176°, soluble in alcohol (1 : 30); freely soluble in acetone and dilute mineral acids; practically insoluble in water.

The pure compound is light-stable, but in the presence of traces of impurities, including water, it becomes photosensitive and it is discolourized. It forms soluble salts with acids, and gives the ordinary reactions of a primary aromatic amine. The drug is protected from light.

Uses : Dapsone is antibacterial (leprostatic), and dermatitis herpetiformis suppressant. Therefore, it is used to treat both lepromatous and tuberculoid types of leprosy. It is cheap, relatively nontoxic and highly active against *Mycobacterium leprae.*

The side-effects are dose-related and include anorexia, nausea, vomiting, headache, dizziness, tachycardia, nervousness and insomnia.

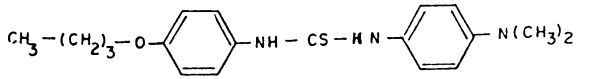
Official

Dapsone, B.P., I.P.
Dapsone Tablets, B.P., I.P., U.S.P.

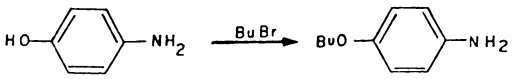
THIAMBUTOSINE

Nomenclature : 1-(4-Butoxyphenyl)-3-(4-dimethylaminophenyl) thiourea.

Brand Names : DPT; Su-1906; Ciba-1906.

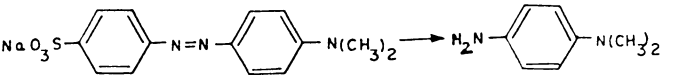


This thiourea derivative is a phenolic ether and also a tertiary aromatic amine. For its synthesis, the phenolic ether intermediate, 4-butoxyaniline is prepared from 4-aminophenol.

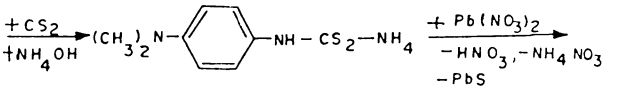


4-Aminophenol 4-Butoxyaniline

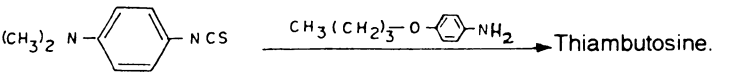
The other intermediate, 4-dimethylaminophenyl isothiocyanate, is synthesized by catalytic reduction of methyl orange, converting the resulting substituted diamine into an ammonium N-aryl dithiocarbamate by means of carbon disulphide and ammonium hydroxide and then heating with lead nitrate to obtain the required isothiocyanate. Reaction of the two intermediates yields thiambutosine.



Methyl orange 4-Dimethylaminoaniline



Ammonium N-aryl dithiocarbamate



It is a white powder, almost insoluble in water.

Uses : Like dapsone and solapsone, it is used in the treatment of leprosy in the form of injection and tablets.

The medicinal value of thiombutosine is limited due to the development of resistance within 1 or 2 years. The drug has a very short half-life and its peak serum concentration does not exceed its MIC. It is unsuitable for multiple therapy of leprosy.

Official

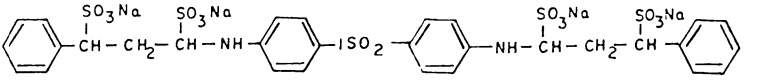
Thiambutasine B.P.

Thiambutosine Tablets, B.P.

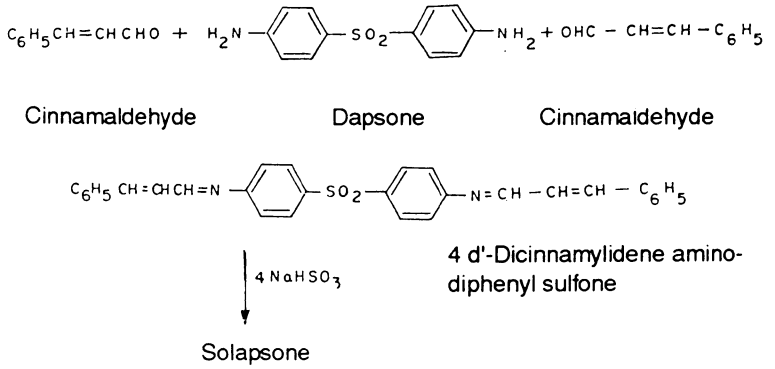
SOLAPSONE

Nomenclature : Tetrasodium 3,3'-diphenyl-4,4'-sulphonylbis (1-anilinopropane-1,3-disulphonate); 1,1'-[Sulfonylbis (p-phenyleneimino)] bis [3-phenyl-1,3-propanedisulfonic acid] tetrasodium salt; Di (γ-phenylpropylamino)-4,4'-diphenylsulfone α,α',γ,γ'-sodium tetrasulfonate; Tetrasodium 4,4'-bis (γ-phenylpropylamino) diphenylsulfone α,γ,α',γ'-tetrasulfonate.

Brand Names : Phenopryldiasulfone sodium; Salapsone, RP 3668; Cimedone; Sulphetrone; Solasulfone; Solasulfonum; Solusulfone.



Solapsone is the sodium salt of a tertrasulphonic acid made by condensing dapsone with cinnamaldehyde (a typical Schiff base preparation) in the cold followed by addition of sodium bisulphite to the resulting conjugated compound, 4,4'-dicinnamylideneaminodiphenyl sulphone.



Solapsone is an almost white powder, becomes anhydrous at 110° *in vacuo;* exceedingly soluble in cold water, giving a neutral solution; practically insoluble in cold alcohol. Acid-catalyzed hydrolysis readily reverses the bisulphide addition reaction, with formation of cinnamaldehyde, sulphurous acid and a dapsone salt.

Uses : Solapsone has the action, uses and side-effects of dapsone. It is given as an antileprotic drug to treat leprosy. It is more slowly absorbed than dapsone and is used in much larger doses.

7

ANTI-TUBERCULAR DRUGS

Tuberculosis is an infectious disease caused by several species of mycobacteria which are collectively called as the tubercle bacilli. *Mycobacterium tuberculosis*, *M. africanum* and *M. bovis* are the most important human pathogens. The most usual site of primary infection is the lung. Tuberculous infection occurs as a result of the inhalation of infected droplets or, in the case of *M. bovis*, by drinking infected milk. The term tuberculosis is used when the infected person has a disease process involving one or more parts of the body.

A tuberculosis patient may not know about his illness for sometime as the symptoms like fever, sweating, cough and headache appear slowly and are mild in nature. When it progresses, there may be breathlessness and palpitation on exertion, blood in sputum and pain in chest or abdomen. These diagnosis is made by positive tuberculin skin test, sputum examination for tubercle bacilli, high E.S.R. and X-ray of lungs showing a cavity at the apex.

Tuberculin, which is a sterile heat-concentrated filtrate from the soluble products of growth and lysis of one or more strains of mycobacteria, is used as diagnostic agent for testing tuberculosis infection. Tuberculin contains a suitable preservative that does not give rise to false-positive reactions. Sensitivity tests to tuberculin are performed in different ways.

Tuberculosis is a difficult disease to treat since tubercle bacilli grow slowly and they develop resistance to the chemotherapeutic agents. Upto 1940, no effective chemotherapeutic agent was available to treat tuberculosis. The treatment was mainly done by nutritive diet, fresh air and rest.

Streptomycin (in 1944), p-aminosalicylic acid and isoniazid (in 1952) were discovered as anti-tubercular drugs. At present, these three compounds in various combination, are considered the primary drugs in the treatment of human tuberculosis. Ethambutol has been discovered as the primary drug for the disease.

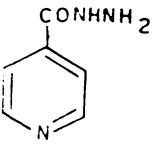
Antitubercular drugs have been studied ever since Koch detected the tubercle bacillus, *Mycobacterium tuberculosis*. Sulfonamides, sulfones, p-aminosalicylic acid, streptomycin, dihydrostreptomycin and tibione were the organic compound used to treat tuberculosis upto 1952.

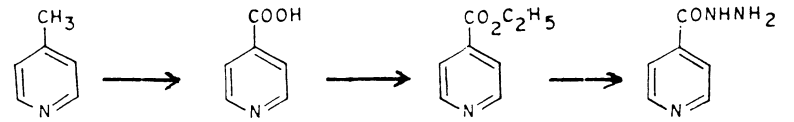
ISONIAZID

Nomenclature : 4-Pyridinecarboxylic acid hydrazide; Isonicotinic acid hydrazide; Isonicotinoylhydrazine; Isonicotinylhydrazine.

Brand Names : INH; Rimitsid; RP 5015; FSR-3 Cedin (Aerosol). Isocid; Neoxin; Hidrasonil; Ertuban; Antimicina; Hyzyd; Isonex; Unicozyde; Zonazide; Hycozid; Niconyl; Isonicazide; Isonicid; Isonicotan; Tubizid; Tibizide; Isobicina; Isozide; Isonilex; Isonindon; Isotebezid; Nicetal; Nikozid; Nitadon; Nyscozid; Pelazid; Raumanon; Retozide; RU-EF-Tb; Tebecid; Tisiodrazide; Tizide; Isozyd; Sauterazid; Nevin; Cotinazin; Dinacrin; Ditubin; Mybasan; Neoteben; Niadrin; Nicozide; Nydrazid; Nidaton; Nicizina; Nicotibina; Pycazide; Pyricidin; Isolyn; Pyrizidin; Rimifon; Robisellin; Isonizide; Neumandin; Isocotin; Tubicon; Tyvid; Tisin; Tibinide; Tubilysin; Tubomel; Tubeco; Atcotibine; Vazadrine; Vederon; Isonidrin; Zinadon. Niplen; TB-Vis; Takazin; Iridrina; Hydrazid.

Isoniazid, the hydrazide of isonicotinic acid, is synthesized from γ-picoline, which by permanganate oxidation is converted in the normal manner into isonicotinic acid. The acid is esterified by means of ethanol and concentrated sulphuric acid. Direct condensation of the ester with hydrazine affords the required hydrazide.





γ-Picoline Isonicotinic acid Ethyl isonicotinate Isoniazid

Isoniazid occurs as colourless, odourless crystals, or white crystalline powder, m.p. 171.4°, soluble in water (1 : 8) and

alcohol (1 : 50); slightly soluble in chloroform and ether. The drug is stored in well-closed containers and protected from light.

Uses : Isoniazid is antibacterial (tuberculostatic), i.e., it has bacteriostatic effect on the tubercle bacilli therein. It is used to treat pulmonary and extrapulmonary tuberculosis. Pyridoxine is often given in conjugation with isoniazid to avert its neurotoxicity.

Many of the adverse effects of isoniazid are related to hypersensitivity; other side-effects being nausea, vomiting and gastro-intestinal effects.

Official

Isoniazid, I.P., B.P.

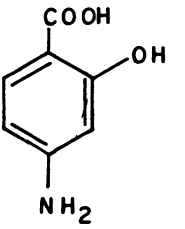
Isoniazid Injection, B.P., U.S.P.

Isoniazid Syrup/Tablets, B.P., U.S.P.

Isoniazid Tablets, I.P., B.P.

PAS

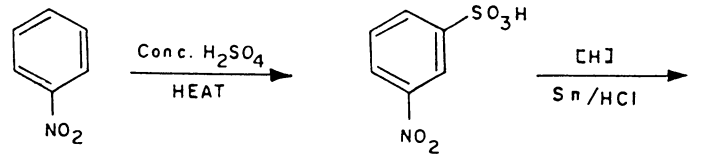
Nomenclature : p-Aminosalicylic acid; 4-Amino-2-hydroxybenzoic acid; 4-Aminosalicylic acid.



Brand Names : Deapasil; Apas; Apacil; Hellipidyl; PAC-C; Pamacyl; Parasal; Pascorbic; Pasolac; Parasalicil, Parasalindon; Pasnodia; Propasa; Rezipas; Sanipirol -4; Pamisyl; Para-Pas.

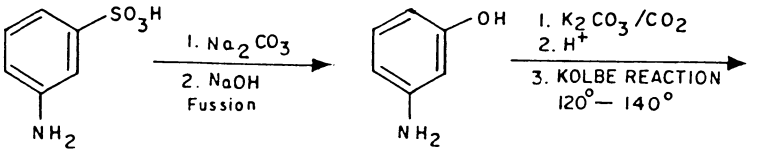
p-Aminosalicylic acid, first proposed for the treatment of tuberculosis by Lehmann in 1964, is prepared by various methods.

1. *m*-Aminophenol, obtained by fusion of *m*-nitrobenzenesulfonic acid, on treatment with potassium carbonate and then with CO_2 (Kolbe reaction), followed by careful acidification yields PAS.

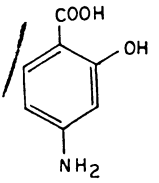


Nitrobenzene

m-Nitrobenzenesulfonic acid

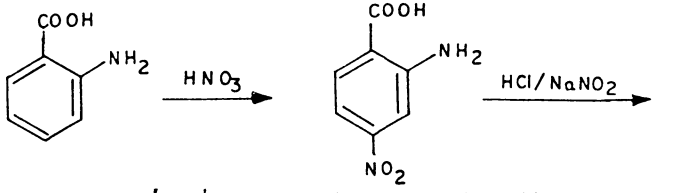


m-Aminophenol

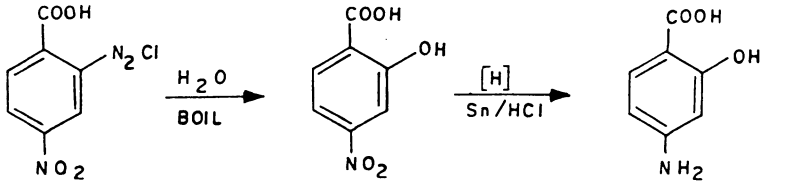


PAS

2. 4-Nitroanthranilic acid, obtained by nitration of anthranilic acid, on diazotization and boiling with water yields 4-nitrosalicylic acid. Reduction of 4-nitrosalicylic acid forms p-aminosalicylic acid.

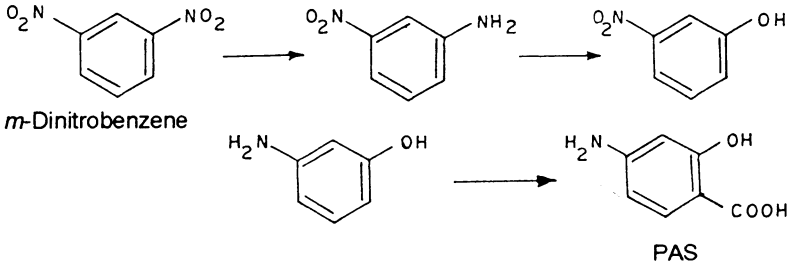


Anthranilic acid 4- Nitroanthranilic acid



PAS

3. PAS may be obtained from *m*-dinitrobenzene as follows:



m-Dinitrobenzene

PAS

It forms minute crystals from alcohol, odourless or slight acetous odour, which darken on exposure to light and air, m.p. 150-151; one gram dissolves in about 500 ml water, in 21 ml alcolol; slightly soluble in alcohol; insoluble in benzene; soluble in dilute nitric acid and dilute sodium hydroxide. At temperatures above 40°, aqueous solutions of PAS and its hydrochloride are readily decarboxylated to give brown solutions consisting mainly of m-aminophenol. The drug is stored at a temperature not exceeding 30° in airtight containers and protected from light.

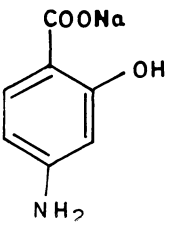
Uses : PAS is a tuberculostatic agent and retards the growth of actively multiplying tubercular bacilli. PAS aids streptomycin or dihydrostreptomycin in the treatment of tuberculosis. It is completely and readily absorbed after oral administration. It is distributed freely and equally to most tissues and fluids with the exception of the cerebrospinal fluid. It is excreted in the urine, both unchanged and as metabolites and has a biologic half-life of about 2 hours.

The main use of PAS is that it delays development of resistance to tuberculotic drugs.

The toxic effects of PAS is that it tends to cause gartro-intestinal disturbances with occasional skin rashes, allergic reactions and hypersensitivity.

SODIUM AMINOSALICYLATE

Brand Names : Aminox; Gabbropas; Pasalon; Pasalon-Rakeet; Passodico; Salvis; Pasid; Tubersan; Sanipirol; Pamisyl sodium; Pasmed sodium; Aminopar; Paramycin; Nippas; Lepasen; Paramisan; Bactylan; Osacyl; Entepas; Enteropas; PAS sodium dihydrate; Aminosalicylate sodium; Aminosalylnatrium; Natrii para-aminosalicylas; Pasalicylum solubile; Sodium-para-amino-salicylate; Sodium PAS; Sodium 4-amino-2-hydroxybenzoate dihydrate; Parasal sodium; Pasara sodium; Pasem sodium; Parapas sodium, Paraminose.



The compound occurs as a yellow-white, odourless, crystalline powder. It is soluble in alcohol; one gram dissolves in 2 ml water; very sparingly soluble in acetone; practically insoluble in ether, chloroform and benzene. Solutions of the sodium salt are more resistant to heat than PAS. Aqueous solutions decompose rapidly, the rate depending on the pH and the temperature.

The pH of maximum stability is in between 7 to 7.5. Two types of reactions are involved in the decomposition process. The first is decarboxylation to form *m*-aminophenol. In the second reaction oxidation of *p*-aminosalicylic acid or of the *m*-aminophenol, or both, is involved in which brown to black pigment is produced. Freshly prepared solutions of pure sodium *p*-aminosalicylate are almost colourless. On standing they develop an amber and finally dark brown or black colour. Solutions should be prepared within 24 hours before administration. The drug is stored at a temperature not exceeding 40^0 in airtight containers and protected from light.

Uses : Like aminosalicylic acid, sodium aminosalicylate is used with isoniazid and streptomycin to treat pulmonary tuberculosis.

Official

Sodium Aminosalicylate, B.P., I.P.

Sodium Aminosalicylate Granules/Capsules, I.P.

Aminosalicylic Acid Tablets, U.S.P.

Aminosalicylate Sodium Tablets, U.S.P.

CALCIUM AMINOSALICYLATE

Nomenclature : Calcium 4-amino-2-hydroxybenzoate; Calcium 4-aminosalicylate, Aminosalicylate calcium.

Brand Names : Para-aminosalicylas; Calcium PAS; Parasa calcium; P.A.C. Paracipan; Pasura calcium; Pasmicina; Aminacyl; Calcii.

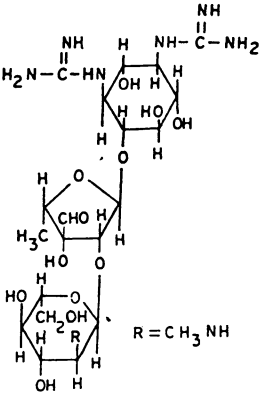
It occurs as cream-coloured, odourless, bitter sweet crystals. Its aqueous solutions decompose slowly and darken in colour. It is hygroscopic; soluble in water (1.7) and slightly soluble in alcohol. Aqueous solutions are unstable and darken in colour. It is stored in airtight containers and protected from light.

It exhibits all the desirable action of *p*-aminosalicylic acid but materially reduces gastro-intestinal irritation.

STREPTOMYCIN

Nomenclature : 4-0-[2-0-(2-Deoxy-2-methylamino-α-L gluco-pyranosyl)-5-deoxy-3-C-formyl-α-L-lyxofuranosyl] N-N'-diamidino-D-streptamine.

Brand Names : Streptomycin A; Estreptomicina.



The antibiotic streptomycin, first isolated from *Streptomyces grises* by Waksman *et al.* in 1944, is produced by submerged cultures. The culture solution is kept in large vats, growth of the microorganism begins at 24-28°C. After separating mycelium and other wastes, the compound is extracted from the filtrate.

Streptomycin is a colourless, odourless, bitter solid. It is soluble in water and is stable up to 28°C. It is usually available as the trihydrochloride, trihydrochloride-calcium double salt, phosphate or sesquisulphate, which occurs as granules or powder. Most salts are hygroscopic and deliquesce on exposure to air, but are not affected by air or light. The salts are very soluble in water, but almost insoluble in alcohol, chloroform and ether. Solutions are laevorotatory.

Acid hydrolysis of streptomycin yields streptidine and streptobiosamine, the compound that is a combination of L-streptose and N-methyl-L-glucosamine.

STREPTOMYCIN SULPHATE

Brand Names : Sesquisulfate; Agri-strep; Streptobrettin, Streptorex, Vetstrep; Sulfato de Estreptomicina; Streptomycini sulfas.

It is a white to light grey or pale buff powder with faint amine-like odour. It is very soluble in water; practically insoluble in alcohol, chloroform and ether; incompatible with acids and alkalies. The sulphate is stable in light and air. Streptomycin and its salts are kept in air-tight containers and protected from light.

Streptomycin sulphate is given by intramuscular injection as a solution in water.

Streptomycin is an aminoglycoside antibiotic mainly used in the treatment of tuberculosis. It is effective in the treatment of plague, tularaemia, and, in conjugation with tetracycline, in brucellosis.

Registance has been observed in strains of most of the organisms reported to be sensitive to streptomycin. Another factor which limits its therapeutic is chronic toxicity. Certain neurotoxic reactions have been observed after the use of streptomycin. They are characterized by vertigo, disturbance of equilibrium and reduced auditory acuity.

In combination with penicillin, streptomycin is used to cure subacute bacterial endocarditis and postoperative infections. Streptomycin is rapidly absorbed after intramuscular injection.

Streptomycin can produce ototoxicity, nepherotoxicity, respiratory depression, muscular paralysis, hypomagnesaemia, hypocalcaemia, hypokalaemia and some other effects like anaemia, purpura, convulsions, visual disturbances, etc.

Official

Streptomycin Sulphate, B.P., I.P.

Streptomycin Sulphate Injection B.P., U.S.P.

Streptomycin Tablets, I.P.

Dihydrostreptomycin Sulphate, I.P.

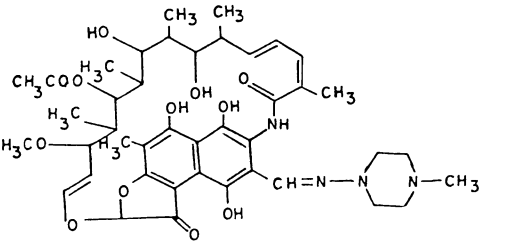
Dihydrostreptomycin Sulphate Injection, I.P.

Sterile Streptomycin Sulphate, U.S.

RIFAMPICIN

Nomenclature : 3-[(4-Methyl-1-piperazinyl) iminomethyl] rifamycin SV.

Brand Names : Rifaldazine; Rifamycin AMP; R/AMP; Rifampin; Rifa; Rifadin; Rifadine; Rifaldin; Riforal; Rifaprodin; Rifobac; Rifoldine; Rimactan; Rifamicinum.



It is a semisynthetic antibiotic obtained by reacting 3-formylrifamycin SV with 1-amino-4-methylpiperazine in tetrahydrofuran.

It occurs as odourless, brick red to reddish brown, crystalline powder; m.p. 183-188° (dec); very slightly soluble in water; freely soluble in chloroform; soluble in ethyl acetate, methyl alcohol and tetrahydrofuran. Rifampicin is a " Zwitterion" with pka 1.7 related to the 4-hydroxy and pka 7.9 related to the 3-piperazine nitrogen. A 1% suspension in water has a pH of 4.5 to 6.5. Rifampicin is stored at a temperature not excerding 15° in airtight containers in an atmosphere of nitrogen and protected from light.

Uses : Rifampicin is antibacterial and antitubercular and is used in the treatment of infections due to mycobacteria. It is usually the most effective drug for administration in association with isoniazid in the primary treatment of pulmonary tuberculosis. It is used to eradicate nasal carriage of *Neisseria meningitidis* and other microorganisms; in non-tuberculous conditions caused by susceptible organisms. No major side-effect has been reported. During intermittent therapy gastro-intestinal disorders, abnormalities in liver function, jaundice, drowsiness, headache, ataxia, dizziness, etc, may occur.

Official

Rifampicin, B.P.

Rifampicin Sodium, B.P.

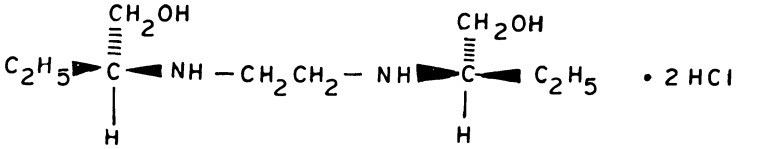
Rifampicin Capsules, U.S. P.

Rifampin and Isoniazid Capsules, U.S.P.

ETHAMBUTOL

Nomenclature : 2,2'-(1,2-Ethanediyldiimino) bis-1-butanol; (+) -2,2' (Ethylenediimino) di-1-butanol; d-N,N'-bis (1-Hydroxymethyl propyl) ethylene diamine.

Brand Names : Dadibutol, EMB; Sural; Tibutol; Myambutol; Ebutol; Etambol.



It is a white, odourless, crystalline powder freely soluble in water (1.1), alcohol (1.4); slightly soluble in chloroform; practically insoluble in ether; m.p. 87-89°.

Ethambutol is stereospecific in activity. The dextro isomer is 16 times as active as the meso isomer and the laevo isomer is even less active than the meso isomer.

Uses : Ethambutol hydrochloride is used with other antituberculous agents in the treatment of tuberculosis. It is rapidly absorbed after oral administration.

Many patients cannot tolerate therapeutic doses of ethionamide and have to discontinue treatment. The most common adverse effects are dose-related : gastro-intestinal disturbances, including anorexia, excessive salivation, a metallic taste, nausea, vomiting, stomatitis, and diarrhoea. Dizziness, drowsiness, headache, postural hypotension, and asthenia may also occur occasionally. Although jaundice is rare, hepatitis may occur in about 5% of patients receiving ethionamide.

Official

Ethambutol Hydrochloride, B.P., I.P.

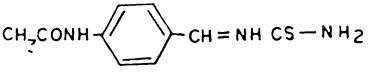
Ethambutol Tablets, B.P., I.P.

Ethambutol Hydrochloride Tablets, U.S.P.

THIACETAZONE

Nomenclature : N-(4-[[(Aminothioxomethyl) hydrazono] methylene] phenyl] acetamide; 2-[[4-Acetylamino) phenyl] methylene] hydrazinecarbothioamide, 4'-Formylacetanilide thiosemicarbazone; p-Acetamidobenzaldehyde thiosemicarbazone; p-Acetylaminobenzaldehyde thiosemicarbazone; p-Acetaminobenzylidenethiosemicarbazone.

Brand Names : Thibone, Thioacetazone; TbI/698, Amithiozone; Sdt 1041; RP 4207; Conteben; Thizone; Norakol; Thionicid; Domakol; Aktivan; Ambathizone; Seroden; Benthiozone; Berkazon; Diasan; Ilbion; Tebalon; Siocarbazone; Tibicur; Thiomicid; Tibion; Tibione; Tebethion; Panrone; Thioparamizone; Myvizone; Thiobicina; Tubercazon; Berculon; Antib; Neustab; Nuclon; Argentinian; Livazone; Benzothiozon; Parazone; Tebezon; Thiotebezin; Thiocarbazil; Thiocarone; Thiosecolo.

It forms minute, pale yellow crystals from alcohol. Taste is 

bitter, m.p. 225-230° (dec); darkens on exposure to light. It is soluble in hot alcohol; very sparingly soluble in cold alcohol; insoluble in water, acetone, benzene, carbon tetrachloride, chloroform, carbon disulphide and petroleum ether.

Uses : Thiacetazone is used in the primary treatment of pulmonary tuberculosis with isoniazid supplemented in the initial phase of treatment, with streptomycin. It is also used in the treatment of leprosy in daily doses similar to those used in tuberculosis.

Gastro-intestinal disorders, hypersensitivity reactions, rashes, and vertigo are the most common side-effects of thiacetazone.

Official

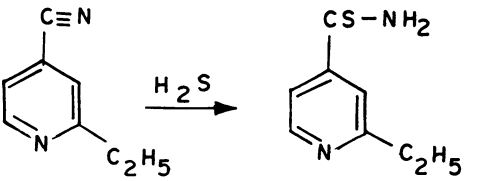
Thiacetazone, I.P.

Thiacetazone and Isoniazid Tablets, I.P.

ETHIONAMIDE

Nomenclature : 2-Ethyl-4-pyridinecarbothioamide; 2-Ethylthioisonicotinamide; 3-Ethylisonicotinamide; 2-Ethylisothionicotinanide; 2-Ethyl-4-thiocarbamoylpyridine; α-Ethylisonicotinoylthioamide.

Brand Names : Amidazine; Ethioniamide; Bayer 5312; Nisotin; 1314 Th; Trecator; Trescatyl, Aetina; Ethimide; Iridocin; Tiomid.



Ethionamide

Ethionamide can be obtained by addition of hydrogen sulphide to the corresponding nitrite in the presence of triethanolamine.

The drug occurs as a yellow, crystalline substance, m.p. 164-166°, very sparingly soluble in water and ether; sparingly soluble in methanol, ethanol and propylene glycol; soluble in hot acetone and dichloroethane; freely soluble in pyridine. It

darkens on exposure to light, with a slight sulphur-like odour. A 1% suspension in water has a pH of 6 to 7. It is stored in airtight containers.

Uses : Ethionamide is a substituted thioamide of isonicotinic acid which has been used with other antituberculous agents for the treatment of tuberculosis, generally when resistance to primary agents has developed. It is a secondary drug in the chemotherapy of tuberculosis and is claimed to be five times less toxic.

Many patients cannot tolerate therapeutic doses of ethionamide. The most common adverse side-effects are gastro-intestinal disorders, excessive salivation, metallic taste, dizziness, headache, etc.

Official

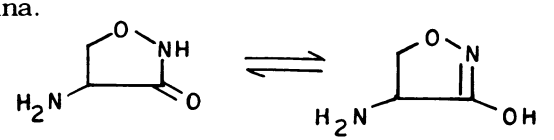
Ethionamide, B.P.

Ethionamide Tablets, B.P., U.S.P.

CYCLOSERINE

Nomenclature : D-4-Amino-3-isozolidinone; D-4-Amino-3-isoxazolidone; (+)-(R)-4-Aminoisoxazolidin-3-one.

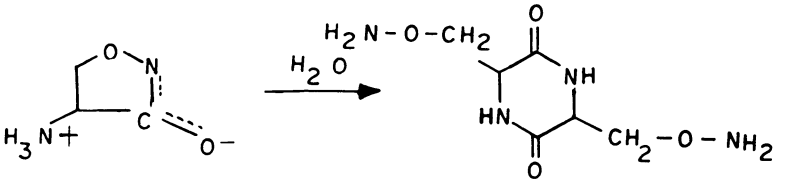
Brand Names : PA-94; Closina; 106-7; Orientomycin; Farmiserina; Micoserina; Oxamycin; Seromycin; D-Cycloserin; Cycloserinum; Cycloserina.



This compound was discovered in 1955 by five independent groups of workers. It has been isolated from three different species of Streptomyces: *Streptomyces garyphalus, S lavendulae,* and *S. orchidaceae.* Its structure was established by acid degradation to serine and hydroxylamine and by hydrogenation to D-serine amide. The compound exists in equilibrium with its enol form. In aqueous solutions, cycloserine will form a dipolar ion that, on standing, will dimerize to 2,5-bis (aminoxymethyl) -3,6-diketopiperazine.

Cycloserine is a white to pale yellow hygroscopic, crystalline material that is soluble in water; m.p. 155-156° (decomp). Aqueous solution of cycloserine has a pH around 6. It forms stable salts with strong acids and bases; the neutral or acid

solutions are unstable. Its racemic mixture is more active than either D-or L-form. It is stored at a temperature not exceeding 25° in airtight containers.



2-5-bis(Aminomethyl)-3, 6-diketopiperazine.

Uses : Cycloserine is a secondary antituberculous agent and is used when primary agents have been ineffective or when their use is precluded due to intolerance or the presence of resistant organisms. It is also used in the treatment of urinary-tract infections unresponsive to other therapy. Its relatively weak potency and frequent toxic reactions limit its use to the treatment of tuberculosis.

Adverse effects of cycloserine are dose-related and include anxiety, confusion, disorientation, depression, irritability and paranoia.

Official

Cycloserine, B.P

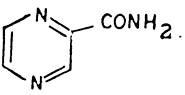
Cycloserine Capsule, B.P.

Cycloserine Tablets, B.P., U.S.P.

PYRAZINAMIDE

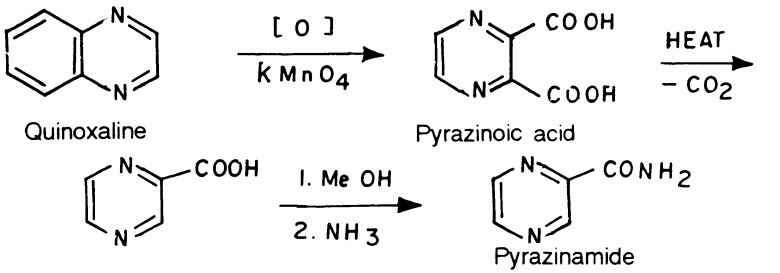
Nomenclature : Pyrazine -2-carboxamide; Pyrazinoic acid amide; Pyrazine carboxylamide.

Brand Names : Addinamide; D-50; Eprazin; Pezetamid; Pyrafat; Pirilene; Piraldina; Tebrazid; Unipyranamide; Zinamide.



This simple pyrazine derivative can be prepared from quinoxaline by oxidation with permanganate, thermal decomposition of the dicarboxylic acid, and esterification with methanol followed by ammonolysis.

Pyrazinamide occurs as a white crystalline, odourless powder, m.p. 189-191°. It is practically insoluble in water and ether; slightly soluble in alcohol and chloroform.



Uses : It is used for patients whose tuberculosis is resistant to other drugs.

It causes a significant incidence of liver damage. With doses of 3 g daily up to 15% of patients may show sign of liver damage. Other side-effects are anorexia, nausea, vomiting, arthralgia, malaise, fever, anaemia and dysuria. Pyrazinamide increases reabsorption of urates and should thus be used with care in patients with a history of gout.

Official

Pyrazinamide, I.P., B.P.

Pyrazinamide Tablets, B.P., U.S.P., I.P.

8

ANTIAMOEBIC AND ANTHELMINTIC DRUGS

Amoebiasis is a world-wide infectious disease caused by a parasitic protozoa, *Entamoeba histolytica*, which usually spreads through contaminated food and water. This disease is common in tropical countries and places where public hygiene and sanitation are poor. The disease occurs mainly in tropical regions. It primarily affects the colon, but other organs like liver, lungs and brain may be involved afterwards. The disease is characterized by gastrointestinal and constitutional symptoms. Since the causative organism of amoebiasis derives its nutrition from the normal bacterial flora of the large intestine, the latter is the chief site of infection. However, in some cases it may spread to other organs of the body of which the liver is the most susceptible. Acute amoebic dysentery is associated with bloody, mucoid stools, abdominal pain and tenesmus. Emetine, and quiniodochlor, halquinol and metronidazole are the agents used to treat amoebic dysentery.

During the acute phase of *intestinal amoebiasis* the patient may have loose motions with or without mucous and blood, besides griping pain in the abdomen which may be severe at the time of evacuation. In chronic amoebiasis, patient may complain of the dull pain in the lower abdomen, alternate constipation and diarrhoea, foul smell in the stools, formation of gases and loss of appetite. In case of liver amoebiasis, the patient may have pain in the right upper abdomen, fever, sweating, loss of weight and anaemia.

The parasitic worms are called helminths. Helminthiasis is

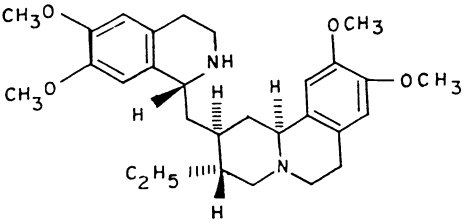
a disease produced by infestation with parasitic worms living in the alimentary canal or in the other tissues of the host. This infection is spread by contact with infected animals, ingestion of infected meat, by animal or human excreta or water or by certain mosquitoes. The worm enter into the body in the form of larvae or egg. The main parasitic worms are roundworms, hookworms, threadworms, tapeworms, guineaworms and filarial worms.

Roundworm *(Ascaris lumbricoides)* is one of the commonest worm affecting human beings. The disease generally spreads through handlling of contaminated food or soil. In areas where sanitation is very poor, children defecate in the area around their homes and in dry climate the eggs of *Ascaris* get airborne and ingested through the mouth. These eggs complete their life cycle in man and are finally lodged in the gut as full adult worms. The disease is also common in those areas where vegetables are grown on soil fertilized by human excreta. Adult worms may cause no symptoms if infestation is light, but severe infestation may lead to abdominal pain, skin radshes, *broncho-pneumonia* and even cause obstruction of the intestines. The diagnosis is usually made when ova are found in the stool or when an adult worm in vomited or passed out in the stools. The adult worm is cylindrical in shape, brown or pinkish in colour and measures 15 to 50 cm in length and 3 to 5 mm in diameter.

The anthelmintics are the drugs used to kill or remove the parasitic worms. The drugs which kill the worms are called vermicidal. The chemical agents used in expelling them are called vermifuges. Piperazine, thiabendazole, mebendazole and dichlorophene are the compounds used as anthelmintic drugs.

EMETINE

Nomenclature : 6',7',10,11-Tetramethoxyemetan; Cephaeline methyl ether; (2, S, 3 R, 11bS)-3-Ethyl-1,3,4,6,7,11b-hexahydro-9,10-dimethoxy-2-[(1R)-1,2,3,4,-tetrahydro-6,7-dimethoxy-1-isoquinolylmethyl]-2H-benzo [a] quinolizine.



Emetine is the principal alkaloid of Ipecac, the ground roots of *Uragoga ipecacuanha* (Family Rubiaceae). It occurs as white amorphous powder, m.p. 74°; turns yellow on exposure to light and heat. It is freely soluble in methanol, ethanol, acetone, ethyl acetate, chloroform; sparingly soluble in water, petroleum ether, solutions of KOH and NaOH; moderately soluble in dilute ammonium hydroxide.

Emetine is obtained from the crude drug by first extracting the total alkaloids with a suitable solvent and then separating them into individual components by chromatographic techniques. It may be obtained synthetically by methylation of naturally occurring cephaeline.

The emetine hydrochloride occurs as a white or very slightly yellowish, odourless, crystalline powder. The salt is freely soluble in water, alcohol, and chloroform. It contains water of crystallization varying from 3 to 8 H_2O. After drying at 105°, it melts at 235-255°. One gram of the hydrated salt dissolves in about 7 ml water. Solids and solutions turn yellow on exposure to light or heat. It is stored in a well-closed container and protected from light.

Uses : Emetine and its hydrochloride have been used as an amoebicide and for lungworm infection. It acts principally in the bowel wall and in the liver. It is used in the treatment of severe intestinal amoebiasis and hepatic amoebiasis, although metronidazole, which is less toxic, is generally preferred.

Adverse effects of emetine therapy include aching, tenderness, stiffness and weakness of muscles in the area of injection following diarrhoea, nausea, vomiting, dizziness and headache.

Official

Emetine Hydrochloride, B.P., I.P.

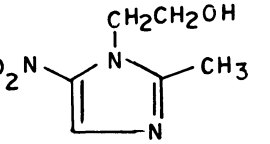
Emetine Injection, B.P., I.P.

Emetine Hydrochloride Injection, U.S.P.

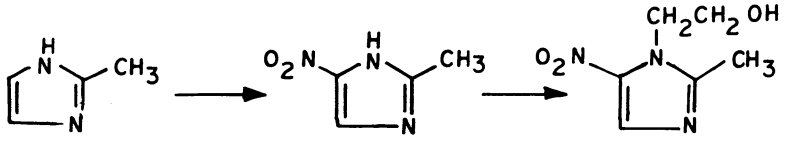
METRONIDAZOLE

Nomenclature : 2-Methyl-5-nitroimidazole-1-ethanol; 1-(2-Hydroxyethyl) -2-methyl-5-nitroimidazole; 1-(β-Ethylol)-2-methyl-5-nitro-3-azapyrrole.

Brand Names : Bayer 5630; RP 8823; Arilin; Clont; Cont; Danizol; Deflamon; Flagyl; Fossyol; Gineflour; Klion; Orvagil; Sanatrichom; Trichazol; Trichocide; Tricho Cordes; Tricho-Gynaedron; Tricocet; Trivazol; Vagilen; Vagimid.



Metronidazole is an imidazole or cyclic amidines which can be synthesized by condensation of compounds containing adjacent carbonyl group (i.e.-CO-CO) with ammonia and formaldehyde (Radziszewski's reaction). Tartaric acid dinitrate and acetaldehyde yields, after thermal decarboxylation, 2-methylimidazole. Nitration, followed by alkylation in the 1-position with ethylene chlorohydrin yields metronidazole.



2-Methylimidazole

Metronidazole

Metronidazole is a pale yellow or cream-coloured crystalline compound, m.p. 150-160°; has limited solubility in water and other organic solvents. It is stable in air but darkens on exposure to light. Therefore, it is protected from light.

Uses : Metronidazole is an antiprotozoal substance and used in the treatment of susceptible protozoal infections, anaerobic becterial infections, dracontiasis (guinea-worm infection), inflammatory bowel disease and as an adjunct to the radiotherapy of malignant neoplasms. Darkened urine may occur when the drug is given in higher doses. The yellow pigment may be a metabolite of metronidazole. The adverse effects of the drug are gastro-intestinal disturbances, nausea, unpleasant taste, headache, anorexia and vomiting.

Official

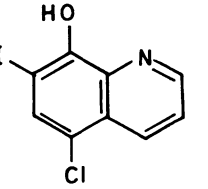
Metronidazole, B.P., I.P.
Metronidazole Tablets, B.P., I.P., U.P.S.
Metronidazole Injection, U.S.P.

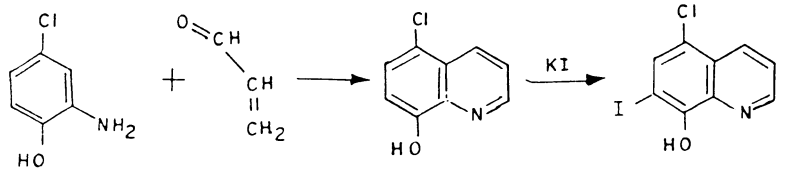
IODOCHLORHYDROXYQUIN

Nomenclature : 5-Chloro-7-iodo -8-quinolinol; 5-Chloro-8-hydroxy-7-iodoquinoline.

Brand Names : Chloroiodoquin, Iodochlorohydroxyquinoline; Iodochloroxyquinoline; Quinoform, Amebil; Alchoquin; Amoenol; Bactol; Barquinol; Budoform; Chinoform; Clioquinol; Cliquinol; Eczecidin; Enteroquinol; Entero-Septol; Entero-Vioform; Enterozol; Entrokin; Hi-Enterol; Iodoenterol; Nioform; Quinambicide; Rometin Vioform.

It is a halogenated derivative of 8-hydroxyquinoline. An aqueous solution of an alkali salt of 5-chloro-8-hydroxyquinoline (prepared by a Skraup's quinoline synthesis) is iodated using potassium iodide and a hypochlorite. The activating phenolic group directs the iodine into the *ortho* position in the homocyclic ring.





2-Amino-4-Chlorophenol | Acraldehyde | 5-Chloro-8-hydroxyquinoline | Iodochloro-hydroxyquin

The compound consists of spongy, brownish-yellow, bulky powder with a slight, characteristic odour, m.p. 178-180° (dec). It darkens on exposure to light. It is practically insoluble in water or alcohol but dissolves in hot ethyl acetate and in boiling acetic acid. It is decomposed by heating with dilute hydrochloric acid, more easily with concentrated sulphuric acid, eliminating vapours of iodine. The drug is stored in airtight containers and protected from light.

Uses : Iodochlorhydroxyquin has been used as topical intestinal anti-infective, and anti-amoebic, taken orally. Oral preparations have now been withdrawn worldwide because of neurotoxicity.

Iodochlorhydroxyquin has antibacerial and anti-fungal activity and is used in creams and ointments in the treatment of skin infections. It is also applied together with a corticosteroid in inflammatory skin conditions complicated by bacterial or fungal infections.

The side-effects of the drug are severe irritation, staining of the skin, discolouring of hairs, neurotoxicity and cerebral disturbances.

Official

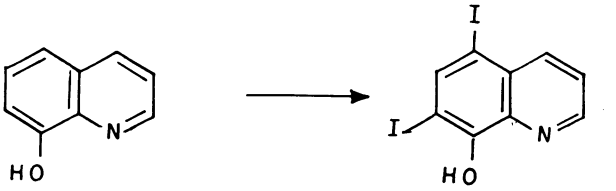
Clioquinol, B.P.
Quiniodochlor, I.P.
Clioquinol Cream, B.P., U.S.P.
Cliquinol Ointment, U.S.P.
Compound Clioquinol Powder, U.S.P.
Hydrocortisone Acetate and Clioquinol Cream, B.P.
Hydrocortisone and Clioquinol Ointment, B.P.
Zinc Paste, Calamine and Cliquinol Bandage, B.P.

DI-IODOHYDROXYQUINOLINE

Nomenclature : 5,7-Di-iodoquinolin-8-ol; 8-Hydroxy-5,7-diiodoquinoline.

Brand Names : Diiodohydroxyquin, Di-iodohydroxyquinoline; Di-iodoxychinolinum; Di-iodoquinoline; Iodoquinol; Diiodoquin.

The compound is the 5,7-di-iodo derivative of 8-hydroxyquinoline, from which it is prepared by direct iodination by the action of iodine monochloride or potassium iodate. The iodine atoms enter the activated benzenoid ring in the positions *ortho*-and *para*-to the directing -OH group.



8-Hydroxyquinoline Di-iodohydroxyquinoline

The compound is a light yellowish to tan-coloured, microcrystalline powder, odourless powder, not readily wetted in water. Practically it is insoluble in water; sparingly soluble in alcohol and ether.

Uses : Di-iodohydroxyquinoline is a luminal amoebicide acting principally in the bowel lumen and is used in the treatment of intestinal amoebiasis. It is given alone in the treatment of asymptomatic cyst-passers. It is also given in the treatment of balantidiasis and the infestation by *Trichomonas hominis (intestinalis).* It has anti-bacterial and anti-fungal activity and has been used topically in various skin conditions, usually along with a corticosteroid.

In high doses for long term, the adverse effects are optic neuritis, optic atrophy, peripheral neuropathy, gastro-intestinal effects such as abdominal cramps, nausea, and diarrhoea. Other side-effects are the same as for iodochlorhydroxyquin.

Official

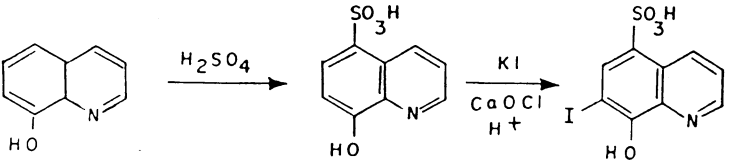
Di-iodohydroxyquinoline, I.P.
Di-iodohydroxyquinoline Tablets, I.P.
Iodoquinol Tablets, U.S.P.

CHINIOFON

Nomenclature : 7-Iodo-8-hydroxyquinoline-5 sulphonic acid.

Brand Names : Anayodin Quinoxyl, Yatren.

It is prepared by sulphonating 8-hydroxyquiniline, subjecting the product to potassium iodide and bleaching powder in the presence of potassium carbonate, precipitating the derived phenol with hydrochloric acid and finally, mixing with sodium carbonate.

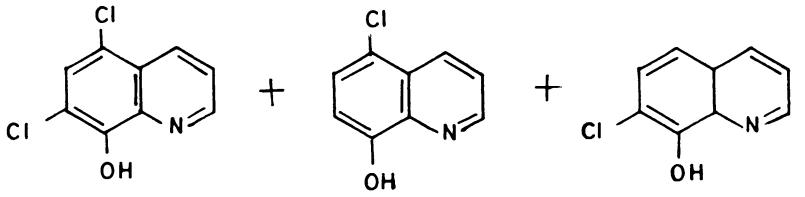


Hydroxyquinoline Chiniofon

Chiniofon is a mixture of 7-iodo-8-hydroxyquinoline-5-sulphonic acid, its sodium salt and sodium carbonate containing about 26-29 per cent of iodine. It is a canary-yellow powder with a slight odour, a bitter taste producing a sweet sensation later on. On adding to water, it effervesces due to reaction with the sodium carbonate and finally dissolves. It forms deep, emerald-green colour with dilute ferric chloride solution and a dense, white precipitate with copper sulphate.

Uses : Chiniofon is used to cure amoebic dysentery, as a surgical dusting powder and in gonorrhoea and diphtheria.

Halquinol : It is a mixture of 5,7-dichloro-8-hydroxyquinoline (57-74%), 5-chloro-8-hydroxyquinoline (23-40%) and 7-chloro-8-hydroxyquinoline (4%). Halquinol is a yellow-white voluminous powder with a faint cresol-like odour; insoluble in water; soluble in most organic solvents. It is protected from light and kept away from metals. Halquinol is antiamoebic, antibacterial and antifungal. It is used to treat bacterial and amoebic dysentery and in skin diseases.



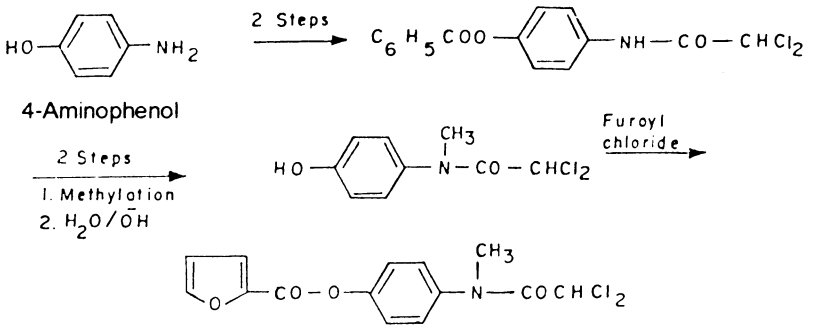
Halquinol

DILOXANIDE FUROATE

Nomenclature : 2, 2-Dichloro-N-(4-hydroxyphenyl)-N-methylacetamide, furoate; 2, 2-Dichloro-4'-hydroxy-N-methylacetanilide furoate; 4-(N-methyl-2, 2-dichloroacetamido) phenyl 2-furoate.

Brand Names : Miforon; Diloxanide 2-furoic acid ester; Furamide; Histomibal.

Diloxanide furoate is an aromatic ester of 2-furoic acid. For its synthesis, 4-aminophenol is treated with chloral cyanohydrin in the presence of pyridine and triethylamine. The resulting phenol is then benzoylated before methylation of the amido group, followed by hydrolysis with 0.5 N sodium hydroxide to give diloxamide. Esterification of diloxanide with furoyl chloride yields diloxanide furoate.



Diloxanide furcate

Diloxanide furoate is a white, odourless, crystalline powder; very slightly soluble in water; slightly soluble in ether and alcohol. It is protected from light.

Uses : It is a luminal amoebicide used in the treatment of intestinal amoebiasis. With metronidazole it is used to treat *Entamoeba polecki* infection.

Flatulence is the most common adverse effect during treatment with diloxanide furoate. Vomiting, pruritis and urticaria may occasionally occur.

Official

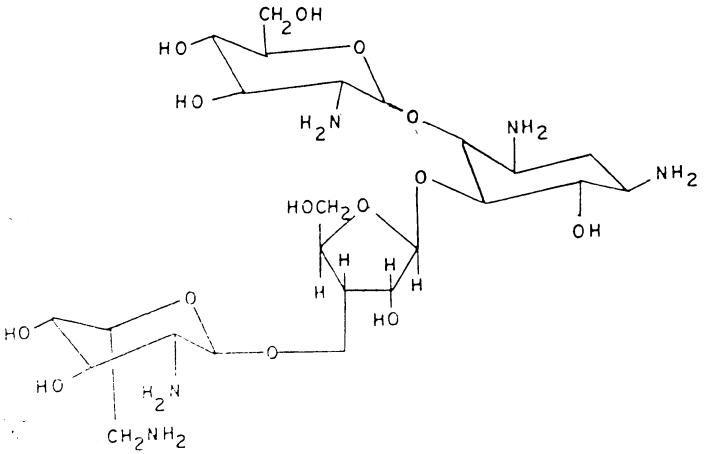
Diloxanide Furoate, B.P., I.P.

Diloxanide Furoate Tablets, B.P., I.P.

PAROMOMYCIN SULPHATE

Nomenclature : 0-2 Amino-2 deoxy-α-D- glucopyranosyl(1→4) 0-[0-2,6-diamino-2, 6-dideoxy-β-L-idopyranosyl-(1→3)-β-D-ribofuranosyl-(1→5)-2-deoxy-D-streptomine.

Brand Names : 1600 Antibiotic; Farmiglucin; Farminosidin; Fi 5853; Gabbromicina; Gabbromycin, Gabbroral; Humatin; Pargonyl; Paramicina; Paricina; Aminosidinum; Sulfuricum; Amminosidina solfato; Catenulin-paromomycin I sulphate; Catenulin sulphate; R 400 sulphate, Neomycine E sulphate.



Paromomycin was isolated in 1959 by Coffey *et al.* from cultures of *Streptomyces rimosus* forma *paromycinus* obtained from soil from Colombia. The antibiotic is very similar to neomycin, consisting of a mixture of two isomers differing only in the configuration in one of the rings. It differs from neomycin in that the 2-deoxystreptamine is linked to 2-deoxy-2-amino-D-glucose

instead of neosamine. Paromomycin consists of two isomers-paromomycins I and II. The combination of D-glucosamine with deoxystreptamine is obtained by partial hydrolysis of both paromomycins and is called paromamine.

Paromomycin occurs as an amorphous, white powder; soluble in water; moderately soluble in methanol; sparingly soluble in absolute alcohol.

Paromomycin sulphate is a creamy white to light yellow, odourless, hygroscopic powder; very soluble in water; practically insoluble in alcohol, chloroform and ether. It is stored in airtight containers.

Uses : Paromomycin sulphate is an aminoglycoside antibiotic which has been taken orally to treat intestinal amoebiasis, bacterial diarrhoea and for the suppression of the intestinal flora prior to surgery.

It may cause partial or total deafness, nausea, vomiting and diarrhoea in large doses.

Official

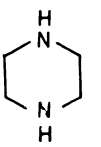
Paromycin Sulfate Capsules/Syrup, U.S.P.

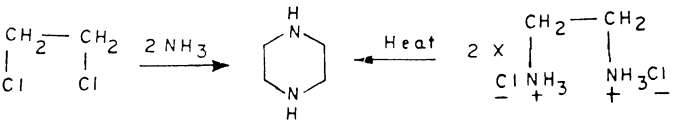
PIPERAZINE

Nomenclature : Hexahydropyrazine; Piperazidine; Diethylenediamine.

Brand Names : Worm-Away; Wurmirazin; Lumbrical; Arthriticin; Dispermine.

It is prepared by the action of alcoholic ammonia on ethylene chloride (Hofmann amine synthesis); by the reduction of pyrazine with sodium in alcohol; by catalytic deamination of diethylenetriamine and of ethylenediamine, and by cyclization of ethylene-diamine by the action of heat on its hydrochloride.





Piperazine is a crystalline solid, m.p. 106°, salty taste, absorbs water and CO_2 from air and freely soluble in water, glycerol and glycols. It crystallizes as leaflets from alcohol and as a low melting hexahydrate from water. It combines with two

equivalents of acids. It is a stronger base than ammonia. It has all the expected properties of a secondary amine. It is stored in airtight containers.

Uses : Piprazine is used as an anthelmintic for the treatment of pinworms and roundworms in children and adults. Piperazine is usually administered as the citrate or phosphate, but dosage is generally stated in terms of the hexahydrate.

Serious adverse effects are rare with piperazine. Overdose may cause nausea, vomiting, diarrhoea, abdominal pain, headache and urticaria.

PIPERAZINE HEXAHYDRATE

Brand Names : Anthalazine; Arpezine; Arthriticine; Ascaril; Dispermin; Eraverm (syrup); Helmifren; Parid; Piavetrin; Tasnon (elixir); Upixon; Vermicompren (syrup); Vermisol; Piperazini hydras; Piperazium hydricum.

It occurs as colourless deliquescent crystals, m.p. 44°; freely soluble in water and alcohol; very slightly soluble in ether. A 5% solution in water has a pH of 10.5 to 12.0. The piperazine of commerce is usually this hydrate. It is kept in well-closed containers.

PIPERAZINE PHOSPHATE

Brand Names : Eraverm (tabl.); Pincets; Pinsirup; Piperaverm; Piperazate; Pripsen; Tasnon (tabl.); Uvilon (tabl.); Piperazini phosphas.

It is a white, odourless, crystalline powder; very slightly soluble in water; insoluble in alcohol. A 1% solution in water has a pH of 6.0 to 6.5. It is stored in well closed containers.

Official

Piperazine Phosphate Tablets, B.P.

PIPERAZINE ADIPATE

Nomenclature : Hexanedioic acid compound with piperazine (1:1); Dietemin; Entacyl; Oxyzin; Vermicompren; Nometan; Vermilass; Oxypaat; Pipadox;' Oxurasin; Adiprazine; Piperazini adipas; Piperazinum adipicum.

It is the neutral salt of piperazine and adipic acid. It occurs as white crystalline powder, m.p. 256-257°; stable to heat and air. It has pleasant, slightly acid taste; dissolves slowly in water (1in 18); practically insoluble in alcohol. It is stored in airtight containers. It has anthelmintic properties.

Official

Piperazine Adipate, I.P., B.P.

Piperazine Adipate Tablets, I.P.

PIPERAZINE CITRATE

Brand Names : Hydrous tripiperazine dicitrate; Pinazan; Pipracid; Exopin; Uvilon; Oxyzin; Helmezine; Piperazini citras; Antepar citrate; Multifuge citrate; Parazine citrate; Oxucide; (3P-2C); Piperaverm (syrup); Pipizan citrate; Pinrou; Piptelate; Ta-verm; Exelmin; Rhomex; Nemadital; Arpezine.

It occurs as a white crystalline or granular powder with a slight odour, m.p. 182-187° (decomp). It contains a variable amount of water. It is soluble in water (1 in 1.5); practically insoluble in alcohol and ether. A 1% solution in water has a pH of about 5. It is kept in well-closed containers.

Piperazine citrate is administered orally. In some commercial products, the dose is expressed in terms of the equivalent amount of piperazine hexahydrate.

It is used as anthelmintic (intestinal pinworms and roundworms).

Official

Piperazine citrate, I.P., B.P.

Piperazine Citrate Elixir, B.P.

Piperazine Citrate Syrup/Tablets, U.S.P.

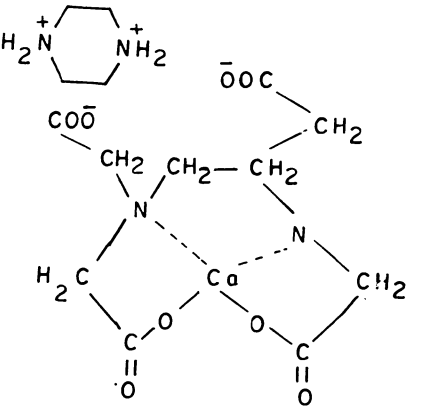
PIPRAZINE CALCIUM EDATHAMIL

Nomenclature : (Ethylenedinitrilo)-tetra-acetic acid piperazine calcium salt.

Brand Names : Piperazine edetate calcium; Piperazine calcium edathamil, Justelmin, Perin.

It is a chelated compound prepared by the action of ethylenediaminetetra acetic acid on piperazine and calcium carbonate. It occurs as white crystals; taste is slightly saline; freely soluble in water but very slightly soluble in alcohol or chloroform. The pH of a 20% aqueous solution is about 5.

It is administered orally in doses expressed in terms of the piperazine hexahydrate equivalent. It is available as a syrup and a wafer.

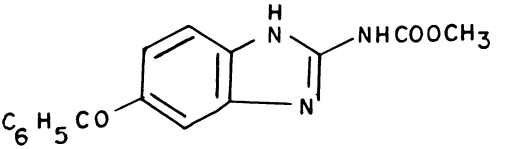


Piperazine calcium Edathamil

MEBENDAZOLE

Nomenclature : (5-Benzoyl-1H-benzimidazol-2-yl)-carbamic acid methyl-ester; 5-Benzoyl-2-benzimidazolecarbamic acid methyl ester; Methyl 5-benzoyl-2-benzimidazolecarbamate.

Brand Names : Ovitelmin; Pantelmin; Telmin; Vermirax; Vermox; R 17635.



Mebendazole, a benzimidazole carbomate derivative, occurs as a white to slightly yellow powder; m.p. 288-289°; practically insoluble in water, alcohol, chloroform, ether and dilute mineral acids; freely soluble in formic acid.

Uses : It is an anthelmintic with activity against most nematode and some cestode. It is poorly absorbed from the gastro-intestinal tract and is used principally to treat infections due to roundworms threadworms, hookworms and whipworm. During treatment with mebendazole, migration of worms with expulsion through the mouth and nose occurred in some patients. It is also used in the treatment of capillariasis.

Side effects have generally been restricted to gastro-intestinal disturbances such as transient abdominal pain and diarrhoea.

Official

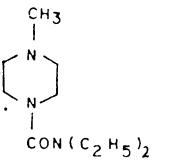
Mebendazole, I.P.

Mebendazole Tablets, U.S.P., I.P.

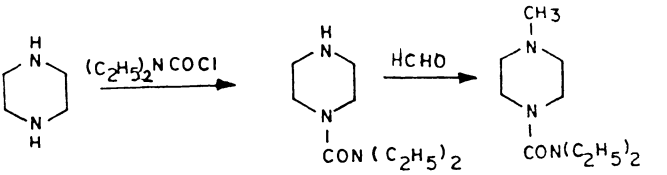
DIETHYLCARBAMAZINE (D.E.C.)

Nomenclature : N, N-Diethyl-4-methyl-1-piperazinecarboxamide; 1-Diethylcarbamoyl-4-methylpiperazine.

Brand Names : Carbamazine, 84L; RP 3799; Banocide; Carbilazine; Caricide; Cypip; Ethodryl; Notezine; Spatonin; Hetrazan.



Diethylcarbamazine, which is 1-diethyl carbamoyl-4-methylpiperazine, is prepared by condensing piperazine with diethylcarbamoyl chloride, $(C_2H_5)_2NCOCl$ (prepared from diethylamine and carbonyl chloride) and then methylating the other nitrogen atom with formaldehyde.



Diethylcarbamazine, m.p. 47-49°, is a crystalline compound. Its hydrochloride is very soluble in water; soluble in chloroform and dioxane.

Diethylcarbamazine Citrate (Brand Names : Franocide; Filazine; Loxuran; Longicid; Dirocide; Filaribits; Hetrazan), m.p. 141-143°, is a colourless, crystalline solid; freely soluble in water; sparingly soluble in cold alcohol; practically insoluble in benzene, acetone, ether, and chloroform. A 1 per cent solution has a pH of 4.1, The drug is stable under various climatic conditions and moisture. It is stored in airtight containers. Solution should be protected from light.

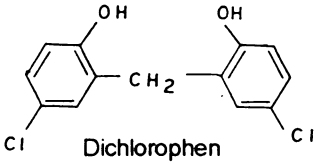
Uses : Diethylcarbamazine is used as an anthelmintic and antifilarial agent.

Official

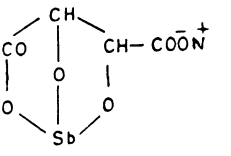
Diethylcarbamazine Citrate (Tablets), I.P., B.P., U.S.P.

Diethylcarbamazine Tablets, I.P., B.P.

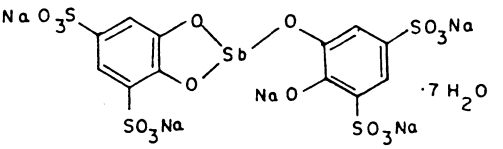
Miscellaneous Anthelmintics



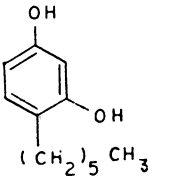
Dichlorophen



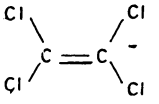
Antimony sodium Tartrate



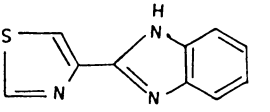
Stibophen



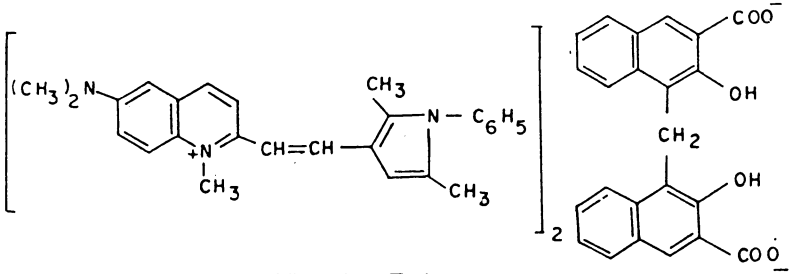
Hexylresorcinol



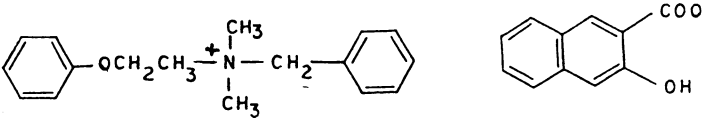
Tetrachloroethylene



Thiabendazole



Viprynium Embonate



Bephenium Hydroxynaphthoate

9

ANTIBIOTICS

Antibiotics are the chemical compounds produced by or derived from various micro-organisms, such as fungi, actinomycetes, bacteria, yeast and molds.

Antibiotics are commonly employed in ailments like diarrhoea, respiratory and urinary tract infections, and nonspecific fevers. Depending upon the type of action, these are called *bactericidal* or *bacteriostatic* antibiotics. Bactericidal are those which kill micro-organisms while bacteriostatics only inhibit their growth. Ordinary bacteriostatic drugs can act as bactericidal in higher concentration. Some act upon specific micro-organisms, whereas others may act on several kinds and known as *'broad spectrum'* antibiotics.

Antibiotics are not only useful in an established condition of infection but are are also effective as prophylactic agents in a variety of situations. Before selecting an antibiotic, the presence of infection must be definitely established. The ideal method of selection is to carry out a bacterial culture sensitivity test in the laboratory before starting the treatment. Self-administration of antibiotics can be very detrimental to health.

The failure of response to antibiotic is frequent due to either to the development of bacterial resistance or to inadequate therapy. The mechanism of the development of drug resistance is quite complex. If the patient postpones the treatment until the infection becomes severe, and stops the drugs as soon as symptoms are relieved without completing a full course due to unavailability of the drug, the bacterial resistance is developed. In some cases, a patient takes either less than the dose prescribed or decreases the frequency of intake advised by the physician,

than this inadequate dose leads to the development of bacterial resistance.

A common misuse of these antibiotics is in employing them where they are ineffective, e.g., virus infections such as measles, chickenpox, and mumps, and the vast majority of infections of the upper respiratory tract which are not cured by *antibiotics*. Another wrong application of these drugs is in fevers of unknown origin. These fevers are usually due to viral or upper respiratory tract infection and these conditions do not generally respond to *antibiotics*. When a disease is associated with an appreciable quantity of pus, necrotic or dead tissues and foreign bodies, then *antibiotics* should not be prescribed alone.

These chemical substances are capable, in small concentrations, to inhibit the life processes or even destroy the other micro-organisms. The action of an antibiotic is very specific. Many of the antibiotics are obtained from fungi but some of them, e.g. bacitracin, colistin, polymyxin B and tyrothricin, are obtained from bacteria. Some antibiotics, e.g. chloramphenicol, are now prepared by chemical means. Penicillins, ampicillin, carbenicillin, chloramphenicol, cephalosporins, polypeptides, streptomycins, tetracyclines, etc. are the important antibiotic drugs.

All antibiotics exhibit two important adverse effects — allergic reactions and superinfections due to other micro-organisms. Allergic reactions to *antibiotics* are usually mild, in the form of skin rashes, fever and joint pain. Superinfections occur because *antibiotics* kill one group of microorganisms, while others keep growing uninhibited. This uninhibited growth of unaffected micro-organisms may occasionally lead to serious consequences and are most difficult to treat.

Chloramphenicol may depress the bone-marrow and neomycin may damage the kidneys.

PENICILLINS

Penicillin was the first antibiotic to be used therapeutically. Until 1944, it was thought that the active principle in penicillin was a single substance. Now it has been known that it is a mixture of penicillins known as F,G,X, and K, from the mould *Penicillium notatum*. These compounds differ chemically in the acid moiety of the amide side chain. Variations in this moiety create differences in antibiotic effect and in chemical-physical

properties. Better yields were achieved using *P. chrysogenum*. Benzylpenicillin (penicillin G) was selectively produced by adding the precursor phenylacetic acid to the fermentation medium.

More than 30 penicillins have been isolated from fermentation mixtures. Some of these occur naturally; others have been biosynthesized by altering the culture media. The term penicillin is now used generally for the entire group of natural and semisynthetic penicillins. They all have the same ring structure and are monobasic acids which readily form salts and esters. In 6-aminopenicillanic acid, the penicillin nucleus, consists of a fused thiazolidine ring and a beta-lactam ring with an amino group at the 6-position.

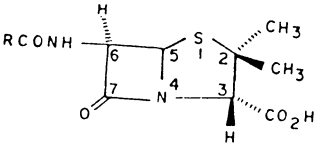
The earlier natural penicillins were produced by adding different side-chain precursors to fermentations of the *Penicillium* mould. For example, benzylpenicillin is obtained with a phenylacetamido side-chain at the 6-position, and phenoxymethylpenicillin (penicillin V) is formed with a phenoxyacetamido side chain. When no side-chain precursor is added to the fermentation medium 6-aminopenicillanic acid itself is obtained. Commercial production of penicillins today depends chiefly on various strains of *P. notatum* and *P. chrysogenum*.

The early commercial penicillin was a yellow to brown amorphous powder. Its stability was maintained in a refrigerator. Now white crystalline material is produced by improved procedures. Its salts well remain stable for years without refrigeration in dry conditions.

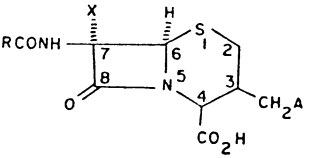
Two primal biosynthetic penicillins, benzylpenicillin and phenoxymethylpenicillin, are considered to be drugs of choice for treating infections caused by gram-positive bacteria. Many semisynthetic penicillins and cephalosporins with broader antibacterial activities and improved pharmacokinetic properties have been added to the group of antibiotics. Additional naturally occurring β-lactam containing structures include the cephamycins, the nocardicins, clavulanic acid and thienamycin. Of these, the cephamycins have also yielded a semisynthetic derivative that has been shown to be effective in controlling bacterial infections in man.

All the naturally occurring forms of these antibiotics have a 4-membered lactam ring. With the exception of the nocardicins the β-lactam ring is fused through the nitrogen and the adjacent tetrahedral carbon atoms to a second heterocyclic ring-a five-membered thiazolidine, pyrroline, or oxazolidine ring for the

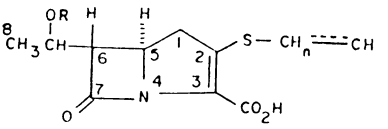
penicillins, thienamycin, clavulanic acid, respectively, or a six-membered dihydrothiazine ring for the cephalosphorins and cephamycins. A structural feature common to all is the carboxyl group on a carbon atom attached to the lactam nitrogen. In addition to this, another feature of penicillins, cephalosporins, cephamycins, and nocardicins is the acylated amino group on the carbon atom opposite the nitrogen of the β-lactam ring. The cephalosporins and the cephamycins have the same basic structure except that the cephamycins have a methoxy function instead of hydrogen on the amide bearing carbon atom (C-7). The stereochemistry around the β-lactam ring of the penicillins and the cephalosporins is the same in both series, i.e. the asymmetric centres at C-5 and C-6 in penicillins correspond to those at C-6 and C-7 in cephalosporins. The amide-bearing carbon atoms has the L- configurations.



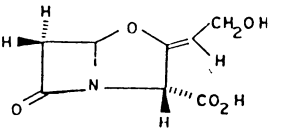
Penicillins



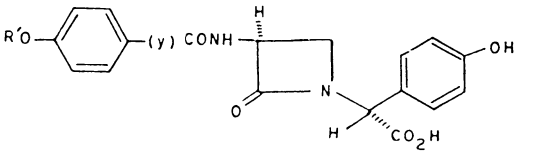
Cephalosporins (X = H)
Cephamycins (X = OCH_3)



Thienamycins



Clavulanic acid



Nocardicins A-G.

Thus penicillin nucleus contains three asymmetric carbon atoms in a fixed spatial arrangement. Any disruption of this arrangement by rupturing either the β-lactam ring or the thiazolidine ring results in a complete loss of antimicrobial activity. Unfortunately the four-membered β-lactam ring has considerable biologic and chemical lability which has created a

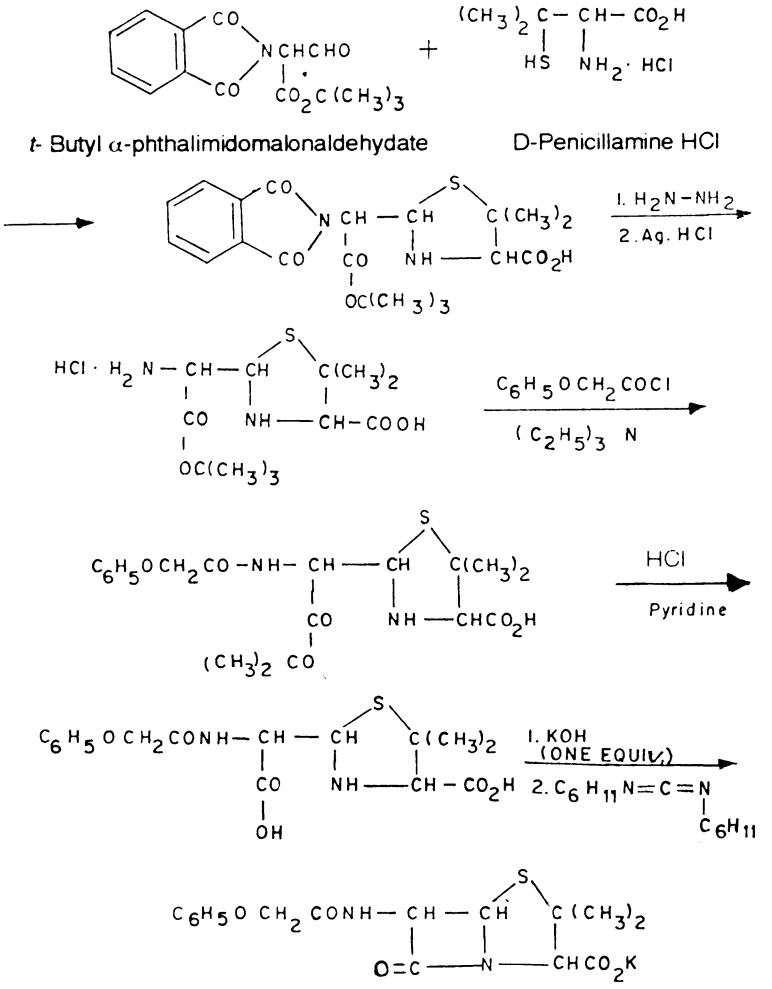
number of problems in the therapeutic utilization of these antibiotics. Biologically, microorganisms resistant to the action of penicillin G produce a β-lactamase (penicillase) which hydrolyzes the β-lactam ring to form inactive penicilloic acid. Chemically, penicillin G is rapidly inactivated when the pH is more acidic than 5 or more alkaline than 8. In acidic conditions penicillin G is converted to penillic acid and to penicilloic acid in alkali. Ideally, aqueous solutions of penicillin G salts should be buffered at pH 6.8 for maximum stability. Penicillins are also inactivated by metal ions such as zinc and copper and by oxidizing agents. The need for penicillin antibiotics with inherent stability in gastric fluids and with resistance to penicillinase led the search and development of other penicillins. Ampicillin, penicillin V, and phenethicillin are characterized by a significant degree of acid stability. Cloxacillin, dicloxacillin, nafcillin, and oxacillin are both acid stable and penicillinase resistant. The introduction of an electron attracting group into the side chain in close proximity to the amide linkage increases the stability of penicillins in gastric acid. Penicillins resistant to the action of penicillinase possess side chains with acyl groups that protect the β-lactam ring through steric hindrance.

In the beginning penicillin was not obtained in pure form. It exhibited varying activity and it was necessary to evaluate it by microbiologic assay. Biologic units are used to express quantitation for penicillin G and penicillin V. Sodium penicillin G has been accepted as the reference standard : 1 unit is the antibiotic activity of 0.6 μg of sodium penicillin G Reference standard. The weight unit relationship of the penicillins will vary with the nature of the acyl substituent and with the salt formed of the free acid. One miligram of sodium penicillin G is equivalent to 1,009 units. One milligram of potassium phenoxymethylpenicillin is equivalent to 1,530 units.

Phenoxymethylpenicillin has been synthesized from t-butyl α-phthalimidomalonaldehydate and D-penicillamine which gives a mixture of two stereoisomers of which one was isolated and used. Treatment with hydrazine followed by acid, removed the phthaloyl protecting group. The resulting amino group was acylated with phenoxyacetyl chloride, the tert butyl ester hydrolyzed with hydrogen chloride, and the carboxyl group so formed ring-closed to give the β-lactam.

The purified penicillins are odourless, white or cream-coloured crystalline powders and strongly dextrorotatory. The ocyl side chain and the cations used to prepare salts of the acid

effect the solubility and other physiochemical properties. Penicillins are generally deteriorated by hydrolysis which is affected by the pH of the solution.



t- Butyl α-phthalimidomalonaldehydate D-Penicillamine HCl

Synthesis of phenoxymethylpenicillin.

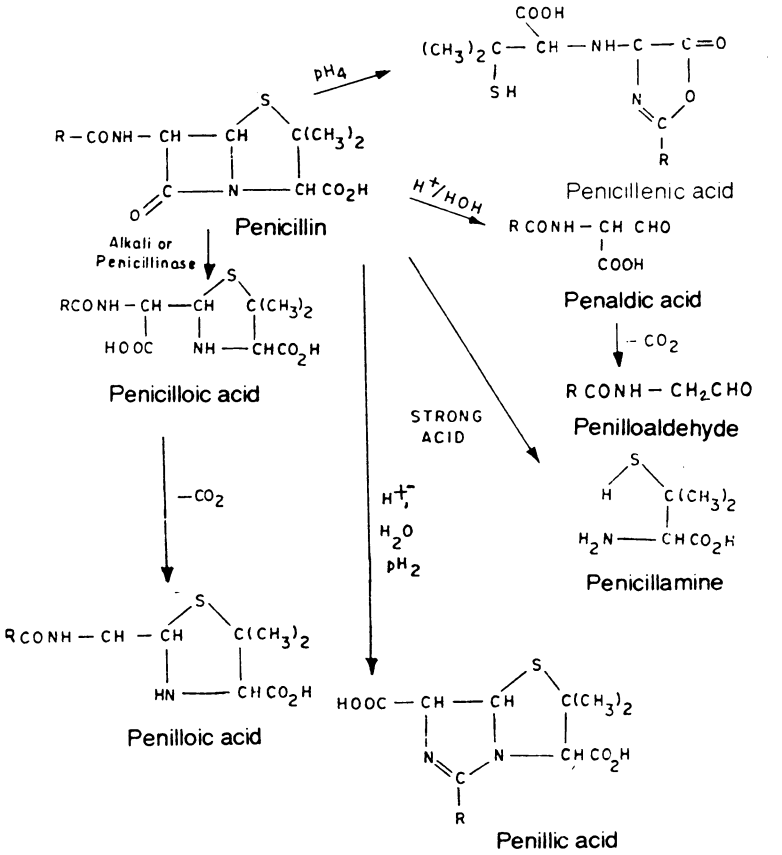
The penicillin molecule can be ruptured in a number of ways. For example, penicillamine is produced by the action of strong acids on acids on penicillins. It is a β,β-dimethyl homologue of cysteine and readily chelates with heavy metals. Penilloaldehydes are produced together with penicillamine under vigorous conditions of degradation. The penilloaldehydes are substituted amides which on further hydrolysis yield the parent

acid. At low pH and particularly in the presence of heavly metal ions (e.g. copper) a penillic acid is formed by a complex series of rearrangements. Under moderately acid conditions the carbonyl group of the side-chain reacts with the β-lactam to give a penicillanic acid. Alkalies rapidly decompose penicillins. Opening the β-lactam ring to give penicilloic acids by the nucleophilic attack of hydroxyl group, which are biologically inactive and the free acids readily lose CO_2 to give penilloic acids.

The formation of penicilloic acids is the basis of the alkalimetric assay for penicillins, in which they are treated with an excess of sodium hydroxide, allowed to stand until ring opening is complete, and the excess alkali determined by titration with standard acids. In the iodimetric assay the penicilloic acid is produced by treatment with alkali and then estimated by reaction with iodine. The β-lactam ring is also hydrolyzed by water in the presence of a bacterial enzyme, penicillinase. It is the production of this enzyme which renders certain strains of bacteria resistant to benzylpenicillin, e.g. some staphylococci. Electrophilic attack by hydrogen ion takes place on the amide side chain. The introduction of an electron-attracting group, particularly in the α-position, into the amide side chain, inhibits the electron displacement involving the carbonyl group and the β-lactam ring. Such penicillins are more acid stable. At controlled pH of aqueous solutions within a range of 6.0 to 6.8, and by refrigeration of the solutions, aqueous solutions of penicillins may be stored for several weeks. Some buffer systems, such as phosphates and citrates, show favourable effect on penicillin stability. These buffers may catalyze penicillin degradation if the pH is adjusted to obtain the requisite ions. Penicillins are inactivated by metal ions such as zinc and copper. Oxidizing agents inactivate penicillins, but reducing agents have little effect on them. Some of the penicillin salts are hygroscopic which should be stored in sealed containers. Temperature affects the rate of deterioration. But the dry salts are stable at room temperature and prolonged heating will inactivate the penicillins.

In the gastrointestinal tract, penicillins are converted by the gastric acid and by the enzymes penicillinases which include beta-lactamase and acylases. The strong gastric acid hydrolyses the amide chain and an opening of the lactam ring, with a result of loss of activity. Beta-lactamase produces an opening of the lactam ring and thus renders the penicillin inactive. Acylases cause the hydrolysis of the amide side chain. These enzymes can

cause the removal of the acyl group and thus produce 6-aminopenicillamic acid (6-APA), a compound having low antibacterial activity. Furthermore, the 6-APA is attacked very easily which leads to the opening of the lactam ring and a complete loss of activity.

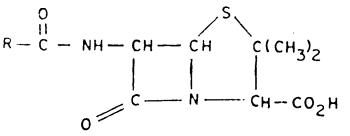


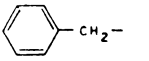
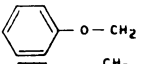
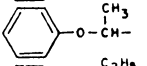
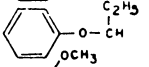
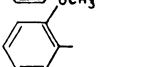
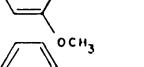
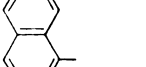
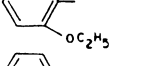
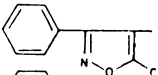
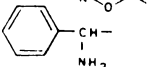
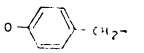
Electrophilic and nucleophilic reactions of penicillins.

There are now four principal classes of penicillins:

1. **Natural penicillins :** In these the acyl portion of the amide side chain consists of a benzyl group or an alkyl group, e.g. penicillin G.
2. **Acid - resistant penicillins :** In these a phenoxy group is attached to the alpha carbon of an alkyl group making up the acyl moiety of the amide side chain, e.g. phenoxymethylpenicillin and phenethicillin.
3. **Penicillinase-resistant penicillins :** In these compounds

Table 1. Structures of penicillins



Generic Name	Chemical Name	R Group
Penicillin G	Benzylpenicillin	
Penicillin V	Phenoxymethylpenicillin	
Phenethicillin	Phenoxyethylpenicillin	
Propicillin	Phenoxypropylpenicillin	
Methicillin	2,6-Dimethoxyphenyl-penicillin	
Nafcillin	2-Ethoxy-1-naphthyl-penicillin	
Oxacillin	5-Methyl-3-phenyl-4-isoazolylpenicillin	
Ampicillin	D-α-Aminobenzyl-penicillin	
Cloxacillin	5-Methyl-3-(2-chlorophenyl) 4-isoxazolylpenicillin	
Dicloxacillin	5-Methyl - 3-(2,6-dichloro-phenyl)-4-isoxazolypenicillin	
Dihydropenicillin F	n-Amylpenicillin	CH_3-$(CH_2)_3$ CH_2-
Penicillin O	Allylmercaptomethyl-penicillin	CH_2=CH-CH_2-S-CH
Penicillin K	n-Heptylpenicillin	CH_3=$(CH_2)_5$ - CH_2-
Penicillin X	*p*-Hydroxybenzyl-penicillin	
Penicillin F	2-Pentenylpenicillin	CH_3-CH_2 CH = CHCH_2-

a ring structure having aromatic properties is attached directly to the carbonyl carbon of the amide side chain. The aromatic ring is substituted at one or both of the ortho positions with groups that appear to act by sterically blocking the attack on the lactam ring by beta-lactamase, e.g. methicillin, nafcillin, oxacillin, cloxacillin and dicloxacillin.

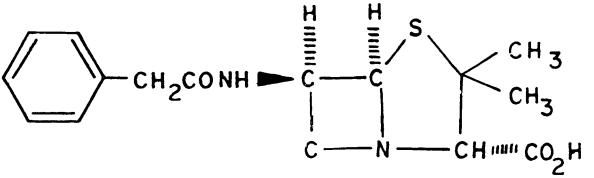
4. **Broad-spectrum penicillins** : Various changes of unspecified nature in the acyl portion of the amide side chain produce penicillins capable of inhibiting microorganisms resistant to penicillin G.

Penicillins act on microorganisms by interfering with the development of the cell wall.

BENZYLPENICILLIN

Nomenclature : 3,3-Dimethyl -7-oxy-6 (phyenylocetyl) amino) -4-thia-1-azabicydo [3.2.0] heptane -2- carboxylic acid.

Brand Names : Crystalline penicillin G. Penicillin: Free penicillin G; Free penicillin II; Benzylpenicillinic acid, Free benzylpenicillin.

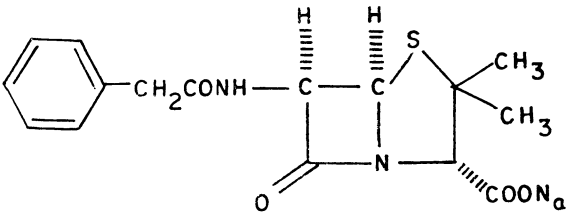


The name of benzylpenicillin is commonly used to describe either benzylpenicillin sodium or benzylpenicillin potassium as these are the forms in which benzylpenicillin is used. Benzyl penicillin is obtained by extraction at ice temperature of the acidified (pH2) aqueous solution of sodium benzylpenicillin with ether or chloroform. When kept dry the acid retains its antibiotic potency for limited periods, but it is rapidly inactivated by small amounts of water. The product formed on slow inactivation by moisture seems to be benzylpenicilloic acid.

Benzylpenicillin is an amorphous white powder; sparingly soluble in water; soluble in methanol, ethanol, ether, ethyl acetate, benzene, chloroform, and acetone and insoluble in petroleum ether; m.p. 80-87°. It forms methyl ester with diazomethane. It is stored at a temperature not exceeding 30° in airtight containers.

BENZYLPENICILLIN SODIUM

Brand Names : Sodium penicillin G; Penicilin G sodium, Sodium penicillin II; Sodium benzylpenicillate; Benzylpenicillinic acid sodium salt; Penicillin; American penicillin; Nalpen G; Novocillin; Penilaryn; Pen-A-Brasive; Veticillin: Crystalline penicillin G.



The sodium salt of 6-phenyl acetamidopenicillanic acid, an antimicrobial acid produced by growing certain strains of *Penicillium notatum* or related organisms or obtained by any other means. It is industrially produced by submerged fermantation using molds mutated from *Penicillium chrysogenum.*

The antibiotic is a white to slightly yellow, moderately hygroscopic, crystalline powder, odourless or with a faint characteristic odour; crystallized from methanol and ethyl acetate mixture. It is very soluble in water; practically insoluble in chloroform, ether, fixed oils, and liquid paraffin; also soluble in alcohol, glycerol, and other primary alcohols. One I.U. or U.S.P. penicillin unit is equivalent to 0.6 μg (0.0005988 mg) of benzylpenicillin sodium. One mg of benzylpenicillin sodium is equivalent to 1670 units. Pure crystalline benzylpenicillin sodium is stable. At pH 5.5 to 6.0 refrigerated solutions may be kept for a few days. Benzylpenicillin is also precipitated by many metal ions. Benzylpenicillin sodium is stored at a temperature not exceeding 30° in airtight containers.

Benzylpenicillin sodium or potassium is hydrolyzed in aqueous solutions by degradation of the β-lactam ring and hydrolysis is accelerated by increased temperature or alkaline conditions; inactivation also occurs under acid conditions. Degradation products include penillic, penicillenic, and penicilloic acids. By buffering solutions to pH 5.5 to 7.5 deterioration is retarded. Dilute solutions are more stable than concentrated ones. The sodium and potassium salts of penicillin are inactivated by the gastric juice, and were not effective when administered orally unless antacids such as calcium carbonate, aluminium

hydroxide and magnesium trisilicate or a strong buffer like sodium citrate were added.

Uses : Benzylpenicillin is used in the treatment of a variety of infections due to susceptible organisms, including abscesses, actinomycosis, anthrax, leptospirosis, Lyme disease, skin infections, including erysipelas, wound infections, gas gangrene, tetanus gonorrhoea; syphilis, yaws, pinta, rat-bite fever, diphtheria, pneumococcal pneumonia, scarlet fever, tonsillitis, Vincent's infection, rheumatic fever, some types of subacute bacterial endocarditis, meningitis, otitis media and osteomyelitis. The drug is also used prophylactically before dental and surgical procedures in patients at risk of developing endocarditis and to prevent a recurrence of rheumatic fever.

The most common adverse effects associated with benzylpenicillin are allergic reactions and of skin rashes.

BENZYLPENICILLIN POTASSIUM

Brand Names : Benzylpenicillin; Benzylpenicillinum kalicum; Crystalline penicillin G; Penicillin; Penicillin G Potassium.

The potassium salt of 6-phenylacetamidopenicillanic acid, an antimicrobial acid, is produced by growing certain strains of *Penicillium notatum or* related organisms or obtained by any other means. It is a white or almost white, moderately hygroscopic, crystalline powder, odourless or with a faint characteristic odour; very soluble in water; practically insoluble in chloroform, ether, fixed oils, and liquid paraffin. The B.P. specifies that a 10% solution in water has a pH of 5.5 to 7.5; the U.S.P. specifies that a 6% solution has a pH of 5.0 to 7.5.

Official

Benzylpenicillin, I.P.

Benzylpenicillin Injection, I.P.

Penicillin Eye Ointment, I.P.

Benzylpenicillin Potassium, B.P.

Benzylpenicillin Potassium Injection/Tablets, B.P.

Fortified Procaine Penicillin Injection, B.P.

Benzylpotassium Sodium, B.P.

Penicillin G Potassium Tablets/Tablets for Oral Solution, U.S.P.

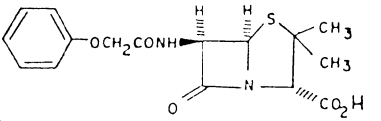
Penicillin G for Injection, U.S.P.

Benzylpenicillin Sodium Injection/Tablets, B.P.
Fortified Procaine Penicillin Injection, B.P.
Penicillin G Potassium Capsules for Injection, U.S.P.

PHENOXYMETHYLPENICILLIN

Nomenclature : 3, 3-Dimethy-7-oxo-6[(phenoxyacetyl) amino] -4-thia -1 azabicyclo [3.2.0] heptane-2-carboxylic acid; 6-Phenoxy-acetamidopenicillanic acid.

Brand Names : Penicillin V: Penicillin phenoxymethyl; Phenoxymethylpenicillin; Phenoxymethylpenicillinic acid; Acipen-V; Apopen;' Distaquaine V; Eskacillin V; Fenacilin; Fenospen; Meropenin; Oracillin; Oratren; Oracillin; Ospen; Pen-Oral; Pen-Vee; Penopenicillin; P-Mega-Tablinen, Stabicillin; V-Cil; V-Cillin; Vebecillin; Phenomycilline.



It is obtained by adding 2-phenoxyethanol to the *Penicillium notatum* on culture medium using yeast autolyzate as a source of nitrogen. It was reported by Behrens and Coworkers in 1948 as a biosynthetic product. It is a white crystalline powder; m.p. 120-128° (dec), odourless or with a slight peculiar odour. It is stable in air up to 37°; relatively stable to pH 1.8; very soluble in water, soluble in polar organic solvents, practically insoluble in vegetable oils and in liquid paraffin. Its activity is 1696 units mg. The biologically active form is the dextrorotatory D-form; the DL-form is half active. L-Penicillin V has little antibiotic activity. The drug is stored in airtight containers.

It is widely used because of its resistance to hydrolysis by gastric juice and its ability to produce uniform concentrations in blood. The free acid requires about 1,200 ml of water to dissolve 1 g. The salt of phenoxymethylpenicillin with N,N'-bis(dehydroabietyl) ethylenediamine (compocillin-V) provides a very long-acting form of this compound. For parenteral solutions, the potassium salt of phenoxymethylpenicillin is usually employed.

PHENOXYMETHYLPENICILLIN POTASSIUM

Brand Names : Antibiocin; Apsin VK; Arcacil; Arcasin; Beromycin; Beromycin 400; Betapen VK; Calciopen K, Cliacil; Compocillin

VK; Distakaps V-K; Distaquaine V-K; Dowpen V-K; DQV-K; Fenoxypen; Icipen; Isocillins; Ispenoral; Ledercillin V-K; Megacillin oral; Oracil-VK; Orapen; Ospeneff; Pedipen; Penagen; Pencompren; Pen-Vee K; Penvikal; Pfizerpen VK; PVK; SK-Penicillin VK; Sumapen VK; Suspen; Uticillin VK; V-Cil-K; V-Cillin K; Veetids; Vepen.

It is a white crystalline powder; odourless or with a slight characteristic odour. It is soluble in water (1 in 1.5), alcohol (1 in 150); practically insoluble in acetone, chloroform, ether, fixed oils, and liquid paraffin. It is stored in airtight containers.

Uses : Phenoxymethylpenicillin is used similarly to benzylpenicillin in the treatment of infections caused by susceptible gram-positive organisms. It is used only for the treatment of mild to moderate infections, and should not be used for chronic, severe or deep-seated infections such as subacute bacterial endocarditis, meningitis, or syphilis.

Phenoxymethylpenicillin is usually well-tolerated but may occasionally cause transient nausea and diarrhoea.

Official

Phenoxymethylpenicillin, B.P.

Phenoxymethylpenicillin Potassium, B.P.

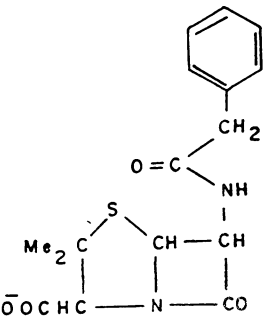
Phenoxymethylpenicillin Potassium Capsules/Tablets, B.P.

Penicillin V Potassium for Oral Solution, U.S.P.

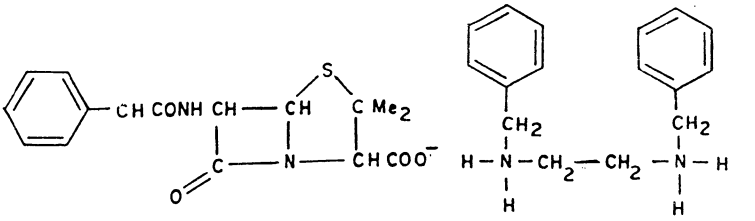
Penicillin V Potassium Tablets, U.S.P.

BENZATHINE PENICILLIN

Nomenclature : Penicillin G Benzathine; Penicillin G Compound with N,N'-dibenzylethylenediamine; N,N'-Dibenzylethylenediamine bis (benzylpenicillin); Dibenzylethylenediamine dipenicillin G; Penicillin G Salt of N,N'-dibenzylethylenediamine.



Brand Names : Benzethacil; Benzathine penicillin G; Diamine penicillin; Beacillin; Megacillin suspension; Bicillin; Cillenta; Permapen; Duropenin; Dibencillin; DBED Penicillin; Penidural; Tardocillin; Dibencil; Lentopenil; Vicin-Neolin; Pen-Di-Ben; Penidure; Moldamin; Extencilline; Longacilina; Longicil; Penadur; Penditan; Cepacilina.



It is the salt of a diamine, two moles of penicillin are available from each molecule of the salt. It is prepared by adding an aqueous solution of one mole N,N'-dibenzylethylenediamine diacetate to an aqueous solution of 2 moles sodium penicillin G.

Benzathine penicillin G is a white odourless, tasteless, crystalline powder, m.p 123-124°; very insoluble in water (1 g in 5000-6000 ml). This solubility property gives the compound great stability and prolonged duration of effect. It is soluble in alcohol (1 in 65); practically insoluble in chloroform and ether. At the pH of gastric juice it is quite stable, and food intake does not interfere with its absorption. It is stored at a temperature not exceeding 30° in airtight containers and protected from light and moisture.

Uses : Benzathine penicillin has the same antimicrobial action as benzylpenicillin, but because of the relatively low blood concentrations of benzylpenicillin produced, its use should be restricted to micro-organisms that are highly susceptible to benzylpenicillin. It is used for the treatment of syphilis and other treponemal infections, such as yaws, pinta, and endemic syphilis. It may be used to cure streptococcal infections, particularly of the upper respiratory tract. It should not be given to patients suffering from gonorrhoea.

Its adverse effects are the same as mentioned benzylpenicillin.

Official

Sterile Penicillin G Benzathine, U.S.P.

Benzathine Penicillin, B.P., I.P.

Benzathine Penicillin Tablets, I.P.

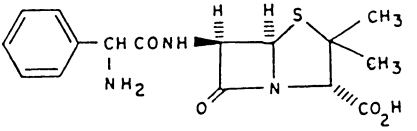
Penicillin G Benzathine Oral Suspension, U.S.P.

AMPICILLIN

Nomenclature : 6-[(Aminophenylacetyl) amino)] -3-3-dimethyl-7-oxo-4-thia-1-azabicyclo [(3.2.0)] heptane -2-carboxylic acid]

6-[D(-)-α-Aminophenylacetamido] penicillanic acid; D(-)-α-Amino-benzylpenicillin.

Brand Names : Ampicillin A; BRL 1341; P 50; Ay 6108; Adobacillin; Alpen; Amfipen; Ampi-Bol; Bonapicillin; Grampenil; Guicitrina; Copharcilin; Nuvapen; Synpenin; Viccillin; Ultrabion; Ampipenin; Amplisom; Ampimed; Ampy-Penyl; Totalciclina; Amipenix S; Amblosin; Ampicin; Amplital; Austrapeen; Binotal; Britacil; Doktacillin; Marisilan; Pen-Bristol; Penbritin; Penbrock; Penicline; Pentrex; Pentrexyl; Ponecil; Polycillin; Q1 Damp; Tokiocillin; Totacillin; Totapen.



Ampicillin is a white or slightly buff-coloured odourless, crystalline powder. Its monohydrate, known as Redicilin, m.p. 202° (decomp), is sparingly soluble in water; practically insoluble in alcohol, acetone, chloroform, ether, and fixed oils. It dissolves in dilute solutions of acids and alkali hydroxides. This antibiotic is active against the same gram-positive organisms that are susceptible to other penicillins, and it is more active against some gram-negative bacteria and enterococcal infections. The α-amino group plays a significant role in the broader activity.

Ampicillin is not resistant to penicillinase, and it produces the allergic reactions and other unwanted effects that are found in penicillin sensitive patients.

Anhydrous form (Brand Names : Ampicillin B; Omnipen; Orbicilina) occurs in crystalline form, m.p. 199-202° (dec). compared to hydrated form, anhydrous compound is more stable on storage, less soluble in water, dimethyl sulphoxide, and has a different crystal structure. It can be converted to ampicillin A by hydration. Ampicillin is stored at a temperature not exceeding 30° in airtight containers.

AMPICILLIN SODIUM

Brand Names : Sodium ampicillin; Alpen-N-Amcill-S; Cilleral, Domicillin; Omnipen-N; Pen A/N; Penbritin-S; Penialmen; Polycillin-N; Principen/N; Ampicillinnatrium; Ampicillinum Natricum; The sodium salt of ampicillin.

It occurs as a white to off-white odourless, crystalline or amorphous, hygroscopic powder; decomposes at about 205°. It is soluble in water (1 in 2) and acetone (1 in 50); slightly soluble

in chloroform; practically insoluble in ether, liquid paraffin, and fixed oils. It is stored at a temperature not exceeding 25° in well-closed containers.

Stability of Ampicillin sodium in aqueous solutions is dependent on many factors including concentration, pH, temperature and the nature of the vehicle. Stability decreases significantly in the presence of glucose, fructose, invert sugar, dextrans and lactate.

AMPICILLIN TRIHYDRATE

Brand Names : Amperil; Ampichel; Ampikel; Ampinova; Amcap; Amplin; Amcill; Acillin; Cymbi; Divercillin; Lifeampil; Morepen; Pensyn; Princillin; Pen-A; Princepen; Ro-Ampen; Trafarbiot; Vidopen; Ukopen.

Ampicillin trihydrate is a white, odourless, crystalline powder; slightly soluble in water; practically insoluble in alcohol, chloroform, ether, and fixed oils. It dissolves in dilute solutions of acids and of alkalies. It is stored at a temperature not exceeding 30° in airtight containers.

Uses : Ampicillin is used in the treatment of a variety of infections due to susceptible organisms, including respiratory tract infections, urinary tract infections, gonorrhoea, enteric infection, meningitis and septicaemica. The dosage of ampicillin will depend on the severity of the disease, the age of the patient and their renal functions; the dose should be reduced in renal failure. Ampicillin is usually administered by mouth as the trihydrate and by injection as the sodium salt.

Adverse effects of Ampicillin are identical to that of benzylpenicillin sodium. Allergic reactions occur in sensitised persons. Skin rashes are among the most common side-effects. Gastro-intestinal adverse effects particularly diarrhoea and also nausea and vomiting occur quite frequently.

Official

Ampicillin, B.P., I.P.

Ampicillin Capsules, B.P., I.P., U.S.P.

Ampicillin Sodium, B.P., I.P.

Ampicillin Injection, B.P., I.P. U.S.P.

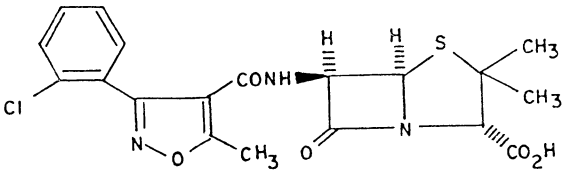
Sterile Ampicillin for Suspension, U.S.P.

Sterile Ampecillin Sodium, U.S.P.

Sterile Ampicillin, U.S.P.

CLOXACILLIN

Nomenclature : 6-[[[3-(2-Chlorophenyl)-5-methyl -4-isoxazolyl] carbonyl amino] 3,3-dimethyl -7oxo-4 thia -1-azabicyclo[3.2.0] heptane 2-carboxylic acid; [3-(0-Chlorophenyl)-5-methyl-4-isoxazolyl) penicillin; (5-Methyl-3-(o-Chlorophenyl)-4-isoxazolyl) penicillin; 6-(3-(o-Chlorophenyl)-5-methyl-4-isoxazoleçarboxamido) penicillanic acid.



Isoxazolyl group is substituted in this antibiotic. The chloro atom ortho to the position of attachment of the phenyl ring to the isoxazole ring enhances the activity of this compound over that of oxacillin.

CLOXACILLIN SODIUM

Brand Names : Sodium cloxacillin; BRL-1621; Bactopen; Cloxapen; Cloxypen; Ekvacillin; Gelstaph; Orbenin; Methocillin-S; Prostaphlin-A; Staphobristol-250°; Staphybiotic; Tegopen; Tepogen.

Cloxacillin sodium, m.p. 170° (decomp), occurs as a white, odourless, hygroscopic, micro-crystalline powder. It is soluble in water (1 in 2.5), alcohol (1 in 30), methanol, pyridine and ethylene glycol; slightly soluble in chloroform. A 10 per cent solution in water has a pH of 5 to 7. Aqueous solutions of cloxacillin sodium are reported to be stable for up to 24 hours at 25°C and for up to 72 hours at 5° . Cloxacillin sodium is stored at a temperature not exceeding 25° in airtight containers.

Benzathine Salt (Brand Names) : Boviclox; Dry-Clox; Noroclox DC; Orbenin dry cow; Triclox.

Uses : Cloxacillin is an isoxazolyl penicillin used to treat infections due to Staphylococci resistant to benzylpenicillin, including infections of the skin and soft tissues, bones and joints, respiratory tract and urinary tracts; otitis media, endocarditis; septicaemia, and meningitis. It is used for the prophylaxis of staphylococcal infections during major surgical procedures, particularly in cardiothoracic and orthopaedic surgery.

Its adverse effects are similar as for Benzylpenicillin sodium.

Official

Cloxacillin Sodium. B.P., I.P.

Cloxacillin Capsules Injection. B.P., I.P.

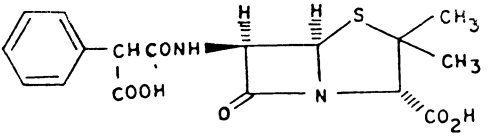
Cloxacillin Sodium Capsules. U.S.P.

Cloxacillin Sodium for Oral Solution. U.S.P.

CARBENICILLIN

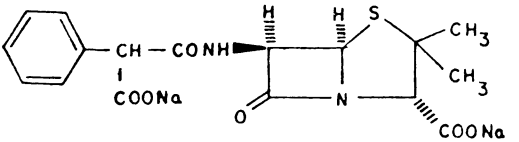
Nomenclature : 6-[(Carboxyphenylacetyl] amino) -3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.8] heptane-2 carboxylic acid;

α-Carboxybenzylpenicillin; 6-(α-carboxyphenylacetamido) penicillanic acid; α-Phenyl (carboxymethylpenicillin); N-(2-Carboxy-3, 3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] hept-6-yl) - 2 -phenylmalonamic acid.



CARBENICILLIN SODIUM

Brand Names : BRL-2064, Carbenicillin disodium; CP-15639-2; Anabactyl; Carbapen; Carbecin; Geopen; Hyoper; Microcillin; Pyocianil; Pyopen; Disodium α-carboxybenzyl penicillin.



Carbenicillin sodium occurs as a white hygroscopic powder. It is soluble in water (1 in 1.2) and alcohol (1 in 25); practically insoluble in chloroform and ether. A 10 per cent solution in water has a pH of 6 to 8. Aqueous solutions of carbenicillin sodium are reported to be stable for up to 24 hours at room temperature.

Carbenicillin is not stable in acids and is inactivated by penicillinases. Carbenicillin sodium is stored at a temperature not exceeding 5° in well-closed containers.

Uses : Carbenicillin is used in the treatment of infections due to *Pseudomonas aeruginosa*, infections due to non-penicillinase producing strains of *Proteus* species, systemic infections, respiratory -tract infections and urinary tract infections.

Adverse effects of carbenicillin are the same as reported for benzylpenicillin sodium. Purpura and haemorrhage have been reported. Pain at the injection site and phlebitis may occur. Electrolytic disturbances, particularly hypokalaemia or hypernatraemia, may follow the administration of large doses of carbenicillin sodium. The most serious possibility being hypersensitivity reactions.

Official

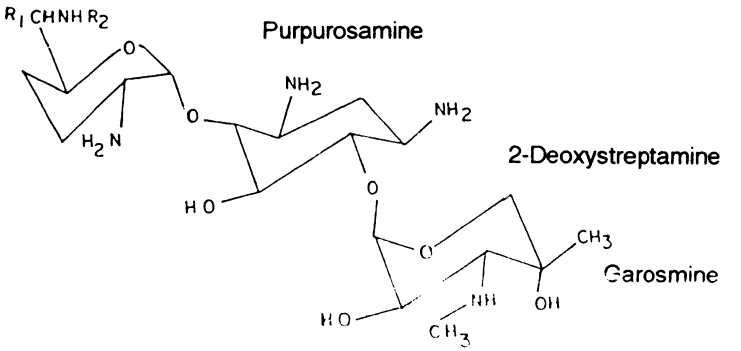
Sterile Carbenicillin Disodium, U.S.P.

Carbenicillin Sodium, B.P.

Carbenicillin Injection, B.P.

GENTAMYCIN

Brand Name : Gentamicin.



Gentamicin C_1 : $R_1=R_2=CH_3$

Gentamicin C_2 : $R_1=CH_3$; $R_2=H$

Gentamicin C_{1a} : $R_1=R_2=H$

Gentamicin is an aminoglycoside antibiotic complex produced commercially by fermentation of *Micromonospor purpurea* or *M. echinospora* and variants thereof (Weinstein and co-workers, 1963). It consists of three closely related components, gentamicins C_1, C_2, C_{1a}, and also gentamicin A which differs from the other members of the complex but is similar to

kanamycin C. Structures of these antibiotics contain 2-desoxystreptamine linked to two saccharide units, these being garosamine and a purpurosamine in the C series gentamicins. Studies on structures were carried out by Cooper *et al.* (1971) and Maehr and Schaffner (1967). Some Commercial samples may contain significant quantities of the major components gentamicin C_{2A} and gentamicin C_{2B}. It contains when dried not less than 590 units of gentamicin per mg. It has a broad spectrum of activity particularly against gram-negative organisms.

Gentamicin occurs as white powder, mp. 102-108°, freely soluble in water, soluble in pyridine, dimethylsulphoxide, in acidic media with salt formation; moderately soluble in methanol, ethanol and acetone; practically insoluble in benzene, and halogenated hydrocarbons.

The melting points of individual gentamicins are as: gentamicin C_1, m.p. 94-100°, gentamicin C_2 m.p. 107-124°. Detailed chromatographic studies indicate that gentamicin contains no less than sixteen compounds. Gentamicin forms salts with minerals and strong organic acids, the sulphate being generally used clinically.

GENTAMICIN SULPHATE

Brand Names : Alcomicin; Bristagen; Cidomycin; Garamycin; Garasol; Genoptic; Gentacin; Gentalline; Gentalyn; Gentibioptal; Genticin; Gentogram; Refobacin; Sulmycin; U-gencin.

Gentamicin sulphate occurs as a white to buff coloured, hygroscopic powder, m.p. 218-137°. It is freely soluble in water; soluble in ethylene glycol and formamide; practically insoluble in alcohol, benzene, chloroform, and ether. It is stored in airtight containers.

Uses : Gentamicin sulphate is used to treat septicaemia, including neonatal sepsis and other severe systemic infections due to gram-negative organisms. It is also used in the treatment and prophylaxis of endocarditis due to streptococci, enterococci and sometimes staphylococci. It has been used for surgical infections prophylaxis, a variety of skin infections for which a topical cream or ointment may be used and in the treatment of burns complicated by pseudomonemia. Gentamicin sulphate injection may be used for serious systemic and genitourinary tract infections caused by gram-negative bacteria, particularly pseudomonas and proteus species. A bone cement impregnated with gentamicin is used in orthopaedic surgery.

All aminoglycoside antibiotics can produce irreversible ototoxicity following systemic treatment. Vestibular damage is more common with gentamicin than hearing loss which is greatest in the high-tone range. Reversible nephrotoxicity may occur and acute renal failure has been reported. Aminoglycosides possess a neuromuscular blocking action and respiratory depression and muscular paralysis have been reported. Hypersensitivity reactions have occurred. For prolonged use of aminoglycosides, hypomagnesaemia, hypocalcaemia, and hypokalaemia have also occurred.

Official

Gentamycin Sulphate, B.P., I.P.

Gentamycin Ointment/Eye drops, B.P.

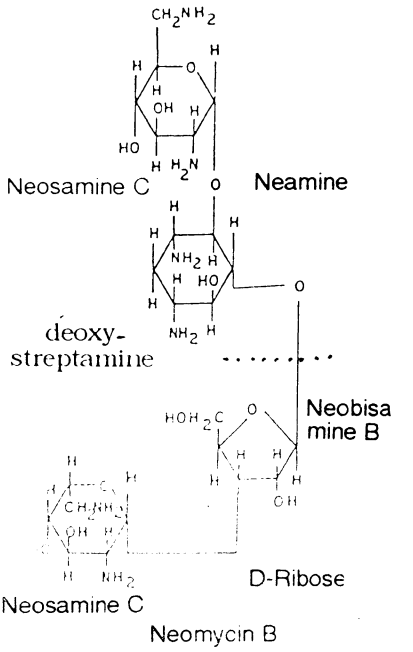
Gentamycin Injecion, B.P., I.P.

Gentamicin Sulfate Injection/Cream/Ointment, U.S.P.

NEOMYCIN

Brand Names : Mycifradin; Myacyne; Fradiomycin; Neomin; Neolate; Neomas; Nivemycin; Pimavecort; Vonamycin Powder V.

Neomycin is a mixture of three substances A, B and C isolated from *Steptomyces fradiae* by counter current distribution. The neomycin A (neamine) is a basic disaccharide which is a common degradation product of neomycins B and C. These neomycins B and C consist of four carbohydrate units and differ only in the configuration of the amino-methyl group in the neosamine ring linked to the ribose unit. Framycetin consists mainly of neomycin B with not more than 3% of neomycin C. Neamine may be obtained by methanolysis of neomycins B and C during which the glycosidic link between the deoxystreptamine and D-ribose is broken. Therefore, neamine is a combination of



deoxystreptamine and neosamine C linked glycosidically at the 4-position of deoxystreptamine. Neomycin B differs from neomycin C by the nature of the sugar attached terminally to D-ribose. The sugar neosamine B differs from neosamine C in its stereochemistry. It has been suggested recently that both the diamino sugars in neomycin C have the L-idose configuration and that the glycosidic link is beta in one attached to D-ribose.

Neomycin complex is an amorphous base soluble in water, methanol and acidified alcohol; practically insoluble in common organic solvents.

Neomycin B (Brand Names : Framycetin; Enterfram; Gramygen; Soframycin; Actilin; Antibiotique EF 185) yields on hydrolysis neamine and neobisamine B.

Neomycin C yields on hydrolysis neamine and neobiosamine.

Neomycin B sulphate (Brand Names : Bykomycin, Fraquinol; Myacine; Neosulf, Neomix; Neobrettin; Tuttomycin) is an amorphous white, tasteless powder. It is soluble in water (6.3 in 1); slightly soluble in alcohols; practically insoluble in acetone, ether and chloroform. Aqueous solutions are fairly stable at pH 2 to 9. Highly purified preparations are very stable to alkali and unstable to acids.

NEOMYCIN SULPHATE

Brand Names : Fradiomycin sulphate; Neomycini sulfas; Mycifradin; Neobiotic.

Neomycin sulphate is a mixture of the sulphates of the antimicrobial substances produced by the growth of certain selected strains of *Streptomyces fradiae*. It occurs as a white or yellowish-white, odourless, hygroscopic, photosensitive, and crystalline powder. It is very soluble in water; slightly soluble in alcohol and insoluble in acetone, chloroform, and ether. It is stored at a temperature not exceeding 30° in airtight containers and protected from light.

Uses : Neomycin sulphate is used to treat infections of the skin and eye due to susceptible staphylococci and other organisms, as well as in ear-drops. A cream containing neomycin sulphate and chlorhexidine hydrochloride has been used for application to the nostrils in the treatment of staphylococcal nasal carriers. It is most useful antibiotic in the treatment of gastrointestinal infections dermatologic infections and acute bacterial peritonitis. It is also employed in abdominal surgery to reduce complication

due to infections from bacterial flora of the bowel. It is very slightly absorbed from the digestive tract, so its oral use does not produce any systemic effect.

Adverse effects of neomycin are the same as in case of gentamicin sulphate. It may cause irreversible deafness when given by injection or by mouth. In large doses it may cause nausea, vomiting, and diarrhoea. Prolonged oral therapy may cause a malabsorption syndrome with steatorrhoea and diarrhoea. Neomycin has a neuromuscular blocking action.

Official

Neomycin Sulphate, B.P., I.P.

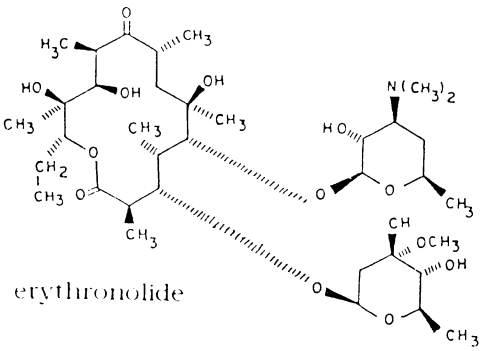
Neomycin Tablets, B.P.

Neomycin and Polymyxin B Sulfates and Bacitracin Zinc Topical Aerosol, U.S.P.

ERYTHROMYCIN

Brand Names : Erythromycin A; Abomacetin; EMU; Ery Derm; Ery-Tab; Erythrocin; Erythromast 36; Erythromid; ERYC; Erycin; Erycinum; Erymysin; Ilotycin; Reticin; Staticin; Torlamicina; E-Mycin; Eritromicina; Erythromycinum.

Erythromycin, a macrolide antibiotic isolated from a culture of *Streptomyces erythreus* by McGuire in 1952, is a mono-acidic base. On hydrolysis, it forms a basic sugar, desosamine, and a neutral sugar, cladinose. There are three erythromycins produced during fermentation, designated as A, B, and C; A is a major and most important component.



Erythromycin A

The amino sugar attached through a glycosidic link to the number 5 carbon atom is desosamine. The tertiary amino nature of desosamine confers a basic character to erythromycin which is involved in the formation of acid salts. The other carbohydrate structure linked as a glycoside to carbon atom 3 is called cladinose. Erythromycins A and B contain the same sugar moieties, desosamine, and cladinose. They differ in position 12 of the aglycone, erythronolide, A having an hydroxyl substituent. Component C contains desosamine and the same aglycone present in A but differs by the presence of mycarose, instead of cladinose.

Erythromycin is a bitter compound, white or slightly yellow, odourless, slightly hygroscopic crystals or powder; crystallized from water; m.p. 135-140°. After melting at 135-140°, it resolidifies and melts again at 190-193°. It readily forms salts with acids. It is slightly soluble in water; less soluble at higher temperatures; soluble in alcohol, methyl alcohol, chloroform and 2 M hydrochloric acid. Saturated aqueous solutions develop an alkaline pH in the range of 8.0 to 10.5. It is extremely unstable at a pH of 4 or lower. The optimum pH for stability of erythromycin is near neutrality. It is stored in airtight containers and protected from light.

The free base erythromycin may be used in oral dosage. In order to reduce its bitter taste and to provide more acceptable pharmaceutical forms for its administration, two types of derivatives of erythromycin are prepared. One type of derivatives are salts formed by acids such as the glucoheptonate, lactobionate and stearate. The other type of derivatives are produced by esterification of the hydroxyl group of the desosamine moiety, such as the ethyl carbonate, ethyl succinate and propionate (estolate). The carbonate ester is hydrolyzed in the gastrointestinal tract to the active base before absorption. However, the ethyl succinate and propionate esters are biologically active themselves and need not be hydrolyzed to show anti-infective action. In gastrointestinal tract, these compounds may be partially hydrolyzed and on absorption provide a more rapid onset and higher and more prolonged therapeutic concentration in the blood.

The glucoheptonate (gluceptate) and lactobionate salts are water-soluble which may be administered parenterally. The stearate salt is water-insoluble and tasteless and is used in tablets and suspensions. The ethyl carbonate ester is also water-insoluble and employed for paediatric suspension.

Uses : Erythromycin is used in the treatment of infections due to susceptible organisms. It is often used as an alternative to penicillin in infections due to gram-positive cocci. It may be given as an adjunct to antitoxin in the treatment of diphtheria. A 0.5% ophthalmic ointment it is used to cure infected eyes. A 2% solution is applied in the treatment of acne of vulgaris. Erythromycin thiocyanate is used in veterinary medicine.

Gastro-intestinal disturbances are fairly common with erythromycin, especially with large doses, but serious side-effects are rare. Reversible deafness has occurred after high doses of erythromycin. Hepatotoxicity has been reported after administration of erythromycin, most commonly used as the estolate. Irritation or sensitivity reactions may occur after the topical administration of the drug.

Official

Erythromycin, B.P., I.P.

Erythromycin Tablets, B.P., I.P.

Erythromycin Estolate, B.P., I.P.

Erythromycin Estolate Capsules, B.P., U.S.P.

Erythromycin Estolate Oral Suspension, U.S.P.

Erythromycin Estolate Tablets, I.P., U.S.P.

Erythromycin Stearate, B.P., I.P.

Erythromycin Stearate Tablets, B.P., I.P., U.S.P.

Erythromycin Lactobionate for Injection, U.S.P.

TETRACYCLINES

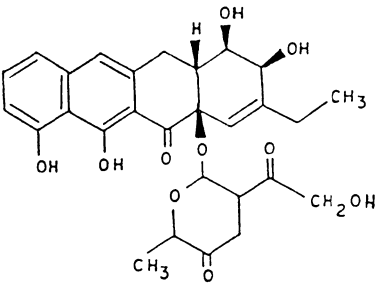
The tetracyclines are a group of actinomycete antibiotics that have a broad spectrum and considerable therapeutic utility. Seven such compounds—tetracycline, oxytetracycline, chlortetracycline, demeclocycline, methacycline, doxycycline and rolitetracycline are used as medicine.

The tetracyclines are obtained by fermentation procedures from Streptomyces species or by chemical transformations of the natural products. The important members of the group are derivatives of an octahydronaphthacene, a hydrocarbon that is consisted of a system of four fused rings (named tetracycline). The first of these compounds, chlortetracycline, was introduced in 1948. Two years later oxytetracycline was obtained.

The tetracyclines were found to be highly effective against rickettsiae, a number of gram-positive and gram-negative bacteria,

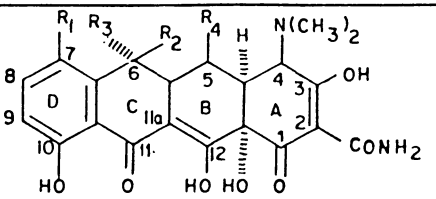
some of the larger viruses, some intestinal amoebae, and the agents responsible for lympho-granuloma, conjunctivities, and psittacosis. Therefore, they are known as "broad spectrum" antibiotics.

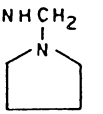
The tetracyclines are closely congeneric derivatives of the tetracyclic naphthelane carboxamide. *Streptomyces flavovirens* produces an antibiotic pillaromycin A that consists of an aglycone related to the tetracyclines with an unusual sugar.



Pillaromycin A

Table : Structures of Tetracyclines



Names	R_1	R_2	R_3	R_4	Brand names
Tetracycline	H	OH	CH_3	H	Achromycin
7-Chlortetracycline	Cl	OH	CH_3	H	Aureomycin
5-Oxytetracycline	H	OH	CH_3	HO	Terramycin
6-Desmethyl-6-deoxy-5-hydroxy-6-methylene tetracycline	H		$=CH_2$	HO	Methacycline
6-Deoxy-5-oxytetracycline	H	H	CH_3	HO	Doxycycline
Rolitetracycline	H	OH	CH_3	H	 at C-2
Minocycline	$N(CH_3)$	H	H	H	
Demeclocycline	Cl	OH	H	H	

All tetracyclines are almost stable and are absorbed adequately in gastro-intestinal tract. These amphoteric compounds are most stable in acid and least stable in alkali. The tetracycline antibiotics are usually used as the hydrochloride salts. Chlortetracycline is the least stable of these antibiotics. They form salts with acids and with bases. In neutral solutions these compounds exist mainly as zwitter ions.

Erratic and unsatisfactory absorption of the tetracyclines takes place when calcium ions and other heavy ions are present in diet or when preparations as aluminium hydroxide-containing antacids are used. Phosphate combinations may be used in tetracycline formulations to reduce the impact of heavy metal ions on absorption. Stable chelate complexes are formed by the tetracyclines with many metals such as calcium, iron and magnesium. Demeclocycline, doxycycline, and methacycline are absorbed more readily than the other tetracycline antibiotics. Their absorption is influenced to a lesser degree by food and milk. Chelation does not play a basic role in the mode of action of the tetracyclines, but it may facilitate transport of the compounds to their sites of action. They act principally by interference with protein synthesis.

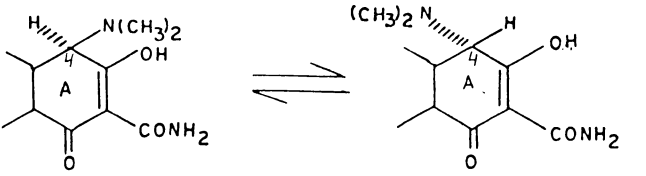
Tetracyclines are often considered the antibiotics of choice for treatment of brucellosis, cholera, relapsing fever, and infections caused by *Chlamydia*, *Mycoplasma*, *Yersinia (Pasteurella)*, rickettsia, and a large number of other infections.

The usual serum half-lives of various tetracyclines are 5-6 hours for chlortetracycline, 8-9 hours for tetracycline, 12-14 hours for demeclocycline and methacycline and 17-19 hours for doxycycline and minocycline. These compounds are eliminated by biliary excretion, glomerular filtration, and metabolism. There is extensive enterohepatic recycling of the tetracycline antibiotics. About 20-50% of the tetracyclines are eliminated by urinal. The rate of renal clearance is slowest for doxycycline and minocycline. Metabolic degradation of these antibiotics is relatively insignificant. Resistance to the tetracyclines developed slowly and becomes a serious problem with pneumococci, straphylococci, streptococci, and some gram-negative pathogens.

The amphoteric antibiotics will crystallize out of aqueous solutions of their salts. The hydrochloride salts are used most commonly for oral administration in the form of capsules due to their bitter taste. Water-soluble salts may be obtained from bases such as sodium or potassium hydroxides. These salts are not stable in aqueous solutions. Water-insoluble salts are

formed with divalent and polyvalent metals. Such calcium salts are used to prepare tasteless suspensions for liquid oral dosage forms.

An interesting property of the tetracyclines is to form epimers, called epi-tetracyclines at carbon atom 4 in solutions of intermediate pH range. Under the influence of the acidic conditions, an equillibrium is maintained within 24-hours containing about equal amounts of the isomers. The 4-epitetracyclines have been isolated and identified.



epi Natural

Srong acids and bases react with the tetracyclines having a hydroxy group of C-6, causing a loss in activity through modification of the C-ring. Strong acids produce dehydration creating unsaturation at C-6, C-5a, which induces a shift in the position of the double bond between carbons C-11a and C-12 to a position between carbon atoms C-11 and C-11a. In this way the more energetically favoured resonant system of the naphthalene group is formed. In th presence of bases, a reaction between the 6-hydroxyl group and the ketone group at C-11 takes place, the bond between C-11 and C-11a is cleaved and the lactone ring, found in the inactive isotetracyclines, is formed.

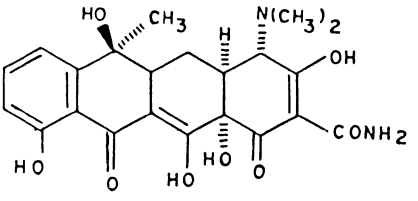
The relationships between chemical structure and the biological activity of tetracyclines have been studied. The substitution on the 5 and 7 carbon atoms and hydroxyl substitution on the 6 carbon atom are not essential for activity. Removal of the 4-dimethylamino group causes a loss of about 75 per cent of the antibiotic effect of the parent tetracyclines. The 4-epitetracyclines are less active than the dedimethyl-amino compounds, suggesting structural conformations in this area may be important in fitting the molecule on a possible enzyme site. A substantial loss of activity by epimerization at carbon atom 5a takes place. Dehydrogenation to form a double bond between carbon atoms 5a and 11a produces a marked decrease in activity. In the same way, dehydration by strong acids of the 6 hydroxyl group and a hydrogen on the 5a carbon atom produces inactive anhydrotetracycline that has an aromatic C

ring. Substitution of bulky groups for one of the hydrogens on the amide nitrogen does not cause any appreciable loss in activity.

TETRACYCLINE

Nomenclature : 4-(Dimethylamino)-1, 4, 4a, 5, 5a, 6, 11, 12a-octahydro-3, 6, 10, 12, 12a-pentahydroxy-6-methyl-1, 11-dioxo-2-naphthacenecarboxamide.

Brand Names : Deschlorobiomycin; Tsiklomitsin; Amtet; Abricycline; Achromycin; Agromicina; Ambramicina; Ambramycin; Bio-Tetra; Bristacycline, Bristaciclina; Cefracycline suspension; Centet; Criseociclina. Cyclomycin; Cyclopar; Democracin; Deltamycin Desamycin; Duratet; G-Mycin, Maytrex; M-Tetra; Hostacyclin; Omegamycin; Panmycin; Nor-Tet; Paltet; Partrex. Piracaps; Polycycline; Purocyclina; Retet; Robitet; Sanclomycine; Steclin; Sumycin; Tet; Teline; Tetra-Bid; Tetrabon; Tetracyn; Tetradecin; Tetraciclina; Tetracyclinum, Tetra-C; Tetra-Co; Tetracap; Tetrachel; Tetralan; Tetram; Tri-Tet; Phosphate Complex; Tetrex.



Tetracycline is the least expensive and most commonly used tetracycline antibiotic. It is a bright-yellow, odourless, crystalline salt, m.p. 170-175° (swells at 165°). It darkens in strong sunlight in moist atmosphere, but is stable in air, neutral and alkaline solutions and in acid solutions having a pH higher than 2. It is soluble in water (1 in 2500), alcohol (1 in 50), methyl alcohol; sparingly soluble in acetone; freely soluble in dilute acids and, with decomposition, in solutions of alkali hydroxides; practically insoluble in chloroform and ether. It is stored in airtight containers and protected from light.

TETRACYCLINE HYDROCHLORIDE

Brand Names : Achro; Achromycin V; Ala Tet; Ambracyn; Artomycin; Cefracycline tablets; Cyclopar; Diacycline; Dumocyclin; Mephacyclin; Partrex; Quadracycline; Quatrex; Remicyclin; Ricycline; Ro-cycline; Stilciclina; Subamycin; Supramycin; Sustamycin; Tefilin; Teline; Telotrex; Tetrabakat; Tetrabid; Tetrablet; Tetrachel; Tetracompren; Tetra-D; Tetrakap; Tetralution; Tetramavan, Tetramycin; Tetrasol; Tetra-wedel;

Topicycline; Totomycin; Triphamycin; Unicin; Unimycin; Vetquamycin-324.

Tetracycline hydrochloride is a yellow, odourless, hygroscopic, crystalline, amphoteric powder. It darkens in moist air when exposed to strong sunlight. It is soluble in water (1 in 10), alcohol (1 in 100), aqueous alkali hydroxides and carbonate solutions; insoluble in acetone, chloroform and ether. Aqueous solutions become turbid on standing due to hydrolysis and precipitation of tetracycline. The potency of tetracycline hydrochloride is reduced in solutions having a pH below 2. It is stored in airtight containers and protected from light.

An insoluble tetracycline phosphate complex (Brand Names : Panmycin Phosphate; Sumycin; Tetradecin Novum; Tetrex; Upcyclin) is made by mixing a solution of tetracycline with a solution of sodium metaphosphate. These agents enhance blood level concentrations over those obtained when tetracycline hydrochloride alone is administered orally.

Uses : The tetracycline has a wide spectrum of activity and is used in the treatment of a large number of infections such as rickettsial infections, including typhus, Rocky Mountain spotted fever, and Q fever; chlamydial infections, including psittacosis, lymphogranuloma, venereum, trachoma, and inclusion conjunctivities; and mycoplasmal infections, especially caused by *Mycoplasma pneumoniae*. Tetracyclines are used in the treatment of brucellosis, plague, tularaemia, chronic bronchitis, chancroid, granuloma inguinale, urinary-tract infections such as non-specific urethritis, malabsorption syndromes such as tropical sprue and Whipple's disease, cholera in conjunction with fluid, relapsing fever, leptospirosis, in early stages of Lyme disease, balantidiasis and chlamydial infections of the eye.

The side-effects of tetracycline include gastro-intestinal disorders, nausea, vomiting, diarrhoea, irritation of mucosa, oesophageal ulceration, hepatotoxicity, allergic oesophageal ulceration, hepatotoxicity, allergic reactions, etc.

Official

Tetracycline, I.P.

Tetracycline Oral Suspension, I.P.

Tetracycline Hydrochloride, B.P., I.P.

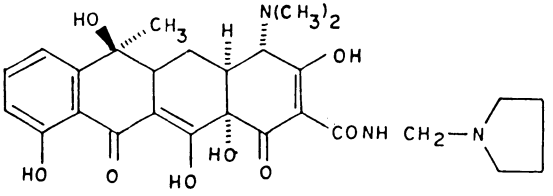
Tetracycline Tablets/Injection/Capsules/Eye Ointment, I.P.

Tetracycline Hydrochloride Capsules/Tablets, U.S.P.

ROLITETRACYCLINE

Nomenclature : 4-(Dimethylamino)-1, 4, 4a, 5, 5a, 6, 11, 12a - octahydro-3, 6, 10, 12, 12a-pentahydroxy-6-methyl-1, 11-dioxo-N-(1-pyrrolidinyl methyl)-2-naphthacene-carboxamide; N-(Pyrrolidinomethyl) tetracycline.

Brand Names : Bristacin; Reverin Superciclin; Syntetrex; Syntetrin; Synotodecin; Tetraverin; Transcycline; Velacicline; Velacycline.



Rolitetracycline is prepared by condensing tetracycline with pyrrolidine and formaldehyde in the presence of t-butyl alcohol. This derivative has been introduced for use by injection. It occurs as a light yellow crystalline powder or fine, pale needles, with a characteristic musty amine-like odour, m.p. 162-165° (dec.). It is more soluble tetracycline and its hydrochloride; soluble in water (01 in 1.1), alcohol (1 in 200), acetone, dilute acids and alkalies; very soluble in ether. It is stored in airtight containers and protected from light.

Uses : Rolitetracycline has antimicrobial activity and uses similar to those of tetracycline hydrochloride.

Shivering and more rarely rigor may be associated with the first few injections of rolitetracycline in infections due to organisms highly sensitive to tetracyclines.

Official

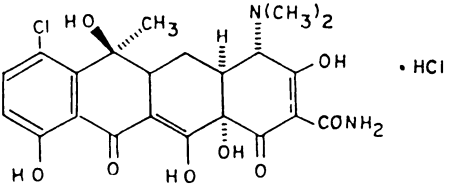
Rolitetracycline for Injection, U.S.P.

Sterile Rolitetracycline, U.S.P.

CHLORTETRACYCLINE HYDROCHLORIDE

Nomenclature : 7-Chloro-4-dimethylamino-1, 4, 4a, 5, 5a, 6, 11, 12a-octahydro-3, 6, 10, 12, 12a-pentahydroxy-6-methyl-1, 11-dioxo-2-naphthacenecarboxamide HCl; 7-Chlorotetracycline HCl.

Brand Names : Aureociclina; Isphamycin; Aureomycin hydrochloride; Acronize hydrochloride; Aureocina hydrochloride; Biomitsin hydrochloride, Biomycin hydrochloride; Chrysomykine hydrochloride.



Chlortetracycline is an antibiotic substance isolated from the substrate of *Streptomyces aureofaciens* by Duggar (1948). It occurs as bright yellow odourless rhomboid crystals, decompsoses above 210°. It is slightly soluble in water and in alcohol; soluble in solutions of alkali hydroxides and carbonates; practically insoluble in acetone, chloroform, dioxane, and ether.

Uses : Chlortetracycline hydrochloride is used similarly as described under tetracycline. Adverse effects are the same as for tetracycline hydrochloride.

Official

Chlortetracycline Hydrochloride. B.P., I.P.

Chlortetracycline Injection, I.P.

Chlortetracycline Capsules, B.P., I.P.

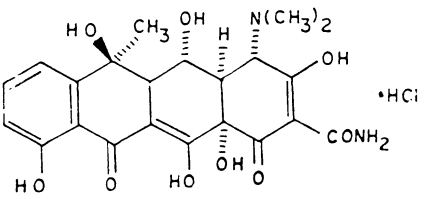
Chlortetracycline Hydrochloride Capsules/Ointment, U.S.P.

Sterile Chlortetracycline Hydrochloride, U.S.P.

OXYTETRACYCLINE HYDROCHLORIDE

Nomenclature : 4-(Dimethylamino)-1, 4, 4a, 5, 5a, 6, 11, 12a - octahydro-3, 5, 6, 10, 12, 12a-hexahydroxy-6-methyl-1, 11-dioxo-2-naphthacenecarboxamide.

Synonyms : Aquacycline; Arcospectron; Bio-Mycin; Duphacycline; Geomycin; Gynamousse; Imperacin (Capsules); Macocyn; Macodyn; Occrycetin; Oxlopar; Oxybiotic; Oxybiocycline; Oxycycline; Oxyject; Stecsolin; Tetra-Tablinen; Toxinal; Terramycin; Tetramel HCl; Ryomycin HCl.



The oxytetracycline antibiotic substance has been isolated from the elaboration products of the actinomycete, *Streptomyces rimosus*, grown on a suitable medium. It occurs as a pale yellow or

yellow or light brown, hygroscopic, stable crystalline powder with a bitter taste. It is soluble in water (1 in 2), alcohol (1 in 45); practically insoluble in chloroform and ether. Concentrated aqueous solutions at neutral pH hydrolyze on standing and deposit crystals of oxytetracycline and the solutions become turbid. Oxytetracycline hydrochloride is inactivated rapidly by deterioration in solutions having a pH of less than 2 and is rapidly destroyed by alkali hydroxide solutions. The amphoteric base and the hydrochloride are absorbed rapidly from the digestive tract readily. Oxytetracycline is stored in airtight containers and protected from light.

Uses : Oxytetracycline has the same antimicrobial activity and uses as described for tetracycline hydrochloride. It is usually used in tablets, the calcium salt in aqueous oral suspensions, and the hydrochloride in capsules and intravenous injections.

Adverse effects of oxytetracycline are the same as described for tetracycline hydrochloride. It may produce less tooth discolouration than most other tetracyclines.

Official

Oxytetracycline Hydrochloride, B.P., I.P.

Oxytetracycline Capsules/Injection, U.S.P., B.P., I.P.

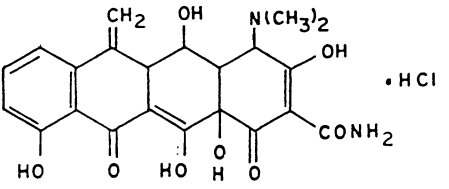
Oxytetracycline Hydrochloride Capsules, U.S.P.

Sterile Oxytetracycline Hydrochloride, U.S.P.

METHACYCLINE HYDROCHLORIDE

Nomenclature : 4-Dimethylamino-1, 4, 4a, 5, 5a, 6, 11, 12a - octahydro-3, 5, 10, 12, 12a - pentahydroxy-6-methylene-1, 11-dioxo-2-naphthacene carboxamide; 6-Methylene oxytetracycline HCl.

Brand Names : GS-2876 (methacycline); Methylenecycline hydrochloride; Metacycline hydrochloride; Metacyclini Chloridum; Adriamiana; Ciclobiotic; Germiciclin; Globociclina; Megamycine; Metadomus; Metilenbiotic; Londomycin; Optimycin; Rondomycin; Physiomycine; Rindex.



Methacycline is synthesized by chemical modification of oxytetracycline. Its antibiotic spe-

ctrum is similar to the other tetracyclines but its potency is greater than the other such compounds. The greater stability of methacycline is due to the modification at carbon atom 6. The substitution of the 6-hydroxy group markedly increases the stability of ring C to both acids and alkalies, by preventing the formation of anhydrotetracyclines by acids and of isotetracyclines by bases.

Methacycline hydrochloride, m.p. 205° (decomp.), is a yellow to dark yellow crystalline powder. It is slightly soluble in water (1 in 100) and in alcohol (1 in 300); practically insoluble in chloroform and ether; soluble in dilute solutions of sodium hydroxide. It should be stored in tight and light-resistant containers in a cool place.

Uses : Methacycline hydrochloride has the same antimicrobial activity, adverse effects and uses as described for tetracycline hydrochloride.

Official

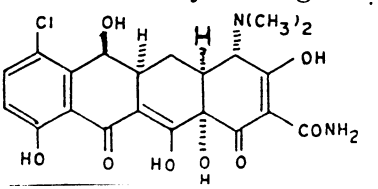
Methacycline Hydrochloride Capsules, U.S.P.

Methacycline Hydrochloride Oral Suspension, U.S.P.

DEMECLOCYCLINE

Nomenclature : 7-Chloro-4-dimethylamino-1, 4, 4a, 5a, 6, 11, 12a-octahydro-3, 6, 10, 12, 12a - pentahydroxy-1, 11-dioxo-2-naphthacenecarboxamide; Demethylchlortetracycline; 7-Chloro-6-demethyltetracycline.

Brand Names : RP 10192; Bioterciclin; Declomycin; Deganol; Ledermycin; Periciclina.



Demeclocycline hydrochloride is an antimicrobial substance produced by the growth of certain strains of *Strepomyces aureofaciens* and first isolated by McCormick *et al.* (1957). It differs from chlortetracycline only by the absence of the methyl group on carbon atom 6. The stability of ring C is enhanced to both acid and alkali due to the absence of this methyl group. It occurs as a yellow, odourless, crystalline powder. It is slightly soluble in water (1 in 30-60), methyl alcohol (1 in 50), and alcohol; practically insoluble in acetone, chloroform, and ether; soluble in aqueous solutions of alkali hydroxides and carbonates. Similar to the other tetracyclines, it may cause infrequent photosensitivity reactions.

Demeclocycline hydrochloride (Brand Names : Clortetrin; Demetraciclina; Detravi's Meciclin; Mixocine). Demeclocycline and its salts are kept in airtight containers and protected from light.

Uses : Demeclocycline has the antimicrobial activity and uses described for tetracycline hydrochloride. It is excreted more slowly and effective blood concentrations are maintained for a longer period.

Adverse effects of demeclocycline are the same as for tetracycline hydrochloride.

Official

Demeclocycline Hydrochloride, B.P.

Demeclocycline Capsules, B.P.

Demeclocycline Hydrochloride Capsules/Tablets, U.S.P.

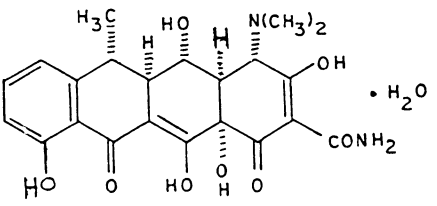
Demeclocycline Oral Suspension, U.S.P.

Demeclocycline Hydrochloride and Nystatin Capsules/Tablets, U.S.P.

DOXYCYCLINE

Nomenclature : 4-(Dimethylamino)-1, 4, 4a, 5, 5a, 6, 11, 12a-octahydro-3, 5, 10, 12, 12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide; α-6-Deoxy-5-hydroxytetracycline monohydrate; α-6-Deoxyoxytetracycline monohydrate; 5-Hydroxy-α-6- deoxytetracycline monohydrate.

Brand Names : Doxitard; Liviatin; Vibramycin; Vibravenos; GS-3065.



Doxycycline, m.p. 201° (decomp.), was first obtained by a chemical transformation of oxytetracycline but it is now synthesized by catalytic reduction of methacycline or by reduction of a benzyl mercaptan derivative with Raney nickel catalyst. In the 6-α-methyl epimer, the orientation of 6-methyl group is different from that in the tetracyclines. The 6α-methyl epimer is three times more active than its 6α-epimer. The absence of the 6-hydroxyl group produces a compound that is highly stable to acids and bases and that has long biologic half-life. It is also very well absorbed from the gastrointestinal tract, thus allowing a smaller dose to be administered.

DOXYCYCLINE HYDROCHLORIDE

Brand Names : Doxycycline hydrate; Vibramycin hydrate; Doxy-II (Caps); Doxy-Tablinen; Vibra-Tabs; Retens; Nivocilin; Tenamicin; Tatradox; Hydromycin; Doxigalumicina; Tecacin, Mespafin, Roximycin.

Doxycycline hydrochloride occurs as a yellow hygroscopic crystalline powder which crystallizes from ethanol and hydrochloric acid mixture. It chars without melting at about 201°. It is biologically more active than the corresponding 6β-epimer hydrochloride. Doxycycline hydrochloride is soluble in water (1 in 3) and methyl alcohol (1 in 4); sparingly soluble in alcohol; practically insoluble in chloroform and ether; soluble in solutions of alkali hydroxides and carbonates. Doxycycline and its salts are stored in airtight containers and protected from light.

Uses : Doxycycline hydrochloride is used for the same purposes as tetracycline hydrochloride. It is readily absorbed and excreted more slowly than most other tetracyclines and effective blood concentrations are maintained for longer periods. The adverse effects as the same as for tetracycline hydrochloride

Official

Doxycycline Hydrochloride, B.P.

Doxycycline Capsules, B.P.

Doxycycline Hyelate Capsules/for Injection, U.S.P.

Doxycycline Hyclate Delayed-Release Capsules, U.S.P.

Sterile Doxycycline Hyclate, U.S.P.

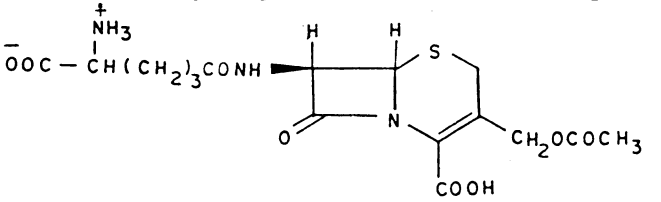
Doxycycline Calcium Oral Suspension, U.S.P.

Doxycline Hyclate Tablets, U.S.P.

CEPHALOSPORINS.

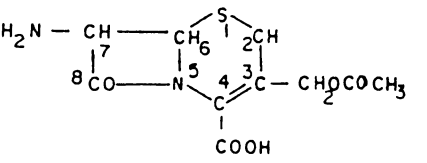
The cephalosporins are antibiotics obtained by Brotzu (1945) from species of the fungus *Cephalosporium* whose culture medium was active against typhoid. Componds having three different chemical structures have been isolated from *Cephalosporium*. One of these, cephalosporin P_1, has a steroid structure. It possesses low antibacterial properties and is not used as medicine. Another antibiotic, cephalosporin C, possesses

an α-aminoadipoyl side chain and a β-lactam ring, but on hydrolysis it does not yield penicillamine as in case of penicillin.



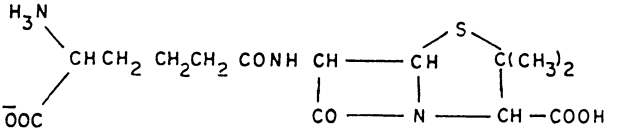
Cephalosporin C

The removal of the side-chain from cephalosporin C gives 7-aminocephalosporanic acid (7-ACA) which provides a means of synthesizing a whole new range of cephalosporins. Treatment with nitrosyl chloride yields an intermediate iminolactone which is then hydrolyzed with water to give α-hydroxyadipic acid and 7-aminocephalosporanic acid.



7-Aminocephalosporanic acid

The antibiotic cephalosporin N, isolated from *C. salmosynnematum*, is an interesting compound. The unusual zwitterionic side chain produces a compound less effective against gram-positive organisms than are other penicillins. However, it is more active than penicillin G against a number of gram-negative organisms and some salmonellae.

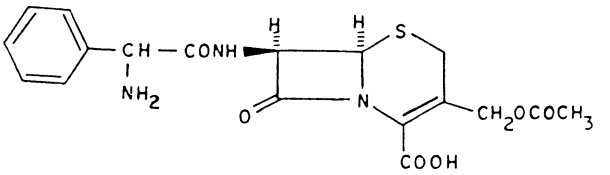


CEPHALEXIN

Nomenclature : 7-(D-2-Amino-2-phenylacetamido)-3-acetoxymethyl-Δ^3-cephem-4-carboxylic acid; 7-(D-α-Aminophenylacetamido) cephalosporanic acid; 7-[(Aminophenylacetyl) amino]-3-methyl-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxyl acid.

Brand Names : Ausocef; Cefadros; Cefaloto; Cefibacter; Ceporexime, Cex, Derantel, Efalexin; Farexin; Fergon 500; Garasin; Ibilex; Iwalexin; Larixin; Lexibiotico; Llonexina; Madlexin;

Mamalexin; Mecilex; Neolexina; Ohlexin; Oracocin; Rinesal; Sencephalin; Syncl; Taicelexin; Tokiolexin; Xahl.



Cephalexin has antibacterial activity similar to that of ampicillin. It occurs as a white to cream-coloured, crystalline powder with a characteristic odour. It is slightly soluble in water; practically insoluble in alcohol, chloroform, and ether. Cephalexin is a first-generation cephalosporin antibiotic. It is stored at a temperature not exceeding 30° in airtight containers and protected from light.

Uses : Cephalexin is used to treat infections of the respiratory and urinary tracts and of skin and for otitis media.

Side-effects of cephalexin include nausea, vomiting, diarrhoea, and abdominal discomfort. Allergic reactions such as skin rashes, urticaria, eosinophilia, angioedema and anaphylaxis may occur.

Official

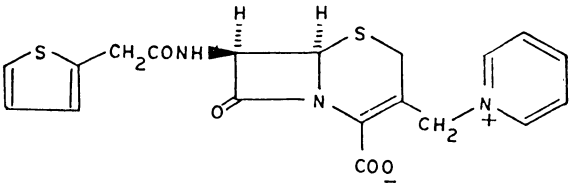
Cephalexin, B.P.

Cephalexin Capsules/Tablets, B.P., U.S.P.

Cephalexin for Oral Suspension, U.S.P.

CEPHALORIDINE

Nomenclature : 1-[{2-Carboxy-8-oxo-7-(2-thienylacetyl) amino}-5-thia-1-azabicyclo {4.2.0} oct-2-en-3-yl}-methyl] pyridinium hydroxide inner salt; N-[7-(2'-Thienylacetamidoceph-3-yl-methyl)]-pyridinium-2-carboxylate.



Brand Names : Ceflorin; Cepaloridin; Cer; Faredina; Cefaloridin; Ceporan; Ceporin; Cilifor; Intrasporin; Keflodin; Keflordin

(obsolete); Lloncefal; Sefacin; Cepalorin; Deflorin; Kefspor; Loridine; Alipornia; Ampligram; Floridin.

When cephalosporin C produced by the growth of certain strains of various cepalosporium species, or 7-ACA is reacted with organic bases such as pyridine, a nucleophilic displacement of the acetyloxy group takes place. The pyridinium compound so obtained is more potent than its acetoxyl analogue.

Cephaloridine is a white crystalline powder. It is soluble in water; slightly soluble in alcohol; practically insoluble in chloroform and ether. It is decolourized when exposed to light. It deteriorates rapidly in aqueous solutions which should be used within 24 hours of their preparation when stored at 2° to 15°C. It is stored in airtight containers at a temperature of 8° to 15°C and protected from light.

Uses : Cephaloridine is used in the treatment of infections of skin, soft tissues, bone, joint, respiratory and urinary tracts. Its use, however, has been limited by nephrotoxicity.

Allergic reactions, including skin rashes, urticaria, eosinophilia, fever reactions resembling serum sickness and anaphylaxis may occur in patients receiving cephaloridine. It is considered to be the most nephrotoxic of the cephalosporins, and for this reason is seldom used. Acute and fatal renal failure may occur.

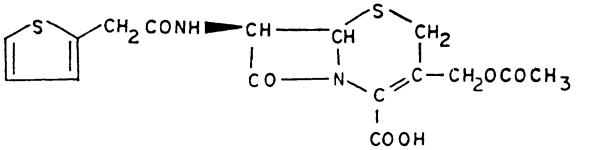
Official

Cephaloridine, B.P., I.P.

Cephaloridine Injection, B.P., I.P.

CEPHALOTHIN

Nomenclature : 7-(2-Thienylacetamido) cephalosporanic acid; 7-(Thiophene-2-acetamido) cephalosporanic acid; 3-[(Acetyloxy) methyl]-8-oxo-7-[(2-thienylacetyl) amino] -5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylic acid; 3-(Hydroxymethyl)-8-oxo-7-[2-(2-thienyl)-acetamido]-5-thia-1-azabicyclo [4.2.0]-oct-2-ene-2-carboxylic acid acetate.



It melted at 160-161°; $[\alpha]_D^{20}$ + 50°

SODIUM CEPHALOTHIN

Brand Names : Averon-1, Cefalotin; Cephation; Ceporacin; Cepovenin; Ephalotin; Coaxin; Keflin; Lospoven; Microtin; Synclotin; Toricelocin.

Sodium cephalothin occurs as a white to off-white, odourless, crystalline powder. It is freely soluble in 0.9% sodium chloride solution, glucose solutions and water (1 in 3.5); slightly soluble in alcohol; practically insoluble in chloroform, ether and most other solvents. Aqueous solutions of cephalothin sodium are stable for 12 hours at 25° and for 48 hours at 5°. Solution of cephalothin sodium may darken on storage at room temperature. Its spectrum of activity is broader than that of penicillin G. It is poorly absorbed from the gastrointestinal tract. It is relatively nontoxic and is acid stable. It is excreted rapidly through the kidneys, about 60% is lost within 6 hours of administration. The drug is stored at a temperature not exceeding 25° in airtight containers.

Uses : Cephalothin sodium is similarly used to cephaloridine.

Allergic reactions are identical to that of cephaloridine. Neutropenia, leucopenia, thrombocytopenia and haemolytic anaemia have occasionally been reported. Nephrotoxicity has occurred in patients with existing renal impairment. There may be pain at the injection site. Gastro-intestinal adverse effects have been reported rarely.

Official

Cephalothin Sodium, B.P.

Cephalothin Injection, B.P.

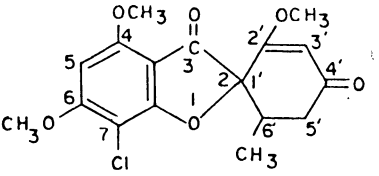
Cephalothin Sodium Injection, U.S.P.

Sterile Cephalothin Sodium, U.S.P.

GRISEOFULVIN

Nomenclature : 7-Chloro-2', 4, 6-trimethoxy-6'-methylspiro [benzofuran-2 (3H), 1'-[2] cyclohexene]-3, 4'-dione, 7-chloro-4, 6-dimethoxy coumeran-3-one-2-spiro-1'-(2'-methoxy-6' methylcylohex-2'-en-4'-one).

Brand Names : Amudane; Curling factor; Fulcin; Futvicin; Grifulvin; Grisactin; Grisovin; Gris-PEG; Grysio; Lamoryl; Likuden; Neo-Fulcin; Poncyl; Spirofulvin; Sporostatin.



Griseofulvin in an antifungal substance produced by the growth of certain strains of *Penicillium griseofulvum*. It is a white, or yellowish-white, bitter, odourless, thermostable powder that may be crystallized as needles, m.p. 220°. It is insoluble in water; slightly soluble in alcohol and in methyl alcohol; soluble in chloroform; freely soluble in dimethylformamide and in tetrachloroethane. In dried state it is stable for at least 20 months. It is stored in well-closed containers.

Uses : Griseofulvin is administered by mouth in the treatment of tinea (ringworm) infections. It is given for infections of the scalp, hair, and nails, and for infections of the skin which do not respond to topical treatment.

Side-effects are usually mild and transient and consist of mainly of headache, skin rashes, dryness of the mouth, an altered sensation of taste, and gastro-intestinal disturbances. Angioedema, erythema multiforme, exfoliative dermatitis, proteinuria, leucopenia and other blood dyscrasias, candidiasis, paraesthesia, photosensitisation, and severe headache have been reported occasionally. Depression, confusion, dizziness, insomnia, and fatigue have also been reported.

Official

Griseofulvin, B.P.

Griseofulvin Tablets, B.P., U.S.P.

Griseofulvin Oral Suspension, U.S.P.

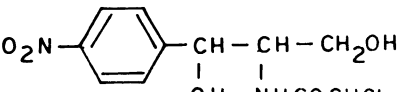
Ultramicrosize Griseofulvin Tablets, U.S.P.

CHLORAMPHENICOL

Nomenclature : 2, 2-Dichloro-N-[2-hydroxy-1-(hydroxymethyl)-2-(4-mitrophenyl) ethyl] acetamide; D-Threo-N-dichloroacetyl-1-p-nitrophenyl-2-amino-1, 3-propanediol.

Brand Names : Aquamycetin; Austracol; C.A.F.; Alficetyn; Amphicol, Anacetin; Chemicetina; Chlomycol; Chloramex;

Chloramfilin; Chloramsaar; Chlorasol; Chloricol; Chlorocaps; Chlorocid; Chloromycetin; Chloronitrin; Cidocetine; Ciplamycetin; Cloramficin; Cloramicol; Clorocyn; Cloromisan; Cylphenicol; Duphenicol; Embacetin; Enicol; Enteromycetin; Furmicetina; Fenicol; Globenicol; Interomycetine; Intramycetin; Juvamycetin; Kamaver; Kemicetine; Klorita; Leukomycin; Levomicetina; Levomycetin; Loromisin; Mastiphen; Medichol; Micloretin; Micoclorina; Microcetina; Mychel; Mycinol; Novomycetin; Opelor; Pantovernil; Paraxin; Quemicetina; Ronfenil; Stanomycetin; Synthomycetine; Tega-cetin; Tevcocin; Tifomycine; Treomicetina; Unimycetin; Veticol, Viceton; Septicol; Sintomicetino; Sno-Phenicol.



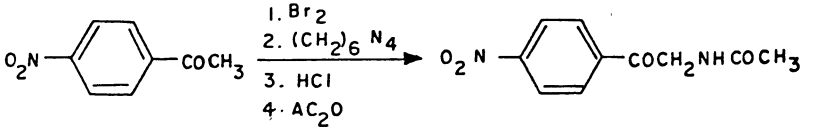
Chloramphenicol was isolated by Ehrlich and coworkers in 1947 from *Streptomyces venezuelae*. It was the first antimicrobial substance widely used as broad spectrum antibiotics.

It possesses two asymmetric carbon atoms in the acylamidopropanediol carbon chain giving rise to *threo* and *erythro* forms. By relating the structure to L-*norephedrine*. L-*pseudonorephedrine*. and D-serine it was assigned as D-(-) *threo* configuration.

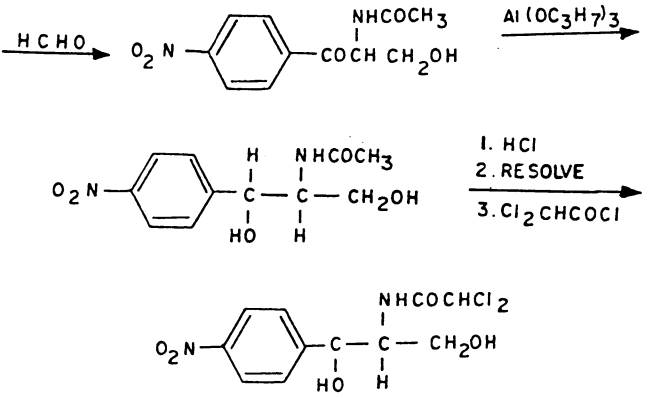
Chloramphenicol has been synthesized by a number of routes and all the commercial material is now prepared synthetically. One of the best synthesis is from p-nitroacetophenone as the starting material. Bromination of the methyl group followed by reaction with hexamine gives an amino ketone which is acetylated, hydroxy-methylated, and reduced with aluminium isopropoxide (Meerwein-Ponndort reduction). The DL-*threo* form so obtained predominantly was purified by crystallization. After removal of the acetyl group by hydrolysis, the *threo*-racemate is resolved with D-camphor sulphuric acid and finally reacted with dichloroacetyl chloride.

A large number of structural analogues of chloramphenicol have been synthesized to study correlation of structure to antibiotic action. It has been found that the p-nitrophenyl group may be replaced by other aryl substituent without any loss in activity. Substitution on the phenyl ring with different nitro groups does not cause a great decrease in activity. However, the maintenance of the aromatic character of this group is essential. A conversion of the alcohol group on carbon atom 1 of the side

chain to a keto group causes an appreciable loss in activity. Thus, numerous analogues have been prepared but they have all shown only similar activity or greater toxicity.



p-Nitroacetophenone



Chloramphenicol

Chloramphenicol occurs as a white to greyish-white or yellowish-white, fine crystalline powder or fine crystals, needles, or elongated plates, m.p. 149-153°. It sublimes in high vacuum. It is soluble in water (1 in 400), alcohol (1 in 2.5), propylene glycol (1 in 7); freely soluble in acetone, ethyl acetate, methanol and butanol and slightly soluble in ether. It is stored in airtight containers and protected from light.

Uses : Chloramphenicol is used as an antibacterial in serious infections due to *Haemophilus influenzae*, in severe respiratory-tract infections, anaerobic infections, rickettsial infections such as typhus and Rocky Mountain spotted fever, and for a variety of eye infections due to sensitive organisms. It has also been used in skin infections. The liability of chloramphenicol to provoke life-threatening adverse effects, particularly bone-marrow aplasia, has severely limited its clinical usefulness. It should not be given for minor infections and should be discontinued immediately on the appearance of toxic symptoms. In addition to its depression of the bone marrow, haemolytic anaemia has occurred in some persons. Abnormal distension, vomiting,

hypothermia, pallid cyanosis, irregular respiration and circulaory collapse followed by death have occurred in premature and other newborn infants receiving large doses of chloramphenicol. Hypersensitivity reactions may occur especially after topical use.

OFFICIAL

Chloramphenicol, B.P., I.P.

Chloramphenicol Eye Drops/Eye Ointment/Ear Drops, B.P.

Chloramphenicol Palmitate, B.P., I.P.

Chloramphenicol Palmitate Mixture, B.P.

Chloramphenicol Palmitate Oral Suspension, I.P., U.S.P.

Chloramphenicol Sodium Succinate, B.P.

Chloramphenicol Sodium Succinate Injection, B.P.

Chloramphenicol Ophthalmic Ointment/Solution, U.S.P.

Chloramphenicol Capsules, B.P., U.S.P.

Chloramphenicol Cream/Otic Solution, U.S.P.

Chloramphenicol and Hydrocortisone Acetate for Ophthalmic Suspension, U.S.P.

Chloramphenicol and Polymyxin B Sulfate Ophthalmic Ointment, U.S.P.

Chloramphenicol, Polymyxin B Sultate, and Hydrocortisone Acetate Ophthalmic Ointment, U.S.P.

Chloramphenicol and Predinisolone Ophthalmic Ointment, U.S.P.

Sterile Chloramphenicol Sodium Succinate, U.S.P.

Chloramphenicol Oral Suspension, B.P.

10

ANTIFUNGAL AGENTS

Fungal infections are due to poor host resistance and are now common worldwide. Antifungal agents are used to treat various fungal infections of hair, mucous membranes, nails, or skin. The fungi of the genera *Candida* (Condidiasis), *Epidermophyton*, *Microsporum* and *Trichophyton* (tinea, ringworm) produce fungal infection. The systemic fungal infections include localized or disseminated blastomycosis, cryptococosis, candidiasis and other invasive infections. Antifungal agents are employed locally, e.g. antibiotics (nystatin, pimaricin, hamycin) or they may be employed systematically, e.g. antibiotics (griseofulvin, amphotericin B), azole derivatives and flucytosine. Fatty acids in perspiration have been found to be fungistatic.

PROPIONIC ACID

Nomenclature : Propanoic acid, Methylacetic acid, Ethylformic acid.

$$CH_3\ CH_2\ COOH$$

Propionic acid occurs in sweat and dairy products in small amounts. It can be obtained from wood pulp waste liquor by a fermentation process using bacteria of the genus *Propionibacterium*. It is synthesized by oxidizing n-propyl alcohol or propaldehyde with acidified dichromate :

$$\underset{\text{n-Propyl alcohol}}{CH_3\ CH_2\ CH_2\ OH} \xrightarrow[K_2Cr_2O_7,\ H^+]{[O]} CH_3\ CH_2\ CHO + H_2O$$

$$CH_3\,CH_2\,CHO \xrightarrow{[O]} CH_3\,CH_2\,COOH$$

Propaldehyde

α-Substituted chloro- or bromo-acids are readily prepared from propionic acid by the Hell-Volhard method. The anhydrous acid is chlorinated or brominated in the presence of red phosphorus. The phosphorus trihalide first converts the acid into the acyl chloride or bromide, and this compound is readily halogenated in the α-position. Addition of cold water hydrolyzes the acyl halide; e.g.

$$CH_3\,CH_2\,COOH \longrightarrow \underset{\text{Propionyl bromide}}{CH_3\,CH_2\,COBr} \longrightarrow \underset{\text{2-Bromoprop-ionyl bromide}}{CH_3\,CHBr\,COBr}$$

$$\longrightarrow \underset{\text{2-Bromopropionic acid}}{CH_3\,CHBr\,COOH}$$

Propionic acid is a clear, corrosive, oily liquid with slightly pungent, disagreeable, rancid odour; b.p. 122°. It can be salted out of water solutions by the additions of $CaCl_2$ or other salts. It is soluble in water, alcohol, ether and chloroform. It has fungicidal action and its salts have the same antifungal properties to that of the free acid. The free acid may be used to treat fungal infections like athlete's foot. It is nontoxic, nonirritant and readily available; stored in airtight containers.

SODIUM PROPIONATE

Brand Names : Sodium propanoate; Mycoban.

Sodium propionate occurs as transparent, colourless crystals or white granular crystalline powder. It is odourless or with a slight characteristic odour resembling acetic and butyric acids and are deliquescent in moist air. It is soluble in water (1 in 1) and alcohol (1 in 25); practically insoluble in chloroform and benzene; stored in airtight containers. Sodium propionate is most effective at pH 5.5 and generally is used in a 10% ointment, powder or solution alone or in combination with other propionates, caprylates or other antifungal agents for the treatment of dermatophyte infections. Eye-drops containing sodium propionate (5%) are also used. It is used in veterinary medicine and as esterifying agent.

Zinc Propionate : It occurs as needles or plates and is freely soluble in water and sparingly soluble in alcohol. It decomposes in moist atmosphere to form propionic acid. It is used as a fungicide. especially on adhesive tape to reduce irritation cause by fungi and bacterial action.

UNDECYLENIC ACID

Nomenclature : 10-Undecenoic acid; 10-Hendecenoic acid; 9-Undecylenic acid.

Brand Names : Declid; Renselin; Sevinon; Acidum; Undecylenicum.

It consists mainly of undec-10-enoic acid and occurs in sweat.

$$CH_2 = CH(CH_2)_8\ COOH$$

It is prepared by vaccum distillation of castor oil in which pyrolysis of ricinoleic acid takes place. It occurs as a colourless or pale yellow clear liquid or a white to pale yellow crystalline mass with a characteristic odour like perspiration and a bitter or acrid taste.

$$CH_3\ (CH_2)_5\ CHOH\ CH_2\ CH = CH\ (CH_2)_7\ COOH$$

Ricinoleic acid

$$\downarrow \text{ heat in vacuum}$$

$$CH_3\ (CH_2)_5\ CHO \quad + \quad CH_2{=}CH\ CH_2\ (CH_2)_7\ COOH$$

n-Heptyl aldehyde (40%) Undecylenic acid (20%)

Undecenoic acid is practically insoluble in water; freely soluble in alcohol, chloroform, ether and fixed and volatile oils; m.p. 24.5°. It is stored in airtight containers at a temperature of 8 to 15°; protected from light.

Zinc Undecylenate : It is a fine white powder; practically insoluble in water, alcohol, and ether, m.p. 115-116°. It can be prepared by dissolving zinc oxide in dilute undecylenic acid and concentrating the solution. It is stored in well-closed containers and protected from light.

Uses : Undecenoic acid and its zinc salt are applied topically in the prophylaxis and treatment of dermatophytic infections of superficial areas. Undecenoic acid is applied to the skin in concentrations of 2% to 10%, and zinc undecenoate in concentrations of up to 20%. They are used in creams, ointments,

or powders, often in conjunction with other. Internally, a very pure form is used in capsules to cure psoriasis and neurodermatitis.

Irritation may rarely occur after the topical application of undecenoic acid or its salts.

Offical

Zinc Undecenoate, B.P.

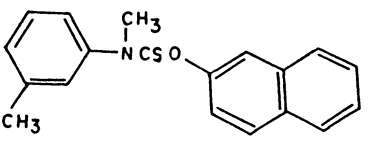
Zinc Undecylenate Ointment, I.P.

Compound Undecylenic Acid Ointment, U.S.P.

TOLNAFTATE

Namenclature : Methyl (3-methylphenyl) carbamothioic acid 0-2-naphthalenyl ester; *m.* N-Dimethylthiocarbanilic acid 0-2-naphthyl ester; 0-2-Naphthyl *m.* N-dimethylthiocarbanilate; 2-Naphthyl N-methyl-N-(3-tolyl) thionocarbamate.

Brand Names : Naphthiomate T: Sch 10144; Aftate; Chinofungin; Focusan; Hi-Alazin; Sporiline; Tinactin; Tinaderm; Tonofal.



Tolnaftate is an O-ester of thiocarbanilic acid; the carbanilic acid being phenylcarbamic acid.

It is a white to creamy-white fine powder, odourless or with a slight odour, m.p. 110-112°: practically insoluble in water; sparingly soluble in methanol and ethanol; soluble in chloroform, acetone and carbon tetrachloride; stored in airtight containers.

Uses : Tolnaftate is an antifungal agent used topically as a 1% solution, powder, or cream in the treatment of tinea infections and of pityriasis versicolour. It is used with nystatin when candidal infections are present.

Skin reactions including irritation and pruritus may occur; contact dermatitis has been reported.

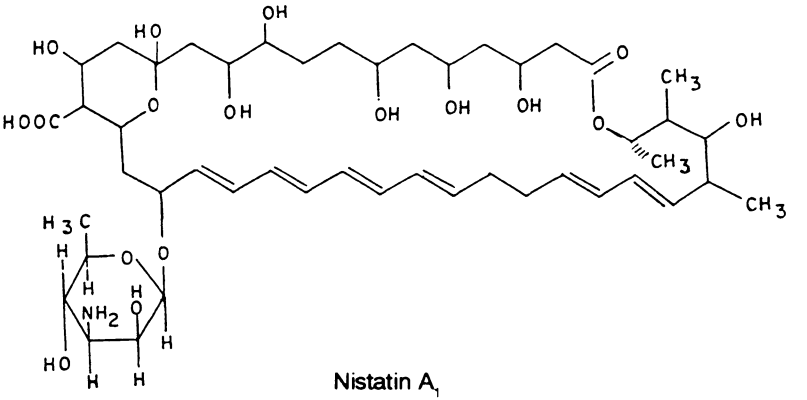
Offical

Tolnaftate, B.P.

Tolnaftate Cream/Gel/Powder, U.S.P.

NYSTATIN

Brand Names : Fungicidin, Biofanal; Diastatin; Candex; Candio-Hermal; Mycostatin; Moronal; Multilind; Nystan; Nystavescent; O-V Statin; Nistatina; Nystatinum.



Nistatin A_1

Nystatin is an antifungal substance produced by the growth of certain strains of *Streptomyces noursei*. It contains mainly tetraenes, the principal component being nystatin A_1. It is a valuable substance used to treat both internal and local infections of *Candida albicans*. The sugar moiety attached to the aglycone is mycosamine, 3,6-dideoxy-3-amino-D-mannose.

Nystatin is a light yellow to light brown hygroscopic powder with a characteristic cereal-like odour; gradually decomposes above 160° without melting by 250°. It exhibits strong reducing properties. It is very soluble in water; slightly soluble in methanol; insoluble in alcohol, chloroform, and ether, freely soluble in dimethyl formamide. It is unstable to moisture, heat, light and air, and its solutions are inactivated rapidly by acids and bases. Solutions and aqueous suspensions begin to lose activity soon after preparation. Aqueous suspensions are stable for 10 minutes on heating to 100° at pH 7.0; also stable in modertely alkaline media. It is stored at a temperature between 2 to 8° in airtight containers and protected from light.

Uses : Nystatin is used for the prophylaxis and treatment of candidiasis of the skin and mucous membranes, especially that caused by *Candida albicans*. It is also given as eye-drops or as a bladder wash.

Nausea, vomiting, and diarrhoea have occasionally been reported after the oral administration of nystatin. Irritation may

occur rarely after the topical use of nystatin, and allergic contact dermititis has been reported.

Offical

Nystatin, B.P.

Nystatin Tablets, B.P.

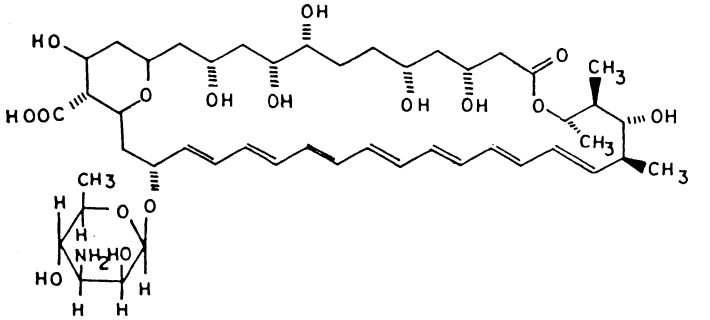
Nystatin Ointment, B.P., U.S.P.

Nystatin Vaginal Tablets/Suppositories, U.S.P.

Nystatin Topical Powder, U.S.P.

AMPHOTERICIN

Brand Names : Amphotericin B; Anfotericina B; Amphozone; Fungizone; Fungilin; Ampho-Moronal.



Amphotericin is a polyene antifungal antibiotic produced by *Streptomycetes nodosus* M4575 obtained from soil of Orinoco river region of Venezuela. The antibiotic material was a mixture of two compounds, Amphotericins A and B. The B compound is more active and used for its broad-spectrum activity against a number of deep-seated and systemic infections caused by yeast-like fungi.

The compound is an amphoteric substance which occurs as a yellow to orange odourless powder. It decomposes gradually above 170°. It is practically insoluble in water, alcohol and in ether; slightly soluble in dimethylformamide and methyl alcohol; soluble in dimethyl sulphoxide and propylene glycol. Solids and solutions appear stable for long periods between pH 4 and 10 when stored at moderate temperatures out of contact with light and air. Amphotericin is precipitated from solution of sodium chloride. It is stored at 2° to 8° in airtight containers and

protected from light. Under these conditions, it does not significantly deteriorate or lose potency for at least 1 year.

Amphotericin is very poorly absorbed from the gastro-intestinal tract, and therefore, it is preferred to administer as intravenous infusion. The aqueous solutions should be used within 24 hours before deterioration.

Uses : Amphotericin is used to treat severe systemic mycotic infections. It has been given for the treatment of American mucocutaneous and cutaneous leishmaniasis and to cure cryptococcal meningitis.

Solutions of amphotericin irritate the venous endothelium and may cause pain at the site of injection. Common adverse effects are headache, nausea, fever, vomiting, chills, malaise, muscle and joint pains, anorexia, diarrhoea, gastro-intestinal cramp and cardiac problems.

Official

Amphotericin, B.P.

Amphotericin B Cream/for Injection/Lotion/Ointment. U.S.P.

HAMYCIN

Brand Name : Primamycin.

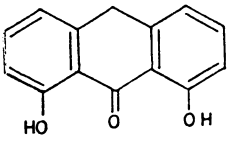
Hamycin is a polyene antibiotic complex produced by *Streptomyces primprina*. At one time, hamycin was believed to be identical to trichomycin and candicidin. Subsequent HPLC studies have shown the three polyene antibiotics to be different compounds. Structural study showed that hamycin was a mixture of components A, B, C and D.

Hamycin occurs as a yellow amorphous powder with no definite melting point. It decomposes at 160°. It is an amphoteric compound which is almost insoluble in water, benzene, chloroform, lower aliphatic alcohols and ether; soluble in basic solvents such as pyridine, collidine, and in aqueous lower alcohols. In concentrated sulphuric acid it forms stable blue colour.

Hamycin has been reported to have antifungal and antitrichomonal properties. It has been administered topically and by mouth in a variety of fungal infections.

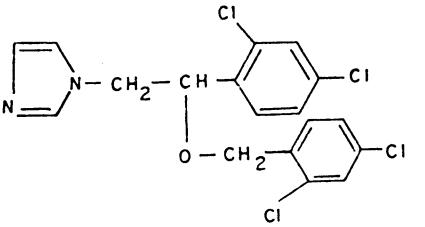
Miscellaneous Agents

Dithranol (anthralin) is a yellow powder; insoluble in water; soluble in organic solvent. It is a fungicide and used to treat ringworm, chronic dermatoses and psoriasis.



Dithranol

Miconazole is an imidazole derivative. Its nitrate is white, crystalline powder; very slightly soluble in water. It is used topically to cure fungal infections.



Miconazole Nitrate

Official

Dithranol, B.P., I.P.

Dithranol Ointment/Paste, B.P.

Miconazole Nitrate, B.P.

11

ANTIMALARIAL DRUGS

Malaria is one of the most serious protozoal infection in man and is caused by infection by any four species of *Plasmodium*. The disease is characterized by successive chills, fever with rigor, anaemia and sweats. The *Plasmodium vivax* (benign tertian), *Plasmodium falciparum* (estivo-autumnal; malignant tertian) and *Plasmodium malariae* (quartan) are widely distributed and occur most frequently in tropical and sub-tropical countries. *Plasmodium ovale* (ovale tertian) is not very common.

All species of *Plasmodium* have two hosts, a vertebrate and a mosquito that acts as both vector and definitive host. The malaria organism requires times in both hosts to complete its multistage life cycle. Infection in man is caused by injection of *sporozoites* by the bite of a female anopheles mosquito. The salivary glands of the infected mosquito contain a large number of sporozoites and they enter into blood stream of the host. Some of the *sporozoites* rapidly enter into liver cells where they undergo *exoerythrocytic* propagation forming tissue *schizonts* which mature and release thousands of merozoites into the blood on rupture of the cell. When the erythrocytes burst then chilling is felt and fever is produced. The merozoites can infest more red-blood cells and start a new life-cycle. After several erythrocytic cycles, some erythrocytic forms develop into sexual *gametocytes* which eventually give rise to the sexual cycle in the mosquito.

Again during the mosquito bite of an infected person these merozoites (known as male and female gametocytes), enter mosquito from the peripheral blood. In the gut of the mosquito the female gametocyte fertilizes to zygote to form oocyst which

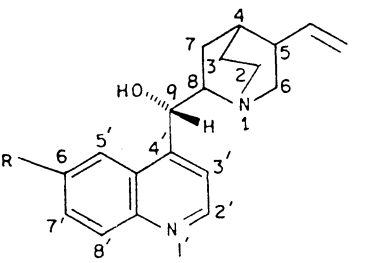
utimately gives rise to sporozoites and they eventually reach the salivary glands of the mosquito.

Antimalarial drugs may kill the sporozoites as soon as they are introduced into the bloodstream by the bite of a mosquito (sporozoitocide drugs); they kill the parasite as it exists in the schizont stage (exoerythrocytic schizontocide drugs); they inhibit the development of schizonts during the erythrocytic stage (erythrocytic schizontocide drugs); they kill the parasite as it exists in the gametocyte stage (gametocytocide drugs); they prevent sporogony in the mosquito by their effect on the gametocytes in the blood of the vertebrate host (sporozoitocide drugs).

Cinchona alkaloids (quinine), 4-aminoquinolines (chloroquine, amodiaquine), 8-aminoquinolines (primaquine), 8-aminoacridines (mepacrine), biguanides (proguanil), diaminopyrimidines (primethamine), quinoline methanol (mefloquine) and some miscellaneous drugs (sulfonamides, sulfones, tetracycline) are used as antimalarial agents.

CINCHONA ALKALOIDS

Cinchona consists of various species and is found in Colombia, Ecuador, Peru and Bolivia. Pelletier and Caventon (1820) isolated the alkaloids quinine and cinchonine from Cinchona bark. Woodward and Doering (1945) syhthesized quinine in the laboratory. The crude drug contains about 35 alkaloids, of which quinine, quinidine, cinchonine and cinchonidine are the most abundant and the most important compounds. The average commercial yields of alkaloids from Cinchona bark are: quinine (5%), quinidine (0.1%), cinchonine (0.3%) and cinchonidine (0.4%). Some of Cinchona alkaloids (e.g. quinicine and cinchonicine) are amorphous. The amount of alkaloids present vary considerably in different species and hybrids. The cultivated bark contains 7-10% total alkaloids of which about 70% is quinine.



Cinchona alkaloids possess four asymmetric centres, carbons 3, 4, 8 and 9. All the cinchona alkaloids are identical in configuration at C-3 and C-4. Four different isomers may exist as a result of different configurations

at C-8 and C-9. The differences in orientation give rise difference in the optical rotation of the alkaloids.

Stereochemical changes at C-8 have little effect on antimalarial activity. Quinine, quinidine, cinchonine and cinchonidine are active against *P. vivax*. Inversion at C-3 does not have important effect on activity. When the configuration at C-9 is changed to form *epi* isomers, the compounds become inactive. If the secondary alcohol group is modified by any way, the activity decreases markedly. The entire quinuclidine nucleus has been shown to be unnecessary for activity. However, α-aryl-β-tertiary amino alcohol system about the central C-9 is essential for activity.

After oral administration, the Cinchona alkaloids are absorbed readily and almost completely with peak blood-level concentrations occurring in 1 to 4 hours. When administration is stopped, blood levels fall off very quickly. A single dose of quinine is disposed of in about 24 hours. Therefore, repeated doses are to be administered. Soluble quinine salts produce higher initial blood levels than are obtained with the free base. In animals, quinine is concentrated mainly in pancreas, liver, spleen, lung and kidney. Small amounts of the drug are present in the blood, muscle or connective and nervous tissues. In liver oxidation of quinine forms a hydroxy group at 2'-position of the quinoline ring. The resulting degradation products, called carbostyrils, are not toxic, eliminated readily and possess lower antimalarial activity than the parent compound. The carbostyrils may be oxidized to dihydroxy compounds.

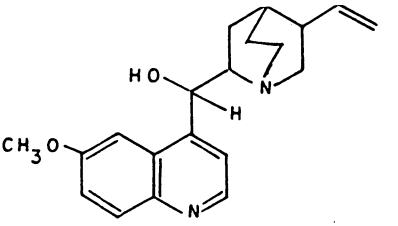
The long-term administration of quinine in normal therapeutic doses may give rise to a train of symptoms known as cinchonism, characterized by tinnitus, headache, nausea, and disturbed vision in its mild form. Other side effects are vomiting, abdominal pain, diarrhoea, vertigo, fever, pruritus, and rashes. Some patients are hypersensitive to quinine and even small doses may give rise to cinchonism together with other hypersensitivity reactions including angio-oedema and asthma. Thrombocytopenia, hypoprothrombinaemia, and haemolysis may occur and organulocytosis has been reported. The symptoms of overdosage include gastro-intestinal, central nervous system, and cardiovascular disturbances. Visual disturbances are normally reversible but may be permanent, and may rarely include sudden blindness. Severe poisoning can produce convulsions, coma, respiratory depression and death. Large doses of quinine can induce abortion, and congenital

malformations. However, quinine should not be withheld from pregnant women with life-threatening malaria.

In addition to antimalarial action, Cinchona alkaloids are antipyretic. It has been used for the treatment of night cramps or "restless legs". The antimalarial action of Cinchona alkaloids may be obtained by oral, intravenous or intramuscular administration. Intravenous injections may cause severe cardiovascular depression leading to generalized collapse.

QUININE

Nomenclature : 6'-Methoxycinchonan-9-ol.



Most of the quinine is obtained from the bark of *Cinchona ledgeriana* and its hybrids *(C. officinalis)* (Family Rubiaceae) which contains about 8% quinine. Cinchona trees grow wildly in South America and are cultivated in Java. The powdered bark is mixed with sodium hydroxide solution and slaked lime, and the liberated alkaloids are extracted with hot petroleum. The extract is separated and shaken with the required quantity of hot, very diluted sulphuric acid. The alkaloids pass into the aqueous layer as sulphates. The separated aqueous solution is cooled, and the sparingly soluble quinine sulphate crystallizes.

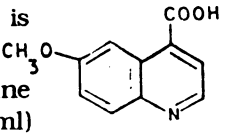
The pure quinine, m.p. 177°, crystallizes as colourless needles with 3 molecules of water of crystallization. It is efflorescent, losing 1 molecule of water at 20° under normal conditions and losing 2 molecules in a dry atmosphere.

Quinine occurs as a laevorotatory, odourless, white crystalline powder possessing an intensely bitter taste. One gram dissolves in 1900 ml water, 760 ml boiling water, 0.8 ml alcohol, 80 ml benzene, 1.2 ml chloroform, and 250 ml dry ether; almost insoluble in petroleum ether. It is stored in well-closed containers and protected from light.

It behaves as a diacidic base and forms salts with two equivalents of an acid. The salts are of two types. The acid or di-acid salts and the neutral salts. The neutral salts are formed by involvement of only tertiary nitrogen in the quinuclidine nucleus. When both basic nitrogens are involved, the acid salts are

formed. The quinoline nitrogen is very much less basic than the quinuclidine nitrogen. The mono-acid salts of quinine are generally much less soluble in water than the di-acid salts.

On oxidation with chromic acid quinine is decomposed to form quininic acid.



Quininic acid

Test for quinine : To about 20 ml of a quinine salt solution (1 in 1000), bromine water (0.25 ml) was added, shaken well and then dilute ammonia solution was mixed. A bright green colour is formed.

QUININE SULPHATE

Brand Names : Quininium sulphate; Basic Quinine sulphate; Chinnini sulphas; Chininum sulphuricum; Quinini sulphas.

Quinine sulphate is prepared from the crude bark by alkalinizing the powdered cinchona and extracting with a hot, high-boiling petroleum ether to remove the alkaloids. Careful addition of dilute sulphuric acid to the extract forms sulphates The quinine sulphate crystallizes first. The crude alkaloidal sulphate is decolourized and recrystallized to get commercial form. Commercial quinine contains 2-3% of hydroquinine and cinchonidine as impurities. Pure quinine sulphate is obtained by neutralizing quinine with dilute sulphuric acid and crystallizing the resulting sulphate from hot water which contains 8 moles of water, but it loses one mole very rapidly even at 20°. On exposure to air at ordinary temperature it gradually loses 5 more moles of water.

Quinine sulphate occurs as colourless or white, odourless, fine acicular crystals or crystalline powder, darkening on exposure to light. It is slightly soluble in water, alcohol, chloroform; practically insoluble in ether. It is stored in airtight containers and protected from light.

Uses : Quinine is an antimalarial drug rapidly acting blood schizontocide with activity against *Plasmodium falciparum, P. vivax, P. ovale* and *P. malariae.* It is used orally for the treatment of uncomplicated attacks of falciparum malaria due to chloroquine-resistant strains and for severe or complicated malaria.

Quinine possesses many toxic side effects. When it is used for a long time, its side effects are ringing in the ear, headache, nausea, disturbance of vision, tinnitus in addition to vomiting,

abdominal pain, diarrhoea, vertigo, fever, pruritus and rashes. In common these symptoms are known as cinchonism.

Official

Quinine Bisulphate, B.P., I.P.

Quinine Bisulphate Tablets, B.P., I.P.

Quinine Dihydrochloride, B.P., I.P.

Quinine Dihydrochloride Injection, B.P., I.P.

Quinine Ethyl Carbonate, I.P.

Quinine Hydrochloride, B.P., I.P.

Quinine Hydrochloride Tablets, I.P.

Quinine and Urethane Injection, I.P.

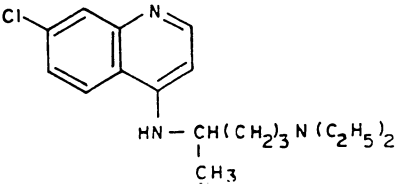
Quinine Sulphate, B.P., I.P.

Quinine Sulphate Tablets, B.P., I.P., U.S.P.

Quinine Sulphate Capsules, U.S.P.

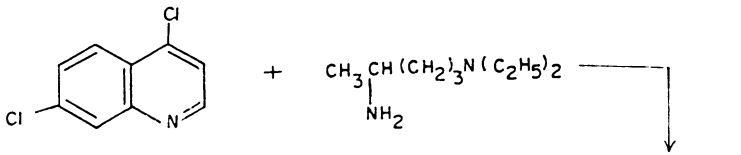
CHLOROQUINE

Nomenclature : N^{14} - (7-Chloro-4-quinolinyl) - N, N^{1} - diethyl-1, 4-pentanediamine; 7-Chloro - 4-(4'-diethylamino-1'-methylbutyl-amino) quinoline.



Brand Names : SN 7618, RP 3377; Aralen; Nivaquine B; Sanoquin; Artrichin; Bipiquin; Reumachlor; Bemaphate; Resoquine.

Chloroquine is prepared by cendensing 4,7-dichloroquinoline with 4-amino-1-diethylaminopentane in phenol solution.



4, 7-Dichloroquinoline

4-Amino-1-diethylaminopentane

Chloroquine

Chloroquine, m.p. 87°, occurs as a white or slightly yellow, odourless, crystalline powder; the taste is bitter. It is soluble in water (1 in 3); soluble in chloroform and ether.

CHLOROQUINE PHOSPHATE

Brand Names : Arechin; Avloclor; Imagon; Malaquin; Chingaminum; Chlorochinum diphosphoricum; Chloroquine diphosphate; Chloroquine phos; Chloroquini diphosphas; Chloroquini phosphas; Quingamine; SN-7618; Resochin; Silbesan, Tresochin.

Chloroquine Phosphate, m.p. 193-195°, is a white, odourless powder which slowly discolours on exposure to light. It is freely soluble in water (1 in 4); very slightly soluble in alcohol; practically insoluble in chloroform, ether and benzene.

CHLOROQUINE SULPHATE

Brand Names : Chloroquine sulph; Chloroquini sulfas; RP-3377; Nivaquine.

It is a white, odourless crystalline powder; soluble in water (1 in 3); practically insoluble in alcohol, sparingly soluble in chloroform and ether.

Uses : Chloroquine is used to cure malaria. It may be given as the phosphate, sulphate or hydrochloride.

Side effects include headache, gastro-intestinal disturbances like nausea, vomiting and diarrhoea, pruritus and skin eruptions.

Official

Chloroquine Phosphate, B.P., I.P.

Chloroquine Phosphate Injection, B.P.

Chloroquine Phosphate Tablets, B.P., U.S.P.

Chloroquine Sulphate, B.P., I.P.

Chloroquine Sulphate Injection/Tablets, B.P., I.P.

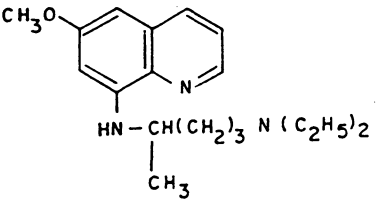
Hydroxychloroquine. Sulphate, B.P.

Hydroxychloroquine Tablets, B.P.

Chloroquine Hydrochloride Injection, U.S.P.

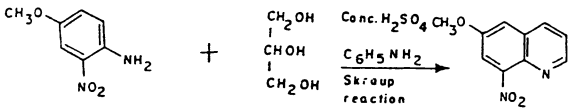
PAMAQUINE

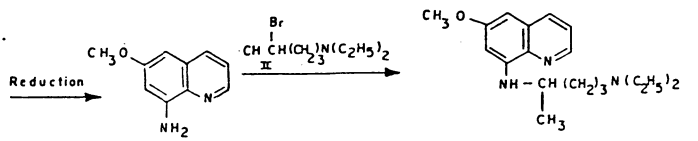
Nomenclature : N^1, N^1-Diethyl-N^4-(6-methoxy-8-quinolyl)-1, 4-pentanediamine; 8-[4-(Diethylamino)-1-methylbutyl}amino]-6-methoxyquinoline.



Brand Names : Plasmochin; Aminoquin; Praequine; Beprochine; Gamefar; Quipenyl; Plasmoquine.

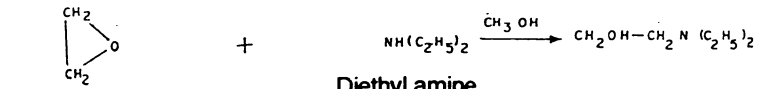
It was the first successful 8-aminoquinoline derivative which was introduced by Germans in 1826. It may be synthesized by condensing 6-methoxy-8-aminoquinoline (I) with 1-diethylamino-4-bromopentane (II).





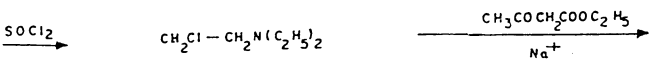
Pamaquine

In a modified process pamaquine is synthesized by condensing ketal with 6-methoxy-8-aminoquinoline :

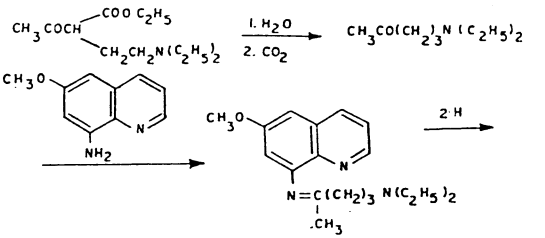


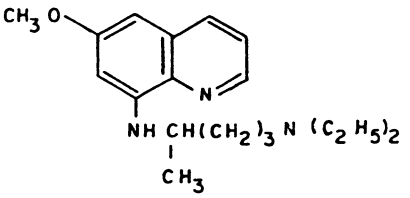
Ethylene oxide

Diethyl amine



Chloroethyl dimethyl amine





Pamaquine

Pamaquine occurs as dark yellow oil.

Pamaquine phosphate (Brand Names : Primachin phosphate; Primaquini diphosphas; Primaquinium phosphate; SN-13, 272) is an orange-red, odourless, crystalline powder. It is soluble in water (1 in 16); practically insoluble in chloroform and ether. It is protected from light.

Uses : Primaquine is an antimalarial effective against exoerythrocytic forms of the plasmodia parasite, and is a gametocyticide.

Primaquine is generally well tolerated at normal therapeutic doses. Adverse effects include abdominal cramps, gastric distress, nausea and vomiting, headache, visual disturbance, and pruritus.

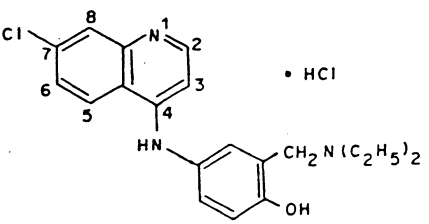
Official

Primaquine Phosphate Tablets, U.S.P.

AMODIAQUINE

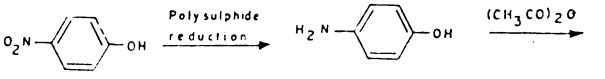
Nomenclature : 4 [(7-Chloro-4-quinolinyl) amino]-2-[(diethylamino) methyl] phenol; 4-[(7-Chloro-4-quinolyl) - amino]-α-(die-thylamino)-o-cresol; 7-Chloro-4-(3-diethylaminomethyl-4-hydroxyanilino) quinoline; 7-Chloro-4-(3-diethylamino-methyl-4-hydroxyphenylamino) quinoline; 4-(3'-Diethylamino-methyl-4-hydroxyanilino)-7-chloroquinoline.

Brand Names : CAMAQI; Camoquin; Flavoquine; Miaquin; Amodiachin hydrochloride; Amodiaquini hydrochloridum, SN-10, 751.

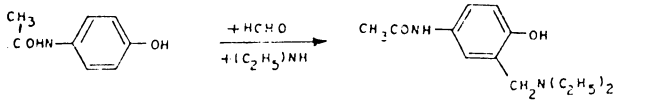


Amodiaquinone contains a diethylamino-substituted amino-group in position 4 of quinoline and a chlorine atom

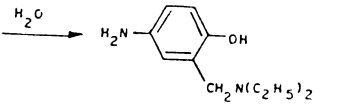
in position 7; the substituent attached at C-4 is aromatic and possesses a phenolic group. For its preparation, 4-amino-2-(diethylaminomethyl) phenol is synthesized from p-nitrophenol which is then condensed with formaldehyde and diethylamine related to the Mannich reaction, followed by removal of the protective group by hydrolysis.



p-Nitrophenol p-Aminophenol

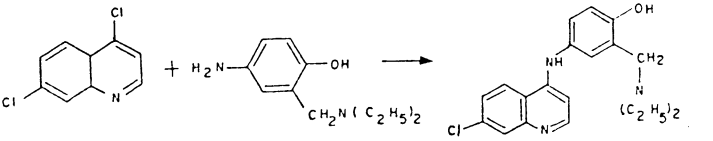


4-Acetamidophenol 4-Acetylamino-2-(diethylamino-methyl) phenol



4-Amino-2-(diethylaminomethyl) phenol

This 4-amino-2-(diethylaminomethyl) phenol condenses with 4, 7-dichloroquinoline to yield amodiaquine.



4,7-Dichloroquinoline Amodiaquine

Amodiaquine, m.p. 208°, is a crystalline base which is used medicinally in the form of its dihydrochloride. It is stored in airtight containers.

AMODIAQUINE HYDROCHLORIDE

Brand Names : CAMAQI; Camoquin; Flavoquine; Miaquine.

Amodiaquine hydrochloride occurs as a yellow, odourless bitter crystalline powder, m.p. 150-160°. It is soluble in water; sparingly soluble in alcohol; very slightly soluble in benzene, chloroform and ether. A 2% aqueous solution has a pH of 3.6 to 4.6. It is stored in airtight containers.

Uses : Amodiaquine hydrochloride is an antimalarial drug which has an action similar to that of chloroquine. Amodiaquine is highly effective against *Plasmodium vivax* and *P. falciparum* infections, being three to four times as active as quinine. However, it has no effect on *P. falciparum*.

In therapeutic doses amodiaquine hydrochloride can give rise to side-effects similar to those of chloroquine.

Official

Amodiaquine Hydrochloride, B.P., I.P.

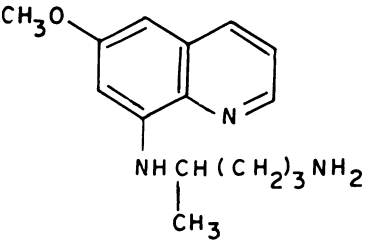
Amodiaquine Tablets, B.P., I.P.

Amodiaquine Hydrochloride Tablets, U.S.P.

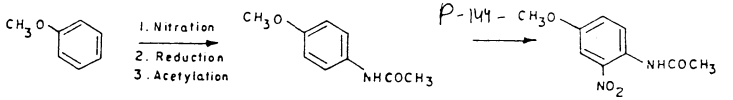
PRIMAQUINE

Nomenclature : N^{14}-(6-Methoxy-8-quinolinyl)-1, 4-pentanediamine; 8-(4-Amino-1-methylbutylamino)—6-methoxyquinoline.

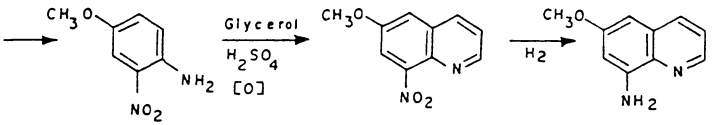
Brand Name : SN 13272.



Primaquine is a quinolinic antimalarial which retains the 6-methoxyl group of the quinine model. The basic side chain is attached at C-8 in place of C-4 position. The starting compound for the preparation of primaquine is 4-amino-3-nitroanisole, which is prepared from anisole by normal synthetic reactions. A Skraup reaction converts this compound into 6-methoxy-8-nitroquinoline by heating a mixture of the aniline, glycerol, sulphuric acid and an oxidizing agent (usually nitrobenzene or arsenic acid). The reduction of 6-methoxy-8-nitroquinoline yields 8-amino-6-methoxyquinoline.



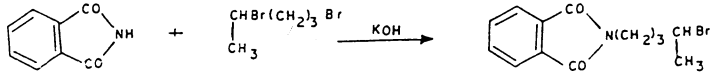
Anisole 4-Acetylamino anisole 4-Acetylamino-3-nitroanisole



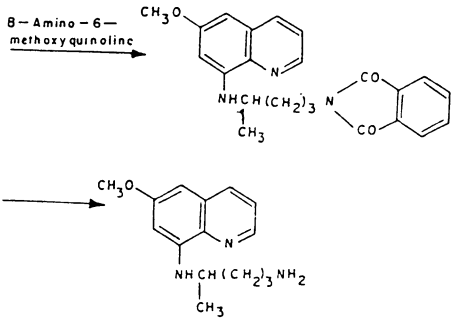
4-Amino-3-nitroanisole

8-Amino-6-methoxyquinoline

The side chain is introduced by using the Gabriel primary amine synthesis. 4-Bromo-1-phthalimidopentane is prepared by reacting 1,4-dibromopentane and phthalimide which is condensed with the aminoquinoline. The phthalyl group is then removed either by direct hydrolysis or by forming an intermediate compound with hydrazine which is decomposed by dilute acids:



Phthalmide 1,4-Dibromopentane 4-Bromo-1-phthalimidopentane



Primaquine

Primaquine is a viscous liquid, b.p. 175-179°; soluble in ether; protected from light. Its diphosphate salt is used as antimalarial drug.

PRIMAQUINE PHOSPHATE

Brand Names : Primachin phosphate; Primaquini diphosphas; Primaquinium phosphate; SN-13, 272.

It is an orange-red, odourless, crystalline, bitter powder, m.p. 197-198°. It is moderately soluble in water, insoluble in chloroform and ether. The aqueous solutions are acidic to litmus. The compound is protected from light.

Uses : Primaquine is antimalarial and effective against plasmodia parasite.

Primaquine is generally well tolerated at normal therapeutic doses. Adverse effects include abdominal cramps, gastric distress, nausea and vomiting, headache, visual disturbances, and pruritus.

Official

Primaquine Phsophate, B.P.

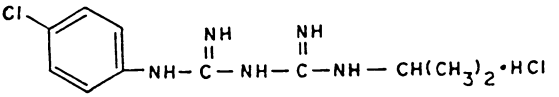
Primaquine Tablets, B.P.

Primaquine Phosphate Tablets, U.S.P.

PROGUANIL HYDROCHLORIDE

Nomenclature : 1-(4-Chlorophenyl)-5-isopropylbiguanide hydrochloride.

Brand Names : Bigumalum; Chloriguane hydrochloride; Chloroguanide hydrochloride; Proguanide hydrochloride; Proguanili hydrochloridum; RP-3359; SN-12,837; Guantol; Paludrine.



Proguanil hydrochloride is a white, odourless, bitter, crystalline powder that is slightly soluble in water, more soluble in hot water, soluble in alcohol (1 in 40); practically insoluble in chloroform and ether. It is stable in air but slowly darkens on exposure to light. Therefore, it is protected from light.

Uses : Proguanil is used as an antimalarial drug and to reduce transmission of infection. It is active against pre-erythrocytic forms and is a slow blood schizontocide.

Proguanil hydrochloride is well tolerated after usual doses; after large doses vomiting, epigastric discomfort, haematuria, and renal irritation may occur.

Official

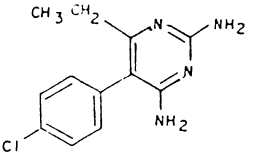
Proguanil Hydrochloride, B.P., I.P.

Proguanil Tablets, B.P., I.P.

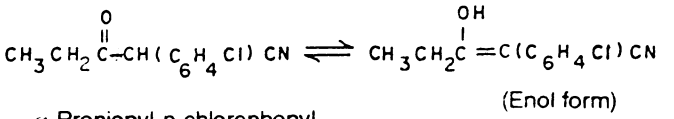
PYRIMETHAMINE

Nomenclature : 5-(4-Chlorophenyl)-6-ethyl-2,4-pyrimidine diamine; 2, 4-Diamino-5-(p-chlorophenyl)-6-ethylpyrimidine.

Brand Names : RP 4753; Daraprim; Chloridin; Darapram, Malocide; Tindurin; BW-50-63; Pirimetamina.

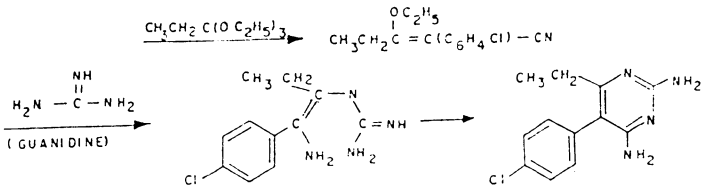


Pyrimethamine is a fully substituted pyrimidine. It can be prepared from open-chain compounds by cyclization reactions. In one method, it is synthesized from α-propionyl-p-chlorophenylacetonitrile, which is converted into the ethyl ether by the action of ethyl orthopropionate. This ether reacts with guanidine to give a product which cyclizes to form pyrimethamine.



α-Propionyl-p-chlorophenyl-acetonitrile (keto form)

(Enol form)



Pyrimethamine is a white, odourless, crystalline powder, m.p. 240-242°. It is practically insoluble in water, slightly soluble in ethanol and in dilute hydrochloric acid; soluble in boiling ethanol; very sparingly soluble in propylene glycol and dimethylacetamide at 70°; stored in airtight containers and protected from light. It is slowly but completely absorbed from the gastro-intestinal tract. It is present in the liver, lungs, kidney and spleen and is excreted through the urine.

Uses : Pyrimethamine is an antimalarial drug which is effective erythrocytic schizontocide against all human malaria especially in most infections due to *P. vivax* and *P. falciparum.*

Pyrimethamine with sulphadoxine is usually well-tolerated but severe and sometimes fatal reactions have been reported. Severe cutaneous reactions include erythema, multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

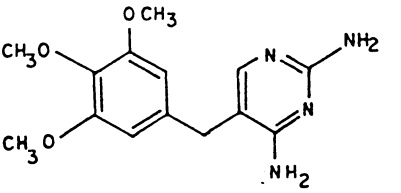
Official

Pyrimethamine, B.P.
Pyrimethamine Tablets, B.P., U.S.P.

TRIMETHOPRIM

Nomenclature : 5-[(3, 4, 5-Trimethoxyphenyl) methyl]-2,4-pyrimidinediamine; 2,4-Diamino-5-(3, 4, 5-trimethoxybenzyl) pyrimidine.

Brand Names : Monotrim; Proloprim; Syraprim; Tiempe; Trimanyl; Trimopan; Trimpex; Wellcoprim; BW-56-72; NSC-106568; Trimethoprimum; Trimethoxyprim.



Trimethoprim is prepared from gaunidine and β-ethoxy- 3, 4,5-trimethoxybenzyl benzalnitrile. It occurs as white to cream, odourless, bitter crystalline powder, m.p. 199-203°. It is very slightly soluble in water; slightly soluble in alcohol, methanol and acetone; soluble in acetone (1 in 55) and benzyl alcohol; practically insoluble in ether and carbon tetrachloride. It is stored in airtight containers and protected from light.

Uses : Trimethoprim is an antibactrial agent used for the treatment of infections due to sensitive organisms like infections of the urinary and respiratory tracts. It has been used in conjunction with sulphonamides in the treatment of chloroquine-resistant malaria but has not achieved wide acceptance. Side effects include pruritus, skin rash, fever, nausea, vomiting, and sore mouth.

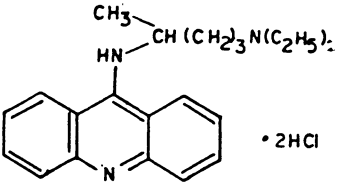
Official

Trimethoprim, B.P., I.P.

QUINACRINE OR MEPACRINE HYDROCHLORIDE

Nomenclature : N^{14}-(6-Chloro-2-methoxy-9-acridinyl)-N^1, N^1-diethyl-1,4-pentanediamine dihydrochloride; 6-Chloro-9[{4- (diethylamino)-1-methlbutyl} amino]-2-methoxyacridine dihydrochloride.

Brand Names : Atabrine 2HCl; Atebrine 2 HCl; RP 866; SN 390; Cinacrine 2HCl; Erion; Acriquine; Acrichine; Palacrin; Metoquine, Italchin.



Quinacrine hydrochloride occurs as a yellow, bitter crystalline powder. It is sparingly soluble in water (1:35); more soluble in hot water; slightly soluble in alcohol and insoluble in ether, benzene, and acetone; pH of a 1% aqueous solution is about 4.5. The yellow colour that quinacrine imparts to the urine and the skin is temporary and should not be mistaken for jaundice. It is stored in airtight containers and protected from light.

Uses : Quinacrine was formerly used for the suppression and treatment of malaria but it has been replaced by chloroquine and other antimalarials. It is used in the treatment of giardiasis, for the expulsion of tapeworms and neoplastic effusions in the pleura or peritoneum. Adverse effects include dizziness, headache and mild gastro-intestinal disturbances.

Official

Quinacrine Hydrochloride Tablets, U.S.P.

12

TRANQUILLIZERS

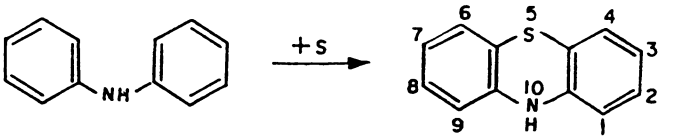
Some drugs are used to treat psychiatric disorders, i.e. abnormalities of mental function. These drugs are known as psychotropic drugs or psychoactive drugs. The drugs which induces a mental state free from agitation and anxiety and renders the patient calm and peaceful are termed as tranquillizers.

Anti-psychotic drugs are used to treat psychoses like schizophrenia, mania, senile dementia and behaviour disorders in children. Tranquillizing agents exert a unique type of selective central nervous depression. They act differently from the barbiturates and other sedatives which act by producing a general central nervous system depression. They give strong sedation without producing sleep and produce a state of indifference and disinterest. They are effective in reducing excitation, agitation, aggressiveness and impulsiveness which are not controlled by the ordinary sedative-hypnotics and central relaxants.

The Rauwolfia alkaloids, benzoquinone derivatives (benzquinamide), phenothiazine derivatives (chlorpromazine, prochlorperazine, piperacetazine, etc.), diphenylmethane derivatives (hydroxyzine, benactyzine) and some other compounds (chlorprothixene, thiothixene, haloperidol, etc.) are employed as tranquillizing agents.

Phenothiazine Derivatives

Phenothiazine (dibenz-1, 4-thiazine) is a heterocyclic compound prepared by cyclization of diphenylamine with sulphur in the presence of iodine or aluminium chloride :



Phenothiazine is a yellow, crystalline compound in which the basic character of the nitrogen atom is so minimized that it forms no stable salts with acids. It is used in veterinary practice as an anthelmintic and certain of its derivatives, usually prepared by replacement of proton of nitrogen atom, are of medicinal importance.

The nature and the position of substituents on the phenothiazine nucleus strongly effect activity. The activity is increased by replacing the hydrogen of C-2 by chlorine (chlorpromazine), trifluoromethyl (triflupromazine) or a dimethylsulphonamide group (thioperazine). Tranquillizing activity does not change due to substitution on C-2 such as thioalkyl (thioridazine, thioethylperazine) and octyl groups (butaperazine, acetophenazine, carphenazine). Tranquillizing activity is lost due to a ring substituent in positions 1, 3, 4 or simultaneous substitution in both aromatic rings. Optimum tranquillizing activity is observed with the three-carbon side chain connecting the nitrogen of the phenothiazine ring and the more basic side-chain nitrogen. Compounds containing two-carbon side chains still possess a moderate central depressant activity, but these compounds have antihistaminic and antiparkinsonism effects. If length and polarity of the side chain is changed, tranquillizing effect is lost.

If a small group like methyl is substituted at the β-position of the side chain, tranquillizing activity is reduced while antihistaminic and antipruritic effects are enhanced. Substitution on the side chain with a large or polar groups such as phenyl, dimethylamino or hydroxyl results in loss of tranquillizing activity. The laevo isomer of the side chain is more active than the dextro isomer for β-methyl analogues. Substitution of the piperazine group (prochlorperazine, trifluoperazine) in place of the terminal dimethylamino moiety on the side chain increases potency. Substitution of $-CH_2$ CH_2OH for the terminal methyl group on piperazine (perphenazine, fluphenazine) increases the potency. Dimethylamino compounds produce a parkinson-like syndrome (tremors, rigidity, salivation) while piperazine derivatives produce dyskinetic reactions. Dimethylamino and alkylpiperidyl-type derivatives result in skin and liver disorders and blood dyscrasias. Quaternary derivatives of the side chain nitrogen do

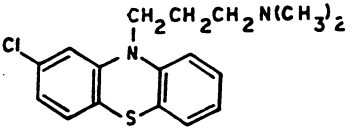
not dissolve in lipids and their penetration in the central nervous system is lost.

The phenothiazines produce a lesser degree of central depression than the barbiturates or benzodiazepines. Adverse effects of phenothiazine therapy may include as dry mouth, constipation, urinary retention, mydriasis, agitation, tachycardia, electrocardiographic changes, postural hypotension, miosis, blurred vision, allergic reactions, jaundice, etc.

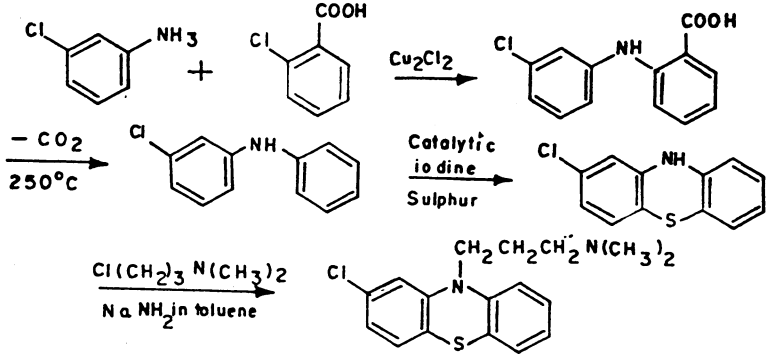
CHLORPROMAZINE

Nomenclature : 2-Chloro-N, N-dimethyl-10H-phenothiazine-10-propanamine; 2-Chloro-10-(3-dimethylaminopropyl) phenothiazine.

Brand Names : 2601 A; HL 5746; RP 4560; SKF 2601-A; Chlorderazin; Chlorpromados; Contomin; Esmind; Fenactil; Novomazina; Promactil; Prozil; Plegomazin; Sanopron; Aminazine; Ampliactil, Amplictil, Promazil, Chlor-Promanyl; Proma; Elmarin; Wintermin.



Chlorpromazine is a derivative of 2-chlorophenothiazine which may be synthesized by the cyclization of 3-chlorodiphenylamine with sulphur in the presence of a catalytic quantity of iodine to yield phenothiazine system. The attachment of the side-chain amino group is carried out as the chloride in the presence of sodamide:



Chlorpromazine is a white to creamy-white powder or waxy solid with amine odour; m.p. 56-58°. It darkens on prolonged exposure to light. It is stored in airtight containers and protected from light.

CHLORPROMAZINE HYDROCHLORIDE

Brand Names : Hebanil; Hibanil; Hibernal; Klorpromex; Largactil; Largaktyl; Megaphen; Promacid; Chloractil; Chlorazin; Sonazine; Torazine; Torazina; Marazine; Propaphenin; Taroctyl.

It is an odourless, white or creamy-white crystalline powder, m.p. 179-180°. It decomposes on exposure to air and light becoming yellow, pink, and finally violet. It is soluble in water (1 in 0.4), alcohol (1 in 1.3) and chloroform (1 in 1); practically insoluble in ether and benzene; slightly acidic to litmus; stored in airtight containers and protected from light.

Uses : Chlorpromazine has sedative, anti-emetic, antipruritic, serotonin-blocking and weak antihistaminic properties. It is used in the management of psychotic conditions, to control hyperkinetic states and aggression. It controls excitement and agitation. It is anti-emetic and is used to control the nausea and vomiting.

The phenothiazines and related neuroleptic produce a lesser degree of central depression than the barbiturates or benzodiazepines. The adverse effects of phenothiazine include dryness of mouth, constipation, urinary retention and mydriasis.

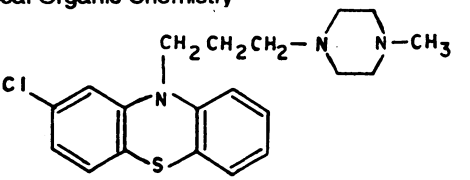
Official

Chlorpromazine, B.P.
Chlorpromazine Suppositories, B.P. U.S.P.
Chlorpromazine Hydrochloride, B.P., I.P.
Chlorpromazine Elixir, B.P.
Chlorpromazine Injection, B.P., I.P.
Chlorpromazine Tablets, B.P., I.P.
Chlorpromazine Hydrochloride Injection/Syrup/Tablets, U.S.P.

PROCHLORPERAZINE

Nomenclature : 2-Chloro-10 -[3-(4-methyl-1-piperazinyl) propyl]-10H-phenothiazine; 3-Chloro-10-[3-(4-methyl-1-piperazinyl] phenothiazine.

Brand Names : Bayer A 173; RP 6140; SKF 4657; Nipodal; Tementil; Kronocin; Capazine; Emelent; Meterazine.



Prochlorperazine is a clear, pale yellow, viscous liquid, sensitive to light. It is very soluble in water; freely soluble in alcohol, chloroform, and in ether. It has a piperazine side-chain.

Prochlorperazine dimaleate (Brand Names : Compazine; Emetiral; Nibromin A; Stemetil), m.p. 228°, is a white or pale yellow, almost odourless, crystalline powder; very slightly soluble in water and alcohol; practically insoluble in chloroform and ether; stored in airtight containers and protected from light.

Uses : Prochlorperazine has uses, actions and adverse effects similar to those of chlorpromazine.

Official

Prochlorperazine Maleate, B.P.

Prochlorperazine Tablets, B.P.

Prochlorperazine Mesylate, B.P.

Prochlorperazine Injection, B.P.

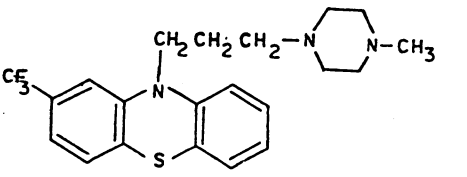
Prochlorperazine Suppositories, U.S.P.

Prochlorperazine Edisylate Injection/Oral Solution/Syrup, U.S.P.

TRIFLUOPERAZINE

Nomenclature : 10-[3-(4-methylpiperazin-1-yl)-propyl]-2-(trifluoromethyl)-10H-phenothiazine; 2-Trifluoromethyl-10-[3¹-(1-methyl-4-piperazinyl) propyl] phenothiazine.

Trifluoperazine has the same side-chain at position 10 as prochlorperazine. It is synthesized by condensation of the same chloro-amine with 2-trifluoromethylphenothiazine which is prepared by cyclization of 3-trifluoromethyldiphenylamine with sulphur. It has a piperazine side-chain.



Free base-has b.p. 202-210.

Trifluoperazine hydrochloride (Brand Names : Triftazin,

Triphthazine; Iatroneural; Jatroneural; Eskazinyl; Eskazine; Modalina; Stelazine; Terfluzine; Triflurin). It is a cream coloured, fine, odourless, slightly hygroscopic, crystalline powder, m.p. 242-243°. It is freely soluble in water; insoluble in dilute base, ether and benzene; stroed in airtight containers and protected from light.

Uses : Trifluoperazine is a phenothiazine with actions, uses and adverse effects similar to those of chlorpromazine.

Official

Trifluoperazine Hydrochloride Injection/Syrup/Tablets, U.S.P.

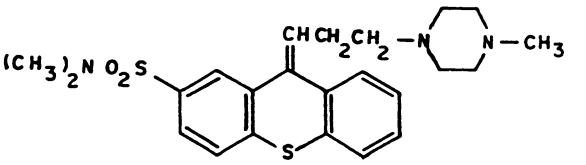
Trifluoperazine Hydrochloride, B.P.

Trifluoperazine Tablets, B.P.

THIOTHIXENE

Nomenclature : N, N-Dimethyl-9-[3-(4-methyl-1-piperazinyl) propylidene] thioxanthene-2-sulphonamide; *cis*-9-[3-(4-Methyl-1-piperazinyl) propylidene]-2-(dimethylsulphonamido) thioxanthene.

Brand Names : Tiotixene; Navane; Navaron (Obsolete); Orbinamon.



Thiothixene is a white to tan-coloured, almost odourless crystalline powder, *cis*-isomer m.p. 147-149°; *trans*-isomer, m.p. 123-125°; *cis-trans*-isomer mixture, m.p. 114-118°. It is practically insoluble in water; soluble in dehydrated alcohol(1 in 110), chloroform (1 in 2) and ether (1 in 120); slightly soluble in acetone and in methyl alcohol; stored in airtight containers and protected from light.

Thiothixene hydrochloride (Brand Names : CP-12252-1; Tiotixene hydrochloride) occurs as white crystalline powder with a slight odour; soluble in water (1 in 8), alcohol and chloroform; practically insoluble in acetone and ether; stored in airtight containers and protected from light.

Uses : Thiothixene is a thioxanthene with general properties similar to those of chlorpromazine.

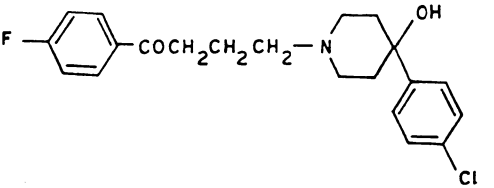
Official

Thiothixene Hydrochloride Injection/Oral Suspension, U.S.P.

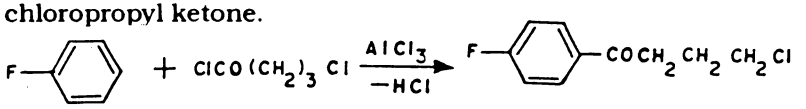
HALOPERIDOL

Nomenclature : 4-[4-(4-Chlorophenyl)-4-hydroxy-1-piperidinyl]-1-(4-fluorophenyl)-1-butanone; 4-[4-(p-Chlorophenyl)-4-hydroxypipieridino]-4'-fluorobutyrophenone.

Brand Names : R 1625; Aloperidine; Brotopon; Einalon S; Eukystol; Haladol; Halosten; Keselan: Linton, Peluces; Serenace; Serenase.

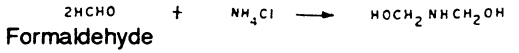


For the preparation of haloperidol fluorobenzene is reacted with 4-chlorobutanoyl chloride in the presence of fused aluminium chloride (Friedel-Crafts reaction) to form p-fluorophenyl 3-chloropropyl ketone.

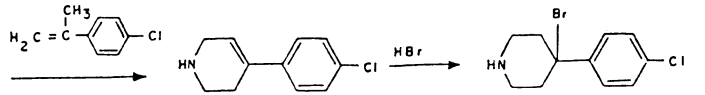


Fluorobenzene 4-Chlorobutanoyl chloride p-Fluorophenyl 3-chlorobutyl ketone

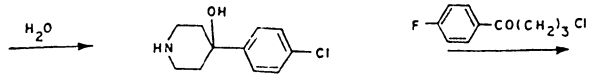
In the next step 4-(*p*-chlorophenyl)-4-hydroxypiperidine is synthesized by treating p-chloro-α-methylstyrene with formaldehyde and ammonium chloride (Mannich reaction), which is then condensed with *p*-fluorophenyl 3-chlorobutyl ketone.



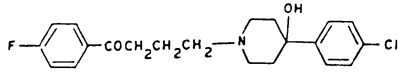
Formaldehyde



p-Chloro-α-methylstyrene



4-(p-Chlorophenyl)-4-hydroxypiperidine



Haloperidol

Haloperidol, m.p. 148-150°, is a white to faintly yellowish, oldourless, amorphous or microcrystalline powder. It is practically insoluble in water; soluble in alcohol (1 in 50), chloroform (1 in 20) and slightly soluble in ether; stored in airtight containers and protected from light.

Uses : Haloperidol is a butyrophenone with actions and uses similar to those of the phenothiazine, chlorpromazine. It is a major tranquillizer used in the management of the agitated states, mania, aggressiveness and hallucinations. It is used for its sedative and potent anti-emetic effects.

The adverse effects of haloperidol resemble to those of phenothiazines with a piperazine side chain. The extrapyramidal reactions, parkinson-like symptoms, impaired liver function and blood dyscrasias are observed as side effects.

Official

Haloperidol, B.P.

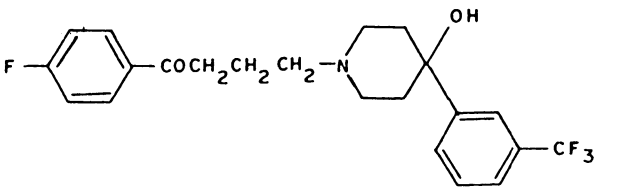
Haloperidol Injection/Tablets, B.P.

Haloperidol Oral Solution/Injection, U.S.P.

TRIPERIDOL

Nomenclature : 4'-Fluoro-4-[4-hydroxy-4(α,α,α — trifluoro-*m*-tolyl) piperidino] butyrophenone; *p*-Fluoro-4-[4 -hydroxy-4'(3"-trifluoromethyl) phenyl] piperidinobutyrophenone.

Brand Names : Trifluperidol hydrochloride; Psicoperidol hydrochloride; Psychoperidol hydrochloride; R 2498.



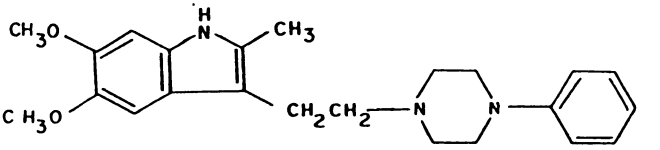
Triperidol, m.p. 200-202°, a butyrophenone, is a crystalline substance.

Uses : Triperidol is a sedative and antipsychotic agent. It controls excitement, agitation, and other psychomotor disturbances. It is used to treat mania and schizophrenia.

OXYPERTINE

Nomenclature : 5,6-Dimethoxy-2-methyl-3-[2-(4-phenyl-1-piperazinyl) ethyl]-1H-indole; 1-[2-(5, 6-Dimethoxy-2-methyl-3-indolyl) ethyl]-4- phenylpiperazine.

Brand Names : Win 18501-2; Equipertine; Forit.

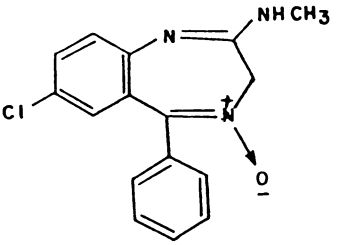


Uses : Oxypertine is a neuroleptic used in the treatment of psychoses. Adverse effects are the same as for phenothiazines.

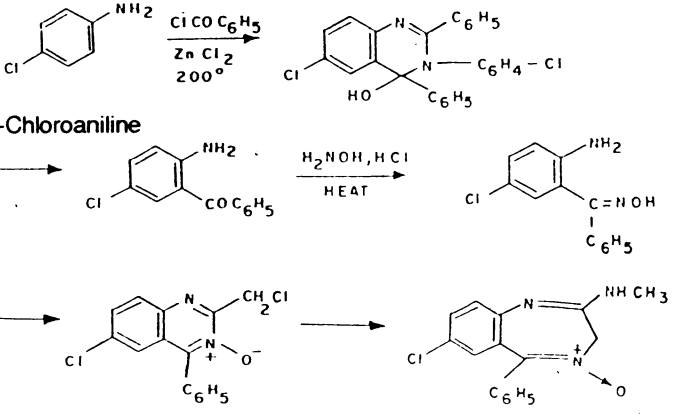
CHLORDIAZEPOXIDE

Nomenclature : 7-Chloro-N-methyl-5-phenyl-3H-1,4-benzodiazepin-2-amine 4-oxide; 7-Chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine 4-oxide.

Brand Names : Metaminodiazepoxide; Methaminodiazepoxide; Libritabs; Menrium; Mesural; Multum; O.C.M.; Risolid; Silibrin; Sonimen; Tropium; Zeisin; Zetran.



Chlordiazepoxide is a derivative of 1, 4-benzodiazepine. It was synthesized by Sternbach and co-workers from *p*-chloroaniline:



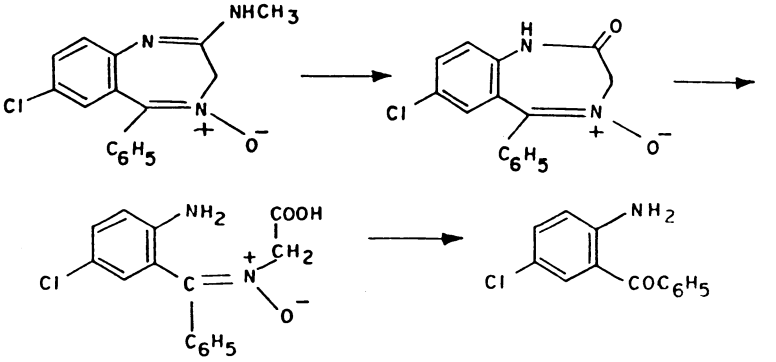
p-Chloroaniline

Chlordiazepoxide

Chlordiazepoxide is a light yellow compound, m.p. 236-237°, used as hydrochloride; stored in airtight containers and protected from light.

Chlordiazepoxide hydrochloride (Brand Names : Ansiacal; Bent; Benzodiapin; Calmoden; Cebrum; Chlordiazachel; Corax, Diazachel, Droxol; Elenium, Equibral; J-Liberty; Kalmocaps; Labican, Lentoran, Librium, Mildmen; Napton; Novosed; Psichial; Psicosan; Psicoterina; Reliberan; Sophiamin; Seren vita; SK-Lygen; Tensinyl; Timosin; Trakipeal, Viansin; Viopsicol).

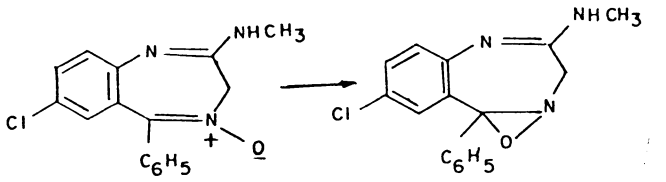
Chlordiazepoxide hydrochloride is a colourless crystalline substance, light sensitive and highly soluble in water but unstable in aqueous solution due to hydrolysis to the lactam, an amino acid and finally 2-amino-5-chlorobenzophenone.



2-Amino-5-chlorobenzophenone

These are the major metabolites of chlordiazepoxide, all primarily excreted in the urine. The decomposion products are detected on silica gel thin-layer chromatography.

On exposure to light, chlordiazepoxide hydrochloride undergoes the nitrone rearrangement to give a 4, 5-epoxide :



4,5-Epoxide

Uses : Chlordiazepoxide has psychosedative properties used as sedative and minor tranquillizer. Its abuse may lead to habituation or addiction.

Official

Chlordiazepoxide, B.P.

Chlordiazepoxide Tablets/Capsules, B.P.,U.S.P.

Chlordiazepoxide Hydrochloride, B.P.

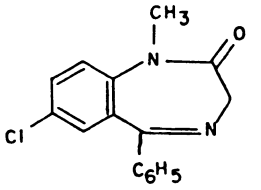
Chloridiazepoxide Hydrochloride Capsules, U.S.P.

Sterile Chloradizepoxide Hydrochloride, U.S.P.

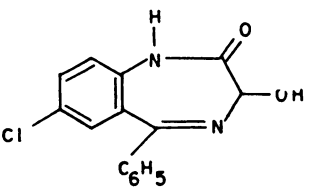
DIAZEPAM

Nomenclature : 7-Chloro-1, 3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one; 7-Chloro-1-methyl-5-phenyl-3H-1, 4-benzodiazepin-2 (1H)-one.

Brand Names : Diacepin; La III; Ro 5-2807; Wy 3467; NSC-77518; Aiupram; Ansiolin; Apaurin; Apozepam; Atensine; Atilen; Bialzepam; Calmpose; Ceregulart; Diazemuls; Dipam; Eridan; Evacalm; Faustan; Lembrol; Levium; Morosan; Neurolytril; Noan; Pacitran; Paxate; Paxel; Relanium; Sedapam; Seduxen; Setonil; Stesolid; Stesolin; Tranimul; Tranquase; Tranquo-Tablinen; Valium; Valrelease; Vival; Vivol.



Diazepam



Oxazepam

Diazepam is a white or yellow, odourless, crystalline powder, m.p. 125-126°. It is slightly soluble in water; soluble in alcohol and freely soluble in chloroform; stored in airtight containers and protected from light. Diazepam is metabolized in the liver, one of the metabolic compound is the 3-hydroxy derivative, known as oxazepam, which is also a sedative and muscle relaxant.

Uses : Diazepam is a benzodiazepine having anticonvulsant, anxiolytic, sedative, muscle relaxant, and amnestic properties. It is used in the treatment of anxiety and tension states, as sedative and premedicant, in the control of muscle spasm, as in tetanus and in the management of alcohol withdrawal symptoms. It is given in cases of minor surgery, endoscopy, in dentistry to calm the patient.

Its prolonged use may lead to habituation or addiction.

Official

Diazepam, B.P.

Diazepam Capsules, B.P., U.S.P.

Diazepam Injection, B.P.

Diazepam Tablets, B.P., U.S.P.

Diazepam Extended-release Capsules, U.S.P.

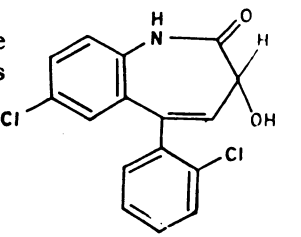
LORAZEPAM

Nomenclature : 7-Chloro-5-(2-chlorophenyl)-1,3-dihydro-3-hydroxy-2H-1,4-benzodiazepin-2-one.

Brand Names : Wy-4036; Almazine; Ativan; Emotival; Lorax; Lorsilan; Psicopax; Tavor; Temesta; Wypax.

Lorazepam is a white, odourless, crystalline powder, m.p. 166-168°. It is practically insoluble in water; sparingly soluble in alcohol; slightly soluble in chloroform; stored in airtight containers and protected from light.

Uses : Lorazepam is a benzodiazepine with actions, adverse effects and uses similar to those of diazepam.



Official

Lorazepam, B.P.

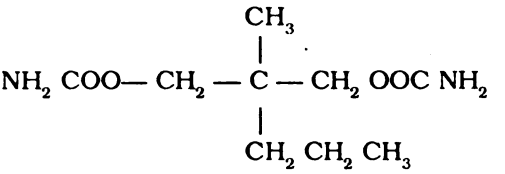
Lorazepam Injection/Tablets, U.S.P.

MEPROBAMATE

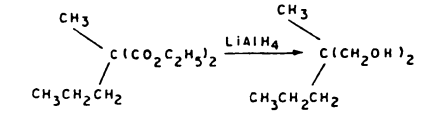
Nomenclature : 2-Methyl-2-propyl-1, 3-propanediol dicarbamate; Carbamic acid 2-methyl-2-propyltrimethylene ester.

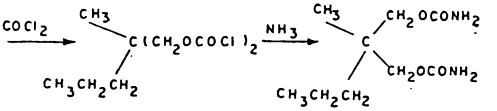
Brand Names : Procalmadiol; Procalmidol; Amosene; Anastress; Andaxin; Aneural; Apascil; Arcoban; Artolon; Atraxin; Ayeramate; Bamo 400; Biomate; Calmax; Calmiren; Cap-O-Tran; Cirpon; Crestanil; Cyrpon; Ecuanil; Equanil; Equinil; Fas-Cile 200; Gadexyl; Harmonin; Hartol; Holbamate; Kesso-Bamate; Klort; Larten; Lepetown; Libiolan; Mar-Bate; Mepantin; Mepavlon; Meposed;Meprin; Meprindon; Meproban; Meprocompren; Meprol; Meprosin; Meprospan; Meprotabs; Meprotan; Meprotil; Meptran; Mesmar; Miltaun; Miltown; Morbam; My-trans; Nervonus; Oasil;

Panediol; Perequil; Perquietil; Pertranquil; Placidon; Placitate; Probamyl; Promate; Protran; Quaname; Quanil; Reostral; Restenil; Robamate; Sedazil; Seril; Setran; Sowell; Tamate; Trankvilan; Tranlisant; Tranquilan; Tranquilax; Tranquiline; Urbil; Urbilat; Vio-Bamae.



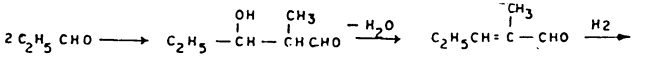
Meprobamate is the dicarbmate of 2-methyl-2-n-propyl-1, 3-propanediol. It may be synthesized from diethyl methyl-n-propylmalonate as :

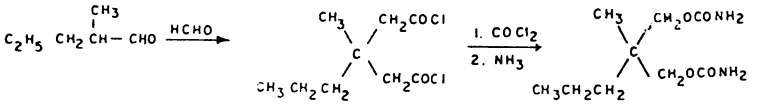




Meprobamate

In an another procedure meprobamate may be synthesized from propionaldehyde :





Meprobamate

Meprobamate is a white, odourless crystalline powder, m.p. 104-106°, with characteristic bitter taste. It is slightly soluble in water and ether; soluble in alcohol (1 in 7) and acetone; stored in airtight containers. The substance is stable in dilute acid and alkali and is not broken down by gastric or

intestinal juices. It belongs to the carbamate group of anxiolytics.

Uses : Meprobamate is used in the treatment of anxiety and tension; sometimes as a muscle relaxant in the management of muscle spasm.

Drowsiness is the most frequent side-effect of meprobamate in addition to nausea, vomiting, diarrhoea, paraesthesia, weakness, headache, dizziness, ataxia and disturbances of vision.

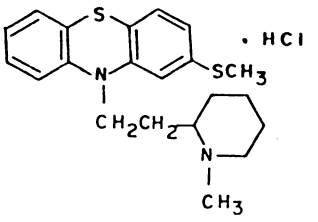
Official

Meprobamate, B.P., I.P.

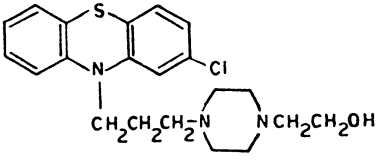
Meprobamate Tablets, B.P., I.P., U.S.P.

Meprobamate Oral Suspension, U.S.P.

Miscellaneous Agents



Thioridazine Hydrochloride



Perphenazine

Thioridazine hydrochloride is a white or slight yellow crystalline powder with slight odour; soluble in water; stored in airtight containers and protected from light. It possesses sedative properties and is used to manage psychotic states.

Official

Thioridazine Hydrochloride Oral Solution, U.S.P.

Thioridazine Hydrochloride Tablets, U.S.P.

Thioridazine Oral Suspension U.S.P.

Thioridazine Tablets B.P.

Perphenazine is a white or creamy-white, odourless powder; practically insoluble in water; soluble in alcohol, chloroform, ether and dilute hydrochloride. It is stored in airtight containers and protected from light. It has sedative properties and used to manage psychotic conditions.

Official

Perphenazine Injection, B.P., U.S.P.
Perphenazine Oral Suspension, U.S.P.
Perphenazine Syrup, U.S.P.
Perphenazine Tablets, B.P., U.S.P.

13

HYPNOTICS

Insomnia (sleeplossness) is produced by various factors such as emotional trauna, fear, apprehension, anguish or certain diseases. Hypnotics are the central nervous system depressants which produce sleep to reduce restlessness and emotional tension. A sedative is a drug that reduces excitement without producing sleep. Hynotics and sedatives both induce depression of the central nervous system, the difference being mainly quantitative. The patient can not be easily awakened until the effect of the hypnotic reduces.

The action of hypnotics and sedatives varies with the dosage. When hypnotics are used in large amounts, they produce anaesthetic state and even death in some case. Hypnotics are generally used in insomnia, anxiety and restlessness.

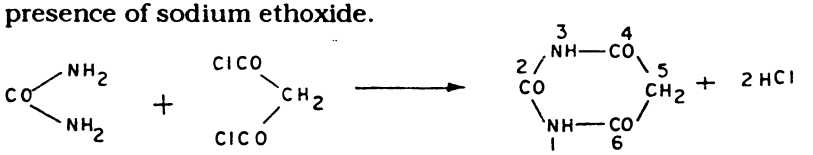
The hypnotic drugs include urea derivatives - diureides (barbiturates) and related ureides (glutethimide), benzodiazepines, alcohols (chloral hydrate), aldehydes (paraldehyde), acetylated carbinols (ethinamate), miscellaneous (meprobamate, methaqualone and scopolamine) and inorganic ions.

Drugs like morphine and pethidine possess analgesic and hypnotic properties.

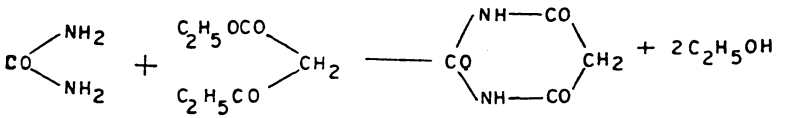
Barbiturates

Barbiturates are cyclic ureides (the condensation products of urea with carboxylic acids) derived from malonic acid. They are most widely used as sedative or hypnotic drugs, and some are introduced intravenously for the production of light general anaesthesia. Based on the old name barbituric acid for

malonylurea the parent compound of the group, they are called barbiturates. Structurally they are derivatives of hexahydropyrimidine. Barbituric acid is prepared by condensing urea with the acid chloride of malonic acid or with ethyl malonate in the presence of sodium ethoxide.

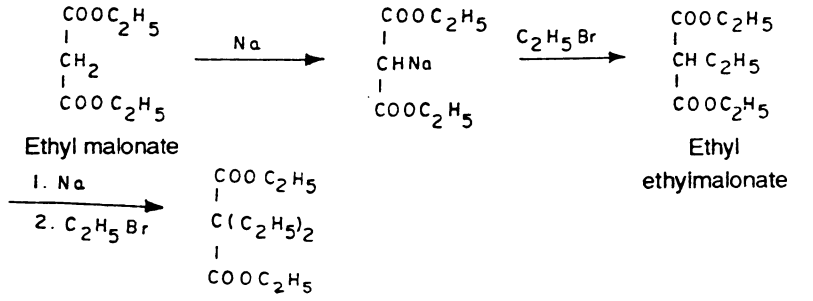


Urea Malonyl chloride Barbituric acid



Ethyl malonate

If thiourea is used in place of urea in the condensation, thiobarbiturates are formed which contain sulphur atom attached to the C-2 position. Employment of N-methylurea in this reaction yields 1-methybarbiturates. For the preparation of substituted barbituric acids, dialkyl malonic ester is prepared as :



Ethyl malonate Ethyl ethylmalonate

Ethyl diethylmalonate

All the barbiturates are colourless, crystalline solids which are not very soluble in water. They form sodium salts which are soluble in water. The barbiturates, though having much lower dissociation constants, are also acidic in character. Alkaline solutions of barbiturates give precipitates of copper complexes with copper sulphate in aqueous pyridine.

Both hydrogen atoms in position 5 of barbituric acid must be replaced for maximal activity. Increasing the length of an alkyl chain in the 5-position enhances the potency up to 5 or 6 carbon atoms. Beyond 6 carbons, depressant action decreases and convulsant action may be observed. Branched, cyclic or

unsaturated chains in the 5-position generally produce a lesser duration of action than that of normal saturated chains. Compounds with alkyl groups in the 1 or 3 position may have a shorter onset and duration of action. Replacement of oxygen by sulphur on the 2-carbon shortens the onset and duration of action. Thiobarbiturates are much more lipid soluble in the unionized form than are the corresponding oxygen analogs. Therefore, rapid onset and short duration of action are observed with thiobarbiturates.

The barbiturates are used as sedative and hypnotics. They are also applied to suppress a variety of convulsions with origins in the central nervous system, including those from tetanus, meningitis, cholera, epilepsy, eclampsia, insulin overdosage and poisoning by strychnine and similar drugs. They are also employed to produce anaesthesia. In combination with morphine and scopolamine, the barbiturates are used in producing obstetric amnesia.

The adverse effects of barbiturates include inconvenience, extreme depression, excitement or even mania. Some persons are hypersensitive in which skin lesions such as edema or scarletinal-like rashes are formed. The respiration and the circulation are depressed slightly by anaesthetic doses. Relatively large doses may cause prolonged coma, fall in blood pressure and paralysis of the respiratory centre. Habituation to the barbiturates is common. Abrupt withdrawal of the drug from an addicted person results in delirium, convulsions, insomnia, nausea, cramps, vomiting, orthostatic hypotension, visual and auditory hallucination.

Acyclic Ureides

The acyl derivatives of urea are called as ureides which include barbiturates and many substitution products of pyrimidine and purine. The amino groups of urea may be acylated by monobasic or polybasic acids to yield either acyclic or cyclic ureides. An acyclic monoureide has the structure R-CO-NH-$CONH_2$; an acyclic diureide is R-CO-NH-CO-NH-COR. In all ureides at least one of the nitrogen atoms is joined by two carbonyl groups (-NH-CO-NH) which will form a water-soluble salt in the presence of alkali hydroxide. In general ureides are neutral compounds.

The acyclic ureides are prepared from the corresponding alkyl or dialkylmalonic acid. Acetic acid is formed by decarboxylation. The acid halides of these or their α-halo

derivatives are condensed with urea to form the desired ureides.

$$(C_2H_5)_2\,C(COOH)_2 \xrightarrow[-CO_2]{\text{Heat}} (C_2H_5)_2CHCOOH \xrightarrow{PBr_3}$$

Diethylmalonic acid — Diethylacetic acid

$$(C_2H_5)_2CBr{-}COBr \xrightarrow{H_2NCONH_2} (C_2H_5)_2CBrCONHCONH_2$$

α-Bromo diethylacetic bromide — (urea) — Carbromal

Ureides are hydrolyzed by hot, dilute alkalis with formation of hydrolysis products of urea and a salt of the particular acid.

The acyclic ureides possess weak depressant activity. Relatively high doses are required to produce hypnosis. They are mainly used as sedative in the treatment of simple anxiety and nervous tension.

Bromisovalum and ectylurea are the acyclic ureides.

Amides and Imides

Glutethimide, methyprylon and methaqualone are the cyclic amides and imides effective as sedative and hypnotic drugs.

Alcohol and their Carbamates

Ethanol is a prominent compound used as sedative and hypnotic. The hypnotic activity of the normal alcohols increases as the molecular weight and lipid solubility increase. Branching of the alkyl chain increases activity. Substitution of a hydrogen by a halogen also increases the action.

Amylene hydrate, chlorobutanol, ethchlorvynol, meparfynol and ethinamate are some alcohols used as hypnotic drugs.

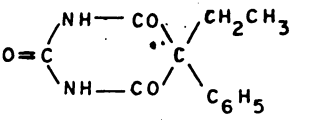
Aldehydes, Ketones and Dervatives

Chloral hydrate, chloral betaine, petrichloral and paraldehyde are the carbonyl compounds used as hypnotic drugs.

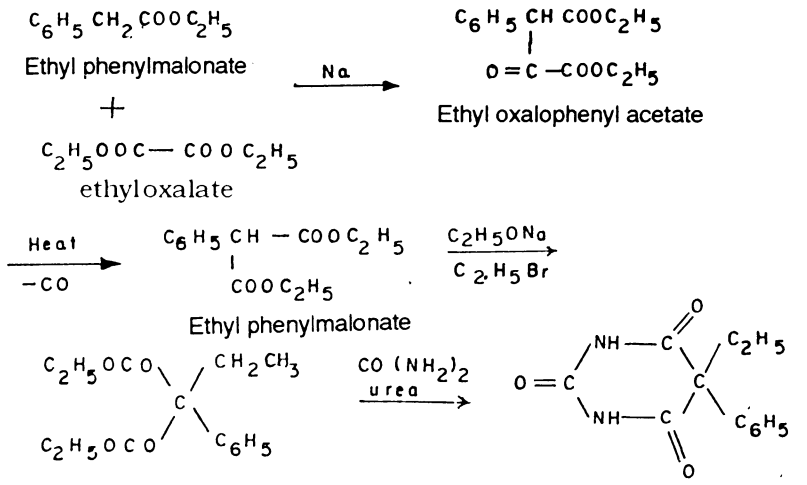
PHENOBARBITONE

Nomenclature : 5-Ethyl-5-phenyl-2,4,6-(1H,3H,5H)-pyrimidinetrione; 5-Ethyl-5-phenylbarbituric acid.

Brand Names : Phenylethylmanonylurea; Gardenal; Barbenyl; Barbiphenyl; Luminal; Phenobarbital; Dormiral; Euneryl; Neurobarb; Barbipil; Lubrokal; Lubergal; Phenyral; Cratecil, Nunol; Phenonyl; Phenobal; Noptil; Agrypnal; Eskabarb: Etifen; Gardepanyl; Somonal



Phenobarbitone is prepared by reacting ethyl phenyl acetate with ethyl oxalate in the presence of sodium (Claisen condensation) to form ethyl oxalophenyl acetate, a ketonic ester which decomposes when distilled, with loss of carbon monoxide and formation of ethyl phenylmalonate. The ethyl group is introduced by means of sodium ethoxide and ethyl bromide to form ethyl ethylphenylmalonate which is then reacted with urea to yield phenobarbitone.



Phenobarbitone occurs as colourless crystalline powder, m.p. 174-178°; soluble in water (1 in 1000), alcohol (1 in 10); sparingly soluble in chloroform soluble in aqueous solutions of alkali carbonates and hydroxides and ammonia.

Phenobarbitone Sodium (Brand Names : Sol phenobarbital; Sol phenobarbitone; Luminal sodium, Gardenal sodium) is a white, bitter, hygroscopic crystalline powder. One gram dissolves in about 1 ml water, about 10 ml alcohol; insoluble in ether. Aqueous solutions are alkaline to litmus and phenolphthalein and are unstable. It is stored in airtight containers.

Uses : Phenobarbitone is anticonvulsant and hypnotic used as a antiepileptic agent to control tonicclonic and partial seizures.

Adverse effects of barbiturates include respiratory depression, sedation, and occasional allergic reactions. Nystagmus and ataxia may occur with excessive doses as well as prolonged coma and cardiovascular depression. Abuse may lead to habituation or addiction. Purpura, exfoliative dermititis, erythema multiforme and necrolysis have also been reported.

Official

Phenobarbital Tablets/Sodium/Sodium Injection, U.S.P.

Phenobarbitone, B.P., I.P.

Phenobarbitone Elixir, B.P.

Phenobarbitone Tablets, B.P., I.P.

Phenobarbitone Sodium, B.P., I.P.

Phenobarbitone Injection, B.P.

Phenobarbitone Sodium Tablets, B.P., I.P., U.S.P.

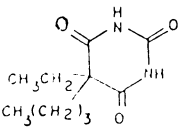
Barbitone Sodium Tablets, I.P.

BUTOBARBITONE

Nomenclature : 5-Butyl-5-ethyl-2, 4, 6 (1 H, 3H, 5H) - pyrimidine-trione; 5-Butyl-5-ethylbarbituric acid.

Brand Names : Butethal, Soneryl, Neonal, Butobarbital, Etoval.

Butobarbitone is a white crystalline, odourless powder with slightly bitter taste, m.p. 124-127°. It is slightly soluble in water; freely soluble in alcohol and in chloroform; soluble in ether and in aqueous solutions of alkali hydroxides, carbonates and ammonia by forming salts.



Uses : Butobarbitone is used as hypnotic and sedative. The adverse effects are the same as for barbiturates in general. Abuse may lead to habituation or addiction.

Official

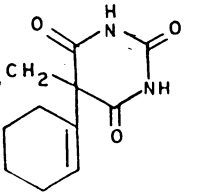
Butobarbitone, B.P.

Butobarbitone Tablets, B.P.

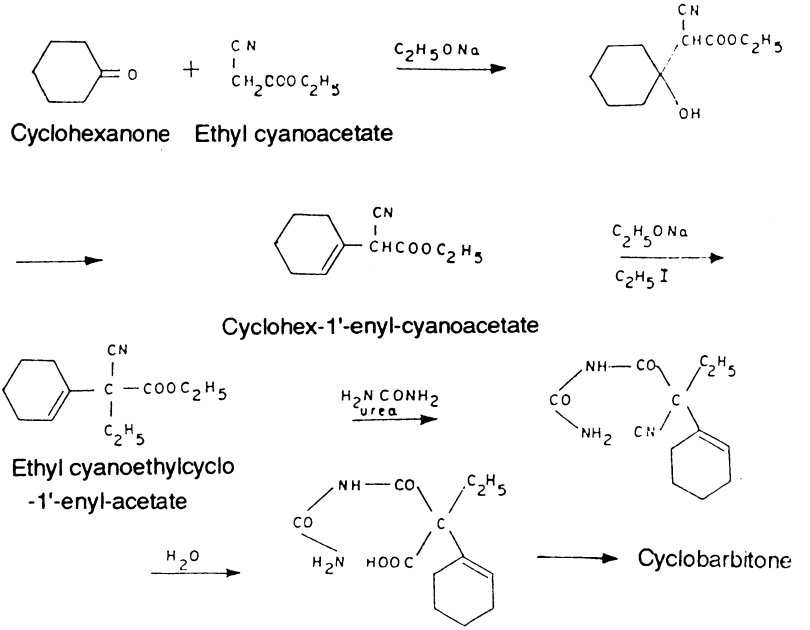
CYCLOBARBITONE

Nomenclature : 5-(1-Cyclohexen-1-yl)-5-ethyl-2, 4, 6 (1H, 3 H, 5H)-pyrimidinetrione; 5-(1-Cyclohexen-1-yl-5-ethylbarbituric acid.

Brand Names : Cyclobarbital, Hexemal; Tetrahydrophenobarbital; Cavonyl; Cyclodorm; Cyklodorm; Fanodormo; Irifan; Namuron; Palinum; Phanodorm; Phanodorn; Philodorm; Pralumin; Pro-Sonil; Sonaform.



Cyclobarbitone contains a cyclohex-1-enyl group in the 5-position. It is prepared by condensing ethyl cyanoacetate with cyclohexanone in the presence of sodium ethoxide or pyridine to yield ethyl cyclohex-1'-enylcyano acetate. With sodium ethoxide and ethyl iodide this ester is alkylated to give ethyl cyanoethylacyclohex-1'-enylacetate. This reactive cyano-ester is condensed with urea to form an open-chain cyanoureide. Hydrolysis of the -CN group afforded an acid which cyclizes spontaneously to cyclobarbitone.



It occurs as shiny crystals, insipid bitter taste, m.p. 171-174°; very slightly soluble in cold water, appreciably soluble in hot water. One gram dissolves in 5 ml alcohol, and 20 ml ether. It is stored in airtight containers.

Uses : It has central depressant (hypnotic, sedative) activity used as an anaesthetic and sedative.

Cyclobarbitone Calcium : (Brand Names : Hexemal calcium; Itridal, Kollerdormfix; Pronox; Cyclobarbital calcium) is a white or slightly yellowish, crystalline powder. It is slightly soluble in water and alcohol; practically insoluble in chloroform and in ether; stored in airtight containers; used as hypnotic and sedative.

Official

Cyclobarbitone, I.P.

Cyclobarbitone Tablets, I.P.

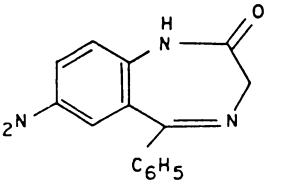
Cyclobarbitone Calcium, B.P.

NITRAZEPAM

Nomenclature : 1,3-Dihydro-7-nitro-5-phenyl-2H-1,4-benzodiazepin-2-one.

Brand Names : LA-1; Ro 4-5360; Benzalin; Calsmin; Eatan; Eunoctin; Mogadan Mogadon; Nelbon; Neuchlonic; Nitrados; Nitrenpax; Paxisyn; Pelson; Radedorm; Relact; Somnased; Somnibel; Somnite; Sonebon; Sonnolin; Surem; Unisomnia.

Nitrazepam is a yellow, crystalline powder, m.p. 224-226°. It is practically insoluble in water; slightly soluble in alcohol and in ether; sparingly soluble in chloroform; stored in well-closed containers and protected form light.



Uses : Nitrazepam is used as a hypnotic and in epilepsy. The side effects may include drowsiness, fatigue, confusion and ataxia.

Official

Nitrazepam, B.P.

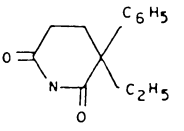
Nitrozepam Capsule, B.P., U.S.P.

Nitrozepam Tablets, B.P., U.S.P.

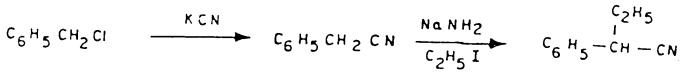
GLUTETHIMIDE

Nomenclature : 3-Ethyl-3-phenyl-2,6-piperidinedione; 2-Ethyl-2-phenylglutarimide.

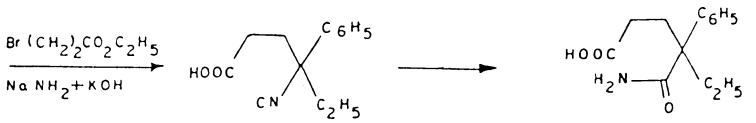
Brand Names : Elrodorm; Doriden-sed; Doriden; 2-Ethyl-2-phenylglutarimide.



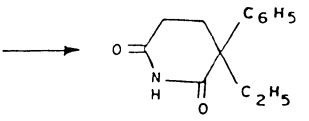
For the synthesis of glutethimide, benzyl chloride is converted into benzyl cyanide; this is ethylated to α-phenylbutyronitrile which on treatment with 3-bromopropionic ester yields a substituted hexanoic acid. Partial hydrolysis with 85% sulphuric acid yields the amide which spontaneously cyclizes to form glutethimide.



Benzyl cyanide — Benzyl chloride — α-Phenylbutyronitrile



Hexanoic acid — Amide



Glutethimide

Glutethimide occurs as odourless, white crystalline powder, m.p. 102-103°; practically insoluble in water, soluble in alcohol (1 in 5), chloroform (1 in < 1), ether (1 in 12), acetone, ethyl acetate and methanol. A saturated solution in water is acidic to litmus. It is stored in airtight containers and protected from light.

Uses : Glutethimide is a hypnotic and sedative. In therapeutic doses side-effects include nausea, headache, excitement, hang-over, blurred vision and sometimes skin rashes. Abuse may lead to habituation or addiction.

Official

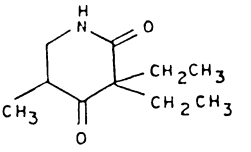
Glutethimide B.P.

Glutethimide Tablets, B.P., U.S.P.

Glutethimide Capsules, U.S.P.

METHYPRYLONE

Nomenclature : 2,4-Dioxo-3, 3-diethyl-5-methylpiperidine; 3, 3-Diethyl-2, 4- dioxo-5-methylpiperidine.



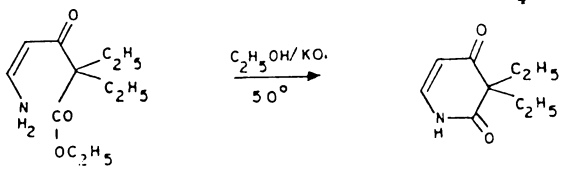
Brand Names : Noctan; Dimerin; Noludar.

Methyprylone is a derivative of 2, 4-piperdinedione which is synthesized by condensing methyl formate with diethyl-acetoacetic ester by means of sodium in toluene. An aqueous solution of the product is then heated with ammonium chloride to form the corresponding amino derivative. This is dissolved in ethanol and heated with 50 per cent KOH solution at 50° to condense carboxyl group with the amino group. The potassium derivative upon acidification yields a tetrahydropyridine which combines with formaldehyde in the presence of sodium sulphite to give 5-hydroxymethyl derivative, which upon catalytic reduction gives methyprylone

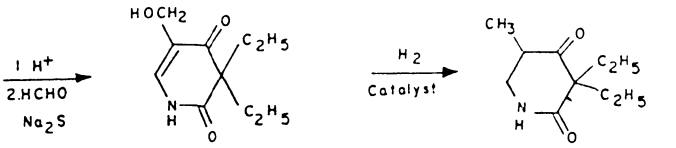
$$HCOOCH_3 + CH_3COC(C_2H_5)_2COOC_2H_5 \xrightarrow[\text{Toluene}]{Na}$$

Methyl formate — Diethylacetoacetic ester

$$NaOCH = CH\ CO\ C\ (C_2H_5)_2\ COOC_2H_5 \xrightarrow[NH_4Cl]{heat}$$



Amino derivative



5-Hydroxymethyl derivative — Methyprylone

Uses : Methyprylone, a piperidinedione derivative, is administered as a sedative and hypnotic in the form of tablets.

In therapeutic doses side effects include nausea, headache, excitement, hang-over, blurred vision and sometimes skin rashes. Abuse may lead to habituation or addiction.

Official

Methyprylone Capsules, U.S.P.

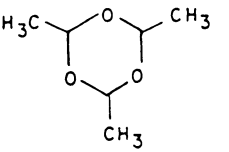
Methyprylone, B.P., U.S.P.

Methyprylone Tablets, B.P., U.S.P.

PARALDEHYDE

Nomenclature : 2, 4, 6-Trimethyl-1, 3, 5-trioxane.

Brand Names : Paracetaldehyde; Paraldehydum; The trimer of acetaldehyde.



Paraldehyde is a polymer of acetaldehyde prepared by the polymerization of acetaldehyde catalyzed by HCl and H_2SO_4 at medium to high temperature. When a drop of concentrated H_2SO_4 is added to acetaldehyde, a vigorous reaction takes place. The polymerization to paraldehyde is controllable if concentrated HCl is used in place of H_2SO_4. At the end of the reaction, the product is shaken with a dilute solution of sodium bicarbonate, separated, dried over fused potassium carbonate and fractionally distilled.

Paraldehyde is a colourless liquid, b.p. 123-126°, with characteristic aromatic odour and warm, but disagreeable acrid taste; neutral to litmus. It is soluble in 8 parts of water at 25°, in 17 parts boiling water; miscible with alcohol, chloroform, ether and volatile oils. It is solidified at 12° to form a crystalline mass which should be liquefied before use. It has solvent action upon rubber, polystyrene and styrene acrylonitrile copolymer, therefore, paraldehyde should not be taken in plastic syringes made with these materials. It gives acetaldehyde on heating with dilute HCl or on warming with concentrated H_2SO_4. It may be oxidized to form acetic acid on storage. Since oxidation occurs more rapidly in opened, partially filled containers, the drug should not be dispensed from container that has been opened for more than 24 hours.

Uses : Paraldehyde is a hypnotic and sedative with anticonvulsant effects.

As paraldehyde decomposes on storage, deaths from corrosive poisoning have followed the use of such material. It has an unpleasant taste and imparts a smell to the breath; it may cause skin rashes.

Official

Paraldehyde, B.P., I.P.

Paraldehyde Injection, B.P.

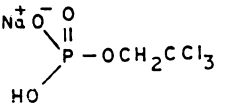
Sterile Paraldehyde, U.S.P.

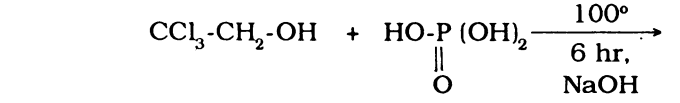
TRICLOFOS-SODIUM

Nomenclature : 2, 2, 2-Trichloroethanol dihydrogen phosphate.

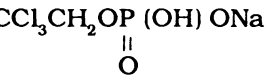
Brand Names : Sch-10159; Sodium Trichlofos; Trichloryl; Tricloryl; Triclos.

This salt of an ester is prepared by esterification of trichloroethanol with orthophosphoric acid by heating at 100° for six hours. The mixture is cooled, diluted, and the triclofos extracted with an organic solvent. Extraction of the organic phase with sodium hydroxide solution furnishes an aqueous solution of triclofos sodium. The compound is crystallized on addition of acetone.





Trichloroethanol — Orthophosphoric acid



Triclofos sodium

Triclofos sodium is a white, odourless, hygroscopic powder. It is soluble in water (1 in 2); slightly soluble in alcohol; practically insoluble in ether; stored in airtight containers. A 2%

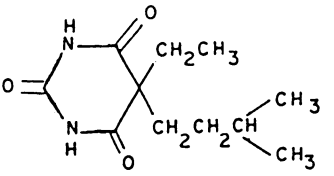
solution in water has a pH of 3.0 to 4.5. Aqueous solutions slowly decompose, liberating chloride and phosphate ions.

Uses : Triclofos sodium has hypnotic and sedative action similar to chloral hydrate. It is not corrosive to skin and mucous membranes.

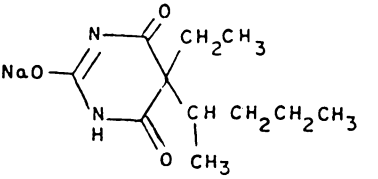
Official

Trichlofos Sodium, B.P.
Trichlofos Elixir, B.P.
Trichlofos Tablets, B.P.

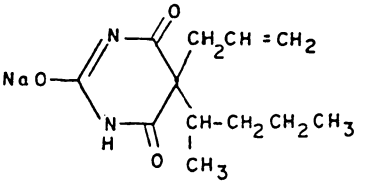
Miscellaneous Hypnotics



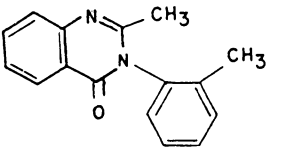
Amylobarbitone



Pentobarbitone Sodium



Quinalbarbitone Sodium
(Secobarbital Sodium)



Methaqualone

Official

Amylobarbitone, B.P., I.P.
Amylobarbitone Sodium, B.P., I.P.
Amylobarbatone Sodium Capsules/Tablets, B.P.
Amobarbital Elixir/Tablets/Sodium Capsules, U.S.P.
Phenobarbitone Capsules/Tablets, B.P.
Phenobarbitone Elixir, U.S.P., B.P.
Secobarbital Elixir/Sodium Capsules/Sodium Injection, U.S.P.
Secobarbital Sodium and Amobarbital Sodium Capsules, U.S.P.
Methaqualone Tablets, U.S.P.

14

GENERAL ANAESTHETICS

General anaesthetics depress the central nervous system and produce loss of consciousness.

General anaesthesia is the controlled, reversible depression of the functional activities of the central nervous system producing loss of sensation and consciousness. The stages of anaesthesia vary for all agents producing general anaesthesia.

Stage I (Cortical stage) : Analgesia is produced, consciousness persists, but the patient is sleepy due to depression of the higher cortical centres.

Stage II (Excitement) : Loss of consciousness occurs, but depression of higher motor centres involving the brain stem and the cerebellum leads to excitement and delirium.

Stage III (Surgical Anaesthesia) : The activity of spinal cord reflexes is minimized, and skeletal muscle relaxation is obtained. In this stage most of the operations are performed.

Stage IV (Medullary Paralysis) : Respiratory failure and vasomotor collapse occur due to depression of vital functions of the medulla and the brain stem.

General anaesthetics are administered either by inhalation or by intravenous or sometimes muscular injection. Chloroform, cycloprapone, enflurane, ether, fluroxene, halothane, isoflurane, nitrous oxide and trichloroethylene are given by inhalation.

General anaesthesia may be produced by different type of compounds. The saturated hydrocarbons possess an anaesthetic effect which increases from methane to octane and then decreases. Cyclopropane and ethylene are used as anaesthetic drugs.

The anaesthetic potency of the lower hydrocarbons is increased as hydrogen is successively replaced by halogen; the order of increment is as : methane, methyl chloride, dichloromethane, chloroform, carbon tetrachloride, ethyl chloride, trichloroethylene and halothane.

An ideal anaesthetic agent should be inert, potent, non-flammable, non-irritating to mucous membranes and non-toxic. It should produce rapid and smooth induction and should be compatible with other anaesthetics.

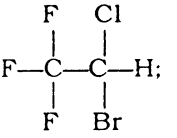
An ideal anaesthetic agent should produce unconsciousness, analgesia, and muscle relaxation suitable for all surgical procedures and be metabolically inert and rapidly eliminated. No single agent in safe concentrations fulfils all these requirements. The activity of any anaesthetic is dependent on its ability to reach the brain.

Adverse effects which may occur during general anaesthesia include involuntary muscle movements, hiccup, coughing, bronchospasm, laryngospasm, hypotension, cardiac arrhythmias, respiratory depression, emergence reactions, and postoperative nausea and vomiting.

HALOTHANE

Nomenclature : 2-Bromo-2-chloro-1, 1, 1-trifluoroethane; 1, 1, 1-Trifluoro-2, 2-chlorobromoethane.

Brand Names : Bromochlorotrifluoroethane; Alotano; Fluothane; Rhodialothan; Halothanum; Phthorothanum.



CF_3-CHBrCl

Halothane is prepared from trichloroethylene by the following reaction :

$$CCl_2{=}CHCl \xrightarrow{+HCl} CCl_3 - CH_2Cl \xrightarrow{HF} CF_3 - CH_2Cl \xrightarrow{\downarrow Br_2} CF_3\,CHBrCl$$

Halothane is a clear, mobile, dense, non-flammable, highly volatile liquid; odour is chloroform-like characteristic, sweetish, and unpleasant; b.p. 50°. It is slightly soluble in water (1 in 400); miscible with dehydrated alcohol, chloroform, ether, trichloroethylene and fixed oils. Halothane is soluble in rubber. In the presence of moisture it reacts with many metals. It is stored at a temperature of 8° to 15° in airtight containers and protected from light.

Uses : Halothane is a volatile anaesthetic administered by inhalation. It is non-inflammable and is not explosive when mixed with oxygen. It is not irritant to skin and mucous membranes. Anaesthesia is rapidly and easily induced and recovery is quick and complete. It is also used as refrigerants.

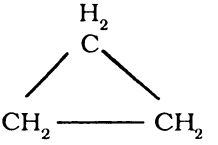
Halothane has depressant action on the cardiovascular system and reduces blood pressure; signs of overdosage are bradycardia and profound hypotension. Hepatic dysfunction, hepatitis and necrosis have been reported following the use of halothane.

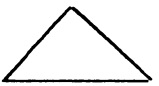
Official

Halothane, B.P.

CYCLOPROPANE

Nomenclature : Trimethylene.





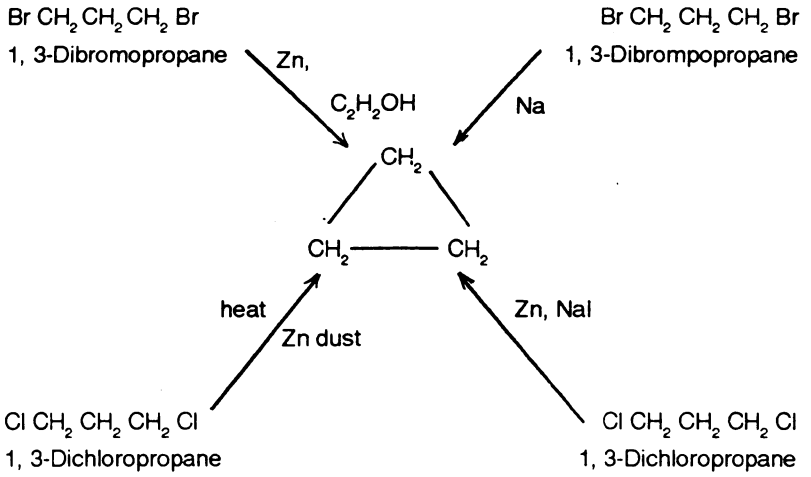
Cyclopropane is prepared form

(a) 1, 3-dibromopropane with zinc and alcohol in absence of water;

(b) by the action of sodium vapour on 1, 3-dibromopropane;

(c) from 1, 3-dichloropropane heated with an excess of zinc dust, iodine and ethanol in 80% yield;

(d) from 1, 3-dichloropropane with zinc in presence of sodium iodide.



Cyclopropane is a colourless flammable gas with a characteristic odour and pungent taste supplied in compressed form in metal cylinders; m.p. -127°; b.p. -33°. It is very soluble in alcohol, chloroform and ether; soluble in fixed oils; liquefies at 4-6 atms. Concentrated H_2SO_4 absorbs the gas readily. Cyclopropane forms an explosive mixture with air in a concentration range from 3 to 8.5 per cent. Rich oxygen mixtures are therefore to be avoided. It is stored in metal cyclinders in a special room which should be cool and free from flammable materials. The cyclinder sould be painted orange.

Uses : Cyclopropane is an anaesthetic administered by inhalation.

Cyclopropane depresses respiration; it may cause bronchospasm, cardiac arrhythmias, nausea, vomiting, headache and liver necrosis.

Offical

Cyclopropone, B.P., I.P.,

DIETHYL ETHER

Nomenclature : 1, 1'-Oxybisethane; Ethoxyethane.

Brand Names : Ether; Ethyl oxide; Diethyl oxide; Sulphuric ether; Anaesthetic ether.

$CH_3\ CH_2—O—CH_2\ CH_3$; $C_2\ H_5\ O\ C_2\ H_5$

Diethyl ether can be prepared by heating an ethyl halide with dry sodium ethoxide (Williamson's synthesis).

$$CH_3CH_2ONa + BrCH_2CH_3 \longrightarrow CH_3CH_2OCH_2CH_3 + NaBr$$

On a large scale ether is produced by dehydration of ethanol or by hydration of ethylene, both processes being carried out in the presence of sulphuric acid. Alcohol reacts with concentrated sulphuric acid to form ethyl hydrogen sulphate which on heating with alcohol at high temperature yields ether and sulphuric acid.

$$\underset{\text{Ethanol}}{CH_3CH_2OH} + \underset{\text{Sulphuric acid}}{HOSO_2OH} \longrightarrow CH_3CH_2OSO_2OH + H_2O$$

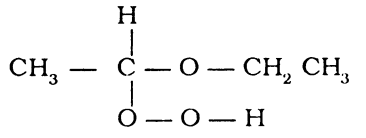
$$CH_3CH_2OCH_2CH_3 + H_2SO_4$$

Ether

Diethyl ether is a colourless, very mobile and volatile, highly flammable liquid with characteristic sweetish, pungent odour; b.p. 35°; taste is burning. It tends to form explosive peroxides under the influence of air and light. It is soluble in water (1 in 12-15); miscible with alcohol, chloroform, petroleum ether and fixed and volatile oils. Peroxides may be removed from ether by shaking with 5% aqueous ferrous sulphate solution. Addition of naphthols, polyphenols, aromatic amines and aminophenols has been recommended for the stabilization of ethyl ether. It is very slowly attacked by ordinary oxidizing agents. Phosphorus pentachloride has no action on it in the cold. Hot, concentrated acids may decompose it, with formation of esters or halides; e.g.

$$(CH_3CH_2)_2O + 2HI \longrightarrow 2\,CH_3CH_2I + H_2O$$

Upon long standing in contact with air, ether peroxides are formed. Their formation is accelerated by ultraviolet light and sunlight. In well-filled containers the peroxides will form in about 6 months, but after 1 year in old ether the content of peroxides decreases and aldehydes are formed from the alcohol present. These peroxides are non-volatile and remain as a residue when such ether sample is evaporated. When heated to about 100°C, they explode with terrific force.



Ether peroxide

The peroxide may be destroyed by shaking the ether with an aqueous solution of a reducing agent, such as ferrous sulphate, ferric chloride, sodium hydrosulphite, catechol or by filtering it through activated alumina. The ether should be stored up to 15° in dry airtight containers and protected from light.

Uses : Ether is an anaesthetic administered by inhalation. It also possesses analgesic and muscle relaxant properties. It is also used as a solvent for waxes, fats, oils, perfumes, alkaloids and gums; as an important reagent in organic synthesis (Grignard and Wurtz type reactions), for easily removable extractant of hormones from plants and animal tissues and in the manufacture of gun powder.

Ether has irritant action on the mucous membrane of the respiratory tract. It may cause vasodilation, capillary bleeding, malignant hyperpyrexia, convulsions, etc.

Official

Anaesthetic Ether, B.P., I.P.

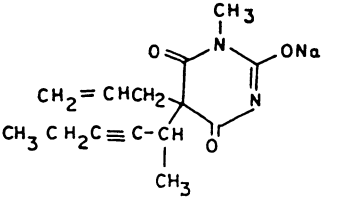
Methoxy furane, B.P.

Vinyl Ether, B.P.

METHOHEXITAL SODIUM

Nomenclature : 1-Methyl-5-(1-methyl-2-pentynyl)-5-(2-propenyl)-2, 4, 6- (1H, 3H, 5H) - pyrimidinetrione sodium salt.

Brand Names : Brevital; Brevital sodium; Brevimytal sodium; Brietal sodium; Compound 25398; Enallynymalnatrium; Methexitone sodium.



Methohexital, m.p. 92-96°; is an example of barbiturates substituted in the 1-position. Methohexital sodium is a white, hygroscopic odourless powder; soluble in water. It should be stored in airtight containers.

Uses : It is used for the induction of general anaesthesia and a hypnotic state by administration intravenously.

Coughing, sneezing, laryngeal spasm, abnormal muscle movements and hiccuping may occur. Other side effects are respiratory depression, sedation and allergic reactions. Abuse may lead to habituation and addiction.

Official

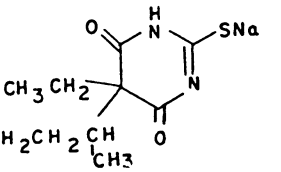
Methohexitone Injection, B.P.

Methohexital Sodium for Injection, U.S.P.

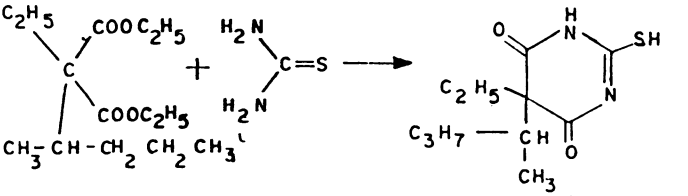
THIOPENTAL SODIUM

Nomenclature : 5-Ethyldihydro-5-(1-Methylbutyl)-2-thioxo-4, 6-(1H, 5H) - pyrimidinedione monosodium salts.

Brand Names : Thiomebumal sodium; Penthiobarbital sodium; Thiopentone sodium; Thionembutal; Pentothal sodium; Nesdonal sodium; Intraval sodium; Trapanal; Thiothal sodium; Penthiobarbital sodique; Soluble thiopentone; Thiopental sodium.



By the use of thiourea in place of urea, thiobarbiturates can be prepared which have -CS- instead of -CO- at position 2. Thiopentone is the sulphur analogue of pentobarbitone, which is synthesized by condensing thiourea with ethyl ethyl-1-methylbutylmalonate :



Thiopentone

Thiopental sodium is a white to yellowish-white, hygroscopic powder with alliaceous, garlic-like odour. It is soluble in water (1 in 1.5); partly soluble in alcohol; practically insoluble in ether and petroleum ether. Aqueous solutions are alkaline to litmus. Solutions decompose on standing; on boiling precipitation occurs. The drug is stored in airtight containers and protected from light.

Uses : Thiopentone sodium is administered intravenously for the induction of anaesthesia and for hypnosis.

Coughing, sneezing, laryngeal spasm or bronchiospasm may occur as side effects.

Official

Thiopentone Sodium, B.P., I.P.

Thiopentone Injection, B.P., I.P.

Thiopental Sodium for Injection, U.S.P.

TRICHLOROETHYLENE

Nomenclature : Trichloroethene; Ethinyl trichloride.

Brand Names : Tri-Clene; Trielene; Trilene; Trichloran; Trichloren; Algylen; Trimar; Triline; Tri; Trethylene; Westrosol; Chlorylen; Gemalgene; Germalgene.

$$ClCH = CCl_2$$

Trichloroethylene is usually prepared —

(a) from *sym*-tetrachloroethane by elimination of hydrochloric acid (by boiling with lime);

(b) by passing tetrachloroethane vapour over calcium chloride catalyst at 300° or without catalyst at 450°-470°, and

(c) by treating acetylene with chlorine in the presence of calcium oxide.

$$\underset{\text{Acetylene}}{CH \equiv CH} \xrightarrow{2Cl_2} \underset{\substack{\text{Acetylene}\\ \text{tetrachloride}}}{CHCl_2—CHCl_2} \xrightarrow[-HCl]{CaO} \underset{\substack{\text{Trichloro-}\\ \text{ethylene}}}{CHCl = CCl_2}$$

Trichloroethylene is a clear, colourless or pale blue, non-flammable, mobile liquid, b.p. 88°, with peculiar odour resembling that of chloroform. It is practically insoluble in water; miscible with ether, alcohol and chloroform, most of fixed and volatile oils. It is slowly decomposed by light in the presence of moisture with formation of HCl. Trichloroethylene for medicinal purposes may contain some thymol and ammonium carbonate (about 100 mg/100 ml) as a stabilizer.

Uses : Trichloroethylene is a weak volatile anaesthetic administered by inhalation; mainly used in short surgical procedures. It is also used as a solvent for fats, waxes, resins, oils, rubber, paints and varnishes; in degreasing in dry cleaning; in the manufacture of organic chemicals, pharmaceuticals, such as chloroacetic acid.

The side effects include ventricular arrhythmias, nausea, vomiting and light-headedness. Moderate exposures can cause

symptoms similar to alcohol inebriation. Higher concentrations can cause narcotic effect. Deaths occurring after heavy exposure is due to ventricular fibrillation. Prolonged contact with trichloroethylene can cause dermatitis, eczema, burns and conjunctivitis.

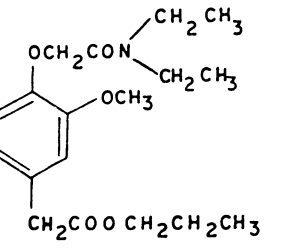
Official

Trichloroethylene, B.P.

PROPANIDID

Nomenclature : Propyl-4-diethylcarbamoylmethoxy-3-methoxyphenyl acetate.

Brand Names : Bayer-1420; FBA-1420; TH-2180; WH-5668.



Propanidid, b.p. 210-212°, is a pale greenish-yellow viscous liquid with a slight odour. It is very slightly soluble in water; miscible with alcohol, chloroform and ether.

Propanidid has been used as an intravenous anaesthetic for rapid induction and for maintenance of anaesthesia of short duration.

Official

Propanidid, B.P.

15

LOCAL ANAESTHETICS

Local anaesthetics are drugs which, when applied directly to peripheral nervous tissue, block nerve conduction and abolish all sensations in the part supplied by the nerve. They are generally applied to somatic nerves and act on axons, cell body, dendrites, and synapses. These agents are applied topically or by localized injection in dental and surgical procedures to prevent pain.

A local anaesthetic should not be irritant, toxic, unstable and painful. It should produce anaesthesia without causing the damage of nerve cells. The duration of anaesthetic effect should be sufficient for carrying out the operation. It should be sterilized without difficulty.

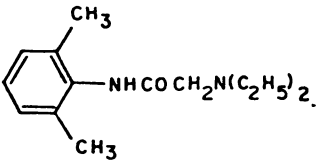
Surface or topical anaesthetics act by blocking the sensory nerve endings in the skin or mucous membranes. The drug should possess high penetration power. Local or infiltration anaesthesia is produced by injection directly into the required part to be operated in small amounts.

Local anaesthetics are natural agents (e.g. cocaine), synthetic nitrogenous compounds (e.g. procaine, benzocaine, lidocaine, cinchocaine), synthetic non-nitrogenous compounds (e.g. benzyl alcohol, propanediol) and miscellaneous drugs with local action (e.g. clove oil, phenol, chlorpromazine, etc.).

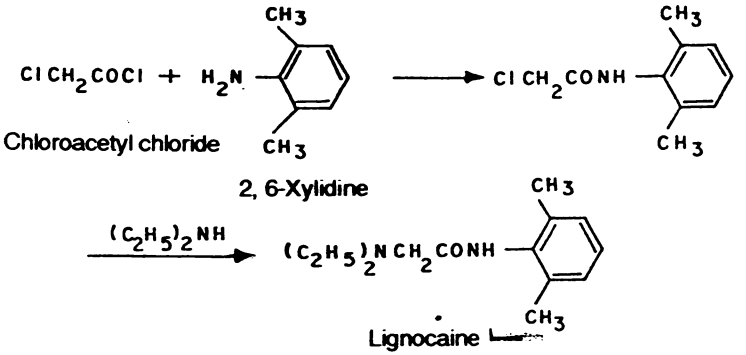
LIGNOCAINE

Nomenclature : 2-(Diethylamino)-N-(2,6-dimethylphenyl) acetamide; 2-Diethylamino-2', 6'-acetoxylidide.

Brand Names : Lidocaine; Xylocaine; Xylotox; Leostesin; Rucaina; Isicaine; Duncaine; Xylestesin; Anestacon; Gravocain; Lidothesin; Xylocitin.



Lignocaine is an amino-amide. This is prepared from 2, 6-xylidine (2, 6-dimethylaniline) by treating with chloroacetyl chloride to yield the corresponding chloro-amide. The product is reacted with diethylamine to form lignocaine.



Lignocaine, m.p. 68-69°, is a white, crystalline odourless substance which is insoluble in water; soluble in alcohol, ether, benzene, chloroform and oils.

Lignocaine hydrochloride (Brand Names : Xylocard; Xyloneural; Lignostab; Nurocain) m.p. 127-129°, is a white crystalline odourless powder which is soluble in water, alcohol and chloroform. The hydrochloride or amine is the most stable local anaesthetic. The ester-type local anaesthetics are generally prone to hydrolysis in aqueous solution.

Uses : Lignocaine is a local anaesthetic and antiarrhythmic.

Lignocaine has systemic adverse effects mainly involves the central nervous system and the cardiovascular system. Excitation of the CNS may be manifested by restlessness, excitement, nervousness, dizziness, tinnitus, blurred vision, nausea and vomiting, muscle twitching and tremors and convulsions. Numbness of the tongue and perioral region may appear. Excitation may be transient and followed by depression with drowsiness, respiratory failure, and coma.

Officials

Lignocaine Hydrochloride, B.P., I.P.
Lignocaine and Adrenaline Injection, B.P., I.P.
Lignocaine Hydrochloride Gel, B.P.

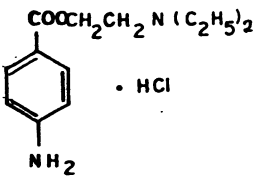
Lignocaine Hydrochloride and Chlohexidine Gluconate Gel, B.P.
Lignocaine Hydrochloride Injection, B.P.
Lidocaine Hydrochloride Jelly/Injection, U.S.P.
Lidocaine Topical Aerosol, U.S.P.

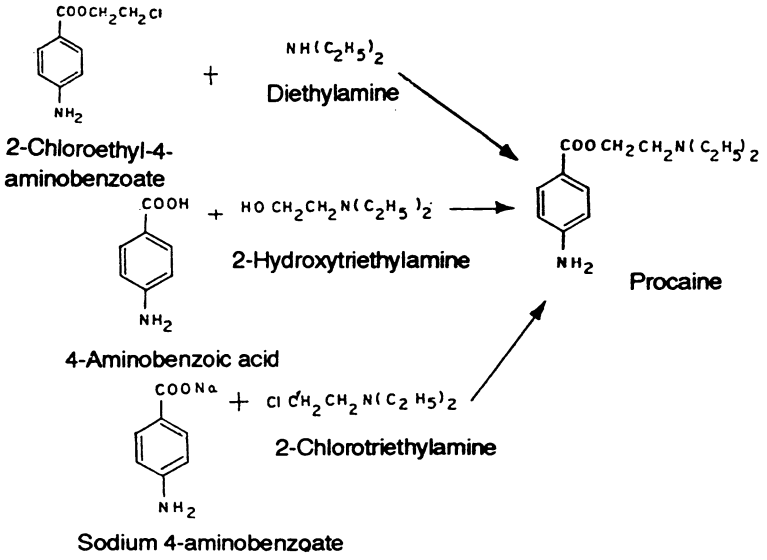
PROCAINE HYDROCHLORIDE

Nomenclature : 4-Aminobenzoic acid 2-(diethylamino) ethyl ester hydrochloride.

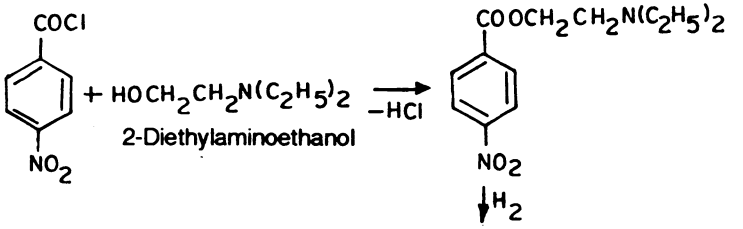
Brand Names : Novocain; Ethocaine; Neocaine; Syncaine; Scurocaine; Allocaine; Anesthesol; Anestil; Cetain; Isocaine-Asid; Isocaine-Heisler, Atoxicocaine; Naucaine; Bernacaine; Irocaine; Juvocaine; Jenacain; Kerocaine; Paracain; Planocaine; Aminocaine; Eugerase; Sevicaine; Topocaine; Westocaine.

Procaine is an important non-irritant local anaesthetic. It is a diethylamino analogue of benzocaine. It is prepared by heating the 2-chloroethyl ester of 4-aminobenzoic acid with diethylamine under pressure, by esterifying 4-aminobenzoic acid with 2-hydroxytriethylamine in the presence of concentrated sulphuric acid, or by heating sodium 4-aminobenzoate with 2-chlorotriethylamine at 120-130°.





Another method of preparation of procaine is by interacting 2-diethylaminoethanol with p-nitrobenzoyl chloride, followed by reduction of the 2-diethylaminoethyl p-nitrobenzoate.



p-Nitrobenzoyl chloride Procaine

Procaine, m.p. 61°, is hygroscopic and occurs as plates. It is highly soluble in water; soluble in alcohol, ether, benzene and chloroform.

Procaine is used as its monohydrochloride which is a white, odourless, crystalline powder, m.p. 153-156°, benumbing taste, stable in air. It is soluble in water and alcohol; slightly soluble in chloroform and acetone; practically insoluble in ether. Procaine is much stable at pH 3.6. It is protected from light.

At a storage temperature of 6° the shelf-life of the solution is 5 weeks and it is 9 weeks at -10°. The procaine molecule is oxidized at the aromatic amine portion. This type of breakdown can be controlled by nitrogen flushing of the solution and by addition of an antioxidant.

Uses : Procaine is used as local anaesthetic. It is widely used in dentistry and for the production of spinal anaesthesia. The hydrochloride is usually given subcutaneously with adrenaline; the function of the adrenaline is to localize and so prolong the effect of the procaine by virtue of its peripheral vasoconstrictor action.

Adverse effects of procaine are similar to lignocaine.

Official

Procaine, B.P., I.P.

Procaine and Adrenaline Injection, B.P., I.P.

Procaine and Phenylephrine Hydrochloride Injection, U.S.P.

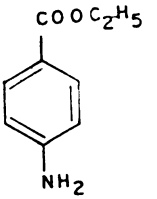
Procaine and Tetracaine Hydrochlorides and Levonordefrin Injection, U.S.P.

Procaine Hydrochloride Injection, U.S.P.

Sterile Procaine Hydrochloride, U.S.P.

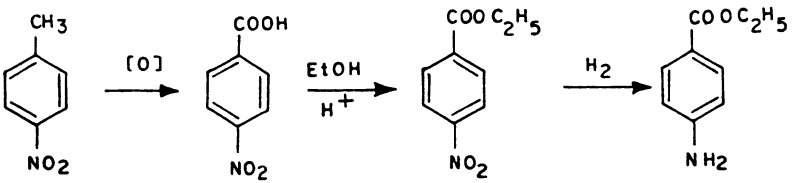
BENZOCAINE

Nomenclature : p-Aminobenzoic acid ethyl ester; Ethyl p-aminobenzoate.



Brand Names : Aethoform; Americaine; Anesthesin; Anesthone; Orthesin; Parathesin.

Benzocaine is the ethyl ester of 4-aminobenzoic acid which is prepared from 4-nitrotoluene by oxidation to 4-nitrobenzoic acid followed by esterification and reduction.



4-Nitrotoluene 4-Nitrobenzoic acid Ethyl 4-nitrobenzoate Benzocaine

Benzocaine has the chemical characters of an ester and a base. The amino group attached to aromatic ring can be diazotized. The diazonium salt so prepared couples with 2-naphthol in alkaline solution to give an orange-red azo-dye.

Benzocaine is a colourless, odourless crystalline powder, m.p. 88-92°; stable in air; slightly soluble in water (1 in 2500), soluble in alcohol (1 in 8), chloroform (1 in 2), ether (1 in 4), dilute acids, almond oil or olive oil. Benzocaine is destroyed when boiled with water. It forms a water soluble complex with caffeine which is less hydrolyzed in comparison to benzocaine. Benzocaine hydrochloride is too irritant since aqueous solutions are extensively hydrolyzed to an acid reaction.

Benzocaine is stored in well-closed containers and protected from light.

Uses : Benzocaine is a local anaesthetic used for the local relief of pain associated with dental conditions, sore throats, haemorrhoids, anal pruritus, and ear pain. It has also been used for pain relief in minor cuts, scrapes, burns and sunburn, muscular pains, strains, and sprains. Benzocaine is used in

creams, ointments, lotions, gels, solutions, and suppositories in concentrations up to 20% for topical analgesia and anaesthesia.

The adverse effects are similar to those of lignocaine.

Official

Benzocaine Sulphate, I.P.

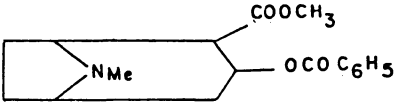
Benzocaine, B.P., I.P.

Benzocaine Cream/Ointment/Topical Aerosol, U.S.P.

COCAINE

Nomenclature : 3-(Benzoyloxy)-8-methyl-8-azabicyclo [3.2-1] octane-2-carboxylic acid methyl ester.

Brand Names : Benzoylmethylecgonine; Ecgonine methyl ester benzoate.



Cocaine is an alkaloid isolated from the leaves of *Erythroxylon coca* and other species of *Erythroxylon* (Family: Erythroxylaceae). The leaves contain about 1 per cent of total alkaloids. The total alkaloids are separated from the powdered leaves by treatment with alkali followed by extraction with benzene. The alkaloids are obtained as sulphates or hydrochlorides by extracting the benzene layer with dilute acid. Pure cocaine is obtained by fractional crystallization of the total alkaloidal salt.

Cocaine is manufactured by converting ecgonine, obtained by hydrolysis of other coca alkaloids such as cinnamylcocaine. The methyl ester is transformed into benzoyl derivative by the action of benzoyl chloride.

Test for cocaine : Cocaine is warmed with concentrated sulphuric acid and then diluted with water. It gives a pleasant odour of methyl benzoate, and on standing a crystalline precipitate of benzoic acid.

Cocaine, m.p. 96-98°, is a colourless crystalline powder. It is slightly volatile above 90°, but the sublimate is not crystalline. It is practically insoluble or very slightly soluble in water; soluble in alcohol, chloroform, ether and arachis oil.

Cocaine hydrochloride, m.p. 197°, is a colourless, odourless hygroscopic crystalline powder which is soluble in water, alcohol, chloroform and glycerol; practically insoluble in ether and fixed

oils. It is stored in well-closed containers and protected from moisture and light.

Aqueous solutions containing cocaine hydrochloride (5%) and phenol (0.5%) remained clear and colourless for a year at 0° to 4°, room temperature and 37°.

Uses : Cocaine is topical anaesthetic (narcotic).

Side effects of cocaine are similar to those of lignocaine. Systemic absorption of small doses may slow the heart. Topical application of cocaine to the cornea can cause corneal damage. Cocaine is abused for its stimulant effects on the central nervous system. It may give rise to psychotic states and hallucinations, nausea, vomiting, loss of appetite, weight loss, fatigue, rapid pulse, fever and rapid, shallow respiration.

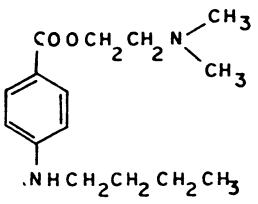
Official

Cocaine, B.P., I.P.

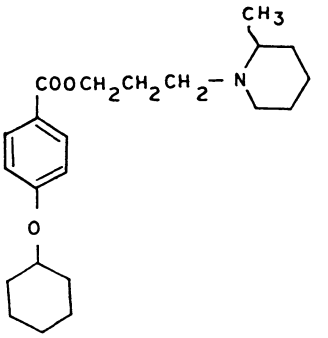
Cocaine Eye Ointment, I.P.

Cocaine Hydrochloride, B.P., I.P.

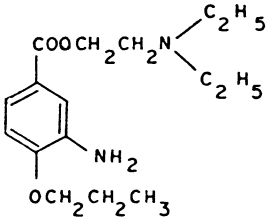
Miscellaneous Anaesthetics



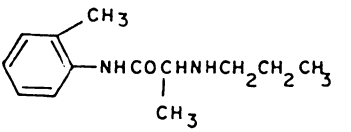
Amethocaine



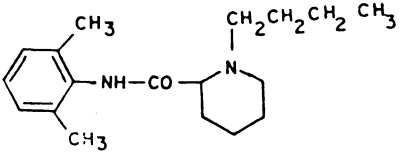
Cyclomethycaine



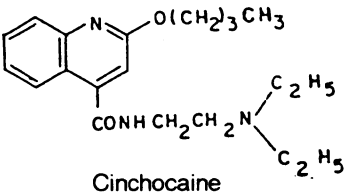
Proxymetacaine



Prilocaine



Bupivacaine



Cinchocaine

Official

Amethocaine Hydrochloride, B.P.
Amethocaine Eye Drops, B.P.
Cyclomethycaine Sulphate, B.P.
Proxymetacaine Hydrochloride, B.P.
Proxymetacaine Hydrochloride Eye Drops, B.P.
Bupivacaine Hydrochloride, B.P.
Bupivacaine and Adrenaline Injection, B.P.
Bupivacaine Hydrochloride Injection, B.P.
Cinchocaine Hydrochloride, B.P., I.P.
Prilocaine Hydrochloride, B.P.

16

ANTIDEPRESSANT DRUGS

Mental depression, like anxiety states, is a common psychiatric condition. If it is a more serious condition, then it can disrupt the normal social life and may derive the individual to commit suicide. Antidepressant drugs are used to treat depressed persons. The common symptoms of mental depression are feeling of guilt, tension, anxiety, emotional withdrawal and in case of endogenous depression, motor retardation. In manic depression extreme swings in mood characterized by mood elation, hyperactivity, uncontrolled thought and speech followed by severe depression and suicidal tendencies are observed.

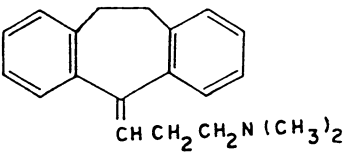
The drugs used as antidepressant are divided as tricyclic antidepressants and monoamine oxidase inhibitors. Tricyclic antidepressants cause changes in the electroencephalogram similar to those produced by the phenothiazines. Their mode of action as antidepressant is not completely clear. Some of them have marked sedative action and some possess tranquillizing properties. Dibenzazepine, dibenzocycloheptene and related derivatives are the tricyclic antidepressants.

Monoamine oxidase is the enzyme mainly responsible for metabolising monoamines such as noradrenaline. These drugs may act by increasing the concentration of amines in the brain. The mechanism of their action as antidepressant in not fully understood.

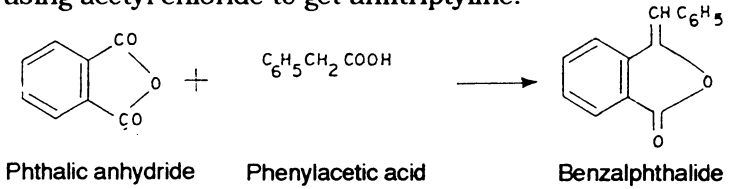
AMITRIPTYLINE

Nomenclature : 3-(10, 11-Dihydro-5H-dibenzo *[a, d]*-cyclohepten-5-ylidene)-N, N-dimethyl-1-propanamine. 10, 11-Dihydro -N, -N-dimethyl-5H-dibenzo *[a, d]* cycloheptene -Δ5, γ-propylamine.

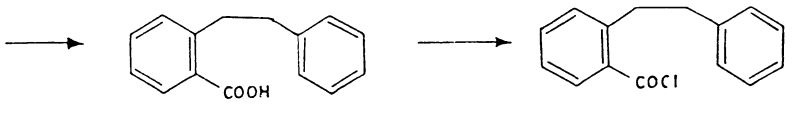
Brand Names : Ro 4-1575; Triptisol; Tryptanol; Sarotex; Seroten; Laroxyl; Redomex; Adepril.



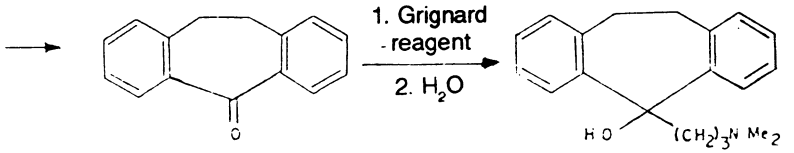
Amitriptyline is prepared from dibenzocycloheptenone. The ketone is synthesized by condensation of phthalic anhydride with phenylacetic acid to give benzalphthalide, which on reduction yields 2-phenethylbenzoic acid; this is converted to the acid chloride, which on treatment with aluminium chloride undergoes cyclization. The ketone is reacted with the appropriate Grignard reagent, followed by hydrolysis of the complex and dehydration using acetyl chloride to get amitriptyline.



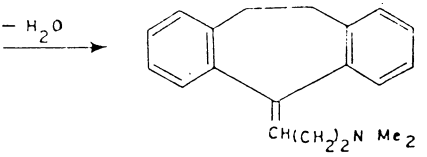
Phthalic anhydride Phenylacetic acid Benzalphthalide



2-Phenethylbenzoic acid Acid chloride



10, 11-Dihydro-5H-dibenzo [a, d] cyclohepten-5-one



Amitriptyline

Amitriptyline hydrochloride (Brand Names : Amitid; Amitril; Deprex; Domical Elavil; Endep; Lentizol; Miketorin; Saroten; Tryptizol) is an odourless, colourless or white powder. It is soluble in water (1 in 1), alcohol (1 in 1.5) chloroform (1 in 2) and

methanol (1 in 1); practically insoluble in ether; m.p. 196-197°; stored in a well-closed container.

Uses : Amitriptyline is a tricyclic antidepressant used in the treatment of mental depression, and for nocturnal enuresis in children.

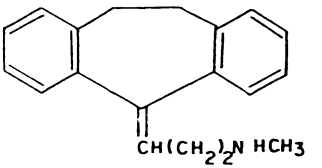
Many side-effects of amitriptyline and other tricyclic antidepressants are caused by their antimuscarinic action. These include dry mouth, sour or metallic taste, constipation, urinary retention, blurred vision and disturbances in accommodation, palpitation, tachycardia, and impotence. Many other side effects have also occurred.

Official

Amitriptyline Embonate, B.P.
Amitriptyline Embonate Mixture, B.P.
Amitriptyline Hydrochloride, B.P., I.P.
Amitriptyline Tablets, B.P., I.P.
Amitriptyline Hydrochloride Tablets/Injection, U.S.P.

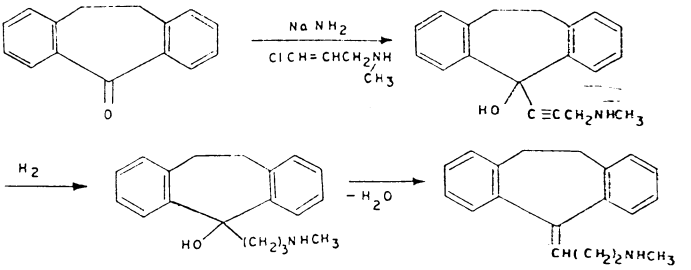
NORTRYPTYLINE

Nomenclature : 3-(10, 11-Dihydro-5H-dibenzo *[a, d]* -cyclohepten 5-ylidene)-N-methyl-1-propanamine.



Brand Names : Desitriptilina; Desmethylamitriptyline; Avantyl; Aventyl; Allegron; Noritren; Ateben; Psychostyl; Sensaval.

This is a lower homologue of amitriptylline which is manufactured from the dibenzocycloheptenone by condensation with N-methyl-β-chloroallyl amine, followed by reduction and dehydration.



Nortriptyline hydrochloride (Brand Names : Acetexa,

Altilev; Nortrilen; Norzepine; Pamelor; Sensival; Vividyl), m.p. 213-215°, is a white powder, with a slight characteristc odour. It is soluble in alcohol, water and chloroform; practically insoluble in ether, acetone, benzene; stored in a well-closed container and protected from light.

Uses : Nortriptylline has actions, uses and adverse effects similar to those of amitriptylline.

It is less sedating than amitriptyline.

Official

Nortriptyline Hydrochloride, B.P.

Nortriptyline Capsule, B.P.

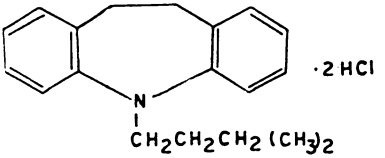
Nortriptyline Tablets, B.P.

Nortriptyline Hydrochloride Capsules/Oral Suspension, U.S.P.

IMIPRAMINE HYDROCHLORIDE

Nomenclature : 10, 11-Di-hydro-N, N-dimethyl-5H-dibenz *[b, f]* azepine *[b, f]* azepine-5-propanamine; 5-(3-Dimethylaminopropyl)-10, 11-dihydro-5H-dibenz-*[b, f]* azepine.

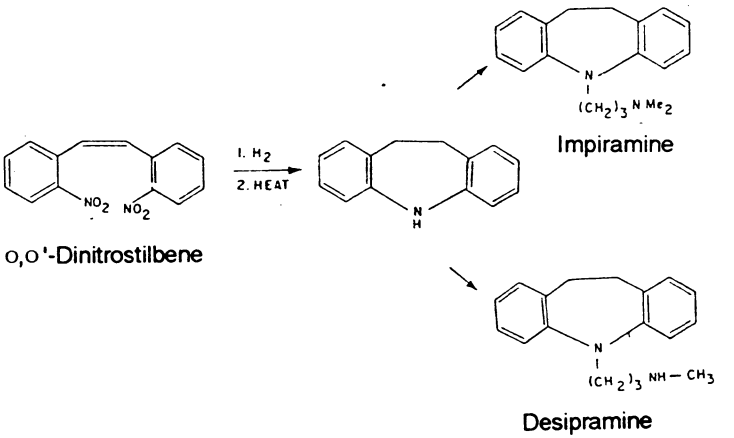
Brand Names : Berkomine; Deprinol; Dyna-Zina; Efuranol; Imavate; Tofranil; Chrytemin; Imiprin; Iramil; Imidol; Melipramin; Dimipressin; Pryleugan; Presamine; Feinalmin; Imilaryle; Iprogen; Janimine; Imizine hydrochloride; G-22355 hydrochloride; Antideprin hydrochloride.



Imipramine is synthesized by reduction of o,o'-dinitrostilbene, and heating the resulting 2, 2'-diaminodibenzyl and its hydrochloride to 280° to give o-iminodibenzyl. This reacts with the appropriate alkyl halide in the presence of sodamide to give impiramine (b.p. 160°) and desipramine :

Imipramine hydrochloride, m.p. 174-175°, is a white or slightly yellow, odourless, crystalline powder; soluble in water (1 in 2), alcohol, chloroform and acetone; practically insoluble in ether. It acquires a yellow to reddish colour under the influence of light. It is stored in airtight containers and protected from light.

Uses : Imipramine is a tricyclic antidepressant with actions and uses similar to those of amitriptyline.



Official

Imipramine Hydrochloride, B.P., I.P.
Imipramine Tablets, B.P., I.P.
Imipramine Hydrochloride Tablets/Injection, U.S.P.

PHENELZINE

Nomenclature : (2-Phenethyl) hydrazine; β-Phenylethylhydrazine.

$$C_6H_5\ CH_2\ CH_2\ NHNH_2$$

Phenelzine is an aralkyl derivative of the inorganic base, hydrazine, NH_2-NH_2. It is synthesized from 2-phenylethanol, which on treatment with phosphorus pentachloride yields phenethyl chloride which on condensation with hydrazine produces phenethylhydrazine.

$$C_6H_5\ CH_2\ CH_2\ OH \rightarrow C_6H_5\ CH_2\ CH_2\ Cl \rightarrow C_6H_5\ CH_2\ CH_2\ NH\ NH_2$$

Phenelzine is a liquid, b.p. 74O.

Phenelzine sulphate (Brand Names : W-1544a; Nardil; Estinerval; Kalgan; Nardelzine; Phenodyn; Stinerval) is a white or yellowish white powder with a peculiar odour; soluble in water (1 in 7); practically insoluble in alcohol, chloroform, and ether; stored in a cool place in airtight containers and protected from light.

Uses : Phenelzine is used in the treatment of neurotic or a typical depression.

Adverse effects of phenelzine include orthostatic hypotension, dizziness, drowsiness, headache, weakness and fatigue, dryness of mouth, constipation, nausea and vomiting.

Official

Phenelzine Sulphate, B.P.

Phenelzine Tablets, B.P.

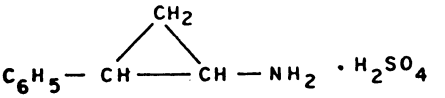
Phenelzine Sulphate Tablets, U.S.P.

TRANYLCYPROMINE SULPHATE

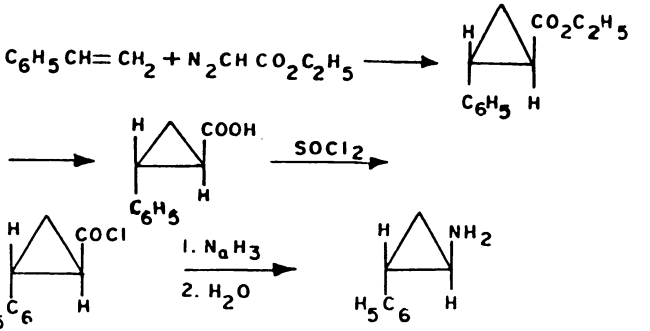
Nomenclature : *trans*-2-Phenylcyclopropanamine.

Brand Names : SKF trans-385; Parnitene sulphate; Parnate; Tylciprine.

This cyclopropane derivative is prepared from styrene and ethyl diazoacetate which yields ethyl 2-phenylcyclopropane carboxylate.



Hydrolysis of the carboxylate forms a mixture of *cis* and *trans* - 2-phenylcyclopropane carboxylic acid which produced respective acid chlorides with thionyl chloride. Treatment with sodium azide in boiling toluene followed by hydrolysis of the isocyanate (Curtius reaction) gives the desired compound.



Tranylcypromine sulphate occurs as a white crystalline powder; odourless or with a faint odour of cinnamaldehyde. It is soluble in water (1 in 20); very slightly soluble in alcohol and in ether; practically insoluble in chloroform; stored in well-closed containers.

Uses : Actions, uses and adverse effects of tranylcypromine are similar to those of phenelzine.

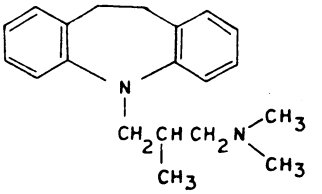
Official

Tranylcypromine Sulphate, B.P., U.S.P.

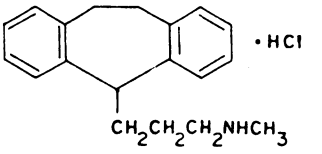
Tranylcypromine Tablets, B.P.

Tranylcypromine Sulfate Tablets, U.S.P.

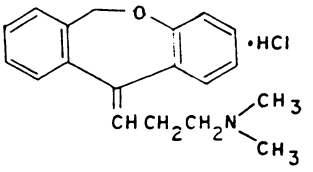
Miscellaneous Tricyclic Antidepressants



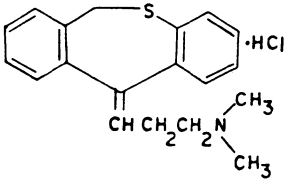
Trimipramine maleate



Protriptyline Hydrochloride



Doxepin Hydrochloride



Dothiepin Hydrochloride

Official

Trimipramine Maleate, B.P.

Trimipramine Tablets, B.P.

Protriptyline Hydrochloride, B.P.

Protriptyline Tablets, B.P.

Doxepin Hydrochloride, B.P.

Doxepin Capsules, B.P.

Dothiepin Hydrochloride, B.P.

Dothiepin Capsules, B.P.

17

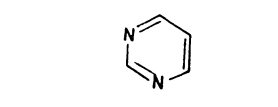
ANALEPTICS

Analeptics stimulate the central nervous system and, in large doses, they cause generalized convulsions. Thus, these drugs have a wide range of effects of which, stimulation of breathing is only one. Many forms of illness, both mental and physical, involve a depression of mental activity. Analeptics often stimulate respiratory centre and other centres. The vasomotor centre, which maintains the constriction of the blood vessel walls, is frequently affected. Some analeptic agents increase vasoconstrictions. These result in an increased peripheral resistance to the flow of blood, thereby causing an elevation of blood supply.

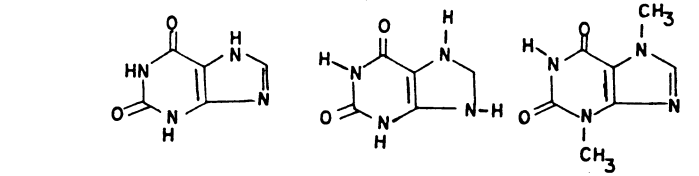
Picrotoxin, pentylenetetrazol, nikethamide, doxapram, ethamivan, lobeline and purine bases (caffeine) are the drugs used as analeptics to counteract respiratory depression and coma arose from overdosage of central depressant agents.

Purines, Pyrimidines and Related Heterocyclic Compounds

Purine is a close-chain compound containing the fused carbon-nitrogen skeletons of pyrimidine and imidazole. Purine and pyrimidine bases are constituents of the nucleic acids. The purine bases occur in nature primarily as oxidized derivatives. The basic analogues of purines, known as alkaloids, occur in plants. The three most common naturally occurring xanthines include caffeine, theobromine and theophylline which have diuretic properties.



Pyrimidine Imidazole Purine



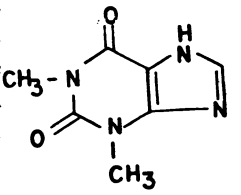
Xanthine Uric acid Theobromine

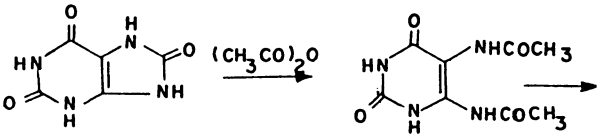
THEOPHYLLINE

Nomenclature : 3,7-Dihydro-1,3-dimethyl-1H-purine, 2,6-dione. 1, 3-Dimethylxanthine.

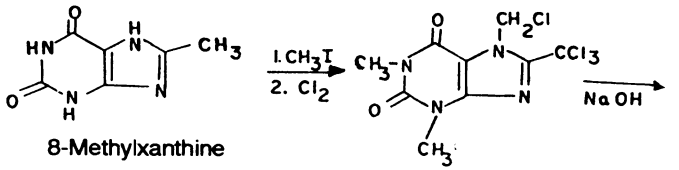
Brand Names : Afonilum; Armophylline, Bronchoretard; Accurbron; Bronkodyl; Elixicon; Labid; Physpan; Rona-Phyllin; Slo-Phyllin; Sustaire; Theal tabl; Theocap; Theoclear; Theocontin; Theo-Dur; Theocin; Theolair; Theophyl-SR; Theolix; Theograd; Theosol; Theostat; Theovent; Uniphyllin.

Theophylline has stronger diuretic properties than caffeine. It occurs in small amounts in tea. For its preparation 1, 3, 7, 8-tetramethylxanthine is first obtained from uric acid which is chlorinated to produce tetrachloro-derivative by substitution in the methyl groups in positions 7 and 8. This compound is converted into theophylline by heating with alkalies in which elimination of HCHO from a hydroxymethylamino [-N (CH_2 OH)-] group takes place.

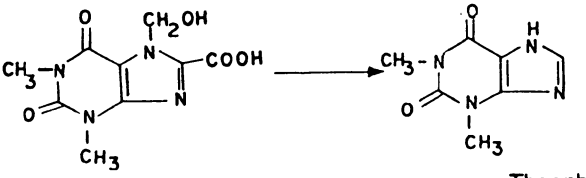




Uric acid Diacetyl derivative



8-Methylxanthine



Theophylline

Theophylline is also prepared from the product of the condensation of dimethylurea with cyanoacetic acid.

Theophylline, m.p. 270-274°, is a white, odourless, crystalline powder; soluble in alcohol (1 in 80); slightly soluble in water, chloroform and ether; soluble in solutions of alkali hydroxides, in aqueous ammonia and in mineral acids; stored in well-closed containers.

Uses : Theophylline relaxes smooth muscles, myocardium and central nervous system. It is used as diuretic, cardiac stimulant, smooth muscle relaxant, vasodialator; for the relief of bronchospasm in asthma, bronchitis, emphysema and acute respiratory infections; to relieve apnoea.

The side-effects of theophylline and its derivatives are gastro-intestinal irritation and stimulation of the central nervous system. It may cause nausea, vomiting, abdominal pain, gastro-intestinal bleeding, insomnia, headache, anxiety, restlessness, vertigo and palpitation.

Official

Theophylline, B.P., I.P.

Theophylline Capsules, U.S.P.

Theophylline Hydrate, B.P.

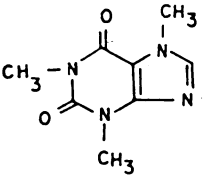
Theophylline, Ephedrine Hydrochloride and Phenobarbitol Tablets, U.S.P.

Theophylline and Guaifenesin Tablets, U.S.P.

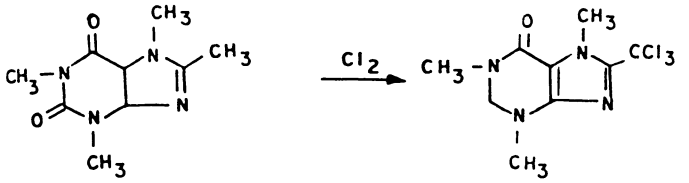
CAFFEINE

Nomenclature : 3, 7-Dihydro-8-[2-hydroxyethyl)-methylamino]-1,3,7-trimethyl-1H-purine -2, 6-dione; 8-[(2-Hydroxyethyl) methylamino] caffeine; 1, 3, 7-Trimethylxanthine.

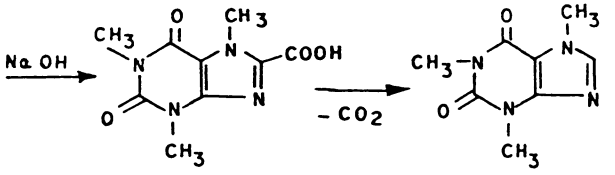
Brand Names : Thein; Guaranine; Methyltheobromine; NO-Doz; Coffeine.



Caffeine is a purine which occurs in tea, coffee, male leaves; also in guarana paste and cola nuts. It is usually extracted from tea dust or damaged tea. It can be prepared from uric acid which occurs in abundant amounts in guano. Uric acid is first converted into 1,3,7,8-tetramethylxanthine as described under theophylline. Finally, the methyl group originally introduced in the 8 position is eliminated by chlorination, followed by heating with water or alkali.



1, 3, 7, 8-Tetramethyl-xanthine



Caffeine

Caffeine, m.p. 230°, sublimes at 178°, occurs as odourless, silky white, usually matted together, or white crystalline powder. It effloresces in air; is soluble in water (1 in 60); freely soluble in boiling water and chloroform; slightly soluble in alcohol and in ether. It dissolves in concentrated solutions of alkali benzoate, salicylates, citrates and cinnamates. It is a weak base. Its aqueous solutions are neutral to litmus. Caffeine is stored in airtight containers. A cup of coffee or tea contains about 60 mg of caffeine.

Caffeine can be identified by *murexide test* by treating it with concentrated nitric acid. The mixture is dried on a water-bath, cooled and treated with a drop of dilute ammonia to produce deep-purple colour. This test is also positive for uric acid, theophylline, and many other purine derivatives.

Uses : Caffeine is a central nervous stimulant. It is used as a cardiac and respiratory stimulant and as a diuretic.

Adverse effects of caffeine are the same as described under theophylline.

Official

Caffeine, B.P., I.P.

Aspirin and Caffeine Tablets, B.P.

Caffeine Citrate, I.P.

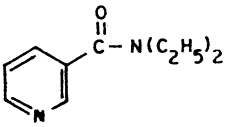
Caffeine Hydrate, B.P.

Caffeine and Sodium Benzoate Injection, U.S.P.

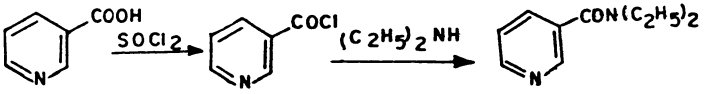
CORAMINE

Nomenclature : N, N-Diethyl-3-pyridinecarboxamide; N, N-Diethylnicotinamide; Pyridine-3-carboxylic acid diethylamide.

Brand Names : Nikethamide; Nicotinic acid diethylamide; Anacardone; Astrocar; Carbamidal; Cardamine; Cardiamid; Cardimon; Coracon; Cordiamin; Corediol; Cormed; Cormid; Corvitol; Corvotone; Dynacoryl; Eucoran; Inicardio; Niamine; Nicamide; Nicor; Nicorine; Nikardin; Pyricardyl; Salvacard; Stimulin; Ventramine.



Coramine is the diethylamide of nicotinic acid. It is prepared by converting nicotinic acid into its acid chloride by thionyl chloride and treating the product with diethylamine.



Nicotinic acid Coramine

Coramine is a colourless or slightly yellow oily liquid or crystalline mass with a slight characteristic odour and a faintly bitter taste followed by a faint sensation of warmth, m.p. 24-26°, b.p. 296-300°. It is miscible with water; alcohol, chloroform, and ether; incapatible with sodium carbonate solutions which cause precipitation.

Uses : Coramine is a respiratory stimulant. It has an intermediate central stimulant effect. It is injected to counteract respiratory depression following administration of depressant drugs such as the barbiturates. It has low toxicity.

Official

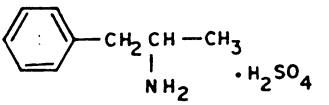
Nikethamide, B.P., I.P.

Nikethamide Injection, B.P., I.P., U.S.P.

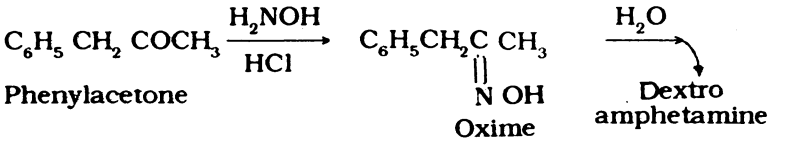
DEXTROAMPHETAMINE SULPHATE

Nomenclature : d-α-Methylphenethylamine sulfate; d-1-Phenyl-2-aminopropane sulfate; α-Methylbenzene ethanamine sulfate;

Brand Names : Dexedrine sulphate; Afatin; Dexamphetamine, Dexampex; d-Amfetasul; Domafate; Obesedrin; Dexten; Maxiton; Sympamin; Albemap; Dadex; Adrex; Dexalone; Amsustain; Betafedrina; Diocurb; Amphetamine sulphate.



Dextroamphetamine (Amphetamine) is a mobile, colourless with liquid amine-like odour and acrid burning taste, b.p. 200-203°. It is prepared from phenylacetone as follows :



Phenylacetone

Oxime

Amphetamine is a strong base and forms an alkaline solution in water. It contains an asymmetric carbon atom, and the synthetic compound is the (±) - mixture. It is resolved by fractional crystallization of the D-tartrates followed by treatment with 10% H_2SO_4. It may be prepared from phenylalanine. Dextroamphetamine sulphate, the dextrorotatory isomer of amphetamine, is a white, odourless, crystalline powder; m.p. above 300°; soluble in water (1 in 10) and alcohol (1 in 800); practically insoluble in ether; stored in well-closed containers.

Uses : Dextroamphetamine is a sympathomimetic agent with adrenergic activity. It has marked stimulant effect on the central nervous system.

The side-effects of dexamphetamine are overstimulation of the central nervous system, insomnia, nervousness, restlessness, irritability and euphoria. Excessive use may lead to tolerance and physical dependence.

Official

Dextroamphetamine Sulfate Elixir/Tablets/Capsules, U.S.P.

18

ADRENERGIC DRUGS

The *adrenergic* or *sympathomimetic* drugs are agents that mimic the responses obtained as a result of stimulation of the sympathetic or adrenergic nerves. Most of these compounds contain an intact or a partially substituted amino (NH_2) group.

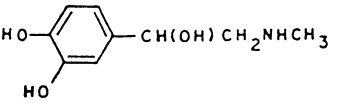
Adrenaline is a hormone which is secreted by adrenal medulla. It exerts various pharmacological actions like cardiac stimulation, increase in blood pressure, constriction of smaller arterioles, relaxation of bronchial muscles and stimulation of central nervous system. These actions stimulate the effects which are produced by the stimulation of adrenergic nerves. Adrenergic agents exert similar actions.

Adrenergic drugs are used for raising blood pressure (e.g. noradrenaline, metaraminol), as central stimulants (e.g. amphetamine), as smooth muscle relaxants (e.g. adrenaline, salbutamol), in allergic reactions (e.g. adrenaline, ephedrine), for local vasoconstrictor effect (e.g. adrenaline, naphazoline, phenylephrine) and for suppressing the appetite (e.g. phenteramine). Adrenergic compounds contain hydoxyl groups substituted in the 3-and 4-positions of the benzene ring (e.g. catecholamines). Some of the compounds lack the hydroxyl groups and known as non-catecholamines.

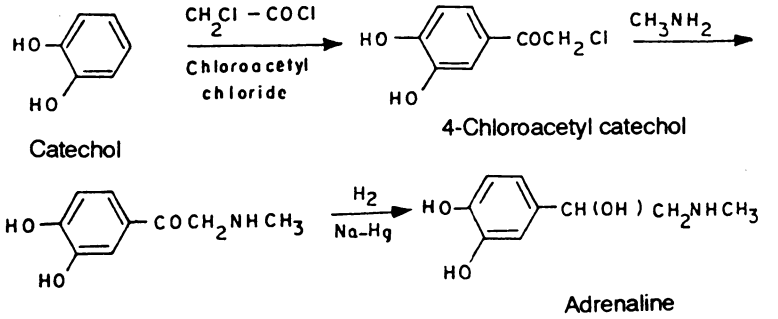
ADRENALINE

Nomenclature : 4-[1-Hydroxy-2-(methylamino) ethyl]-1, 2-benzenediol; 3, 4-Dihydroxy - α [(methylamino) methyl] benzyl alcohol.

Brand Names : Epinephrine; Adrenalin; Suprarenin; Suprarenalin; Epirenamine; Levorenin.



Adrenaline is the active hormone produced by the adrenal medulla in most species; occurs as the l-form in animals and man. It may be obtained from the adrenal glands of certain mammals or may be prepared from catechol as:.



The synthetic substance is the (±)-mixture. It is resolved by crystallization of the D-tartrate. The l-form of adrenaline has at least twelve times the biological activity of its d-form enantiomorph.

Adrenaline, m.p. 211-212°, is a white or creamy-white, odourless, crystalline powder. It darkens in colour on exposure to air and light. It is sparingly soluble in water; practically insoluble in alcohol, chloroform, ether, fixed and volatile oils. Adrenaline dissolves in solutions of mineral acids and in solutions of sodium or potassium hydroxides, but not in solutions of ammonia or the alkali carbonates. Solutions in water are alkaline to litmus. It is unstable in neutral or alkaline solution which readily becomes red on exposure to air. It is stored in airtight containers, preferably in which the air has been replaced by nitrogen and protected from light.

Uses : Adrenaline is sympathomimetic, vasoconstrictor, cardiac stimulant, and bronchodilator. It is used to counter allergic reactions, anaesthesia, cardiac arrest, to cure asthma, to cause a rise in blood pressure and to enhance the activity of local anaesthetics.

The disadvantages of adrenaline are short duration of action, decomposition of its salts in solution, fear, anxiety, restlessness, tremor, insomnia, confusion, irritability, weakness and psychotic states. Appetite may be reduced, and nausea and vomiting may occur.

Offical

Adrenaline, B.P., I.P.

Adrenaline Maleate Injection, I.P.

Adrenaline Acid Tartrate, B.P.

Adrenaline Injection, B.P.

Adrenaline Solution, B.P.

Compound Adrenaline and Atropine Spray, B.P.

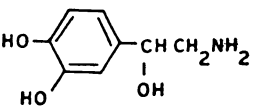
Epinephrine Bitartrate Inhalation Aerosol, U.S.P.

Epinephrine Nasal/Ophthalmic Solution, U.S.P.

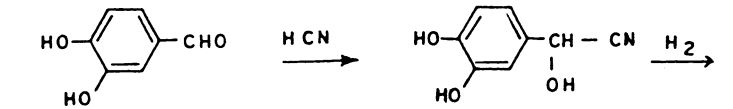
NORADRENALINE

Nomenclature : 4-(2-Amino-1-hydroxyethyl)-1, 2-benzenediol; α-(Aminomethyl)-3,4-dihydroxybenzyl alcohol; 1-(3, 4-Dihydroxyphenyl)-2-aminoethanol.

Brand Names : Norepinephrine; Levarterenol.

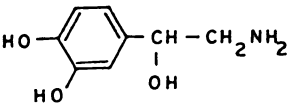


Noradrenaline, the catecholamine, is also a product of the adrenal medulla. It is liberated at sympathetic nerve endings when they are in action. It is the lower homologue of adrenaline and is a primary amine rather than a secondary amine. The l-form, the demethylated precursor of epinephrine, occurs in animals and man. A synthesis identical to that of adrenaline is used. In an another preparative method protocatechuic aldehyde is the starting material.



Protocatechuic aldehyde

Cyanohydrin



Noradrenaline

The racemic mixture can be resolved by formation of (+) - acid tartrates. The dl-form, m.p. 191°, is sparingly soluble in water; very slightly soluble in alcohol, readily soluble in dilute acids and alkalies. L-From, also known as levarterenol, Adrenor and Levophed, occurs as microcrystalline powder, m.p. 216-

218°. l-Form hydrochloride (synonym, Arterenol), m.p. 145-147°, is freely soluble in water. Solutions are slowly oxidized under the influence of light and oxygen.

L-Form Bitartrate (Brand Names : Levarterenol bitartrate; Aktamin; Binodrenal) is a white, crystalline powder, m.p. 102-104°; when anhydrous, m.p. 158-159. It darkens on exposure to air and light. It is soluble in water (1 in 2.5), and alcohol (1 in 300); practically insoluble in chloroform and ether; stored in airtight containers and protected from light.

Uses : Noradrenaline is a sympathomimetic agent used to maintain blood pressure in acute hypotensive states resulting from trauma, central vasomotor depression and haemorrhage.

Adverse effects are similar as described under adrenaline.

Official

Noradrenaline Acid Tartrate, B.P., I.P.

Noradrenaline Injection, B.P.

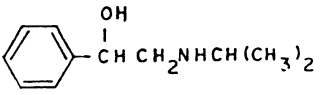
Norepinephrine Bitartrate Injection, U.S.P.

ISOPRENALINE

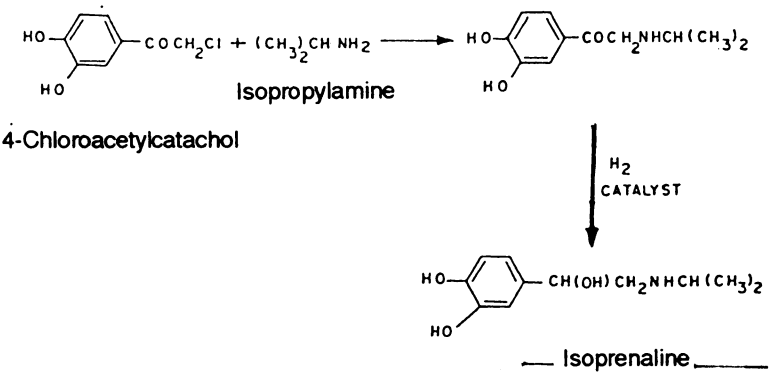
Nomenclature : 4-[1-Hydroxy-2-[1-methylethyl)-amino]ethyl]-1, 2-benzenediol; 3, 4-Dihydroxy-α [(isopropylamino) methyl] benzyl alcohol.

Brand Names : A-21; Aludrine; Aleudrin; Isuprel; Norisodrine; Asiprenol; Asmalar; Neo-Epinine; Novodrin; Isupren; Neodrenal Lomupren, Isopropydrin; Assiprenol; Respifral; Bellasthman; Saventrine; Proternol; Isorenin; Vapo-N-Iso; Isonorin; Isoproterenol; Isopropylarterenol.

Isoprenaline is the synthetic isopropyl homologue of adrenaline. Like adrenaline, it is synthesized from 4-chloroacetyl-catechol, which is condensed with isopropylamine to yield a ketone which is reduced in the presence of a catalyst.



Isoproterenol hydrochloride, m.p. 170-171°, is a white, odourless, crystalline powder. It gradually darkens on exposure to air and light. It is soluble in water and alcohol; practically insoluble in chloroform, ether and benzene. Its aqueous solutions become pink on standing. It is stored in airtight containers and protected from light.



The presence of a larger alkyl (isopropyl) group on the amino group eliminates circulatory effects except palpitation of the heart.

Uses : Isoproterenol is a sympathomimetic agent, chiefly as bronchodilator. It stimulates the central nervous system. It has a powerful stimulating action on the heart and increases cardiac output and rate. It also causes peripheral vasodilation and produces a fall in diastolic blood pressure.

Adverse effects of isoprenaline are the same as described under adrenaline. Prolonged use of isoprenaline may lead to resistance, eventual deterioration and severe damage to the teeth.

Official

Isoprenaline Hydrochloride, B.P.

Isoprenaline Hydrochloride Injection, B.P.

Isoprenaline Sulphate, B.P., I.P.

Isoprenaline Tablets, I.P.

Isoproterenol Hydrochloride Tablets/Injection/Inhalation Aerosol, U.S.P.

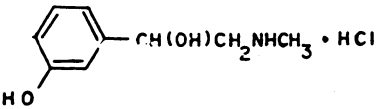
Isoproterenol Sulfate Inhalation Aerosol/Solution, U.S.P.

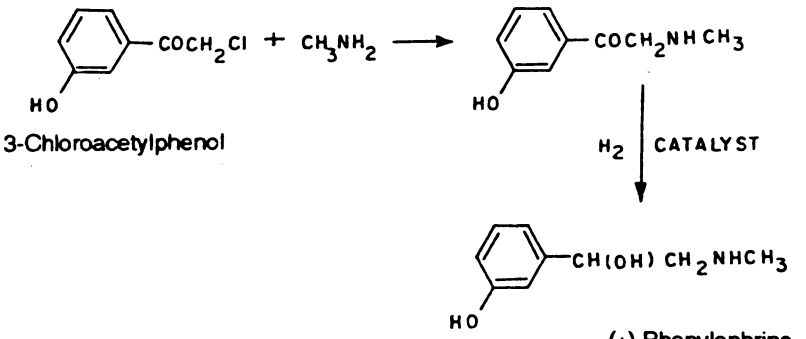
PHENYLEPHRINE HYDROCHLORIDE

Nomenclature : (R)-3-Hydroxy-α-[(methylamino) methyl] benzene methanol hydrochloride; 1-*m*-Hydroxy-α-[(methylamino) methyl] benzyl alcohol hydrochloride.

Brand Names : Adrianol, Fenilfar; Isophrin hydrochloride; Metaoxedrin; Lexatol; Meta Sympatol; Mezaton; Neophryn; Oftalfrine; Pyracort D; Prefrin; Mydfrin.

Phenylephrine is another synthetic compound of adrenaline-like properties. It is prepared by treating 3-chloroacetyl phenol and methylamine and is resolved by fractionation of its d-camphorsulphonic acid salt.

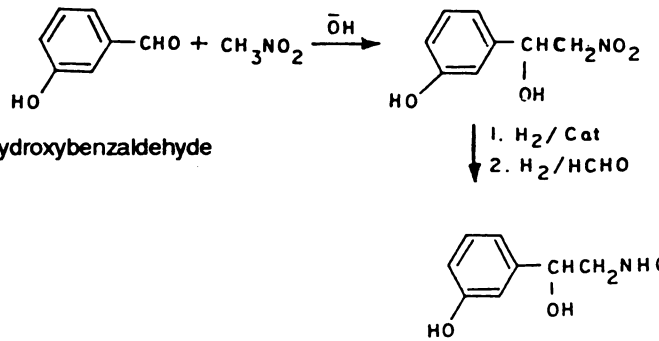




3-Chloroacetylphenol

(±) Phenylephrine

In an another synthesis, phenylephrine is prepared from m-hydroxybenzaldehyde.



m-Hydroxybenzaldehyde

(±) Phenylephrine.

Isoprenaline hydrochloride, m.p. 140-145°, occurs as a white, odourless, bitter crystalline powder. The aqueous solution is neutral to litmus paper. It is soluble in water (1 in 2), and alcohol (1 in 4); stored in airtight containers and protected from light.

Uses : Phenylephrine hydrochloride is a sympathomimetic agent used in the treatment of hypotensive states, e.g.; circulatory failure, spinal anaesthesia, drug-induced hypotension; to produce bronchodilator effects; as a nasal decongestant in rhinitis and sinusitis.

Side effects of phenylephrine are the same as described under adrenaline. It is irritant and may cause local discomfort at the site of application.

Official

Phenylephrine Hydrochloride, I.P., B.P.

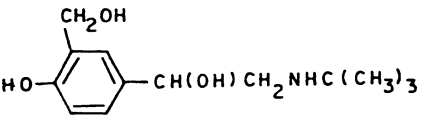
Phenylephrine Injection, B.P.

SALBUTAMOL

Nomenclature : α^1-[[(1,1-Dimethylethyl) amino] methyl]-4-hydroxy-1, 3-benzenedimethanol; α^1-[(*tert* - Butylamino)methyl]-4-hydroxy-*m*-xylene-α, α^1-diol.

Brand Names : Albuterol; AH 3365; Sch-13949 W.

Salbutamol is a white, crystalline powder, m.p. 151°; soluble in water (1 in 70) and alcohol (1 in 25); slightly soluble in ether.



Salbutamol Sulphate (Brand Names : Aerolin; Broncovaleas; Proventil; Sultanol; Venetlin; Ventolin) is a white, odourless powder; soluble in water (1 in 4); slightly soluble in alcohol, chloroform and ether. Salbutamol and its salts are stored in airtight containers and protected from light.

Uses : Salbutamol is a sympathomimetic agent; used as a bronchodilator and in prevention of premature labour; as the base in aerosol inhalers.

Adverse effects of salbutamol are similar as described under adrenaline.

Official

Salbutamol, B.P.

Salbutamol Sulphate, B.P.

Salbutamol Sulphate Injection, B.P.

Salbutamol Tablets, B.P.

8. SILVER NITRATE, $AgNO_3$

Preparation: Silver nitrate is prepared by dissolving metallic silver in hot, slightly concentrated nitric acid.

$$Ag + 2HNO_3 = AgNO_3 + NO_2\uparrow + H_2O$$

The solution is filtered through glass wool and set aside in a dark, dust proof room to crystallize. It is recrystallized from water.

Physical and Chemical Properties

Silver nitrate occurs as colourless or white rhombic or tabular crystals without odour and with a bitter, caustic, metallic taste. It is very soluble in water and sparingly soluble in alcohol. It is not affected by light, when pure. But when it comes into contact with any organic matter such as skin, it is reduced to metallic silver which is grey or greyish black in colour and leaves a stain. The best way to remove this stain is to paint it with tincture of iodine or any iodine solution and remove the iodine with a solution of sodium thiosulphate. When it is heated at 209°C, it melts to a slight, yellow liquid without decomposition. However, on further heating, it slowly decomposes with evolution of oxides of nitrogen, leaving a residue of metallic silver. Aqueous solution of silver nitrate is neutral to litmus. Silver nitrate is photosensitive (affected by light).

On heating it gives metallic silver and nitrogen dioxide.

$$2AgNO_3 = 2Ag + 2NO_2 + O_2$$

With ammonia, it forms a complex known as silver diammino nitrate. The solution is known as ammoniacal silver nitrate and it is prepared by adding strong ammonia solution to silver nitrate solution till the black precipitate formed is dissolved.

$$AgNO_3 + 2NH_3 = Ag(NH_3)_2NO_3$$

Silver diammino nitrate

Further it answers the chemical reactions of silver and of the nitrate ion. Silver nitrate is official in I.P.

exceeding 8° in airtight containers and protected from light.

Uses : Ephedrine, a sympathomimetic agent, has been used to counteract hypotension associated with anaesthesia; as a mydriatic; in allergic reactions and as a CNS stimulant. Ephedrine salts have been used in the symptomatic relief of nasal congestion associated with the common cold, hay-fever, or rhinitis or sinusitis.

Adverse effects of ephedrine are the same as described under adrenaline.

Official

Ephedrine Tablets, I.P.

Ephedrine Sulfate Capsules/Injection/Syrup/Tablets, U.S.P.

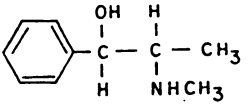
Ephedrine Hydrochloride Tablets, B.P., I.P.

Ephedrine Nasal Drops, B.P.

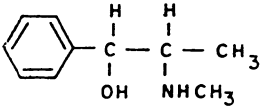
PSEUDOEPHEDRINE

Nomenclature : (+) -(1S. 2S)-2-Methylamino-1-phenylpropan-1-ol; (αR, βR)-β-Hydroxy-α-methylphenethyl-N-methylamine

Brand Names : d-Pseudoephedrine; d-—Ψ-Ephedrine; d-isoephedrine.



Pseudoephedrine
(Threo form)



Ephedrine
(Erythro form)

Pseudoephedrine is obtained from *Ephedra* species; m.p. 119°; sparingly soluble in water (differs from l-ephedrine); freely soluble in alcohol or ether. The drug and its salts are stored in airtight containers and protected from light.

Pseudoephedrine hydrochloride (Brand Names : Novafed; Sinufed; Sudafed; Symptom 2), m.p. 181-182°, is a white crystalline powder with a faint characteristic odour; soluble in water, alcohol and chloroform.

Pseudoephedrine sulphate is also a white, odourless crystalline powder.

Uses : Pseudoephedrine has similar actions and uses as that of

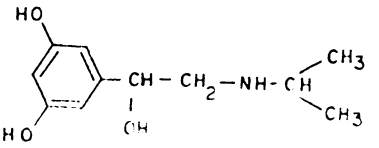
ephedrine; but it has less presser activity and cen[illegible] system effects. Pseudoephedrine is a useful bronch[illegible] is much less active in increasing blood pressure.

Official

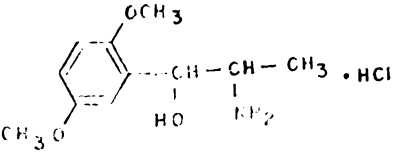
Pseudoephedrine Hydrochloride, B.P.

Pseudoephedrine Hydrochloride Tablets/Syrup, U.S.P

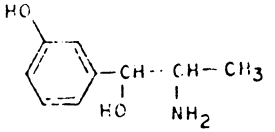
Miscellaneous Agents



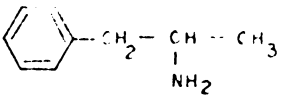
Orciprenaline



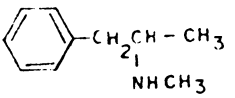
Methoxamine Hydr[illegible]



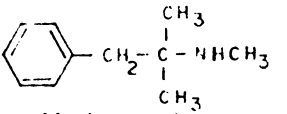
Metaraminol



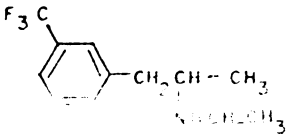
Amphetamine



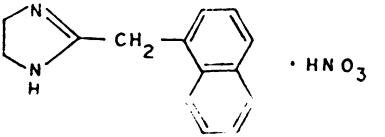
Methylamphetamine



Mephentermine



Fenfluramine



Naphazoline Nitrate

19

ADRENERGIC ANTAGONISTS

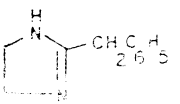
Adrenergic antagonists prevent the response of adrenergic nerve stimulation. These drugs block either alpha (α) or beta (β) adrenergic receptors. Adrenergic blocking agents of the α-type are ergot alkaloids (e.g. ergonovine, ergotamine, dihydroergotamine), yohimbine alkaloids (e.g. yohimbine), and benzodioxanes. The adrenergic blockers apparently possess suitable affinity for adrenergic α-receptors but lack of the intrinsic activity characteristic of the natural neuroeffector.

β-Adrenergic blocking drugs are structurally related to isopropylarterenol. They block the actions of catecholamines mediated through β-receptor stimulation. Thus, the β-receptor stimulating action of adrenaline and isoproterenol are blocked but positive chronotropic effects of calcium, barium, theophylline and digitalis are not affected. Sotalol, timolol, dichloroisoproterenol (DCI), oxprenolol, pindolol, propranol, acebutolol, atenolol, metoprolol and labetalol are the β-adrenergic blocking agents.

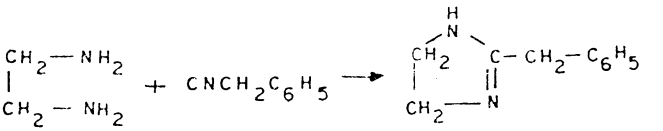
TOLAZOLINE

Nomenclature : 4, 5-Dihydro-2-(phenylmethyl)-1H-imidazole; 2-Benzyl-2-imidazoline.

Brand Names : Benzazoline; Phenylmethylimidazoline; Priscoline; Priscol; Vasodil; Prefaxil; Benzidazol; Vasimid; Kasimid; Artonil; Vasodilatan; Lambril; Glitensol.



Tolazoline is prepared by condensing phenylacetonitrile with the benzenesulphonate



Tolazoline hydrochloride, m.p. 174°, is a white or creamy white, bitter, crystalline powder with slight aromatic odour. It is soluble in water (1 in 1), alcohol (1 in 2), chloroform (1 in 3); practically insoluble in ether. Aqueous solutions are slightly acidic to litmus. The drug is stored in well-closed containers.

Uses : Tolazoline is an anti-adrenergic, and vasodilator; used to reduce pulmonary artery pressure and in the treatment of peripheral vascular disorders, acrocyanosis, arteriosclerosis obliterans, Buerger's disease, Raynaud's disease, frostbite sequelae, thrombophlebitis, etc.

Common side effects of tolazoline include pilo-erection, headache, flushing, tachycardia, cardiac arrhythmias, tingling, chilliness, shivering, sweating, nausea, vomiting, diarrhoea and epigastric pain.

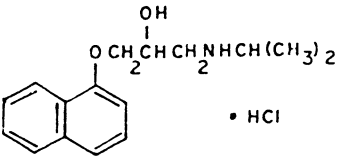
Offical

Tolazoline Hydrochloride Tablets/Injection, U.S.P.

PROPRANOLOL HYDROCHLORIDE

Nomenclature : 1[(1-Methylethyl) amino]-3-(1-naphthalenyloxy)-2-propanol; 1-(Isopropylamino)-3-(1-naphthyloxy)-2-propanol.

Brand Names : Avlocardyl; AY-64043; ICI-45520; NSC-91523; Berkolol; Beta-Neg; Caridorol; Deralin; Dociton; Frekven; Inderal; Inderex; Indobloc; Kemi; Oposim; Pylapron; Rapynogen; Tesnol.



Propranolol is an ether of 1-naphthol. Its hydrochloride occurs as a white or creamy-white, odourless, crystalline powder; soluble in water (1 in 20) and alcohol; slightly soluble in chloroform; practically insoluble in ether, benzene and ethyl acetate. In aqueous solutions propranolol decomposes with oxidation of the isopropylamine side-chain, accompanied by a reduction in pH and discolouration of the solution. Solutions are most stable at pH 3 and decompose rapidly when alkaline. The compound is stored in well-closed containers and protected from light.

Uses : Propranolol is a cardiac depressant (anti-arrhythmic) and adrenergic blocker. It reduces the rates and force of contraction of the heart and decreases the rate of conduction of impulses. It is used in the treatment of hypertension, cardiac arrhythmias, to improve the tolerance to exercise in patients with angina pectoris, bronchial asthma, allergic rhinitis during pollen season, etc.

The most common side effects of propranolol are nausea, vomiting and other gastro-intestinal disturbances, fatigue and dizziness.

Official

Propranolol Hydrochloride Injection, U.S.P.

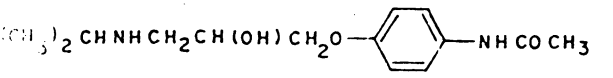
Propranolol Injection, B.P.

Propranolol Tablets, U.S.P., I.P., B.P.

PRACTOLOL

Nomenclature : N-[4-[2-Hydroxy-3-[(1-methylethyl)-amino] propoxy] phenyl] acetamide; 4'-[2-Hydroxy-3-(isopropylamino) propoxy] acetanilide.

Brand Names : AY-21011; ICI-50172; Dalzic; Eraldin.



Practolol, m.p. 134-136°, is soluble in hot isopropanol.

Uses : Practolol is a β-adrenergic blocker with general properties similar to those of propranolol.

In addition to side effects described for propranolol, the other adverse effects of practolol are observed on skin, eyes and mucous membranes, deafness and fibrotic changes.

20

CHOLINERGIC DRUGS

The transmission of a message along the nerves occurs through electric impulses. At the ends of the nerve fibres there is no direct contact between the ends and effector nerves. At the junction, known as synapse, there is a very minute gap which does not allow the transmission of the electric impulse. This transmission is accomplished by chemical mediators, known as neurohumoral agents, which are stored in a vesicle cell. When an electric impulse reaches the vesicle, it releases these chemical mediators which are transmitted through the synapse. The impulses then react with the receptor at the effector cell membrane leading initiations of the impulse at that cell.

Many tissues or organs have been connected with two sets of nerve fibres. One set gets one of the major chemical transmission while the other is utilizing the second one. The effect produced by one agent is opposed to that produced by the other, i.e., if one increases activity, the other decreases it. Those transmitters which mimic the stimulation of the sympathetic nerves are known as adrenergic agents, whereas those which mimic the parasympathetic system are called as cholinergic agents. Thus cholinergic agents are drugs which stimulate the effect of cells innervated by postganglionic parasympathetic cholinergic nerves. The effects of stimulation of cholinergic system by acetylcholine include the stimulation of gastrointestinal smooth muscles, contraction of muscles of urinary bladder, cardiac inhibition, peripheral vasodilation, contraction of pupil of eye, etc.

The enzyme acetylcholinesterase hydrolyses acetylcholine to choline and acetic acid at or near the site of liberation. Drugs that inhibit the action of acetylcholinesterase are known as

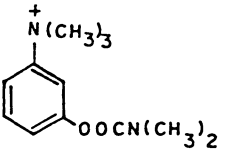
anticholinesterase agents. They prolong the life of acetylcholine, accumulate it at the sites of cholinergic receptor and give rise to effects which are similar to excitation of cholinergic system.

The cholinergic agents are the esters of choline (e.g. acetylcholine, methacholine and carbachol), cholinomimetic alkaloids (e.g. pilocarpine, muscarine and arecholine) and cholinesterase inhibitors (e.g. neostigmine, organophosphorus compounds). Cholinergic drugs and anticholinesterases are used to treat cardiac arrhythmias, for the relief of atony of gut and urinary bladder, for decreasing the intraocular pressure in glaucoma and to relieve muscular weakness in myasthenia gravis.

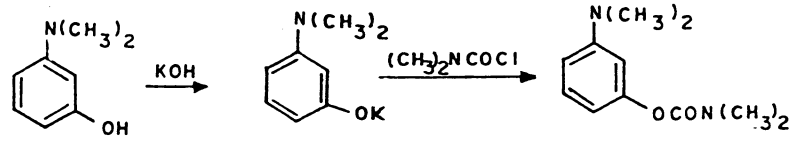
NEOSTIGMINE

Nomenclature : 3[[(Dimethylamino) carbonyl] oxy]-N, N N-trimethyl-benzenaminium; (3-Dimethylcarbamoxyphenyl) trimethylammonium.

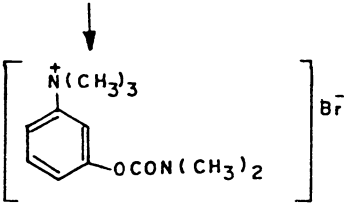
Brand Names : Synstigmin; Proserine; Intrastigmina; Juvastigmin; Neostigmin; Normastigmin; Prostigmine.



Neostigmine is an ester of a substituted carbamic acid. Neostigmine bromide is prepared from 3-hydroxydimethylaniline, which is synthesized from 3-nitroaniline. The 3-hydroxydimethylaniline potassium salt is treated with dimethylcarbamoyl chloride, $(CH_3)_2N$-COCl (prepared from dimethylamine and carbonyl chloride) to give a tertiary base which on treatment with methyl bromide yields the required neostigmine.



3-Hydroxydimethylaniline



Neostigmine

Neostigmine bromide, m.p. 167° (decomp), occurs as a hygroscopic, bitter, odourless, colourless crystals or white crystalline powder. It is soluble in water, alcohol, and chloroform; practically insoluble in ether; stored in airtight containers and protected from light.

Neostigmine methylsulphate also occurs as odourless, colourless crystals or a white crystalline powder; soluble in water and alcohol.

Uses : Neostigmine is cholinergic and used to stimulate peristalsis in post-operative distension, in the treatment of myasthenia gravis, to curtail the muscular relaxation produced by non-depolarising muscle relaxants and in the treatment of paralytic ileus and postoperative urinary retention.

The side effects of neostigmine are chiefly due to excessive cholinergic stimulation and include increased salivation, nausea, vomiting, abdominal cramps and diarrhoea. Allergic reactions have been reported.

Official

Neostigmine Bromide, B.P., I.P.

Neostigmine Tablets/Injection, B.P., I.P.

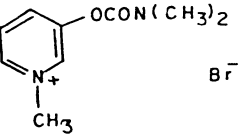
Neostigmine Methylsulphate, B.P., I.P.

Neostigmine Bromide Tablets, U.S.P.

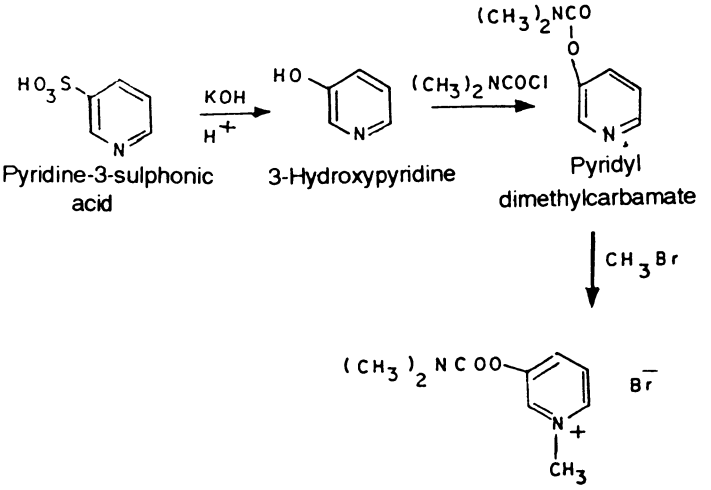
PYRIDOSTIGMINE BROMIDE

Nomenclature : 3-[[(Dimethylamino)-carbonyl]oxy]-1-methylpyridinium bromide; 3-Hydroxy-1-methylpyridinium bromide dimethyl carbamate.

Brand Names : RO 1-5130; Mestinon bromide; Kalymin; Regonol; Pyridostigminium bromide.



This pyridinium salt is an analogue of neostigmine in which the aniline radical is substituted by a heterocyclic ring. For its preparation, pyridine-3-sulphonic acid on fusion with potassium hydroxide and then acidification yields 3-hydroxypyridine. This is treated with dimethylcarbamoyl chloride to yield pyridyl dimethyl carbamate which is quaternized with methyl bromide :



Pyridine-3-sulphonic acid — 3-Hydroxypyridine — Pyridyl dimethylcarbamate

Pyridostigmine bromide

Pyridostigmine bromide, m.p. 152-154°, is a white crystalline powder with an agreeable characteristic odour. It is freely soluble in water, alcohol and chloroform; practically insoluble in ether, acetone and benzene; stored in airtight containers and protected from light.

Uses : The uses and adverse effects of pyridostigmine bromide are similar as mentioned under neostigmine, but is slower in onset and of longer duration. It is mainly used in the treatment of myasthenia gravis. Adverse effects occur less frequently with pyridostigmine treatment than with neostigmine.

Official

Pyridostigmine Bromide, B.P.

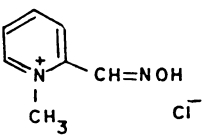
Pyridostigmine Injection/Tablets, B.P.

Pyridostigmine Bromide Syrup/Tablets, U.S.P.

PRALIDOXIME CHLORIDE

Nomenclature : 2-[(Hydroxyimino) methyl]-1-methylpyridinium chloride; 2-Formyl-1-methylpyridinium chloride oxime.

Brand names : 2-PAM Chloride; Protopam Chloride.



Pralidoxime chloride is 2-formyl-1-methylpyridinium chloride oxime. It is white or

pale yellow, odourless crystalline powder; freely soluble in water, m.p. 235-238°.

Uses : Pralidoxime chloride is used as cholinesterase reactivator; as antidote for poisoning by parathion and related pesticides. It is anticholinergic, cholinomimetic, it inhibits cholinesterase, and potentiates the depresser action of acetylcholine. It is most effective by intramuscular, subcutaneous or intravenous administration.

Adverse effects of pralidoximine are drowsiness, dizziness, disturbances of vision, nausea, tachycardia, headache, hyperventilation and muscular weakness.

Official

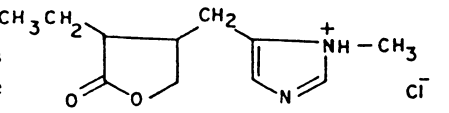
Pralidoxime Chloride Tablets, U.S.P.

Sterile Pralidoxime Chloride, U.S.P.

PILOCARPINE

Nomenclature: 3-Ethyldihydro-4-[1-methyl-1H-imidazol-5-yl) methyl]-2(3H)-furanone.

Brand Names : Chibro pilocarpine; Ocusert Pilo.



Pilocarpine, m.p. 34°, is an alkaloid obtained from the dried leaflets of *Pilocarpus jaborandi* or *Pilocarpus microphyllus* (Family Rut-aceae). It occurs as colourless, translucent, odourless, faintly bitter crystals or as a viscous, hygroscopic, oily liquid. It is soluble in water, alcohol and chloroform; sparingly soluble in ether; stored at a temperature not exceeding 8° in airtight containers; protected from light.

Pilocarpine hydrochloride, m.p. 204-205°, (Brand Names : Almocarpin, Akarpin; Isopto carpine; Pilovisc) is an odourless, hygroscopic, colourless crystalline powder; soluble in water, alcohol and chloroform; practically insoluble in ether; stored in airtight containers and protected from light.

Uses : Pilocarpine is a parasympathomimetic agent with primarily the muscarinic effects of acetylcholine. It is most commonly used to reduce intraocular pressure in the treatment of open-angle glaucoma. It is antiglaucoma and cholinergic agent.

Adverse effects of pilocarpine are the same as for neostigmine. It may produce ciliary spasm, ocular pain and irritation, blurred vision, and headache.

Official

Pilocarpine Hydrochloride, B.P.

Pilocarpine Eye Drops, B.P.

Pilocarpine Nitrate, B.P., I.P.

Pilocarpine Nitrate Ophthalmic Sodium, U.S.P.

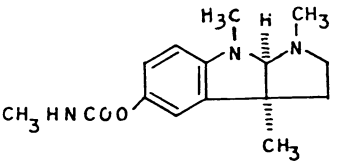
Pilocarpine Ocular System, U.S.P.

Pilocarpine Hydrochloride Ophthalmic Solution, U.S.P.

PHYSIOSTIGMINE

Nomenclature : 1, 2, 3, 3a, 8, 8a-Hexahydro-1, 3a, 8-trimethylpyrrolo [2, 3-*b*] indol-5-ol methylcarbamate (ester).

Brad Names : Eserine; Physostol.



Physostigmine, m.p. 105-106°, is an alkaloid obtained from the calabar bean (ordeal beam, chopnut), the seed of *Physostigma venenosum* (Leguminosae). It occurs as a white, odourless, microcrystalline powder which becomes pink on exposure to heat, light, air, or contact with traces of metals. It is slightly soluble in water; very soluble in chloroform; freely soluble in alcohol; soluble in fixed oils. Under certain conditions the oxidation may proceed to yield eserine blue. The compound is stored in airtight containers and protected from light.

Physostigmine salicylate is prepared by neutralizing an ethereal solution of the alkaloid with an ethereal solution of salicylic acid. Excess salicylic acid is removed from the precipitated product by washing it with ether.

The salicylate, m.p. 185-187°, is a colourless, shining odourless crystalline material or white powder; soluble in water, alcohol or chloroform; slightly soluble in ether. The crystals and their aqueous solutions become red on exposure to heat, light, air and contact with traces of metals. The red solutions are not effective. Therefore, solutions should be kept well closed in light-resistant, alkali-free glass containers and used within a week.

Physostigmine sulphate, m.p. 140°, is a white, deliquescent, odourless, microcrystalline powder; soluble in alcohol and water; slightly soluble in ether. The powder and its aqueous solution become red on exposure to heat, light, air and contact with traces of metals. The red colour may be removed by washing the crystals with alcohol.

The degradation products of physostigmine are eseroline, red coloured compound rubreserine, eserine blue, and esernine brown. The oxidation of eserinol (a phenol) may be prevented by adding sodium sulphite and no red colour will be formed. In solution, physostigmine is first hydrolyzes to methylcarbamic acid and eserinol which is oxidized rapidly to rubreserine. Solutions are most stable at pH 6 and they should not be sterilized by heat. Physostigmine is stabilized up to 6 months on addition of ascorbic acid.

Uses : Physostigmine is cholinergic (anticholinesterase) and used as a miotic, to counteract the dilation of the pupil caused by atropine, homatropine, or cocaine and to decrease intra-ocular pressure in glaucoma.

The adverse effects of physostigmine are the same as described under neostigmine. Toxic effects are usually more severe than those occurring with neostigmine.

Official

Physostigmine Salicylate, B.P., I.P.

Physostigmine Injection, I.P.

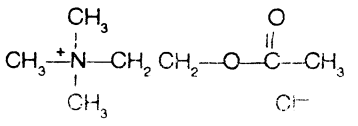
Physostigmine Sulphate, B.P.

Physostigmine Eye Drops, B.P.

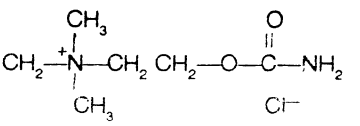
Physostigmine Salicylate Injection, U.S.P.

Physostigmine Salicylate Ophthalmic Solution/Ointment, U.S.P.

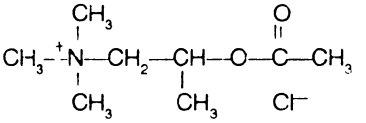
Miscellaneous Cholinergic Agents



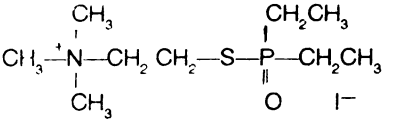
Acetylcholine chloride



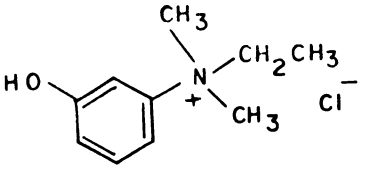
Carbachol chloride



Methacholine Chloride



Ecothiopate Iodide



Edrophonium chloride

21

CHOLINERGIC ANTAGONISTS

Cholinergic antagonists are the agents which act on ganglionic terminations of parasympathetic and sympathetic nervous systems and at the neuromuscular junction of the voluntary nervous system. The useful results from blocking the muscarinic effects of acetylcholine are :

1. *Mydriatic effect* (dilation of pupil of the eye).
2. *Cycloplegia* (a paralysis of the ciliary structure of the eye).
3. *Antispasmodic effect* (lowered tone and motility of the gastrointestinal tract and the genitourinary tract).
4. *Antisecretory effect* (reduction of salivation, reduced perspiration, and reduced acid and gastric secretion).

The cholinergic or parasympathetic blocking agents include atropine and related tropane alkaloids obtained from the plants *Atropa belladonna, Atropa acuminata, Hyoscyamus niger, Scopolia carniolica and Datura stramonium* and synthetic or semisynthetic atropine substitutes. These drugs in therapeutic doses predominantly block the muscarinic actions of acetylcholine.

Solanaceous Alkaloids

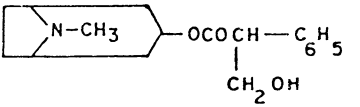
A number of tropine alkaloids having marked physiological activity are found in different organs of Solanaceous plants such as belladonna, hyoscyamus, stramonium and datura. These alkaloids are derivatives of tropine which is a cyclic compound containing the fused carbon-nitrogen skeletons of pyrrolidine and piperidine. Chemically these alkaloids are tertiary bases

and possess a secondary alcohol. These are esters of the bicyclic aminoalcohol, 3-hydroxytropane, or of related aminoalcohols.

ATROPINE

Nomenclature : α-(Hydroxymethyl) benzeneacetic acid -8-methyl-8-azabicyclo [3.2.1] oct -3-ylester; 1α-H; 5α-H-Tropane -3α-ol.

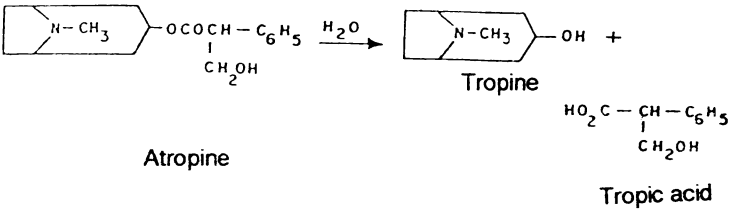
Brand Names : DL-Hyoscyamine; Tropic acid ester with tropine, DL-Tropyl tropate, Tropine tropate.



Atropine is extracted from *Atropa belladonna L., Datura stramonium L., Hyoscyamus muticus or Duboisia* species, or prepared by synthesis. During extraction, partial racemization of the l-hyoscyamine takes place which is completed by treatment with dilute alkali on heating in chloroform solution.

Atropine is the tropyl ester of tropic acid, $C_6H_5CH(CH_2OH)COOH$. For the synthesis of atropine, tropinone is reduced under proper conditions to tropine, which is then used to esterify tropic acid.

Atropine, m.p. 114-118°, is an odourless, white crystalline powder; sparingly soluble in water, readily in alcohol, ether and chloroform. Atropine is optically inactive. It is a monoacid tertiary base, and forms salts with acids. In the presence of acids or alkalies, atropine is hydrolyzed to tropine and tropic acid.



Atropine is soluble in water (1 in 460), alcohol (1 in 2), chloroform (1 in 1) and ether (1 in 25). A saturated aqueous solution is alkaline to phenolphthalein.

Atropine sulphate (Atropisol) : It is prepared by neutralizing atropine in acetone or ether solution with an alcoholic solution of sulphuric acid. The salt occurs as a white crystalline powder; is soluble in water and alcohol; practically insoluble in chloroform and in ether. Aqueous solutions are unstable and should be freshly prepared. Stability is increased in acid solutions of pH

below 6; solutions should be protected from alkalies. It is efflorescent in dry air and should be protected from light to prevent deterioration. Atropine and its salts are stored in airtight containers and protected from light.

Uses : Atropine is anticholinergic, and antimuscarinic alkaloid, has antispasmodic action on smooth muscles and reduces secretions and perspiration. It is used to alleviate the griping caused by vegetable laxatives, in the treatment of smooth muscle spasm, in the symptomatic treatment of parkinsonism, to reduce tremor sialorrhoea and muscular rigidity, and to improve the gait, posture and speech. The antispasmodic action of atropine has been used to facilitate radiological examination of the gut. It depresses the vagus and is used as cycloplegic and mydriatic, in the treatment of iritis and uveitis to immobilize the ciliary muscle and iris.

Atropine has been used in the form of liniment to relieve the pain of muscular rheumatism, sciatica and neuralgia. Atropine is a specific antidote to prevent the 'muscarinic' effect of acetylcholine accumulation such as vomiting, abdominal cramps, diarrhoea, salivation, sweating, bronchoconstriction and excessive bronchial secretion.

Side effects of atropine and other antimuscarinic agents include dryness of mouth, thirst, dilation of the pupils, flushing and dryness of the skin, bradycardia, reduction of tone, constipation, etc. Sometimes vomiting, giddiness and staggering may occur. Toxic doses cause tachycardia, rapid respiration, hyperpyrexia and CNS stimulation.

Official

Atropine, I.P.

Atropine Methobromide/Methonitrate, B.P.

Compound Adrenaline and Atropine Spray, B.P.

Atropine Sulphate, B.P., I.P.

Atropine Sulphate Injection/Tablets, B.P., I.P.

Hyoscyamine Sulphate, B.P.

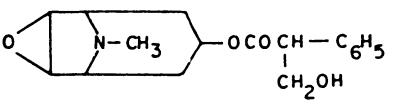
Atropine Sulfate Tablets/Injection/Ophthalmic Ointment, U.S.P.

Atropine Eye Ointment, B.P., I.P.

HYOSCINE

Nomenclature : α-(Hydroxymethyl) benzeneacetic acid 9-methyl -3-oxa-9-azatricyclo [3.3..1-$O^{2,4}$] non-7-yl ester.

Brand Names : Scopolamine; 6, 7-Epoxytropine tropate; Scopine tropate; Transderm-V.



Hyoscine is an alkaloid obtained from various Solanaceous plants especially *Datura metal. Scopolia carniolica. Duboisia myoporoides* and *Hyoscyamus niger.* It is isolated from the mother liquor remaining from the isolation of hyoscyamine. This is the tropyl ester of scopine, a base which is related to tropine but contains an epoxide ring.

The alkaloid is a viscous liquid, laevo-rotatory, slightly soluble in water; very soluble in alcohol, chloroform, acetone and ether m.p. 108.5°. It is hydrolyzed by acids or alkalies, decomposes on standing, and forms crystalline salts with most acids. The hydrobromide salt is most stable and the most popularly accepted.

Hyoscine hydrobromide, m.p. 152°, is efflorescent, odourless, colourless crystalline powder; soluble in water and alcohol, practically insoluble in chloroform and ether; stored in airtight containers and protected from light.

Uses : Hyoscine is an antimuscarinic agent. It is a more powerful suppressant of salivation than atropine. It is effective in the prevention and control of motion sickness and used to treat nausea, acute mania and delirium, peptic ulcer, in the eye for its cycloplegic and mydriatic actions, and to treat parkinsonism.

Adverse effects of hyoscine are the same as for atropine. Hyoscine acts as a narcotic or sedative.

Official

Scopolamine Hydrobromide Ophthalmic Solution Ointment U.S.P.

Methscopolamine Bromide Tablets/Injection, U.S.P.

Hyoscine Butylbromide, B.P.

Hyoscine Butylbromide Injection, B.P.

Hyoscine Butylbromide Tablets, B.P.

Hyoscine Hydrobromide, B.P., I.P.

Hyoscine Eye Drops/Eye/Ointment Tablets B.P

Hyoscine Injection, B.P., I.P.

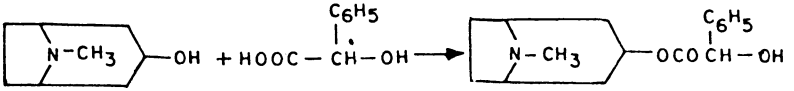
Hyoscine Methonitrate/Methobromide, B.P.

HOMATROPINE

Nomenclature : α-Hydroxybenzeneacetic acid 8-methyl-8-azabicyclo [3.2.1] oct-3-yl ester; 1α, 5αH-Tropane -3α-ol mandelate.

Brand Names : Mandelyltropeine, Tropine mandelate.

Homatropine is a synthetic alkaloid which is a lower homologue of atropine. It is prepared by the interaction of tropine and mandelic acid.



Tropine Mandelic acid Homatropine

Homatropine, m.p. 99-100°, occurs as colourless, odourless crystals or a white crystalline powder. It is hygroscopic, but only slightly soluble in water; soluble in alcohol, benzene, chloroform, ether, acetone and dilute acids.

The hydrobromide or hydrochloride is obtained readily from the free base by neutralizing with hydrobromic or hydrochloric acid. The hydrobromide occurs as colourless, odourless crystals or a white crystalline powder. It is soluble in water and alcohol; slightly soluble in chloroform; very slightly soluble in ether; stored in airtight containers and protected from light.

Homatropine methylbromide, m.p. 210-212°, is the tropine methylbromide ester of mandelic acid. It is prepared by treating homatropine with methyl bromide, thus yielding the quaternary compound. It occurs as a white, bitter, odourless powder that slowly darkens on exposure to light. It is very soluble in water, freely soluble in alcohol; practically insoluble in acetone and ether.

Uses : Homatropine is an antimuscarinic agent with effects similar to those of atropine. When applied to the eye its cycloplegic and mydriatic actions are more rapid and of shorter duration. In combination with ammonium methobromide, homatropine is used to treat peptic ulcer and gastro-intestinal spasm.

Adverse effects of homatropine are the same as discribed for atropine.

Official

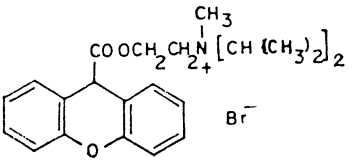
Homatropine Hydrobromide Ophthalmic Solution, U.S.P.

Homatropine Methylbromide Tablets, U.S.P.

PROPANTHELINE BROMIDE

Nomenclature : N-Methyl-N-(1-methylethyl)-N-(2-[9H-xanthen-9-ylcarbonyl] oxy) -2-propanaminium bromide.

Brand Names : Corrigast, Ercotina; Giquel; Pro-Banthine; Prodixamon; Ketaman; Neo-metantyl; Pantheline;



Propantheline is a choline-homologue ester of 9-xanthen-carboxylic acid. It is prepared from the sodium salt of 9-xanthen-carboxylic acid which reacts with 2-diisopropylaminoethyl chloride, $Cl\ CH_2\ CH_2\ N\ [CH\ (CH_3)_2]$ to yield the tertiary amino- ester, 2'-diisopropylaminoethyl 9-xanthencarboxylate. This is reacted with methyl bromide to give the required quaternary salt.

Propantheline bromide, m.p. 159-161°, is a white or yellowish-white odourless, hygroscopic powder. it is very soluble in water, alcohol and chloroform; practically insoluble in ether and benzene; stored in well-closed containers.

Uses : Propantheline bromide is an antimuscarinic agent with peripheral effects similar to those of atropine. It is used in the treatment of peptic ulcer, gastritis, acute pancreatitis, enuresis, hyperhidrosis and spasm of the gastro-intestinal, biliary and urinary tracts.

Side effects of propantheline bromide are similar as for atropine.

Official

Propantheline Bromide, B.P.

Propantheline Tablets, B.P.

Propantheline Bromide Tablets, U.S.P.

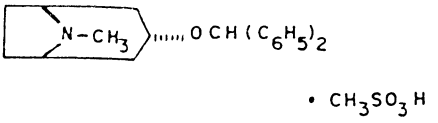
Sterile Propantheline Bromide, U.S.P.

BENZTROPINE MESYLATE

Nomenclature : 3-(Diphenylmethoxy)-8-methyl-8- azabicyclo [3.2.1.] octane methane sulfonate.

Brand Names : Cogentin; Cogentinol; Cobrentin; methane-sulphonate.

Benztropine mesylate, m.p. 143°, is prepared by the action of diphenyldiazomethane on tropine. It is a white, odourless, slightly hygroscopic, crystalline powder; very soluble in water and alcohol; practically insoluble in ether; stored in airtight containers.



Uses : Benztropine mesylate is an anticholinergic, antihistaminic, local anaesthetic and antimuscarinic agent with actions similar to those of atropine. It also has a direct antispasmodic action on smooth muscle. It is used for the symptomatic treatment of parkinsonism and to alleviate the effect induced by drugs such as the phenothiazine derivatives. It may minimize drooling, sialorrhea, masklike facies, oculogyric crises and muscular cramps.

Adverse effects of benztropine mesylate are the same as for atropine. Drowsiness may be severe in some patients. It may produce severe mental disturbances and excitement.

Official

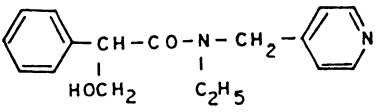
Benztropine Mesylate Tablets/Injection, U.S.P.

TROPICAMIDE

Nomenclature : N-Ethyl-α-(hydroxymethyl)-N-(4-pyridinylmethyl) benzeneacetamide; N-Ethyl-N-(4-pyridylmethyl) tropicamide.

Brand Names : Bistropamide; Mydriacyl.

Tropicamide m.p. 96-97°, is a synthetic derivative of the amide of tropic acid. It is a white, odourless, crystalline powder, slightly soluble in water; soluble in alcohol and chloroform; freely soluble in solutions of strong acids. Solutions for ophthalmic use have a pH of 4.0 and 5.0. Tropicamide is stored in airtight containers and protected from light.



Uses : Tropicamide is anticholinergic (ophthalmic), and antimuscarinic agent with actions similar to those of atropine. Its action is more rapid in onset than other mydriatics.

Adverse effects of tropicamide are the same as for atropine sulphate.

Official

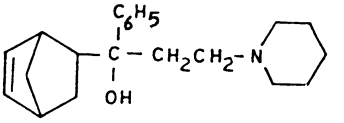
Tropicamide, B.P.

Tropicamide Ophthalmic Solution, U.S.P.

BIPERIDEN

Nomenclature : α-Bicyclo [2.2.1.] hept-5-en-2-yl-α-phenyl-1-piperidinepropanol; α-5-Norbornen -2-yl-α-phenyl-1-piperidine-propanol.

Brand Names : Akinetion; KL 373.



Biperiden, m.p. 112-116°, is a white, odourless, crystalline powder. It is freely soluble in chloroform and methanol; sparingly soluble in alcohol; practically insoluble in water.

Biperiden hydrochloride (Brand Names; Kineton; Akinophyl), m.p. 275° (dec), is a white, odourless, optically inactive, crystalline powder. It is slightly soluble in water, alcohol, chloroform, and ether; sparingly soluble in methanol; stored in airtight containers and protected from light.

Uses : Biperiden is anticholinergic, antimuscarinic and antiparkinsonian agent used to treat all types of parkinosonism, to alleviate the extrapyramidal syndrome induced by drugs, and to eliminate akinesia, rigidity and tremor.

Adverse effects of biperiden are the same as for atropine sulphate.

Official

Biperiden Hydrochloride Tablets, U.S.P.

Biperiden Lactate Injection, U.S.P.

22

DIURETIC DRUGS

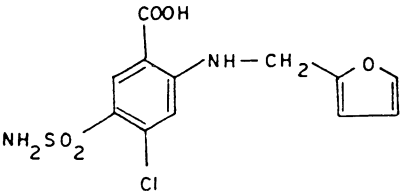
Drugs that increase the rate or output of urine formation by the kidney are called diuretics. They promote the excretion of electrolytes and water from the body. Diuretics act on tubular function (nephron) and do not affect the glomerular filtration rate in causing diuresis. Diuretics increase the quantity of sodium and chloride ions in the urine and the increased salt excretion is being accompanied by an increased water exeretion to maintain osmotic balance. This action is achieved by direct or indirect inhibition of the reabsorption of Na^+ ions by the kidney tubules. The increased urine flow may also be produced by suppressing the secretion of antidiuretic hormone vasopressin from posterior pituitary. Diuretics are used to treat all types of oedema, i.e. disease associated with abnormal retention of salt and water in extracellular parts of the body. The important diseases associated with oedema are congestive heart failure, premenstrual tension, oedema of pregnancy, renal oedema, cirrhosis with ascites and oedema induced by the administration of adrenocorticotropin (ACTH) and other corticosteroids.

The diuretics used are water and osmotic agents, acidifying salts, xanthine derivatives, mercurials, : α, β- unsaturated ketones, sulphonamides and purines, pyrimidines and related heterocyclic compounds. They are also used, alone or in combination with other antihypertensive agents, in the treatment of raised blood pressure.

FUROSEMIDE

Nomenclature : 5-(Aminosulfonyl) -4 chloro-2-[(2-furanylmethyl) amino)] benzoic acid; 4-Chloro-N-furfuryl-5-sulfamoylanthranilic acid.

Brand Names : Frusemide; LB-502; Aisemide; Aluzine; Beronald; Desdemin; Diural; Dryptal; Errolon; Eutensin; Frusemin; Frusid; Fulsix; Fuluvamide; Furesis; Hydro-rapid; Katlex; Lasilix; Lasix; Lowpstron; Macasirool; Nicorol; Profemin; Rosemide; Transit; Trofurit; Urosemide; Urexo.



Furosemide, m.p., 206°, is a derivative both of sulphanilamide and of anthranilic acid. It is a white or slightly yellow, odourless, crystalline powder; practically insoluble in water and chloroform, soluble in alcohol; freely soluble in acetone, dimethylformamide, methanol and solutions of alkali hydroxides; protected from light.

Uses : Furosemide is a potent diuretic with rapid action used to treat oedema, hypertension and renal insufficiency.

The most common side-effects of furosemide are fluid and electrolyte imbalance, allergy, nausea, diarrhoea, blurred vision, yellow vision, dizziness, headache, pancreatitis, photosensitivity, skin rashes and hypotension.

Official

Frusemide, B.P., I.P., U.S.P.

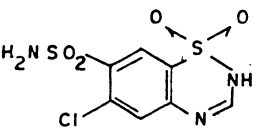
Frusemide Injection, B.P., U.S.P.

Frusemide Tablets, B.P., I.P., U.S.P.

CHLOROTHIAZIDE

Nomenclature : 6-Chloro-2H-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide.

Brand Names : Alurene; Chlorosal; Chlorurit; Chlotride; Diuresal; Diuril; Diurilix; Diurite; Exuril; Urinex; Flumen; Minzil; Neo-Dema; Ro-Chlorozide; Salisan; Salunil; Saluretil; Saluric Warduzide; Yadulan.



Chlorothiazide, m.p. 342-343°, is a white, odourless, crystalline powder; slightly soluble in water, alcohol and acetone; soluble in solutions of alkali hydroxides.

Uses : Chlorothiazide is diuretic and antihypertensive used in the treatment of oedema and hypertension.

Chlorothiazide may cause a number of metabolic disturbances. They may provoke hyperglycaemia and glycosuria in diabetic patients and cause hyperuricaemia and gout in some patients.

Official

Chlorothiazide, B.P.

Chlorothiazide Tablets, B.P., U.S.P.

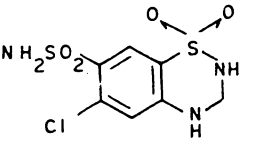
Methyldopa and Chlorothiazide Tablets, U.S.P.

Resespine and Chlorothiazide Tablets, U.S.P.

HYDROCHLOROTHIAZIDE

Nomenclature : 6-Chloro-3,4-dihydro-2H-1, 2, 4-benzothiadiazine-7-sulfonamide-1,1-dioxide.

Brand Names : Aquarius; Bremil; Chlorosulthiadil; Chlorzide; Cidrex; Dichlorosal; Dichlotride; Diclotride; Direma; Disalunil; Esidrex; Esidrix; Fluvin; Hidroronol; Hydril; Hydro-Aquil; Hydro-Diuril; Hydrosaluric; Hydrothide; Hypothiazide; Ivaugon; Jen-Diril; Maschitt; Nefrix; Neo-Codema; Neoflumen; Oretic; Panurin; Ro-Hydrazide; Thiaretic; Thiuretic; Urodiazin; Vetidrex.



Reduction of the 3,4-position of the thiadiazine ring increases activity of the benzothiadiazines, lowers the toxicity and increases the activity by about 10 times. Hydrochlorothiazide is a reduced derivative of benzothiadiazine. It is a white, odourless, crystalline powder, m.p. 273-275°, slightly soluble in water, alcohol and methanol; soluble in acetone; freely soluble in dimethylformamide, n-butylamine and solution of alkali hydroxides; insoluble in ether, chloroform and dilute mineral acids; stored in well closed containers.

Uses : Hydrochlorothiazide is a diuretic with actions, uses and adverse effects similar to those of chlorothiazide.

Official

Hydrochlorothiazide, B.P, I.P.

Hydrochlorothiazide Tablets, B.P., I.P., U.S.P.

Amiloride Hydrochloride and Hydrochlorothiazide Tablets, U.S.P.

Methyldopa and Hydrochlorothiazide Tablets, U.S.P.

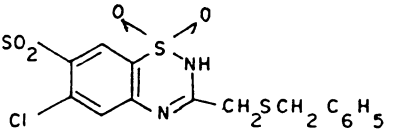
Reserpine and Hydrochlorothiazide Tablets, U.S.P.

Tomolol Maleate and Hydrochlorothiazide Tablets, U.S.P.

BENZTHIAZIDE

Nomenclature : 6-Chloro-3-[(phenylmethyl) thio]-methyl] 2-H-1,2,4-benzothiadiazine-7-sulfonamide-1, 1,-dioxide.·

Brand Names : Aquatag; Benzothiazide; Dihydrex; Diucen; Edemex; ExNa; Exosalt; Fovane; Freeuril; Hy-Drine; Lemazide; Proaqua; Urese.



Benzthiazide, m.p. 238-239°, is a white crystalline powder with a characteristic odour. It is practically insoluble in water, ether and chloroform; slightly soluble in acetone and alcohol; freely soluble in dimethylformamide and in solutions of alkali hydroxides.

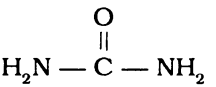
Uses : Benzthiazide is diuretic and antihypertensive with properties similar to those of chlorothiazide.

Official

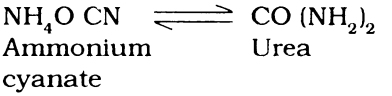
Benzthiazide Tablets, U.S.P.

UREA

Brand Names : Carbamide; Carbonyldiamide; Aquacare; Aquadrate; Basodexan; Keratinamin; Nutraplus; Pastaron; Ureaphil; Ureophil; Urepearl.



Urea is a product of protein metabolism. It is present in human urine in about 3 per cent amount. In laboratory urea is prepared by evaporating a solution of ammonium cyanate to dryness when nearly 95% of ammonium cyanate is converted into urea.



Urea is also prepared from cyanamide by hydrolysis and from carbon dioxide by ammonolysis. One mole of carbon

dioxide reacts with two moles of ammonia to yield ammonium carbamate. The carbamate then decomposes to form urea and water.

Urea is also prepared from ammonia, carbon monoxide and sulphur in methanol.

Urea, m.p. 132-133°, occurs as colourless, transparent, slightly hygroscopic, odourless, prismatic crystals or white crystalline powder or pellets with cooling saline taste. It may gradually develop a slight odour of ammonia on prolonged standing. It is soluble in water, alcohol and methanol; practically insoluble in chloroform and ether; stored in airtight containers. Solutions in water are neutral to litmus and decompose on heating, giving off some ammonia.

$$H_2NCONH_2 + H_2O \xrightarrow{\text{heat}} CO_2 + 2NH_3$$

Solutions of sodium hypochlorite or hypobromite oxidize urea in cold, with formation of nitrogen and carbon dioxide.

$$NH_2—CO—NH_2 + 3NaOBr \longrightarrow CO_2 + N_2 + 3NaBr + 2H_2O$$

Urea has weak basic properties. On combination with acids, crystalline salts e.g., hydrochloride $CO(NH_2)_2 . HCl$, nitrate, $CO(NH_2)_2 . HNO_3$ and the oxalate, are formed.

Urea gives positive *biuret* test. Pure urea should not give the biuret reaction unless heated above the melting point. The material is heated in a dry test-tube above its melting point to form biuret with evolution of ammonia.

$$\underset{\text{urea (2 moles)}}{H_2N\text{-}CO\text{-}NH_2} \xrightarrow{\text{heat}} \underset{\text{Biuret}}{H_2N\text{-}CO\text{-}NH\text{-}CONH_2} + NH_3$$

When ammonia is evolved, the residue is dissolved in water and treated with a few drops of sodium hydroxide and then copper sulphate solution. A distinct violet colour is obtained.

Uses : Urea is a diuretic and antiseptic, used to treat acute increases in intracranial pressure, to maintain the output of urine during surgical procedures and to decrease intra-ocular pressure in acute glaucoma. It is also used to treat infected wounds, to promote granulation and healing and to promote the bacteriostatic activity of sulpha drugs. In industries, urea is used as fertilizer; in animal feeds; it reacted with aldehydes to prepare resins and plastics; condenses with malonic ester to

form barbituric acid; used extensively in the paper industry; in ammoniated dentifrices.

Urea may cause gastric irritation with nausea and vomiting when given by mouth. Intravenous administration may cause headache, nausea, vomiting, confusion and a fall in blood pressure. Topical applications may be irritant to sensitive skin.

Official

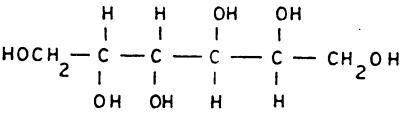
Urea, B.P., I.P.

Urea Cream, B.P.

Sterile Urea, U.S.P.

MANNITOL

Brand Names : Mannite; Manna sugar; Cordycepic acid; Manicol; Mannidex; Diosmol; Osmitrol; Osmosal;



Mannitol is a hexahydric alcohol related to mannose. it is widespread in plants and plant exudates; constitutes about 50 per cent of the 'manna', exudate and in seawead. It is prepared by electrolytic reduction of glucose; by hydrogenation of invert sugar, monosaccharides and sucrose.

Mannitol, m.p. 166-168°, is a white, odourless crystalline powder or granules with a sweet taste. It is soluble in water; slightly soluble in alcohol and pyridine; practically insoluble in ether; soluble in solutions of alkali carbonates and hydroxides.

Uses : Monnitol is diuretic used to increase urine flow in patients with acute renal failure, to reduce intra-ocular pressure prior to ophthalmic procedures, to promote the excretion of toxic substances by forced diuresis, as diluent and excipient in pharmaceutical preparations, as a bulk sweetener, for determination of the glomerular filtration-rate, to treat patients with renal failure.

In industry mannitol is used with boric acid in the manufacturing of dry electrolytic condensers for radio applications; in making artificial resins and plasticizers; in analytical chemistry for boron determination; as anticaking and free-flow agent, flavouring agent, lubricant and release agent, stabilizer, thickener and nutritive sweetener.

The most common side effects associated with mannitol

therapy are fluid and electrolyte imbalance, circulatory overload, acidosis, diarrhoea, nausea, vomiting, thirst, headache, dizziness, chills, fever, etc.

Official

Mannitol, B.P.

Mannitol Intravenous Infusion, B.P.

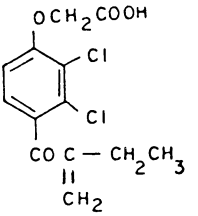
Mannitol Injection, U.S.P.

Mannitol and Sodium Chloride Injection, U.S.P.

ETHACRYNIC ACID

Nomenclature : [2,3-Dichloro-4-(2-methylene-1-oxobutyl] phenyoxy) acetic acid; [2,3-Dichloro-4-(-2-methylenebutyryl) phenoxy] acetic acid.

Brand Names : MK-595; Crinuryl; Edecril; Edecrin; Endecril; Hydromedin; Reomax; Taladren; Uregit.



Ethacrynic acid, m.p. 121-120°, is an unsaturated derivative of a dichlorophenoxyacetic acid. It is a white, odourless, crystalline powder; sparingly soluble in water; soluble in alcohol, chloroform and ether; dissolves in ammonia and in dilute aqueous solutions of alkali hydroxides and carbonates; stored in airtight containers. Sodium salt, called ethacrynate sodium or Lyovac sodium edecrin, is soluble in water.

Uses : Ethacrynic acid is a diuretic and used similarly to chlorothiazide.

The side effects of ethacrynic acid are fluid and electrolyte imbalance, hyponatraemia, hypokalaemia, gastro-intestinal disturbances, hypochloremic, alkalosis, and deafness in patients with uremia. Other adverse effects include confusion, fatigue, nervousness, and apprehensiveness.

Official

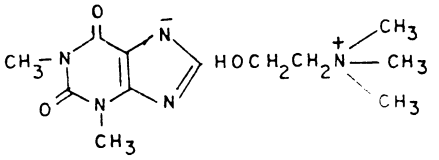
Ethacrynic acid, B.P.

Ethacrynic Acid Tablets, B.P., U.S.P.

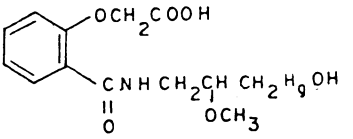
Ethacrynic Sodium for Injection, U.S.P.

Sodium Ethacrynate Injection, B.P.

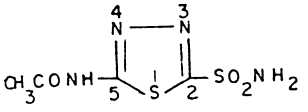
Miscellaneous Diuretics



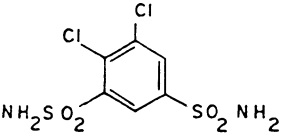
Choline Theaphyllinate



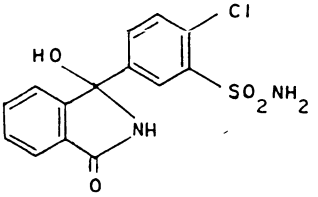
Mersalyl Acid



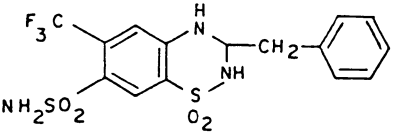
Acetazolamide



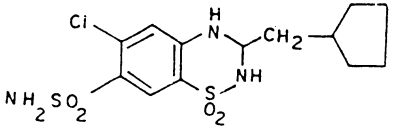
Dichlorphenamide



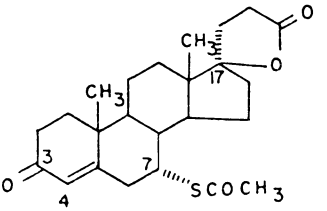
Chlorthalidone



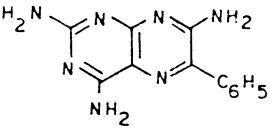
Bendrofluazide



Cyclopenthiazide



Spironolactone



Triamterene

23

CARDIOVASCULAR DRUGS

Cardiovascular system is related to the circulation of the blood and includes heart and blood vessels. Cardiovascular drugs are used for their action on the heart or on other parts of the vascular system to modify the total output of the heart or the distribution of blood to certain parts of the circulatory system. Cardiovascular agents include cardiotonic drugs (Digitalis glycosides), vasodilators (esters of nitrous and nitric acid and some alkaloids, e.g. nicotinyl alcohol, dipyridazole), hypotensive drugs that modify cardiac rhythm (Rauwolfia alkaloids, Veratrum alkaloids and some other compounds like guanethidine, methyldopa, pargyline), antihypercholesterolemic drugs (e.g. clofibrate, dextrothyroxine) and sclerosing agents (e.g. invert sugar, dextrose, ethyl alcohol, iron salts, urea, quinine, soaps, etc.).

ETHYL NITRITE

Nomenclature : Nitrous acid ethyl ester.

Brand Name : Nitrous ether.

$$C_2H_5—NO_2$$

Ethyl nitrite is prepared by the action of sodium nitrite on a mixture of alcohol and sulphuric acid in the cold. In the laboratory ethyl nitrite gas is conveniently generated by placing 20 litres of 90 per cent ethanol in a suitable vessel, diluting with 200 litres of water, and while stirring, adding to the dilute alcoholic nitrosyl chloride.

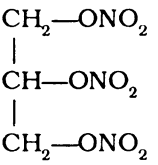
Ethyl nitrite, b.p. 17°, is a colourless or yellowish, clear, flammable, exceedingly volatile liquid with characteristic pleasant, ethereal odour and burning, sweetish taste. It is slightly soluble in water and decomposed by it; miscible with alcohol and ether. On keeping, it gradually decomposes to an acid and oxides of nitrogen are formed. Decomposition is rapid by air, light, and moisture.

Uses : Ethyl nitrite is used as diaphoretic and cardiovascular drug. It may cause methemoglobinemia and hypotension and, in high concentrations, narcosis.

GLYCERYL TRINITRATE

Nomenclature : 1,2,3-Propanetriol trinitrate.

Brand Names : Nitroglycerine; Trinitroglycerol; Trinitrin; Glonoin; Blasting gelatin; Blasting oil; S.N.G.; Angibid; Angiolingual; Anginine; Angorin; Cardamist; Corditrine; Gilucor 'nitro'; Klavikordal; Lenitral; Myoglycerin; Nitrobid; Nitrodisc; Nitro-Dur; Nitroglin; Nitroglyn; Nitrolan; Nitrolar; Nitro-lent; Nitrolingual; Nitro Mack; Nitromel; Nitronal; Nitrong; Nitro PRN; Nitrorectal; Nitroretard; Nitrostat; Nitrozell retard; Nysconitrine; Percutol; Perlingant; Perglottal; Transderm-Nitro; Suscard; Sustac; Tridil; Trinalgon; Trinitrosan; Vasoglyn.



Glyceryl trinitrate is the glyceride of nitric acid. It is prepared by slowly adding glycerol to an ice-cold mixture of concentrated nitric acid and concentrated sulphuric acid in the ratio of 1:4. The solution is carefully passed into ice-cold water when the glyceryl trinitrate is separated as a heavy oil. It is purified by repeated washing with cold water.

Glyceryl trinitrate is a heavy, pale yellow, oily, inflammable, explosive liquid with sweet burning taste. It produces headache on tasting and explodes on rapid heating or when struck with hammer. In impure form it may explode spontaneously. It is slightly soluble in water; soluble in methyl alcohol, alcohol, carbon disulphide, acetone, chloroform, ether and in glacial acetic acid.

Concentrated glyceryl trinitrate is a 9-11% solution of glyceryl trinitrate in alcohol (96%). Dilute nitroglycerin is a mixture of glyceryl trinitrate with lactose., glucose, alcohol, propylene glycol or other suitable inert excipient.

Uses : Glyceryl trinitrate relaxes smooth muscles, including vascular muscles and reduces the blood pressure. It is used as a vasodilator in the prophylaxis and treatment of angina pectoris; for bronchial asthma in dogs.

Adverse effects of glyceryl trinitrate are acute poisoning, occurring in industrial workers; nausea, vomiting, abdominal cramps, headache, mental confusion, delirium, bradypnea, bradycardia, paralysis, convulsions, methemoglobinemia, cyanosis, circulatory collapse and death.

Official

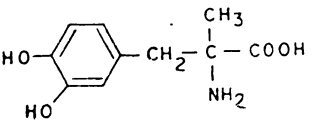
Glyceryl Trinitrate Tablets, B.P.

Nitroglycerin Tablets, U.S.P.

L-METHYLDOPA

Nomenclature : 3-Hydroxy-α-Methyl -L-tyrosine; L-3,-(3, 4-Dihydroxyphenyl)-2-methylalanine; L-α-methyl-3,4-dihydroxy-phenylalanine.

Brand Names : AMD; MK-351; Aldomet; Aldometil; Aldomine; Dopamet; Dopegyt; Dopatec; Medomet; Medopa; Medopren; Methoplain; Sembrina; Presinol.



Methyldopa, m.p. 292-293°, is a colourless or white to yellowish-white odourless fine powder which may contain friable lumps. It is slightly soluble in water and alcohol; practically insoluble in chloroform and ether; dissolves in dilute mineral acids; protected from light.

Uses : Methyldopa is an antihypertensive agent. It reduces the standing blood pressure and supine blood pressure.

Methyldopate hydrochloride is used in pharmaceutical dosage forms.

The most common side-effect is drowsiness. Other common side-effects include depression, psychic effects, impaired mental acuity, nightmares, nausea, dryness of the mouth, nasal stuffiness.

weakness, dizziness, light headedness, headache, oedema and disorders of sexual function.

Official

Methyldopa Tablets, B.P., U.S.P.

Methyldopa and Chlorothiazide Tablets, U.S.P.

Methyldopa and Hydrochlorothiazide Tablets, U.S.P.

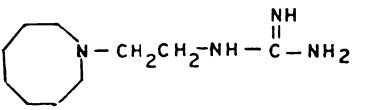
Methyldopa Oral Suspension, U.S.P.

Methyldopate Injection, B.P.

Methyldopate Hydrochloride Injection, U.S.P.

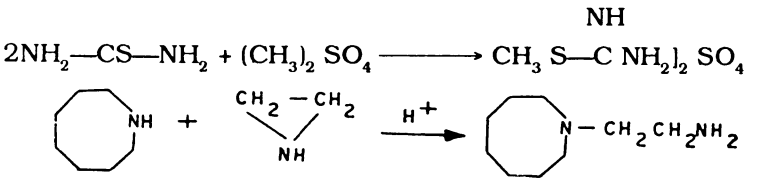
GUANETHIDINE

Nomenclature : [2-(Hexahydro-1-(2H)-azocinyl) ethyl] guanidine.

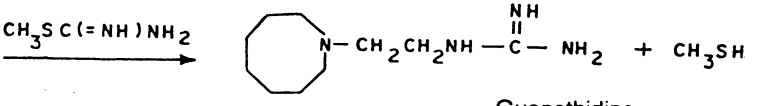


Brand Names : Oktadin; Oktatenzin; Su 5864; Eutensol; Dopom; Octatensine; Sanotensin; Abapresin.

Guanethidine is synthesized from heptamethyleneimine :



Heptamethyleneimine Ethyleneimine



Guanethidine

Guanethidine has strongly basic guanidino group and the weaker tertiary amine group of the hetero-ring.

Guanethidine sulphate (Brand Names : Guethine, Iporal; Isobasin; Ismelin), m.p. 276-281° (dec), is a white or off-white, odourless, crystalline powder which is highly soluble in water; practically insoluble in alcohol, chloroform, and ether; stored in airtight containers and protected from light.

Uses : Guanethidine is an antihypertensive agent, used to treat hypertension.

The most common side-effects of guanethidine therapy are hypotension, and diarrhoea. Dizziness, syncope, muscle weakness, and lassitude are liable to occur.

Official

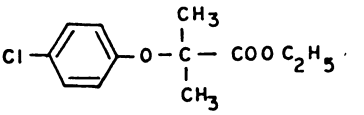
Guanethidine Monosulfate Tablets, U.S.P.

Guanethidine Sulfate Tablets, U.S.P.

CLOFIBRATE

Nomenclature : 2-(4-Chlorophenoxy)-2-methylpropanoic acid ethyl ester; Ethyl 2-(*p*-chlorophenoxy)-2-methylpropionate.

Brand Names : Amotril; Anparton; Apolan; Artevil; Ateculon; Ateriosan; Atheropront; Atromidin; Atromid-S; Bioscleran; Claripex; Cloberate; Clobren-SF; Clofinit; CPIB; Hyclorate; Lipavlon; Liprinal; Neo-Atromid; Normet; Normolipol; Recolip; Regelan; Serotinex; Sklerolip; Skleromexe; Sklero-Tablinen; Ticlobran; Xyduril.



Clofibrate, b.p. 148-150°, is a stable, clear, colourless to pale yellow liquid with a characteristic faintly acrid odour. It is very slightly soluble in water; miscible with alcohol, chloroform and ether; stored in airtight containers and protected from light.

Clofibrate is readily hydrolyzed by serum enzymes in gastrointestinal tract to yield free acid. It is effective in lowering serum triglycerides.

Uses : Clofibrate is used as a hypolipidaemic agent and for the prophylaxis of ischaimic heart disease.

The most common side-effects of clofibrate therapy are gastrointestinal upsets including nausea, vomiting, diarrhoea, dyspepsia, flatulence, and abdominal discomfort.

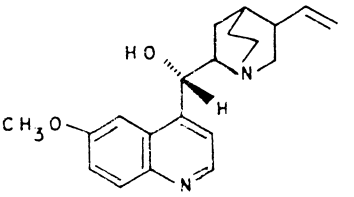
Official

Clofibrate Capsules, B.P., U.S.P.

QUINIDINE

Nomenclature : 6-Methoxycinchonan-9-ol; 6-Methoxy-α-(5-vinyl-2-quinuclidinyl)-4-quinolinemethanol.

Brand Names : Conquinine, Pitayinee; β-Quinine.



Quinidine, m.p. 174-175°, is a dextro-rotatory stereoisomer of quinine which is present is Cinchona barks to the extent of 0.25-3.0 per cent. Most of the compound available in the market is prepared by isomerization of quinine. Quinidine and its salts (e.g. gluconate, sulphate) respond to all the tests for quinine. Both of these alkaloids are distinguished by means of the polarimeter. Quinidine gives blue fluorescence in dilute H_2SO_4. It is very soluble in methanol and chloroform; slightly soluble in alcohol and ether; practically insoluble in petroleum ether.

Quinidine Bisulphate : (Brand Names : Kiditard; Kinichron; Kinidin; Kinidrin; Quiniduran) occurs as colourless, bitter, odourless crystals. It is soluble in water and alcohol; practically insoluble in ether; stored in well-closed containers and protected from light.

Uses : Quinidine has cardiac depressant (antiarrhythmic), antimuscarinic and alpha-adrenergic blocking properties. It is used to maintain sinus rhythm after cardioversion of artrial fibrillation and for the prevention of arrhythmias.

Quinidine causes both cardiac and extracardiac adverse effects. They comonly cause gastro-intestinal irritation with nausea, vomiting and diarrhoea.

Official

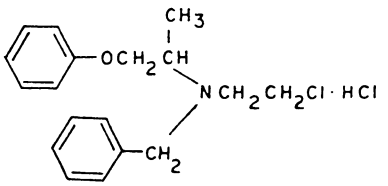
Quinidine Gluconate Injection, U.S.P.

Quinidine Sulfate Tablets, U.S.P., B.P.

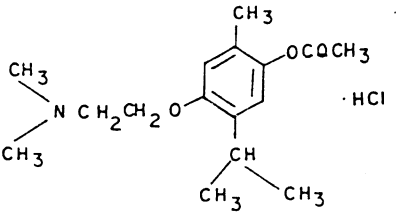
Quinidine Sulfate Capsule, U.S.P.

Quinidine Sulfate Extended Release Tablete, U.S.P.

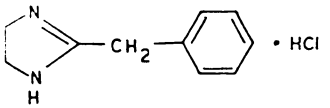
Miscellaneous Agents (Vasodilators)



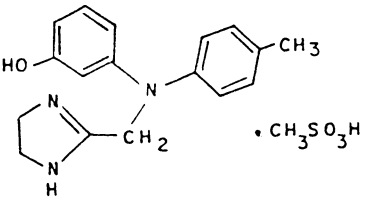
Phenoxybenzamine Hydrochloride



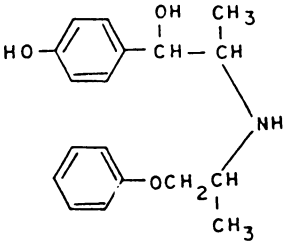
Thymoxamine Hydrochloride



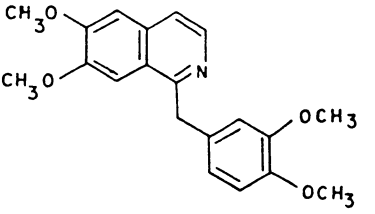
Tolazoline Hydrochloride



Phentolamine Mesylate



Isoxsuprine



Papaverine

24

HYPOGLYCEMIC AGENTS

Insulin is a protein hormone which is secreted by the β-cells of islets of Langerhans of pancreas. If there is a deficiency of insulin in the body, then a disease called diabetes mellitus occurs due to disturbance of carbohydrate, protein and lipid metabolism. The other diseases produced are hyperglycaemia (excessive sugar in the blood) and glucosuria (presence of sugar in urine). The main symptoms of diabetes are polydipsia (increased thirst), polyurea (increased urine), ketonaemia (presence of ketones in blood) and ketourea (presence of ketones in urea). Hypoglycaemic agents are used to lower the blood sugar and to treat diabetes mellitus.

Insulin and insulin preparations, sulphonylureas (e.g. tolbutamide, chlorpropamide, tolazamide, acetohexamide) biguanides and phenformin are used as hypoglycaemic agents.

INSULIN

Insulin is a polypeptide hormone produced by the beta-cells of the Islets of Langerhans of the pancreas of all vertebrates. It is secreted directly into the bloodstream where it regulates carbohydrate metabolism, influences the synthesis of protein and of RNA, and the formation and storge of neutral lipids. It was the first protein for which chemical structure and precise molecular weight were determined.

Insulin consists of two chains of amino acids, the A and B chains, connected by two disulphide bridges. Insulin produced by different species contains the same basic structure but has different sequences of amino acids in the chain . Porcine insulin

differs from human insulin in only one amino acid in the B chain whereas bovine insulin varies from human insulin in the same amino acid in the B chain and in two acids in the A chain.

Commercially insulins are obtained by extraction of bovine or porcine or these mixed pancreases and purified by recrystallization only. An extract which has been recrystallized only once can be separated into 3 components or fractions called as a, b, and c fractions, The 'a' fraction contains high molecular weight substances and is present in very impure preparations. This fraction is purified by repeated recrystallization. The 'b' fraction consists mainly of proinsulin and insulin dimers. In 'c' fraction, insulin, insulin esters, arginine insulin and desamidoinsulin are present. Other pancreatic peptides such as glucagon, pancreatic polypeptide, somatostatin, and vasoactive intestinal peptide are also present in products.

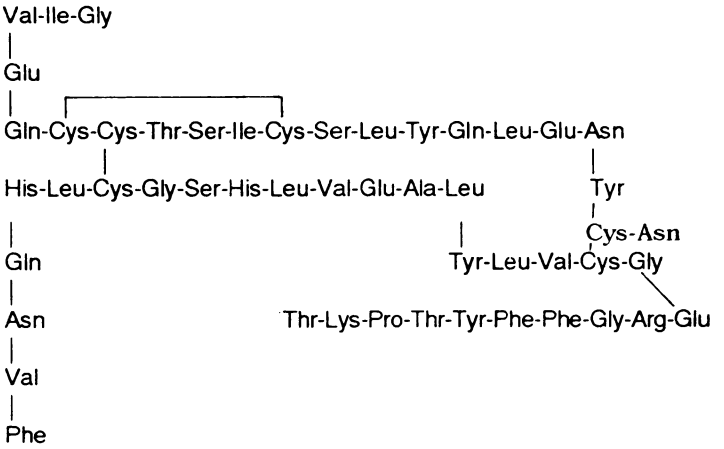
Proinsulin is removed by gel filtration and ion-exchange chromatagraphic techniques. Prior to the discovery of recombinant DNA technology, the major source of insulin was the pancreases of slaughtered animals.

Human insulin, sometimes called semisynthetic human insulin, is now produced by the enzymatic modification of insulin obtained from the porcine pancreas. Human insulin is also produced by the chemical combination of A and B chains which have been obtained from bacteria genetically modified by recombination of DNA technology, or from proinsulin obtained from bacteria or from a precursor obtained from a yeast genetically. Human insulin obtained by recombinant DNA technology is called as biosynthetic human insulin.

Insulin is a protein containing the elements carbon, hydrogen, oxygen, nitrogen and sulphur. The minimum molecular weight is 6000. All crystalline insulin preparations contain small amounts of heavy metals, such as zinc, nickel, cobalt or cadmium as components of the molecule. The amino acid composition and physical structure of mammalian insulin varies only slightly from species to the next, except for the rat and the guinea pig which have large structural differences. Insulin is hydrolyzed by an enzyme, insulinase, which is prepared from hog pancreas

Insulin occurs as an amorphous powder or as crystals, usually obtained as flat rhombohedra and containing 0.4 per cent zinc. It is readily soluble in dilute acids and alkalies. It exists as the dimer in mild acid and as the monomer in 30 per

cent acetic acid. Practically, it is insoluble in pH 4.5 to 7.0. Its isoelectric point is from 5.30 to 5.35.



Human Insulin

Insulin is inactivated when the phenolic, hydroxyl, carboxyl, imidazole and amide groups are blocked by chemical reactions such as acetylation, esterification; or the disulphide bridges are broken by reduction, oxidation or treatment with cysteine. Insulin forms complexes with metals like zinc, nickel, cobalt and cadmium.

Insulin plays a role in :

1. transport of glucose through cell membrane;
2. protein synthesis in muscles, adipose tissue and liver;
3. fatty acid synthesis, increased in liver and adipose tissue;
4. glycogen synthesis in muscle and adipose tissue;
5. glucose uptake, enhanced in muscle, adipose tissue and liver;
6. oxidation phosphorylation, i.e., formation of 'energy rich' phosphate bonds;
7. oxidations in tricarboxylic acid cycle, and
8. formation of glucose-6- phosphate from glucose and ATP + hexokinase.

The role of insulin in the reversible transport of glucose through cell membranes is important. This transport is stereoselective in character and L-glucose is not transported. Insulin does not effect the transport of phosphorylated glucose

through the cell membrane.

A deficiency of insulin yields hyperglycemia, followed by glucosuria, disturbance of electrolyte and water balance, increased fat metabolism and increased amino acid metabolism with increased nitrogen excretion. This results in decrease in blood pressure, collapse of the peripheral blood vessels, failure of kidney function and shock.

Slightly esterified insulin is active and not very strongly antigenic. Unmodified insulin has a rapid onset of activity and a short duration of action.

Proinsulin (Porcine) is a single polypeptide which is composed of the A and B chains of insulin joined together by a polypeptide containing 33 amino acid units and 3 disulphide bridges.

Insulin Injection (Brand names : Actrapid; Endopancrine, Humulin S; Insular; Insulyl; Iszilin; Regular iletin; Velosulin) is a steriled, acidified or neutral solution of insulin. It has a potency of not less than 95 per cent. The potency is 40, 80, 100 or 500 U.S.P insulin units in each ml. The injection containing not more than 100 U.S.P. units/ml is colourless, that containing 500 units may be straw-coloured; substantially free from turbidity and from insoluble matter. Onset of action occurs within 1 hour after injection, reaching its maximum in 2 to 3 hours.

Insulin zinc suspension is a sterile suspension, in a buffered water medium, of insulin modified by the addition of zinc chloride in a manner such that the solid phase of the suspension consists of a mixture of crystals and amorphous material in a ratio of approximately 7:3. It is almost colourless suspension of a mixture of characteristic crystals and many particles have no uniform shape.

Uses : Insulin is used to treat diabetes.

The most frequent complication of insulin therapy is hypoglycaemia resulting hunger, pallor, sweating, palpitations, anxiety and tremulousness. Other symptoms include headache, visual disturbances, slurred speech, paraesthesia of the mouth, alterations in behaviour, and impaired mental ability.

Official

Insulin, B.P.

Insulin Injection, B.P., I.P., U.S.P.

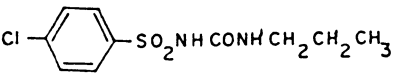
Biphasic Insulin Injection, B.P.

Globin Zine Insulin Injection, B.P., I.P.
Insulin Zine Suspension, B.P., I.P., U.S.P.
Isophane Insulin Injection, B.P.
Neutral Insulin Injection, B.P.
Protamine Zinc Insulin Injection, B.P., U.S.P., I.P.
Extended Insulin Zinc Suspension, U.S.P.
Insulin Human Injection, U.S.P.
Isophane Insulin Suspension, U.S.P.
Prompt Insulin Zinc Suspension, U.S.P.

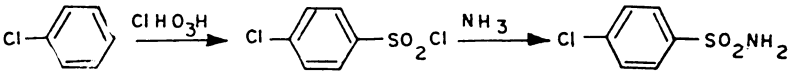
CHLORPROPAMIDE

Nomenclature : 4-Chloro-N-[(propylamino) carbonyl] benzene-sulphonamide; L-(*p*-Chlorophenylsulfonyl) -3-propyl urea.

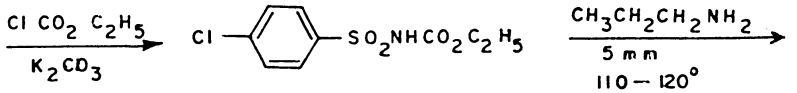
Brand Names : P-607; Adiaben; Asucrol; Catanil; Chloronase; Diabechlor; Diabenal; Diabetoral; Diabinese; Melitase; Millinese; Oradian; Stabinol.

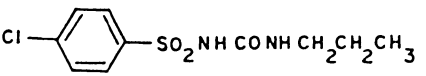


Chlorpropamide, m.p. 127-129°, is a derivative of benzenesulphonamide. It is synthesized from chloro-benzene, which, on treatment with chlorosulphonic acid, yields 4-chlorobenzenesulphonyl chloride. Reaction with excess of ammonia forms the sulphonamide, which is refluxed with ethyl chloroformate to produce ethyl N-4-chlorophenylsulphonyl-carbamate. The substituted urethane on condensation with N-propylamine forms chlorpropamide.



Chlorobenzene





Chlorpropamide

Chlorpropamide is a white, odourless, crystalline powder which is soluble in water at pH 6, practically insoluble at pH 7.3; in alcohol; moderately soluble in chloroform; sparingly soluble in ether and benzene.

Uses : Chlorpropamide is a sulphonylurea hypoglycaemic agent which is used in the treatment of non-insulin-dependent diabetes mellitus.

The side-effects include gastro-intestinal disturbances such as nausea, vomiting, heartburn, anorexia, constipation, diarrhoea, and metallic taste. They may also cause headache, dizziness, weakness, paraesthesia, and tinnitus.

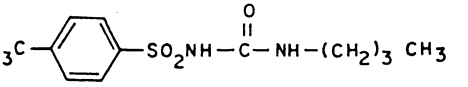
Official

Chloropropamide, B.P., I.P.
Chloropropamide Tabtets, B.P., U.S.P.

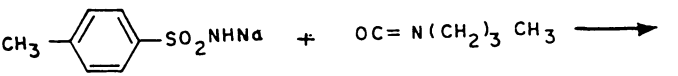
TOLBUTAMIDE

Nomeaclature : N-[(Butylamino) carbonyl] -4-methylbenzenesulfonamide; N-Butyl-3-(*p*-tolylsulfonyl) urea.

Brand Names : D 860; U 2043; Diabetamid; Diasulfon; Glyconon; Orinase; Rastinon; Diabuton; Mobenol; Oterben; Toluina; Diaben; Diabesan; Ipoglicone; Orabet; Oralin; Artosin; Dolipol; Tolbet; Tarasina; Tolbusal; Pramidex; Tolbutone; Willbutamide.

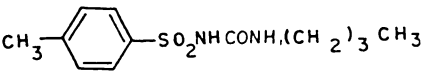


Tolbutamide is pre-pared by condensation of the sodium salt of toluene- p-sulphonamide with n-butyl isocyanate and then by acidification



Toluene-p-sulphonamide sodium salt

n-Butylisocyanate



Tolbutamide

Tolbutamide, m.p. 128-130°, is a white, odourless, crystalline powder which is practically insoluble in water; soluble in

alcohol, acetone, chloroform and dilute solutions of alkali hydroxides; slightly soluble in ether; stored in airtight containers.

Uses : Tolbutamide has actions, uses and side effects similar to those of chlorpropamide. The duration of action is about 10 hours.

Tolbutamide sodium is used intravenously for the diagnosis of mild diabetes mellitus and of functioning pancreatic islet cell adenomas.

Official

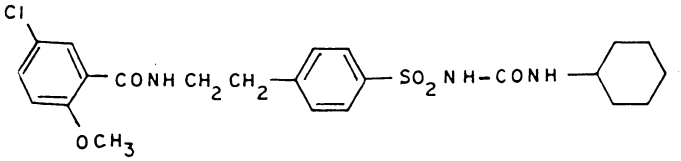
Tolbutamide, B.P., I.P.

Tolbutamide Tablets, B.P., I.P., U.S.P.

GLIBENCLAMIDE

Nomenclature : 5-Chloro-N-(2-(4-[[[(cyclohexylamino) carbonyl] amino] sulfonyl] phenyl) ethyl] -2- methoxybenzamide.

Brand Names : Glybenclamide; Glyburide; HB-419; U-26452; Adiab; Diabeta; Daonil; Euclamin; Euglucon; Gilemal; Glidiabet; Hemi-Daonil; Lisaglucon; Maninil; Micronase; Semi-Euglucon.



Glibenclamide, m.p. 169-170° and 172-174°, is a white, odourless, crystalline powder; practically insoluble in water and ether; soluble in alcohol, chloroform and methanol.

Uses : The actions, uses and adverse effects of glibenclamide are similar to that of chlorpropamide. It is reported to exert a mild diuretic action.

Official

Glibenclamide, B.P.

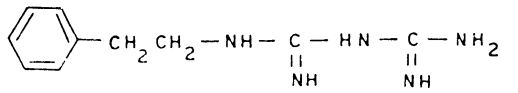
Glibenclamide Tablets, B.P.

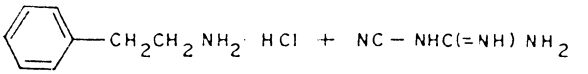
PHENFORMIN

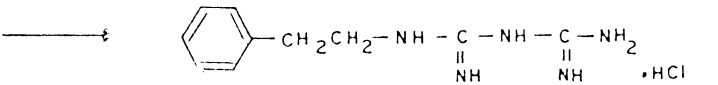
Nomenclature : N-(2-Phenylethyl) imidodicarbonimidic diamide; 1-Phenethylbiguanide.

Brand Names : DBI; β-PEBG; PEDG; Azucaps; D Bretard; Debeone; Debinyl; Diabis; Glucopostin; Retardo; Dibein; Dibiraf; Dibotin; Feguanide; Glyphen; Insoral; Lentobetic; Normoglucina.

Phenformin is prepared by heating cyanoguanidine with phenethylamine hydrochloride.







Phenformin hydrochloride (Synonyms: DBI-TD, Dipar, Meltrol), a biguanide hypoglycaemic agent, m.p. 175-178°, is soluble in water. It functions extrahepatically and acts as an insulin-supporting or reinforcing agent.

Uses : Phenformin is used on maturity-onset diabetes mellitus, especially in patients who have no other complications and the disease cannot be controlled by diet alone.

Phenformin causes lactic acidosis. FDA has declared this substance an imminent hazard to public health.

Official

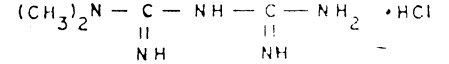
Phenformin Hydrochloride, B.P.

Phenformin Tablets, B.P.

METFORMIN

Nomenclature : N, N-Dimethylimidocarbonimidic diamide; 1,1-Dimethylbiguanide

Brand Names : DMGG; La 6023; Diabetosan; Diabex; Fluamine; Flumamine; Gliguanid.



Metformin hydrochloride, m.p. 218-220°, (Brand Names: Diabefagos, Glucophage, Haurymellin; Meguan; Metiguanide)

is a white, odourless, hygroscopic, crystalline powder; soluble in water and alcohol; practically insoluble in chloroform and ether; stored in airtight containers.

Uses : Metformin is used in non-insulin dependent dia-betes mellitus when diet control fails. It has been reported to increase blood-lipid concentrations.

Metformin causes gastro-intestinal adverse effects with anorexia, nausea, and vomiting. Lactic acidosis has occurred but to a lesser extent than phenformin.

Official

Metformin Hydrochloride, B.P.

Metformin Tablets, B.P.

25

COAGULANTS AND ANTI-COAGULANTS

Coagulation of blood involves the formation of fibrin by a complex phenomenon. The *clotting factors* are the proteins synthesized by the liver. Some of the factors (II or prothrombin-VII, IX and X) are vitamin K dependent for the final stage of their synthesis in the liver. In the process of clotting, each factor undergoes partial proteolysis to form an enzyme (factor Xa). The activated factor then brings about similar proteolysis of the next factor, leading ultimately to conversion of fibrinogen into soluble fibrin and finally, conversion of soluble fibrin into insoluble fibrin (firm clot). The other substances aid the factors in the process of coagulation. The coagulation proceeds along either intrinsic system or extrinsic system. All the reactions necessary for the intrinsic system are already present in the blood in inactive form. The initiators of the extrinsic system are not generally present in the blood; they are added by tissue injury. The intrinsic pathway is a slow pathway and minutes are required for the formation of activated factor Xa. In case of extrinsic pathway, the factor Xa is generated within seconds.

Blood clots are removed from the vascular system by breakdown of fibrin by proteolytic enzyme plasmin or fibrinolysin which is formed from its inactive precursor proplasmin or profibrinolysin. The blood clotting factors are fibrinogen (I), prothrombin (II), thromboplastin (III), ionic calcium (IV), hereditary labile factor (V), accelein (VI), proconvertin (VII), antihemophilic factor (VIII), plasma thromboplastin component (IX), Stuart

Prower factor (X), plasma thromboplastin antecedant (XI), Hageman factor (XII) and fibrin stabilizing factor (XIII).

COAGULANTS

Haemorrhagic state is caused by vascular defects, platelet defects, plasma coagulation disorder or low prothrombin concentration. Coagulants are used to treat severe haemorrhage. Vitamin K_1 (phytomenadione) maintains a normal concentration of prothrombin and other clotting factors in blood plasma. This vitamin is used as an antihaemorrhagic agent. Protamine and thrombin are the other official drugs.

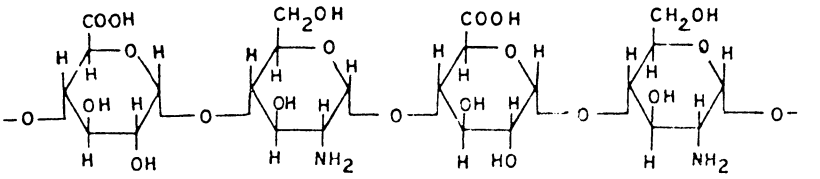
ANTICOAGULANTS

Anticoagulants are the agents which prolong the period of coagulation of blood. They are employed as prophylactics and in the treatment of thrombo-embolic occlusine vascular diseases such as cardiac infraction, pulmonary embolism and venous thrombosis and to prevent thrombosis after operation or by other means.

Heparin inhibits the formation of thrombin from prothrombin, and fibrin from fibrinogen and thus retards the coagulation. The other anticoagulant drugs are coumarins and indanediones (phenindione).

HEPARIN

Brand Name : Heparinic Acid.



Desulphated heparin

Heparin is highly sulphated dextrorotatory active mucopolysaccharide, having specific anticoagulant properties. It is composed of D-glucosamine and D-glucuronic acid residues. Its molecular weight varies from 6,000 to 20,000 depending on source and method of determination. It is a constituent of various tissues especially livers, lung and mast cells in several

mammalian species and isolated from these tissues using suitable methods of isolation. The difference between heparin samples lies in the degree of de-N-sulphation and the extent of 0-sulphation at position 2 of 1 → 4 linked hexuronic acid and position 3 of hexosamine unit. Heparin has been shown to potentiate the activity of angiogenesis promotors. It is a member of the mucopolysaccharides such as chondroitin sulphates A, B and C, keratosulphate, hyaluronic acid and heparitin sulphate. It is a polymer consisting of alternating D-glucuronic acid and 2-amino-2-deoxy-D-glucose units. All the amino groups of the hexoseamine are sulphated.

Heparin has the property of prolonging the clotting time of blood in man and other animals and does not exhibit any other biological action. The exact mechanism of its blood coagulation nature is unknown. It is not active orally and is administered intravenously. The usual clotting time with heparin is from 15 to 20 mimutes.

Heparin Calcium (Brand Name ; Calciparine) is a preparation containing the calcium salt of a sulphated glucosaminoglycan present in mammalian tissues, and having the characteristic property of delaying the clotting of shed blood. It is prepared from the lungs of oxen or the intestinal mucosa of oxen, pigs, or sheep. It is a white, moderately hygroscopic powder, soluble in water; stored in airtight containers.

Heparin sodium (Brand Names : Heprinar; Hepsal; Lipo-Hepin: Liquemin; Lipo-Hepinette; Longheparin; Panheprin; Pularin; Liquaemin sodium; Minihep; Thrombo—Hepin; Thromboliquine Thrombophob; Unihelp) is a preparation containing the sodium salt of a sulphated glucosaminoglycan present in mammalian tissues and having the characteristic property of delaying the clotting of shed blood. It is prepared from the lungs of oxen or the intestinal mucosa of oxen, pigs, or sheep.

Heparin sodium is a white, odourless, moderately hygroscopic powder which is soluble in water; practically insoluble in alcohol, acetone, benzene, chloroform and ether. Ampuled solutions may be stored at room temperature for at least 12 months.

Uses : Heparin is an anticoagulant which inhibits clotting of blood. It is used in the prevention and arrest of deep-vein thrombosis in the treatment of frostbite to prevent gangrene, to treat pulmonary embolism and peripheral arterial embolism, as a precursor to oral anticoagulation, to prevent coagulation

during dialysis and as an adjunct to thrombolytic therapy. Other uses include the anticoagulation of blood samples and the flushing of catheters and cannulas to maintain potency.

Heparin can give rise to haemorrhage and can cause thrombocytopenia. Allergic reactions may occur, such as local irritant effects, necrosis, alopecia and spontaneous fractures.

Official

Heparin Calcium, B.P.
Heparin Injection, B.P.
Heparin Sodium, B.P., I.P.
Anticoagulant Heparin Solution, U.S.P.
Heparin Calcium Injection, U.S.P.
Heparin Lock Flush Solution, U.S.P.
Heparin Sodium Injection, U.S.P.

THROMBIN

Thrombin is an enzyme, serine proteinase, present in blood plasma in the form of a precursor, prothrombin. Its molecular weight is about 33, 580. It plays a central part in the mechanism of blood coagulation by converting the soluble plasma protein, fibrinogen, into insoluble fibrin. Bovine thrombin consists of two polypeptide chains, designated as A and B. The A chain has 49 amino acid residues. It is bound by a disulphide bridge to the B chain which contains about 265 residues and carbohydrate. The prothrombin fraction is prepared by a suitable fractionation technique. The prothrombin is converted into thrombin in solution by the addition of calcium ions and thromboplastin. Thrombin is a white or greyish, amorphous substance.

Uses : Thrombin is a local haemostatic used topically to control haemorrhage from puncture sites or from capillary oozing in surgery.

Official

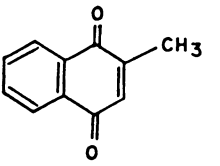
Dried Thrombin, B.P.

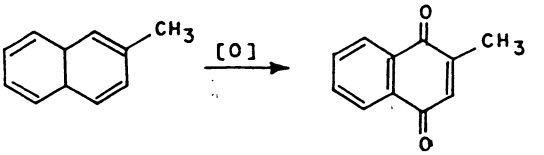
MENADIONE

Nomenclature : 2-Methyl-1,4-naphthalenedione; 2-Methyl-1,4-naphthoquinone.

Brand Names: Menaphthone; Vitamin $K_2(o)$; Vitamin K_3; Kayklot; Kativ G; Kipca; Oil soluble; Kappaxin; Aquakay; Aquinone; Kaergona; Kareon; Kayquinone; Kalklot; Panosine; Synkay; Thyloquinone; Kanone; Klottone; K-Thrombyl; Prokayrit; Koaxin; K-vitan.

Menadione is a synthetic compound analogous in structure to the K group of vitamins, and has similar anti-haemorrhagic properties. It is prepared from 2-methylnaphthalene by oxidation with hydrogen peroxide or with chromium trioxide in acetic acid solution.





Menadione, m.p. 105-107°, is a bright yellow crystalline powder. It is insoluble in water, sparingly soluble in alcohol and methyl alcohol, soluble in ether and vegetable oils: freely soluble in chloroform. The alcoholic solution is neutral to litmus. Solutions may be heated to 120° without decomposition. It is destroyed by alkalies and reducing agents. It is affected by sunlight.

Uses : Menadione is a vitamin which inhibits the glucose metabolism. It has antihaemorrhage action.

Menadione is irritating to mucous membranes, respiratory passages and skin.

Official

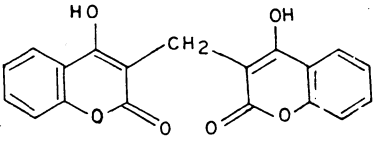
Menadione, I.P., B.P.

BISHYDROXYCOUMARIN

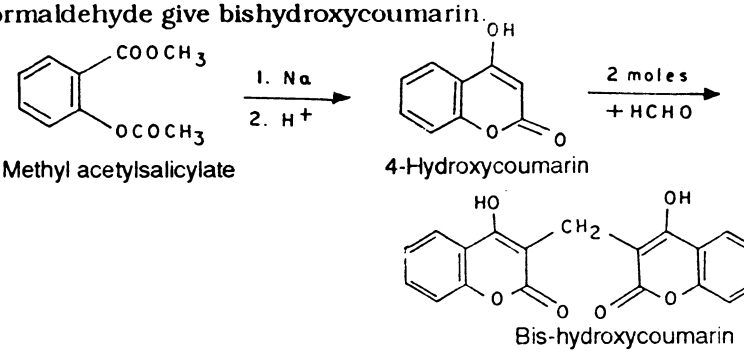
Nomenclature : 3,3'-Methylenebis [4-hydroxy-2-H-1-benzopyran 2-one]; 3,3'-methylenebis [4-hydroxycoumarin].

Brand Names : Dicumarol; Dicoumarolum; Dicumarinum; Dicoumarol; Dicoumarin; Dicumol; Dufalone; Melitoxin.

Bishydroxycoumarin is prepared by the action of sodium on the methyl ester of acetylsalicylic acid to yield the sodium derivative



of 4-hydroxycoumarin. Acidification of the sodium derivative and then condensation of two molecules with one molecule of formaldehyde give bishydroxycoumarin.



Methyl acetylsalicylate

4-Hydroxycoumarin

Bis-hydroxycoumarin

Bishydroxycoumarin is a white or creamy-white crystalline powder with a pleasant faint odour. It is readily soluble in solutions of alkali hydroxides; slightly soluble in chloroform; practically insoluble in water, alcohol and ether.

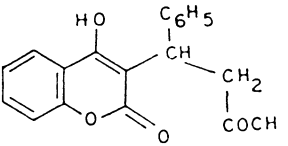
Uses : Bishydroxycoumarin is used orally as anticoagulant in the prophylaxis and treatment of Intravascular clotting. It is employed in postoperative thrombophlebitis, pulmonary embolus, acute embolic and thrombotic occlusion of peripheral arteries and recurrent idopathic thrombophlebitis; to arrest impending gangrene and frostbite.

The side effects of bishydroxycoumarin are haemorrhage, skin necrosis and purple discolouration of the toes.

WARFARIN

Nomenclature : 4-Hydroxy-3-(3-oxo-1-phenylbutyl)-2H-1-benzopyran-2-one; 3-(α-Acetonylbenzyl)-4-hydroxycoumarin.

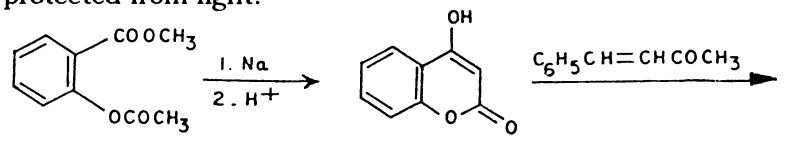
Brand Names : Compound 42; WARF compound-42; Athrombine-K; Coumadin.



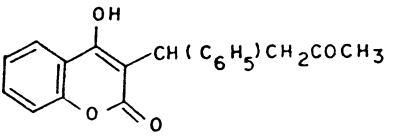
Warfarin is synthesized by treating 4-hydroxycoumarin with benzalacetone by Michael condensation.

Warfarin, m.p. 161°, is a crystalline compound soluble in acetone and dioxane; moderately soluble in methanol, ethanol, isopropanol and some oils; freely soluble in alkaline aqueous solutions, practically insoluble in water, benzene, and cyclohexane. Warfarin has an acidic enol which forms metallic salts and an acetate, m.p. 117-118°, and a ketone

which forms an oxime, m.p. 182-183°, and a 2,4-dinitrophenylhydrazone; stored in well-closed containers and protected from light.



Methyl acetyl salicylate 4-Hydroxycoumarin



Warfarin

Warfarin sodium (Brand Names : Marevan; Prothromadin; Tintorane: Warfilone: Waran) is slightly bitter, white odourless amorphous or crystalline powder. It is decolourized by light; freely soluble in water and alcohol; very slightly soluble in chloroform and ether.

Uses : Warfarin is an anticoagulant which depresses the hepatic vitamin K-dependent synthesis. It is used in the prevention and management of deep-vein thrombosis or pulmonary embolism, in myocardial infraction, stroke and transient ischaemic attacks.

The major risk from warfarin therapy is of haemorrhage from any organ of the body. Skin necrosis is occasionally observed. A purple discolouration of the toes has sometimes been occurred. Other effects include alopecia, fever, nausea, vomiting, diarrhoea, hypersensitivity reactions, priapism, and skin reactions.

Official

Warfarin Sodium, B.P

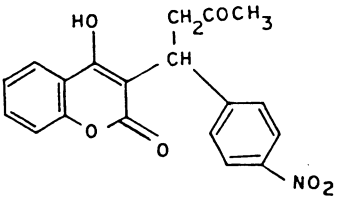
Warfarin Tablets, B.P.

Warfarin Potassium Tablets, U.S.P.

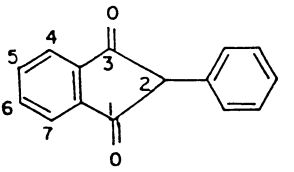
Warfarin Sodium for Injection, U.S.P.

Warfarin Sodium Tablets, U.S.P.

Miscellaneous Antrcoagulants



Nicoumalone



Phenindione

Official

Nicoumalone, B.P., I.P.

Nicoumalone Tablets, B.P., I.P.

Phenindione, B.P., I.P.

Phenindione Tablets, B.P., I.P.

26

HISTAMINE AND ANTI-HISTAMINIC AGENTS

Various sensitising substances, derived from food or environment, cause human allergy and anaphylactic manifestations. These substances, called antigens, release histamine in the body which is β-imidazolylethylamine. An allergic reaction often includes inflammed nasal membranes (rhinitis), running nose, itching in the nose and eyes, coughing, spitting, severe shortness of breath and coma. Allergy is a form of immune reaction in which the individual becomes hypersensitive to a particular substance (an allergen) that may be touched, swallowed, or carried by air into the lungs. Common allergens include pollens, mold spores, household dust, animal dandruff and industrial emissions. Foods, drugs and some toxic plants are also common allergens. When allergens touch or enter the body, they trigger the production of a reactive substance (an antibody) that attaches itself to certain types of body cells : mast cells in the body and basophils in other tissues. This reaction prompts the cells to secret histamine, which acts as an irritant that causes itching, tear formation, and other allergic symptoms.

Histamine brings about numerous physiological effects which are mediated by two sets of receptors, called H_1-and H_2 receptors. The combined effects cause dilatation and increased permeability of capillaries so that fluid and plasma proteins escape to extracellular fluid and produce oedema, bronchiolar constriction, cardiac acceleration and stimulating action on the secretion of gastric acids.

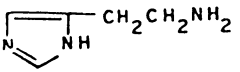
Histamine causes a wide variety of physiological responses. It decreases blood pressure by dilating the capillaries and increases the heart rate. In lungs, histamine acts on smooth muscles producing bronchiolar constriction. In the gastro-intestinal tract, histamine stimulates some excretory glands, causing excess secretion of gastric juice which may produce gastric ulcers. Histamine stimulates the lacrimal (tear) and secretory glands, and takes part in the rapid growth of tissues particularly after wounds.

Antihistamines are the agents which diminish or prevent several actions of histamine in the body. They do not prevent the formation of histamine, but act through competition in the tissues between the agent and histamine. It combines with the receptive substance first before histamine can produce its side effect on the tissue. The antihistamines are used for palliative treatment of allergic reactions such as hay fever, rhinitis, urticaria, mild asthma, nasal discharge, dysentery, irradiation sickness, post operative vomiting, nausea and vomiting of pregnancy. These drugs are generally administered orally or deep intramuscular or slow intravenous injection.

The antihistamines include histamine H_1-receptor antagonists (amino alkyl ethers, ethylenediamines, alkylamines, phenothiazines, piperazines), histamine H_2-receptor (cimetidine) and some miscellaneous agents (cyproheptadine, diphenylpyraline and phenindamine).

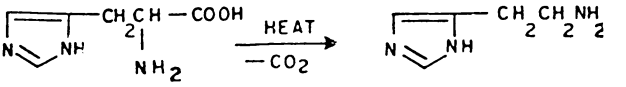
HISTAMINE

Nomenclature : 1H-Imidazole-4-ethanamine; 2-(4-Imidazolyl) ethylamine; 4-Imidazole ethylamine; 5-Imidazoleethylamine; β-Aminoethylimidazole; β-Aminoethylglyoxaline.



Histamine is a potent vasodilator found in normal tissues and blood. It occurs widely in nature, e.g. in ergot and in all the organs and tissues of the human body as a result of putrefactive processes. It stimulates the secretion of pepsin and acid by the stomach. Histamine is converted into the corresponding aldehyde and ammonia by the flavoprotein, diamine oxidase. Some undegraded histamine is excreted in the urine in the form of the N-acetyl and N-methyl derivatives.

Histamine can be obtained by decarboxylation of the amino acid histidine which can be isolated from natural sources or can be prepared synthetically.



Histamine, m.p. 83-84°, is a crystalline compound which is freely soluble in water, alcohol and hot chloroform, and sparingly soluble in ether. It behaves as a di-acid base, forming salts such as the dihydrochloride.

Histamine dihydrochloride (Brand Names : Amin-Glaukosan; Imido; Imadyl; Ergamine; Peremine), m.p. 244-246°, occurs as odourless, hygroscopic, colourless crystalline powder. It is very soluble in water; soluble in alcohol; practically insoluble in chloroform and ether. It is stored in airtight containers and protected from light.

Histamine produces a strong vasodilatation of the capillaries. In large doses it may cause an increase in their permeability, so that fluid and plasma proteins may escape into the extracellular fluid and lead to oedema. In lungs, histamine acts on smooth muscle, producing bronchiolar constriction. It has the effect of stimulating the gastric glands to produce hydrochloric acid. The lacrimal and nasal secretory glands are also stimulated.

Uses : Histamine causes stimulation of smooth muscles and lowers blood pressure by dilating the arterioles and capillaries. It also stimulates various glands of internal secretion, especially the gastric glands.

The main use of histamine is to diagnose impairment of the acid-producing cells of the stomach and in hyposensitization.

The adverse effects of histamine therapy include headache, flushing of the skin, general vasodilation with a fall in pressure, tachycardia, bronchial constriction and dyspnoea, visual disturbance, vomiting, diarrhoea, and other gastro-intestinal effects.

Official

Histamine Phosphate, B.P.

Histamine Phosphate Injection, U.S.P.

Histamine Acid Phosphate, I.P.

Histamine Acid Phosphate Injection, I.P.

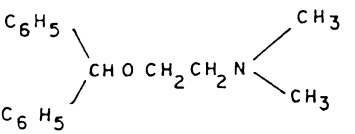
Histamine Dihydrochloride, B.P.

DIPHENHYDRAMINE

Nomenclature : 2-Diphenylmethoxy-N,N-dimethylethanamine.

Brand Names : Alledryl; Allergin; Amidryl;' Bagodryl; Benodin; Benzhydramine; Benylan; Benzantin; Dibendrin; Dibondrin; Dihidral; Diphantine; S 8; Sekundal -D; Syntedril.

Diphenhydramine is a tertiary amine of typically aliphatic character. It is prepared by treating benzhydryl bromide with 2-dimethylaminoethanol in the presence of alkali.



$$(C_6H_5)_2\,CH\,Br + HO\,CH_2\,CH_2\,N\,(CH_3)_2 \longrightarrow (C_6H_5)_2\,CH\,—O—CH_2\,CH_2\,N(CH_3)_2 + HBr$$

Diphenhydramine hydrochloride (Brand Names : BAX; Benadryl; Benocten; Benzehist; Dabylen; Dolestan; Felben; Fenylhist; Halbmond; Rohydra; Valdrene; Wehydry), m.p. 166-170°, is a white, odourless, crystalline powder. It slowly darkens on exposure to light. It is soluble in water, alcohol, acetone and chloroform; very slightly soluble in ether and benzene; pH of 1% aqueous solution is about 5.5. The aqueous solution forms a pink precipitate with saturated Reinecke's salt. It is stored in airtight containers and protected from light.

Uses : Diphenhydramine is an antihistaminic agent; it has pronounced sedative properties and anti-emetic, anti-muscarinic and local anaesthetic actions. It is used to control parkinsonian symptoms and to treat nausea and vomiting. It is included in preparations for coughs and common cold.

As an antihistaminic agent diphenhydramine is given in various allergic conditions and as antispasmodic. It is used to treat urticaria, hay fever, bronchial asthma, vasomotor rhinitis and some dermatoses.

The most common side effects include sedation and drowsiness.

Official

Diphenhydramine Hydrochloride, B.P., I.P.

Diphenhydramine Capsule, B.P., I.P.

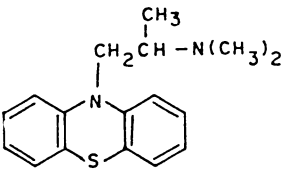
Diphenhydramine Elixir, B.P.

Diphenhydramine Hydrochloride Capsule/Elixir/Injection, U.S.P.

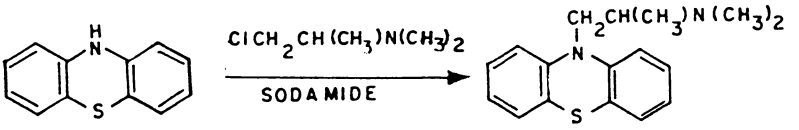
PROMETHAZINE

Nomenclature : N,N,α-Trimethyl-10H-phenothiazine-10-ethanamine; 10-(2-Dimethylaminopropyl) phenothiazine.

Brand Names : Proazamine; RP 3277; RP 3389; Hiberna; Vallergine; Dimapp.



Promethazine is a phenothiazine derivative which is prepared by condensing phenothiazine with $ClCH_2CH(CH_3)N(C_2H_5)_2$ in the presence of sodamide.



Phenothiazine Promethazine

Promethazine is prepared from 10-phenothiazinepropyl chloride and dimethylamine in the presence of copper; and from Grignard complexes of dimethylaminopropyl halide and phenothiazine.

Promethazine, m.p. 60°, is a crystalline compound and used in the form of hydrochloride salt.

Promethazine hydrochloride (Brand Names : Atosil; Fargan; Fenazil; Provigan; Prorex; Diphergan; Ganphen; Fellozine; Remsed; Dorme; Fenegan; Lergigan; Phencen; Phenergan; Promantine; Promine; Protazine; Prothazine; Thiergan), m.p. 230-232° (decomp); is a white, odourless powder which is very soluble in water; soluble in alcohol and chloroform; practically insoluble in ether, acetone and ethyl acetate. It turns blue on prolonged exposure to air and moisture. It is kept in airtight containers and protected from light.

Uses : Promethazine is an antihistaminic agent having some antimuscarinic, antiemetic, antiserotoninergic and local anaesthetic properties. It is given for allergic conditions and to treat burns.

The side effects include sedation, drowsiness, lassitude, dizziness, and inco-ordination. Cardiovascular side-effects are more commonly observed after injection. Bradycardia, tachycardia, increase in blood pressure, hypotension, jaundice and thrombocytopenic purpura have been reported.

Official

Promethazine Hydrochloride, B.P., I.P.

Promethazine Hydrochloride Elixir/Injection/Tablets, B.P., U.S.P.

Promethazine Theoclate, B.P.

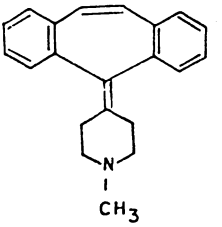
Promethazine Theoclate Tablets, B.P.

Promethazine Hydrochloride Syrup, U.S.P.

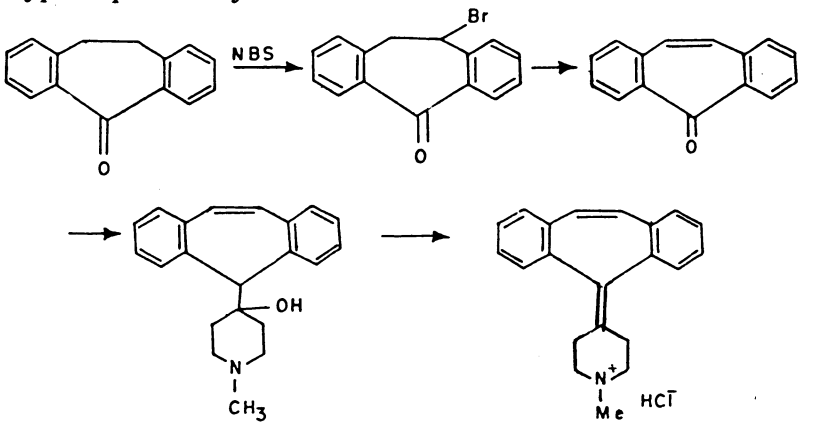
CYPROHEPTADINE

Nomencluture : 4-(5-H-Dibenzo *[a,b]* cyclohepten-5-ylidene) - 1-methylpiperidine; 1-Methyl-4-(5H-dibenzo-*[a,d]* cycloheptenylidene) piperidine.

Brand Name : Periactinol.



Cyproheptadine is synthesized from a ketone consisting of two benzene rings fused in a linear fashion to a seven membered ketone. It is first brominated with N-bromosuccinimide (NBS) and then dehydrobrominated by treatment with triethylamine. The product is reacted with the Grignard reagent, N-methyl-4-piperidyl magnesium chloride, to yield a complex. This is dehydrated by solution in acetic acid and then treated with hydrogen chloride and acetic anhydride to yield cyproheptadine hydrochloride.



Cypropeptadiene hydrochloride

Cyproheptadine, m.p. 112-114°, is a crystalline compound.

Cyproheptadine hydrochloride (Brand Names : Anarexol;

Antegan; Ifrasarl; Nuran; Periactin; Vimicon; Cipractin; Peritol), m.p. 252-254 (decomp), is a white to slightly yellow, odourless, crystalline powder which is soluble in water, alcohol, methanol and chloroform; practically insoluble in ether.

Uses : Cyproheptadine is an antihistamine, antiserotonin and antipruritic agent. It has antimuscarinic activity and is used to suppress the symptoms of allergic reactions and is effective in cold urticaria . It is also used as an appetite stimulant, in treatment of vascular and migraine headaches, Cushing's disease and allergic conditions and to relieve various itching skin conditions.

The side effects are the same as for promethazine. Increased appetite and weight gain may occur.

Official

Cyproheptadine Hydrochloride, B.P.

cyproheptadine Tablets, B.P.

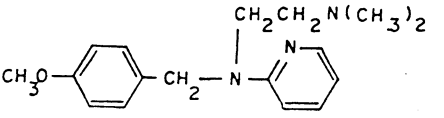
Cyproheptadine Hydrochloride Tablets/Syrup. U.S.P.

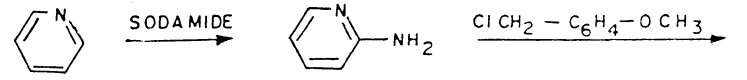
MEPYRAMINE

Nomenclature : N-[(4-Methoxyphenyl) methyl] N',N',-dimethyl-N-2- pyridinyl-1,2-ethanediamine; 2-[(2-Dimethylaminoethyl) (p-methoxybenzyl) amino] pyridine.

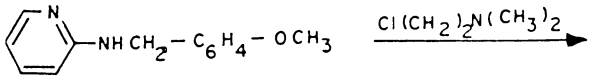
Brand Names : Pyrilamine; Pyranisamine; RP 2786; Neo-Antergan; Anthisan; Antallergan; Harvamine; Isamin; Pyra; Kriptin; Thylogen; Wait's Green; Mountain Antihistamine; Paraminyl ; Maranhist; Histapyran; Histasan; Histalon; Histacap; Coradon; Copsamine, Antamine; Afko-Hist; Mepyren; Neo-Bridal; Pyramal; Stangen; Statomin; Nyscaps; Parmal.

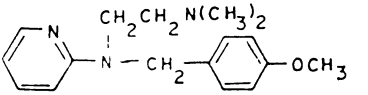
Mepyramine is a substituted 2-aminopyridine which is prepared by heating pyridine in a suitable solvent with sodamide. The nucleophilic amino group enters at the position adjacent to the nitrogen atom.





Pyridine 2-Aminopyridine





Mepyramine

Mepyramine is an oily liquid, b.p. 201°. It is used as maleate salt.

Mepyramine maleate (Brand Names : Dorantamin; Enrumay; Histan; Histatex; Histosol; Paraminyl maleate; Stamine), m.p. 100-101°, is a white or creamy-white, crystalline, odourless powder. It is soluble in water, alcohol and chloroform; slightly soluble in ether. A 2% solution in water has a pH of 4.9 to 5.2. It is stored in airtight containers and protected from light.

Uses : Mepyramine is an antihistamic agent used in the treatment of allergic conditions. It is employed locally for insect bites and stings and for allergic and pruritic skin conditions.

Side effects of mepyramine are the same as described for promethazine.

Official

Mepyramine Maleate, B.P, I., P.

Mepyramine Elixr/Injection, B.P.

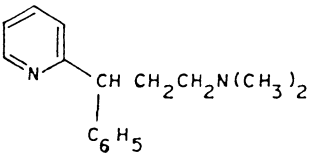
Mepyramine Tablets, B.P., I.P.

Mepyramine Maleate Tablets, U.S.P.

PHENIRAMINE

Nomenclature: N,N-Dimethyl-γ-phenyl (-2-pyridine propanamine; 2-[α-(2-Dimethylaminoethyl) benzyl] pyridine.

Brand Names : Prophenpyridamine; Propheniramine; Avil, Tripoton.



Pheniramine is an oily liquid, slightly yellow in colour with characteristic amine-like odour, b.p. 181°. It is used in the form of maleate (Brand names : Daneral; Inhiston; Trimeton), m.p. 107°; freely soluble in water, alcohol; slightly

soluble in ether, and benzene; pH of 1% aqueous solution is between 4.3 and 4.9. It is protected from light.

Uses : Pheniramine is an antihistamic agent. Side effects are the same as described for promethazine.

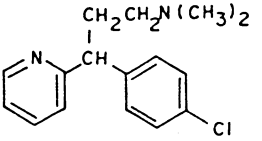
Official

Pheniramine Maleate, B.P., I.P.

Pheniramine Tablets, I.P.

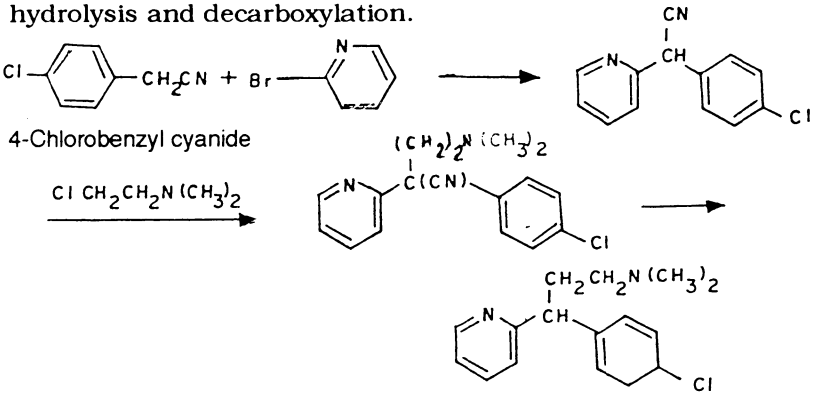
CHLORPHENIRAMINE

Nomenclature : γ-(4-Chlorophenyl)-N, N-dimethyl-2-pyridine-propanamine; 2-[*p*-Chloro-α-(2-dimethylaminoethyl) benzyl] pyridine.



Brand Names : Chlorprophenpyridamine; Chlorphenamine; Haynon.

Chlorpheniramine is synthesized by condensing 4-chlorobenzyl cyanide with 2-bromopyridine. The acetonitrile so obtained is treated with 2-diethylaminoethyl chloride. The cyano group is then removed by hydrolysis and decarboxylation.



4-Chlorobenzyl cyanide

Chlorpheniramine

Chlorpheniramine is an oily liquid, b.p. 142°, used in the form of maleate salt.

CHLORPHENIRAMINE MALEATE

Brand Names : Allerclor; Allergisan; Alunex; Antagonate; Chlormene; Chlor-Trimeton; Chlor-Tripolon; Cloropiril; C-Meton; Histadur; Histalen; Histaspan; Lorphen; M.P. Chlorcaps T.D.;

Piriton; Polaronil (Germany), Pyridamal-100; Teldrin); m.p. 130-135°, is a white, odourless crystalline powder. It is soluble in water, alcohol and chloroform; slightly soluble in ether. A 1% solution in water has a pH 4.0 to 5.0. The drug is stored in airtight containers and protected from light.

Chlorpheniramine is one of the most potent oral antihistamines. The presence of chlorine group of pheniramine in the p-position of the phenyl ring increases 20-fold potency with no appreciate change in toxicity.

Uses : Chlorpheniramine is an outstanding antihistaminic agent which exerts useful protection and causes a moderate degree of sedation. In severe allergies it may be given by injection which may be irritant and transient hypotension or stimulation of the CNS may occur during rapid intravenous injection.

Official

Chlorpheniramine Maleate, B.P. I.P.

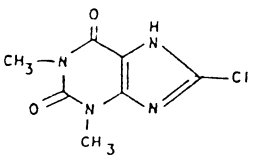
Chlorpheniramine Injection, B.P.

Chlorpheniramine Elixir/Tablets, B.P., I.P.

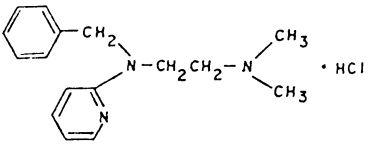
Chlorpheniramine Maleate Syrup/Injection/Tablets, U.S.P.

Dexchlorpheniramine Maleate Syrup Tablets, U.S.P.

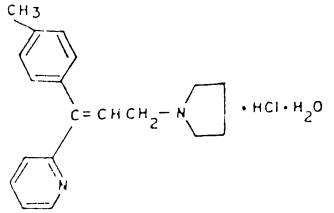
Miscellaneous Agents



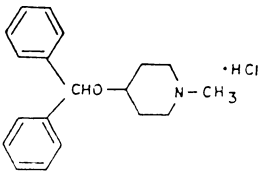
Theoclic Acid



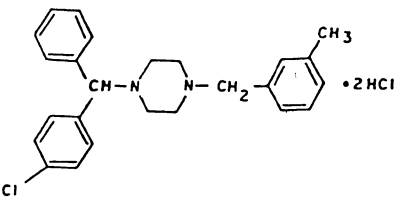
Tripelennamine Hydrochloride



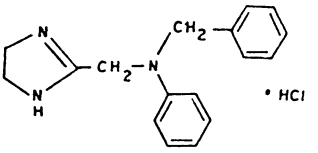
Triprolidine Hydrochloride



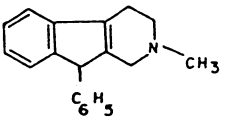
Diphenylpyraline Hydrochloride



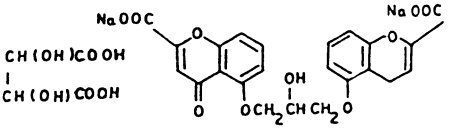
Meclozine Hydrochloride



Antazoline Hydrochloride



Phenindamine Tartrate



Sodium Cromoglycate

27

ANALGESICS AND ANTIPYRETICS

ANALGESICS

Analgesics are the agents which relieve pain without causing loss of consciousness. They are generally used for the relief of moderate to severe pain. The main analgesic agents are morphine and related compounds and some totally synthetic agents, e.g., butorphanol, pentazocine, methadone, etc.

Antipyretics

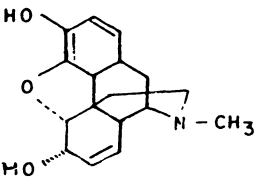
If the body core temperature rises by more than a few degrees in man, then mental changes occur. The commonest manifestation of a change in core temperature is fiver. The hypothalamus plays an important role in thermo-regulatory responses of the body. It controls the body temperature by an increase in sweat gland activity. Many diseases can give rise to fever, the commonest being infection. The increase in temperature is caused by the hypothalamus which reduces heat loss by peripheral vasoconstriction and increases heat production by shivering. Antipyretics are the agents which reduce the body temperature in febrile state. Aspirin, paracetamol and analgin are some antipyretics.

MORPHINE

Nomenclature : 7,8-Didehydro-4,5-epoxy-17-methyl-morphinan-3,6-diol.

Brand Names : Morphium; Morphia; Morphina.

Morphine is the most important alkaloid of opium, *Papaver somniferum* (Family-Papaveraceae). A good grade of opium contains about 10 per cent of morphine. Most of the morphine in opium is present as sulphate or in combination with meconic acid.



For the extraction of morphine, the powdered opium is mixed with calcium chloride solution which reacts with the alkaloidal salt by double decomposition, precipitating calcium meconate and calcium sulphate and leaving the alkaloids in solution as hydrochlorides.

After addition of hot water, the liquid is filtered and sodium sulphate is added to the filtrate to prevent oxidation of the morphine. The liquid is concentrated by evaporation, and sodium acetate is added to precipitate narcotine and other alkoloids, which are separated. The morphine is precipitated by the addition of calcium hydroxide and ammonium chloride, which interact with liberation of free ammonia. Addition of small amount of alcohol helps to induce crystallization of the morphine. Codeine remains in the filtrate. The morphine is purified by washing it with benzene or by recrystallizing its hydrochloride salt.

Morphine, m.p. 254° (decomp.), is a colourless, crystalline compound, very sparingly soluble in water and ether; slightly soluble in ammonia, benzene, alcohol and chloroform; highly soluble in methanol; freely soluble in solutions of fixed alkali and alkaline earth hydroxides, in phenol and cresols. It has an intensely bitter taste. It is a monoacid tertiary base, forming salts with one equivalent of an acid. It has phenolic and basic properties. When morphine is heated with zinc dust, it is decomposed with formation of simpler compounds like pyridine and quinoline.

Tests for Morphine :

1. Morphine is soluble in aqueous sodium hydroxide. Solutions of morphine salt are precipitated on addition of ammonia to form free base which is dissolved on addition of sodium hydroxide.
2. Morphine liberates iodine from iodic acid.
3. When a dilute solution of a morphine salt, acidified with sulphuric acid, is added to a solution of potassium iodate

containing starch mucilage, a deep blue colour is formed.

4. Addition of a drop of ferric chloride to a solution of a morphine salt produces bluish-green colour.
5. Morphine (0.1g) is heated with concentrated sulphuric acid on a water bath for 15 minutes and the cold solution is treated with a few drops of dilute nitric acid, a blood-red colour is formed.

Morphine hydrochloride, m.p. 200° (decomp.), is prepared by neutralizing a hot aqueous suspension of morphine with dilute hydrochloric acid and then concentrating the resulting solution by evaporation to get crystals.

It occurs as colourless, silky, glistering crystals or white crystalline powder. It is soluble in water, glycerine and boiling alcohol; practically insoluble in ether or chloroform. Solutions have a pH of about 5 and may be sterilized by boiling. It is protected from light and kept in well-closed containers.

Morphine Sulphate (Brand Name : MST-1 continus), m.p. 250° (decomp), is prepared in the same manner as the hydrochloride. It occurs as white, odourless, acicular crystals, cubical masses, or crystalline powder. It loses water of crystallization at room temperature and darkens on exposure to light. It is soluble in water (1 in 21), alcohol (1 in 1000); insoluble in chloroform and ether; pH of aqueous solutions is about 4.8. Ampuled aqueous solutions of morphine sulphate turn brown on storage. No loss of analgesic potency and no increase in toxicity have ever been demonstrated for such discoloured solutions. It is protected from light and kept in airtight containers.

Uses : Morphine is a narcotic analgesic agent used for the symptomatic relief of pain, to alleviate the anxiety associated with pain; as general anaesthetic in high doses.

The common side effects of morphine are nausea, vomiting, constipation, drowsiness, and confusion. Dry mouth, sweating, facial flushing, vertigo, bradycardia, palpitation, orthostatic hypotension, hypothermia, restlessness, changes in mood and miosis also occur. Abuse leads to habituation or addiction.

Official

Diamorphine Hydrochloride, B.P.

Diamorphine Injection, B.P.

Morphine Hydrochloride, B.P., I.P.

Morphine Hydrochloride Solution, I.P.

Morphine Injection, I.P.

Morphine Sulphate, B.P., I.P.

Morphine Sulphate Tablets/Injection, B.P., U.S.P.

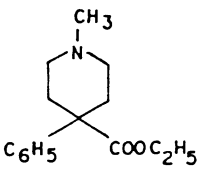
Morphine and Atropine Injection, I.P.

Ethyl Morphine Hydrochloride, B.P., I.P.

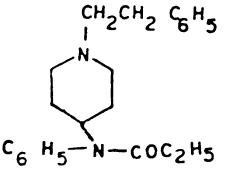
PETHIDINE AND ANALOGUES

Nomenclature : 1-Methyl-4-phenyl-4-piperidinecarboxylic acid ethyl ester; 1-Methyl-4-phenylisonipecotic acid ethyl ester.

Brand Names : Isonipecaine; Meperidine.

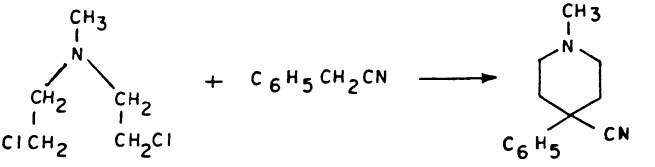


Pethidine



Fentanyl

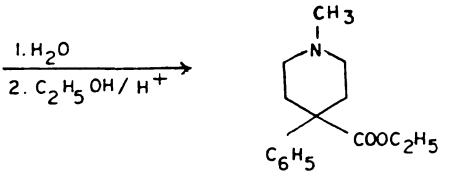
Pethidine is a derivative of piperidine and is synthesized by treating benzyl cyanide with di-(2-chloroethyl) methylamine followed by hydrolysis and esterification of the resultant product.



Di-(2-chloroethyl) methylamine

Benzyl Cyanide

4-Cyano-1-methyl-4-phenylpiperidine



Pethidine

Pethidine is a strong tertiary base and an ester. It is used as a hydrochloride salt which is an analgesic with a morphine-like action.

Pethidine Hydrochloride (Brand Names : Algil; Alodan; Dolantin; Dolestine; Dolenal; Demerol hydrochloride; Dolosal; Endolat; Dispadol; Dolvanol; Dolcontral; Doloneurin (e); Centralgin; Dolopethin; Mefedina; Pantalgine; Sauteralgyl; Spasmedal; Spasmodolin; Mephedine; Lydol; Lidol; Synlaudine). m.p. 186-189°. It is a fine white odourless crystalline powder which is very soluble in water; freely soluble in alcohol, acetone, ethyl acetate and chloroform; practically insoluble in ether and benzene. It is kept in airtight containers and protected from light.

Uses : Pethidine is an analgesic which has actions, uses and side effects of morphine. It is also used as pre-operative medication and as an adjunct to anaesthesia. It has little effect on cough and diarrhoea.

Official

Meperidine hydrochlorde Injection syrup, U.S.P.

Pethidine hydrochloride, B.P., I.P.

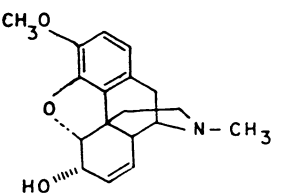
Pethidine Injection/Tablets. B.P., I.P.

Fentanyl Citrate. B.P.

CODEINE

Nomenclature : 7,8-Didehydro-4,5-epoxy-3-methoxy-17-methyl-morphinan-6-ol.

Brand Names : Methylmorphine; Morphine 3-methyl ether; Codicept.



Codeine is an alkaloid which occurs naturally in opium from 0.7 to 2.5 per cent. Commercially codeine is prepared from morphine by methylating the phenolic hydroxyl with methyl iodine in the presence of potassium hydroxide.

Codeine, m.p. 154-156°, occurs as odourless laevorotatory, colourless crystals or white crystalline powder. It effloresces slowly in dry air and is affected by light. It is soluble in water (1 in 120), alcohol (1 in 2), chloroform (1 in 0.5) and ether; almost insoluble in petroleum ether or in solutions of alkali hydroxides. A 0.5% solution in water has a pH of more than 9. It is kept in airtight containers and protected from light.

Codeine is a mono-acid tertiary base and dissolves readily in dilute acids with formation of salts. Its molecule does not contain a free phenolic hydroxyl group like morphine, therefore,

it does not react with alkali hydroxides to form metallic derivatives. It does not give bluish-green colour with ferricyanide and ferric ions and yellow colour with nitrous acid and ammonia as observed in morphine. Generally codeine is used in the form of hydrochloride, sulphate or phosphate salt. The general pharmacological action of codeine is identical to that of morphine but it does not possesses the same degree of analgesic potency.

Codeine hydrochloride is prepared by neutralizing an aqueous solution of codeine with dilute hydrochloric acid and crystallizing the salt, m.p. about 280°. It occurs as small colourless crystals or a white crystalline powder. It is soluble in water, slightly soluble in alcohol; practically insoluble in chloroform and ether; stored in well-closed container and protected from light.

Codeine sulphate, prepared similarly to the hydrochloride salts, occurs as white crystals or white crystalline powder. It is soluble in water (1:30), and alcohol (1:1300); insoluble in ether or chloroform; stored in airtight containers and protected from light.

Codeine phosphate is prepared by neutralizing codeine with phosphoric acid and precipitating the salt from aqueous solution with alcohol. It occurs as odourless, colourless, crystals or a white crystalline powder; affected by light. It is soluble in water, slightly soluble in alcohol; practically insoluble in chloroform and ether. The pH of 2% aqueous solution is 4.6. It is kept well-closed and protected from light.

Uses : Codeine is an analgesic with uses and side-effects similar to those of morphine. It is more potent as an analgesic and has mild sedative effects.

Codeine is also reputed as an antitussive, depressing the cough reflex and is used in cough preparations.

Official

Codeine, B.P.

Codeine Phosphate, B.P., I.P.

Aspirin and Codeine Tablets, B.P.

Codeine Linctus, B.P.

Codeine Phosphate Syrup, I.P.

Codeine Phosphate Tablets, B.P.

Codeine Phosphate Injection, U.S.P.

Dihydrocodeine Tartrate, B.P.

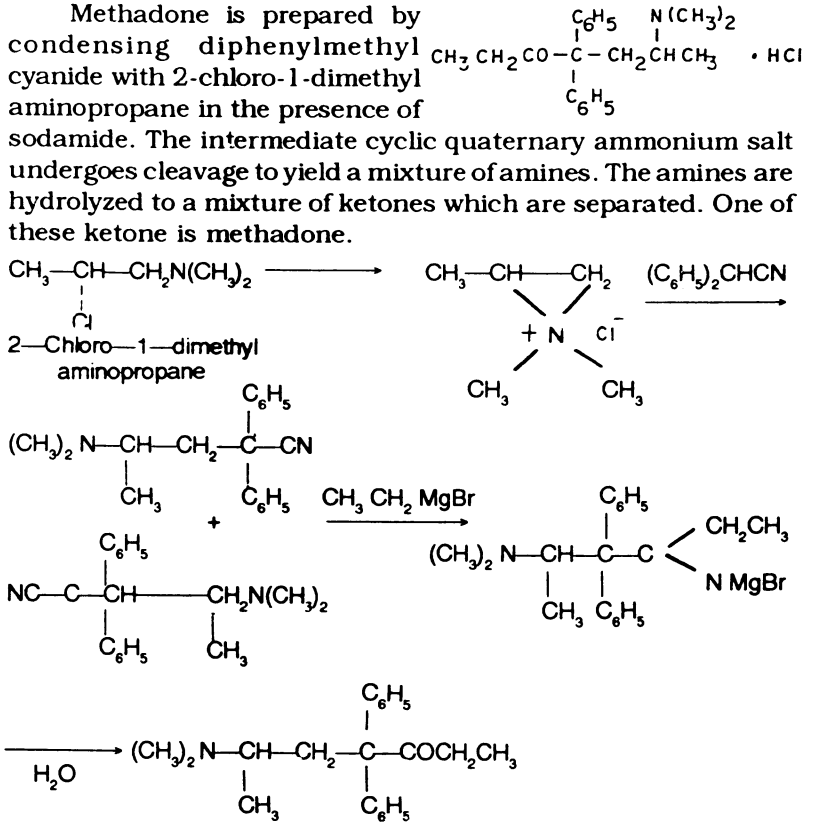
Dihydrocodeine Injection/Tablets, B.P.

METHADONE HYDROCHLORIDE

Nomenclature: 6-Dimethylamino-4, 4-diphenyl-3-heptanone hydrochloride.

Brand Names : Dolophine; Amidine; Phenadone; Adanon HCl; Algidone; Algolysin; AN-148; Butalgin; Amidon HCl; Depridol; Diaminon HCl; Fenadone; Heptadon HCl; Hoechst 10820; Mecodin; Mephenon; Miadone; Moheptan; Physeptone HCl; Tussal.

Methadone is prepared by condensing diphenylmethyl cyanide with 2-chloro-1-dimethyl aminopropane in the presence of sodamide. The intermediate cyclic quaternary ammonium salt undergoes cleavage to yield a mixture of amines. The amines are hydrolyzed to a mixture of ketones which are separated. One of these ketone is methadone.



Methadone

Methadone hydrochloride, m.p. 235°, is a colourless, odourless crystalline powder with a bitter taste. It is soluble in water; freely soluble in alcohol and chloroform; practically insoluble in ether and glycerol. A 1% solution in water has a pH of 4.5 to 6.5.

Uses : Methadone is a potent analgesic with actions, uses and side effects similar to those of morphine. It is used to alleviate many types of pains and has a depressant action on cough centre.

The toxicity of methadone is 3 to 10 times greater than that of morphine. It has analgesic effect twice that of morphine and relatively greater respiratory depressant effect than morphine. Pulmonary oedema after over dose is common.

Official

Methadone Hydrochloride, B.P., I.P.

Methadone Injection, B.P., I.P.

Methadone Linctus, B.P.

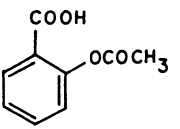
Methadone Tablets, B.P., I.P.

Methadone Hydrochloride Injection/Tablets/Oral Concentrate, U.S.P.

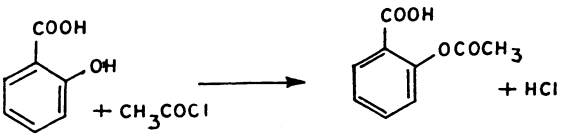
ASPIRIN

Nomenclature : Salicylic acid acetate; 2-(Acetyloxy) benzoic acid; 2-Acetoxybenzoic acid; Acetylsalicylic acid.

Brand Names : Acenterine; Aceticyl; Acetophen; Acetosal; Acetosalin; Acetylin; Acetyl-SAL; Acimetten; Acylpyrin; A.S.A.; Asatard; Aspro; Asteric; Caprin; Colfarit; Contrheuma retard; Delgesic; Duramax; Ecotrin; Empirin; ECM; Endydol; Entrophen; Enterosarine; Helicon; Neuronika; Rhodine; Salacetin; Salcetogen; Saletin; Solpyron; Xara.



Aspirin is prepared by the action of acetyl chloride or acetic anhydride on salicylic acid.



Salicylic acid Aspirin

Aspirin, m.p. 135°, is a colourless, odourless, crystalline powder which is soluble in water (1:300), alcohol (1:6), chloroform (1:17) and ether. It is stable in dry air, but gradually hydrolyses in contact with moisture to acetic and salicylic acids. It is decomposed in boiling water or when dissolved in solutions of

alkali hydroxides and carbonates.

Uses : Aspirin has analgesic, anti-inflammatory and antipyretic properties. It is used for the relief of pains such as headache, dysmenorrhoea, myalgias and toothache. It is also used in inflammatory disorders such as rheumatoid arthritis and to treat colds and influenza.

The most common adverse effects with aspirin therapy are gastro-intestinal disorders such as nausea, dyspepsia and vomiting, irritation of gastric mucosa and increasing in bleeding time.

Official

Acetylsalicylic Acid/Tablets, I.P.

Aspirin Tablets, B.P., U.S.P.

Aspirin and Codeine Tablets, B.P.

Aspirin and Caffeine Tablets, B.P.

Compound Acetylsalicylic Acid/Tablets, I.P.

Dispersible Aspirin and Codeine Tablets. B.P.

Dispersible Aspirin Tablets, B.P.

Paediatric Dispersible Aspirin Tablets, B.P.

Methyl Salicylate, B.P., I.P.

Methyl Salicylate Liniment, B.P.

Methyl Salicylate Ointment, B.P.

Sodium Salicylate, B.P., I.P..

Sodium Salicylate, Mixture, B.P.,

Aspirin Suppositories, U.S.P.

Aspirin Delayed-release Tablets, U.S.P.

Aspirin and Codeine Phosphate Tablets. U.S.P.

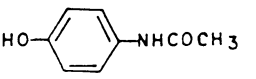
Buffered Aspirin Tablets, U.S.P.

PARACETAMOL

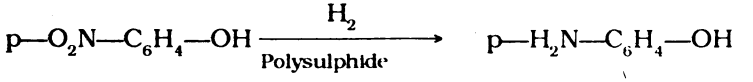
Nomenclature : N-(4-Hydroxyphenyl) acetamide; 4-Hydroxyacetanilide.

Brand Names : Acetaminophen; p-Hydroxyacetanilide; Acamol; Alpiny; Anhiba; Ben-4-ron; Bickie-mol; Dial-a-gesic; Doliprane; Temlo; Valadol; Cetadol; Acetalgin; Enelfa; Exdol; Finimal; Datril; Dirox; Nobedon; APAP; Tabalgin; Tempra, Calpol, Dymadon;

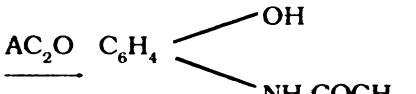
Momentum; Naprinol; Panets; Homoolan; Febrilix; Abensanil; Anaflon; Amadil; Eneril; Tralgon; Hedex; Pacemo; Panex; Panofen; Parmol; Tylenol; Panadol; Lyteca; Apamide; Tapar; Gelocatil; Korum; Paraspen.



This is prepared by reduction of p-nitrophenol in glacial acetic acid, acetylation of p-aminophenol with acetic anhydride or ketone, or from p-hydroxyacetophenone hydrazone.



P-Nitrophenol p-Aminophenol



Paracetamol

Paracetomol, m.p. 169-171°, is a white odourless crystalline powder with a slightly bitter taste. It is soluble in water (1:70); considerably more soluble in hot water (1:20) and in alcohol (1:10); very slightly soluble in chloroform and ether; insoluble in petroleum ether, and benzene. It is kept in airtight containers and protected from light.

Uses : Paracetamol has analgesic and antipyretic properties.

Side-effects of paracetamol therapy are haematological reactions and skin rashes.

Official

Paracetamol, B.P., I.P.

Paediatric Paracetamol Elixir, B.P.

Paracetanol Tablets, B.P., I.P.

Phenacetin, I.P.

Acetaminophen Capsule/Elixir/Tablets, U.S.P.

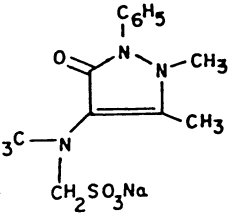
Acetaminophen and Codeine Phosphate Elixir, U.S.P.

ANALGIN

Brand Names : Metamizol; Benalsis; Maxigen; Novaligin.

Analgin is a white, crystalline, odourless powder with a scarcely perceptible yellowish tinge. The taste is bitter. It is freely soluble in water; slightly soluble in alcohol; practically

insoluble in chloroform and solvent ether. It is stored in tightly-closed containers.



When a mixture of analgin (0.1g) in water (2 ml), alcohol (5ml) and dilute hydrochloric acid (0.5 ml) is treated with potassium iodate solution (5 ml), a crimson red colour is produced which darkens on further addition of potassium iodate solution. If analgin is heated with diluted hydrochloric acid, the characteristic odour of sulphur dioxide is produced followed by that of formaldehyde.

Uses : Anagin is an analgesic agent. It relieves pain like headache, neuralgia, muscle pain, arthralgia, postoperative pain, traumatic pain associated with burns, injury, fracture and dental procedures; also used as antipyretic.

Adverse effects of analgin are dyspepsia, epigastric, discomfort, nausea, vomiting, blood dyscrasias, skin rashes, insomnia, agranulocytosis, edema, shock intolerance, hypersensitivity and fall in blood pressure on rapid injection.

Official

Analgin, I.P.

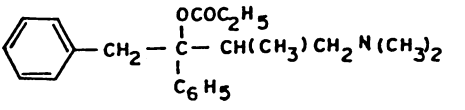
Analgin Tablets, I.P.

DEXTROPROPOXYPHENE

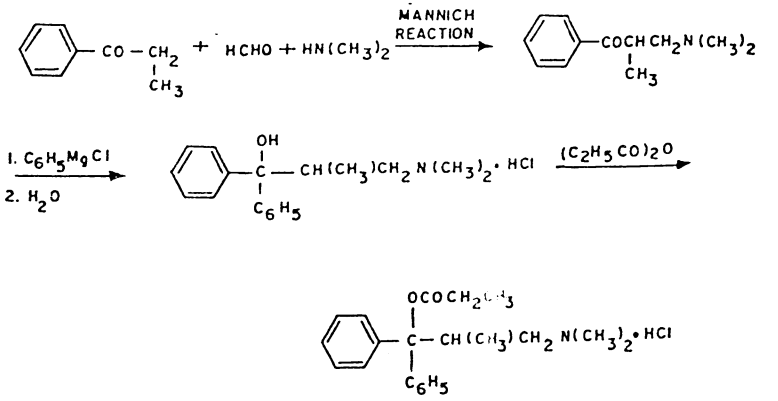
Nomenclature : α-(2-(Dimethylamino)-1-methylethyl)-α-phenyl-benzene ethanol propanoate; α-4-Dimethylamino-3-methyl-1,2-diphenyl-2-butanol propionate.

Brand Names : d-Propoxyphene

This aliphatic tertiary amine base is also an aryl-substituted aliphatic ester of propionic acid. The



substituted isobutyro-phenone required for its synthesis can be prepared by condensation of propiophenone, paraformaldehyde and diethylamine hydrochloride (Mannich reaction). The aminoketone so obtained reacts with the Grignard reagent, benzyl magnesium chloride, which on hydrolysis gives mainly the α-form of a tertiary alcohol hydrochloride. This alcohol is esterified by refluxing with propionic anhydride in the presence of pyridine.



Dextropropoxyphene

The official compound is the hydrochloride of the ester (α-form) since the α-dl-and d-diastereoisomers possess marked analgesic activity in contrast to the β-diastereoisomers which are substantially inactive.

Dextropropoxyphene. m.p. 75-76°, occurs as crystals.

DEXTROPROPOXYPHENE HYDROCHLORIDE

Brand Names : Algafan; Antalvic; Darvon; Depromic; Doloxene; Deprancol; Develin; Dolene; Dolocap; Doraphen; Erantin; Femadol; Harmar; Propox; Propoxychel; Proxagesic); m.p. 163-169°, is a white or slightly yellow odourless powder. It is soluble in water, alcohol, chloroform and acetone; practically insoluble in benzene and ether. It is kept in airtight containers.

The analgesic potency of dextropropoxyphene is almost equal to codeine phosphate and exhibits fewer side-effects. It has no antidiarrhoeal, antitussive or antipyretic effect like most of the other analgesic agents. It is not much effective in deep pain.

Uses : Dextropropoxyphene is an analgesic related to methadone. It is mainly used in conjunction with other analgesics with anti-inflammatory and antipyretic effects.

Adverse effects of dextropropoxyphene are the same as for morphine. Gastro-intestinal effects are the most common. Liver impairment has been reported.

Official

Dextropropoxyphene hydrochloride, I.P; B.P.

Dextropropoxyphene Capsules, B.P.

Proproxyphene Hydrochlorde, Aspirin and Caffeine Capsules, U.S.P.

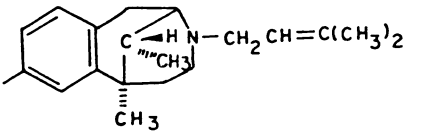
Propoxyphene Napsylate and Aspirin Tablets, U.S.P.

Dextropropoxyphene Napsylate, I.P.

PENTAZOCINE

Nomenclature : 1,2,3,4,5,6-Hexahydro-6,11-dimethyl -3-(3-methyl-2-butenyl) 2,6-methano-3-benzazocin-8-ol.

Brand Names : NSC -107430; Win 20228; Fortalin; Fortalgesic; Fortral; Liticon; Pentagin; Sosigon; Talwin.



Pentazocine, m.p. 145-148°, is a white or creamy-white odourless powder. It is practically insoluble in water; soluble in alcohol (1in15), chloroform (1 in 2) and ether (1 in 3). It is kept in airtight containers and protected from light.

Pentazocine is used as its hydrochloride salt which is a white or pale cream, odourless, crystalline powder. It is soluble in water, alcohol and chloroform; practically insoluble in ether. It is kept in airtight containers and protected from light.

Uses : Pentazocine is an opioid analgesic with actions and uses similar to those of morphine. It is used for the relief of moderate to severe pain. Its analgesic effect declines more rapidly than that of morphine.

The most frequent side-effects of pentazocine are headache, dizziness, nausea and vomiting, sedation, and sweating.

Official

Pentazocine, B.P.

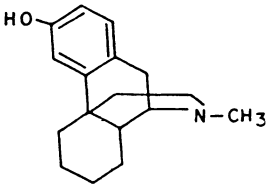
Pentazocine Lactate Injection, B.P., U.S.P.

Pentazocine Hydrochloride, B.P.

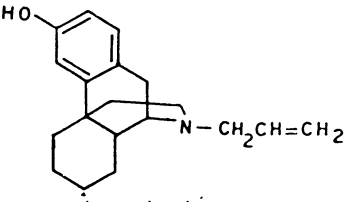
Pentazocine Tablets, B.P.

Pentazocine Hydrochloride and Aspirin Tablets, U.S.P.

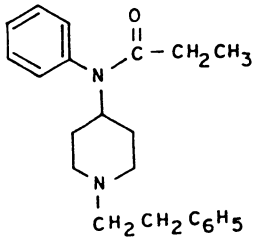
Miscellaneous Agents



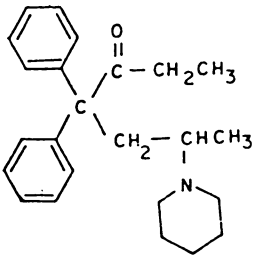
Levorphanol



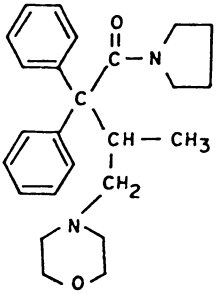
Levaclorphan



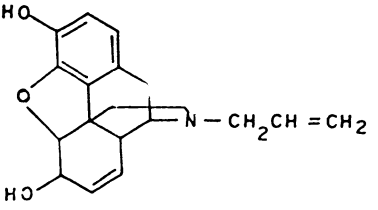
Fentanyl



Dipipanone



Dextromoramide



Nalorphine

28

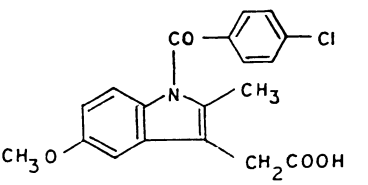
NONSTEROIDAL ANTI-INFLAMMATORY AGENTS

The drugs used to reduce inflammation and the pain arising from it are termed as anti-inflammatory agents. Glucocorticoids, e.g. hydrocortisone and cortisone, are generally used as anti-inflammatory states, but they have many undesirable adverse effects. Nonsteroidal anti-inflammatory agents do not show undesirable effects of steroid therapy. These drugs give symptomatic relief from the pain and inflammation and have analgesic and antipyretic properties. These drugs are used in inflammatory conditions in arthritis, rheumatism, lupus erythematosus and ankylosing spondylitis. They possess lower maximal effects than opioid analgesics. The useful nonsteroidal anti-inflammatory drugs are salicylic acid derivatives (e.g. aspirin), N-arylanthranilic acids, indolyl or arylacetic acid derivatives, and pyrazole derivatives.

INDOMETHACIN

Nomenclature : 1-(4-Chlorobenzoyl)—5-methoxy-2-methyl-1H-indole-3-acetic acid.

Brand Names : Amuno; Artracin; Artrinovo; Artrivia; Confortid; Idomethine; Imbrilon; Inacid; Indacin; Indocid; Indocin; Indomed; Indomee; Indometacin; Indoptic; Indo-Tablinen; Inflazon; Infrocin; Inteban SP; Lausit; Mezolin; Mikametan; Mobilan; Tannex.



Indomethacin is a white to yellow-tan, odourless, crystalline powder. It shows polymorphism having melting points at 155° and 162°. It is practically insoluble in water; soluble in alcohol, chloroform and ether. It is stable in neutral or slightly acidic media; decomposed by strong alkali and in sunshine. It is kept in well-closed containers and protected from light.

Uses : Indomethacin has analgesic, anti-inflammatory and antipyretic properties. It is used in rheumatic disorders, pain conditions and to close a patent ductus arteriosus in premature infants.

The commonest adverse effects with indomethacin therapy are gastro-intestinal disorders, headache, and dizziness. Other side effects are depression, drowsiness, tinnitus, confusion, insomnia, psychiatric disorders, syncope, convulsions, coma, peripheral neuropathy, blurred vision, etc.

Official

Indomethacin, B.P.

Indomethacin Capsules, B.P., U.S.P.

Indomethacin Suppositories, B.P., U.S.P.

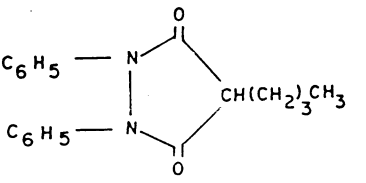
Indomethacin Extended-release Capsules, U.S.P.

PHENYLBUTAZONE

Nomenclature : 4-Butyl-1,2-diphenyl-3,5-pyrazolidinedione.

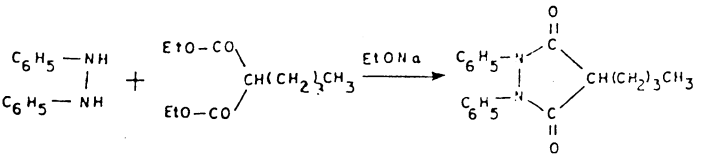
Brand Names : Alindol; Antadol; Anuspiramin; Azolid; Artrizin; Buzon; Butazolidin; Butapirazol; Butidiona; Bunetzone; Betazed; Benzone; Butoz; Butacote; Bizolin; Diphebuzol; Flexazone; Fenibutazona; G 13871; Ecobutazone; Fenotone; Fenilbutina; Elmedal; Fenibutol; Ia-But; Intrabutazone; Intrazone; Mephabutazone; Phenyzone; Pirarreumol-B; Phebuzine Praecirheumin; Reudo; Reudox, R-3-ZON; Robizone-V; Schemergen; Spondyril; Ticinil; Tevcodyne; Zolapen.

Phenylbutazone is synthesized by condensing n-butyl substituted malonic ester with hydrazobenzene (1,2-diphenylhydrazine) in the presence of sodium ethoxide.



Phenylbutazone, m.p. 105°, is a white or off white, odourless, crystalline powder. It is practically

insoluble in water; sparingly soluble in alcohol; soluble in chloroform; ether and aqueous solutions of alkali hydroxides. It is kept in airtight containers and protected from light.



Hydrazobenzene n-Butyl malonic ester

Uses : Phenylbutazone has analgesic, antipyretic and anti-inflammatory properties. It is used in rheumatic disorders, arthritis and Reiter's disease (a condition characterized by arthritis, urethritis and conjunctivitis).

Nausea, vomiting, epigastric distress, diarrhoea, oedema, skin rashes, vertigo, headache and blurred vision may occur. More serious reactions include gastric irritation, ulceration, hepatitis, jaundice, nephritis, renal failure and goitre.

Official

Phenylbutazone Capsules, U.S.P.

Phenylbutazone Suppositories, B.P.

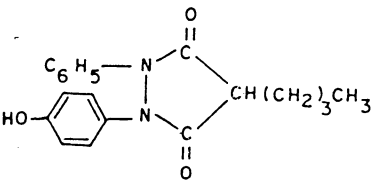
Phenylbutazone Tablets, B.P., U.S.P.

OXYPHENBUTAZONE

Nomenclature : 4-Butyl-1-(4-hydroxyphenyl)-2-phenyl-3,5-pyrazolidinedione; 4-Butyl-2-(p-hydroxyphenyl)-1-phenyl-3,5-pyrazolidinedione.

Brand Names : Butazonic; Crovaril; Flogitolo; Flogoril; Frabel; G 27202; p-Hydroxyphenylbutazone; Neo-Farmadol; Oxalid; Rapostan; Rheumapax; Tandacote; Tanderil; Tandearil; Visubutina.

Oxyphenbutazone is p-hydroxy derivative of pheylbutazone, m.p. 96°. It is a white to yellowish-white, odourless, crystalline powder; practically insoluble in water; soluble in alcohol,



chloroform, ether and solutions of alkali hydroxides forming water soluble metal salts.

Uses : Oxyphenbutazone has similar analgesic, anti-inflammatory, and antipyretic properties similar to phenylbutazone.

Official

Oxyphenbutazone, B.P., I.P.

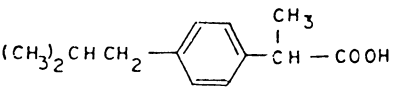
Oxyphenbutazone Tablets, B.P., U.S.P.

Oxyphenbutazone Eye ointment, B.P.

IBUPROFEN

Nomenclature : α-Methyl-4-(2-methylpropyl) benzeneacetic acid; P-Isobutylhydratropic acid.

Brand Names : RD 13621; Adran; Anflagen; Artril 300; Bluton; Brufanic; Brufen; Buburone; Butylenin; Dolgin; Emodin; Epobron; Ibuprocin; Lamidon; Liptan; Motrin; Mynosedin; Napacetin; Nobfelon; Nobfen; Nobgen; Rebugen; Roidenin.



Ibuprofen, m.p. 75-77°, is a white powder or crystals with a characteristic odour. It is practically insoluble in water; soluble in alcohol, chloroform, ether, acetone and aqueous solutions of alkali hydroxides and carbonates. It is kept in airtight containers.

Uses : Ibuprofen has analgesic, anti-inflammatory and antipyretic properties. It is used for the relief of pain in conditions such as dysmenorrhoea, migraine, postoperative pain; rheumatic disorders and joint disorders.

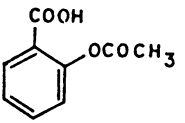
The most frequent adverse effect occurring with ibuprofen are gastro-intestinal disturbances as well as headache, dizziness, nervousness, skin rash, pruritus, tinnitus, oedema, depression, drowsiness, insomnia and blurred vision.

Official

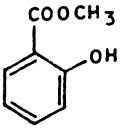
Ibuprofen, B.P.

Ibuprofen Tablets, B.P., U.S.P.

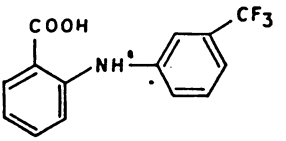
Miscellaneous Agents



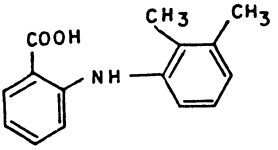
Aspirin



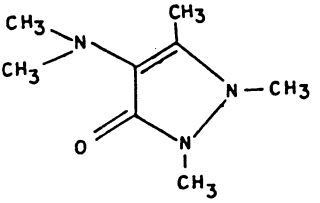
Methyl salicylate



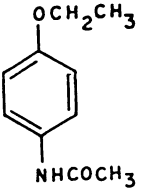
Flufenamic Acid



Mefenamic Acid



Amidopyrine



Phenacetin

29

THYROXINE AND ANTITHYROIDS

Thyroid gland removes inorganic iodides from the blood plasma and produces two active hormones called thyroxine and tri-iodothyronine (liothyronine). Their production is dependent on the adequate supply of iodine from the blood plasma to the gland. These hormones are the amino acids and stored as thyroglobulin in the follicular colloid. Deficiency of thyroid hormones, called hypothyroidism or myxo-edema, reduces all the metabolic processes of the body and affects growth, development and mental retardation. Excessive secretion of thyroid hormones produces hyperthyroidism (thyrotoxicosis or Grave's disease) characterized by increased metabolic rate, increase in heart rate and general state of anxiety and restlessness.

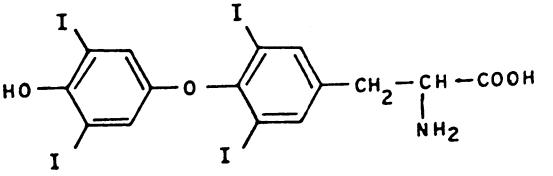
Antithyroid drugs reduce the production of thyroxine and tri-iodothyronine. They are used to treat thyrotoxicosis and given prior to surgical removal of thyroid gland. The most useful drugs are 2-thiouracil derivatives and 2-thioimidazole derivatives. Propylthiouracil, methimazole and carbimazole are the useful antithyroid drugs.

THYROXINE

Nomenclature : o-(4-Hydroxy-3,5-diodophenyl) 3,5-diiodo-tyrosine; 3-[4-(4-Hydroxy-3,5-diiodophenoxy)-3,5-diiodophenyl] alanine.

Thyroxine is a tetraiodo amino acid of the thyroid gland and exerts a stimulating effect on metabolism. Its natural occurrence in the free state has not been reported. It may be a cleavage

product of thyroglobulin. The L-form is twice as active physiologically as the racemic product; the D-form has very less activity.



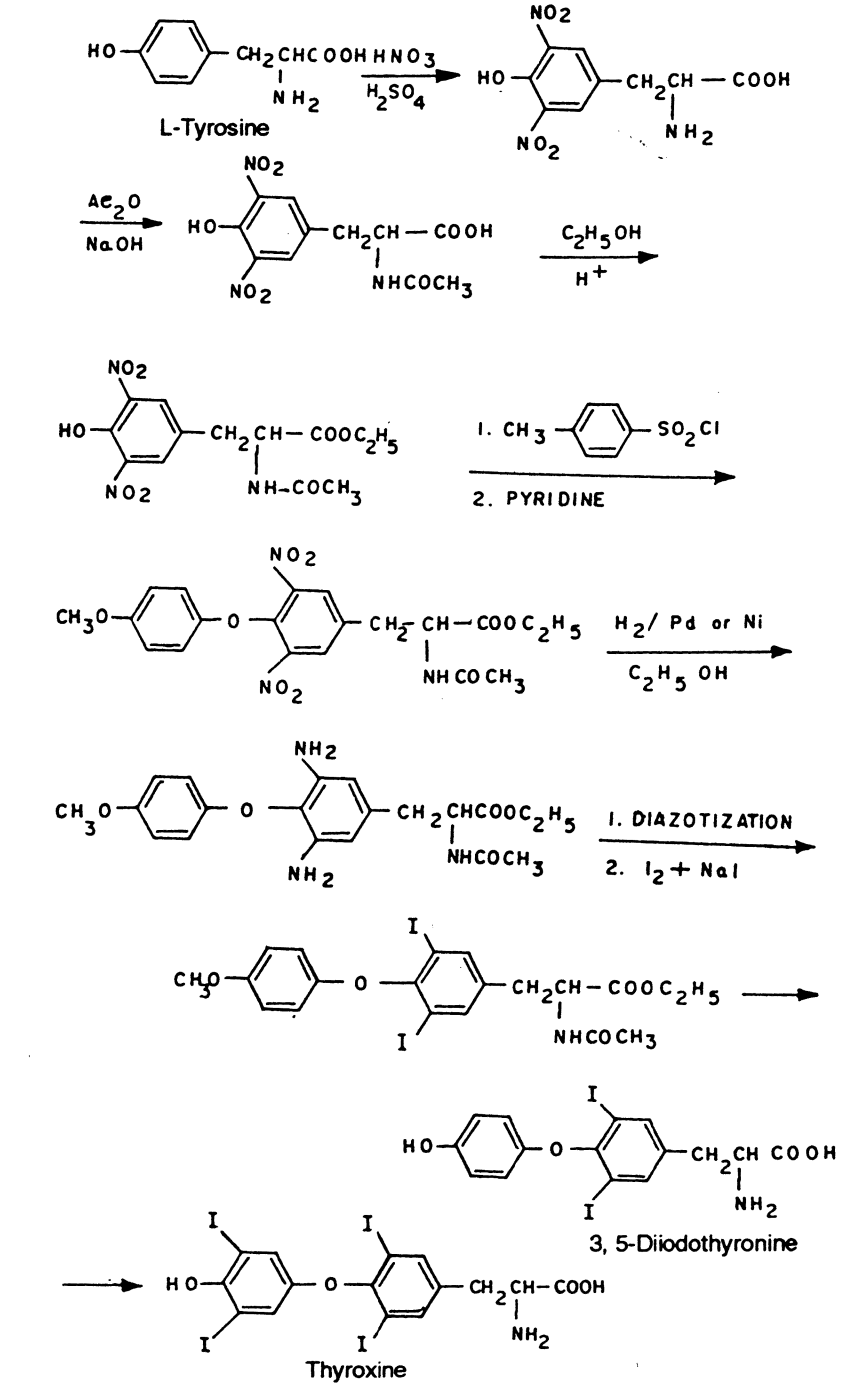
For the synthesis of thyroxine, L-tyrosine is nitrated, the nitro-derivative is acetylated at the amino group, followed by esterification. For the synthesis of 4-methoxyphenyl ether, toluene-4-sulphonyl ester is prepared using tosyl chloride and the ester reacts with 4-methoxyphenol in pyridine to form the desired ether. The nitro groups are reduced, the di-amino tetrazotized, and the tetrazonium salt reacted with iodine in sodium iodide solution to yield the diiodo derivative. Chemical reduction with a mixture of hydriodic acid, red phosphorus and glacial acetic acid produces L-3,5-diiodothyronine, which on iodination in ethylamine gives L-thyroxine.

DL-Thyroxine, needle-like crystals. m.p. 231-233° (decomp), is insoluble in alcohol and other organic solvents. In the presence of mineral acids or alkalies it dissolves in alcohol; soluble in solutions of the alkali hydroxides and in hot solutions of the alkali carbonates.

L-Thyroxine, m.p. 235-236° (decomp), is used in the form of sodium salt, known as sodium Levothyroxine.

Sodium Levothyroxine (Brand Names : L-Thyroxin sodium salt; Levothyroxine sodium; Eltroxin; Euthyrox; Laevoxin; Letter; Levaxin; Levothroid; Oroxine; Synthroid sodium; Thyroxevan). It is the sodium salt of the laevo isomer of thyroxine or prepared synthetically. It occurs as an odourless, white to pale brownish-yellow, tasteless, hygroscopic, amorphous or crystalline powder. It may assume a slight pink colour on exposure to light. It is very slightly soluble in water and chloroform; slightly soluble in alcohol; practically insoluble in acetone, chloroform and ether; soluble in solutions of alkali hydroxides and in hot solutions of alkali carbonates. A saturated solution in water has a pH of about 8.9.

Uses : Thyroxine is used in the treatment of thyroid-deficiency conditions and to treat hypothyroidism occurring in patients after therapy for thyroid cancer.


L-Tyrosine
3, 5-Diiodothyronine
Thyroxine

The adverse effects of thyroid hormones are generally associated with excessive dosage. The effects may include tachycardia, palpitations, anginal pain, cardiac arrhythmias, headache, nervousness, excitability, restlessness, insomnia, cramps in skeletal muscle, muscular weakness, tremors, sweating, flushing, fever, diarrhoea, vomiting and loss of weight.

Official

Thyroid, I.P.

Thyroid Tablets I.P.

Thyroxin Tablets, B.P., I.P.

Thyroxin Sodium, B.P., I.P.

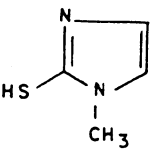
Thyroxin Tablets, B.P.

Levothyroxin Sodium Tablets U.S.P.

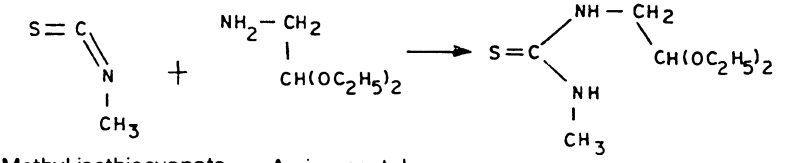
METHIMAZOLE

Nomenclature : 1,3-Dihydro-1-methyl-2H-imidazole-2-thione; 1-Methylimidazole-2-thiol.

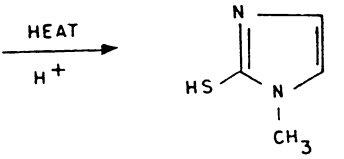
Brand Names : Mercazolyl; Thiamazole; Basolan; Danantizol; Favistan; Frentirox; Mercazole; Metazolo; Tapazole; Thacapzol; Thycapsol; Strumazol.



Methimazole is an imidazoline which is prepared by condensing methyl isothiocyanate with amino acetal and cyclizing the product by heating it with acid.



Methyl isothiocyanate Amino acetal



Methimazole

Methimazole, m.p. 146-148°, is a white to pale buff crystalline powder with a faint characteristic odour. It is soluble in water, alcohol, chloroform and ether; sparingly soluble in ether, petroleum ether and benzene.

Uses : Methimazole is an antithyroid agent used to control hyperthyroidism.

Side-effects occurring with methimazole therapy are nausea, vomiting, gastric distress, headache and skin rashes.

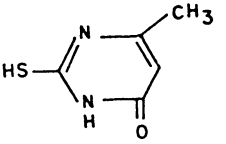
Official

Methimazole Tablets, U.S.P.

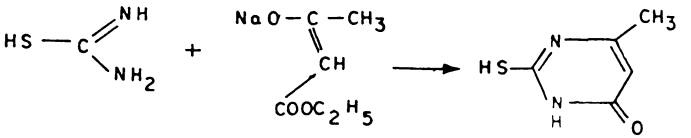
METHYLTHIOURACIL

Nomenclature : 2,3-Dihydro-6-methyl-2-thioxo-4-(1H)-pyrimidinone. 6-Methyl-2-thiouracil; 4-Methyl-2-thiouracil.

Brand Names : MTU; Alkiron; Antibason; Basecil; Basethyrin; Methiacil; Methicil; Methiocil; Muracil; Prostrumyl; Strumacil; Thimecil; Thyreostat I.



Methylthiouracil is a homologue of thiouracil synthesized by condensing thiourea with sodium derivative of ethyl acetoacetate:



Thiourea Sodium ethyl acetoacetate Methylthiouracil

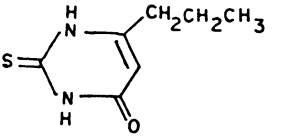
Methylthiouracil, m.p. 326-331° (decomp), is a white odourless crystalline powder which is soluble in boiling water; sparingly soluble in alcohol, chloroform and ether; freely soluble in ammonium hydroxide and in solutions of alkali hydroxides. A saturated aqueous solution is neutral or slightly acidic to litmus. It is protected from light and stored is well-closed containers.

Uses : Methylthiouracil is an antithyroid agent which has been used in the treatment of hyperthyroidism.

The common side effects include nausea, vomiting, gastric distress, headache and skin rashes.

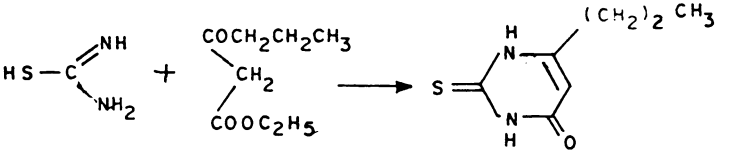
PROPYLTHIOURACIL

Nomenclature : 2,3-Dihydro-6-propyl-2-thioxo-4(1H) pyrimidinone; 6-Propyl-2-thiouracil.



Brand Names : Propacil; Propycil; Procasil; Propyl-Thyracil; Prothyran; Thyreostat II.

Propylthiouracil is prepared by condensation of thiourea with ethyl β-ketohexoate.



Propylthiouracil, m.p. 219-221°, is a white, bitter, crystalline powder which is very slightly soluble in water and ether; sparingly soluble in alcohol; dissolves in aqueous solutions of alkali hydroxides and ammonia. A saturated solution is neutral or slightly acidic to litmus. It is kept in well-closed containers and protected from light.

Uses : Propylthiouracil is an antithyroid agent which depresses the formation of thyroid hormones. It is used to control hyperthyroidism.

Side-effects of propylthiouracil are the same as mentioned for methylthiouracil.

Official

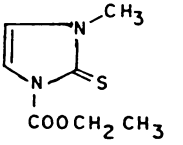
Propylthiouracil, B.P., I.P.

Propythiouracil Tablets, B.P., I.P., U.S.P.

CARBIMAZOLE

Nomenclature : 3-Methyl-2-thioxo-4-imidazoline-1-carboxylate.

Carbimazole, m.p. 314-316°, is a creamy white crystalline powder with a characteristic odour which is slightly soluble in water; used as an antithyroid drug.



Official

Carbimazole, B.P.

Carbimazole Tablets, B.P.

30

DIAGNOSTIC AGENTS

Diagnostic agents are used to detect impaired function of the body or to recognize abnormalities in tissue structure. Compounds used in diagnosis are the chemicals employed to determine normal and pathologic products in urine, blood, faeces and other fluids or excrement. There are some other diagnostic agents which are used directly to or in the body, for example radiopaque substances, compounds for testing functional capacity and compounds modifying a physiologic action.

Diagnostic agents are divided into four major groups as follows :

1. Agents used for radiographic purposes

These agents help to reveal anatomic evidence of the disease. They are radiopagues or X-rays contrast media. These are chemicals which cannot be penetrated by X-rays. They absorb radiation and provide a shadow of positive contrast, due to density difference. Barium sulphate, tentalum metal powder spray, metrizoates, diatrizoates, iothalmates, iodomides, iodipamides, iodoxamic acid, iohexol, vocaramate, etc. are used as radiopaques.

Radionucleids are also used for radiographic purposes. They emit radiation and are hazardous agents. Commonly used agents are I^{131} for thyroid function test and thyroid scanning Tc^{99} for blood pool scanning, etc.

2. Agents used for organ function tests

These include drugs used to test liver excretory function (e.g. sulfobromophthalein sodium, phenoltetrachlorophthalein and

indocyanine green); to test liver metabolic function (e.g. laevulose), to test capacity for detoxification (e.g. sodium benzoate); to measure glomerular filtration rate (e.g. inuline), to measure renal plasma flow and tubular functional capacity (e.g. aminohippuric acid); to test gastric function (e.g. pentagastrin, betazole HCl); to test pancreatic functions (e.g. secretin, tolbutamide sodium); to test hypothalamic-pituitary function (e.g. metyrapone); to test adrenocortical functions (e.g. corticotrophin, tetracosactrin) and to test thyroid function (e.g. protirelin, thyrotrophin).

3. Agents used to determine blood volume and hemopoietic functions

Evans blue, indocyanin green and fluorescein sodium are employed to determine blood volume and hemopoietic functions.

4. Agents used for miscellaneous diagnostic tests

Florerscein sodium is applied topically to the cornea to detect minute foreign bodies or corneal ulcers. Amyloidosis is detected by applying Congo red. Benedicts reagent is used as a diagnotic agent for urine analysis. Clinistix, Multistix and Test Tape are reagent strips impregnated with glucose oxidase, peroxidase and orthotolidine. When dipped into urine, blue colour develops on to the strip due to oxidation of orthotoludine. Diastrix is a specific urine glucose test, based on the same principle, which also indicates a rough estimate of the glucose present quantitatively. Ketostrix are the reagent strips used as "dip and read" test for ketone bodies in urine or serum. These contain sodium nitroprusside and other chemical reagents which provide a purple colour if ketone bodies are present. Multistrix are strips containing multiple reagents to detect glucose, ketone bodies and hematuria etc. on a single strip.

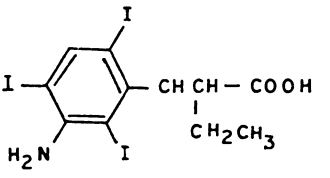
There are number of kits available for simple pregnancy test, e.g. Gravidex and Pregnosis. In these tests chorionic gonadotrophins are measured in urine with the aid of specific antibodies.

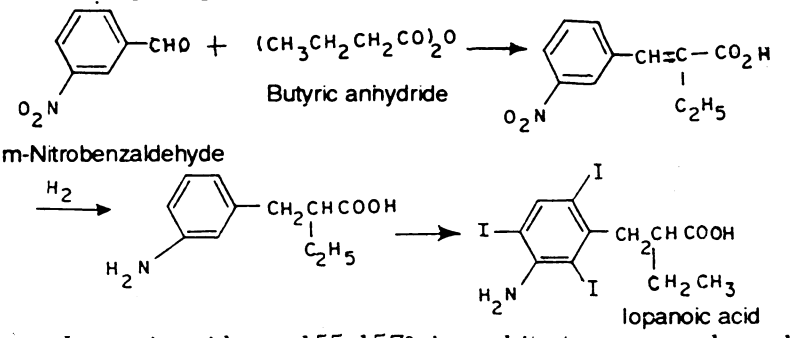
IOPANOIC ACID

Nomenclature : 3-Amino-α-ethyl-2,4,6-triiodobenzene propanoic acid; 3-Amino-α-ethyl-2,4,6-triiodohydrocinnamic acid.

Brand Names : Colepax; Telepaque; Teletrast; Iodopanoic acid.

Iopanoic acid is prepared from the product of a Perkin condensation of m-nitrobenzaldehyde and butyric anhydride by reduction of the double bond and nitro-group, and iodination of the resulting amine in the reactive *otho-* and *para* positions.





Iopanoic acid, mp 155-157°, is a white to cream-coloured powder, odourless or with a distinct faint odour. It is insoluble in water; soluble in alcohol and other organic solvents; soluble in aqueous solutions of alkali hydroxides; protected from light.

Uses : Iopanoic acid is a diagnostic agent (radiopaque medium) used for the examination of the biliary tract. It is given by mouth with a light fat-free meal about 10 to 14 hours before x-ray examination.

Iopanoic acid gives rise to nausea, vomiting, abdominal cramp, diarrhoea, and more rarely, dysuria. Acute renal failure, thrombocytopenia and hypersensitivity reactions have been reported. Iopanoic acid has a uricosuric effect.

Official

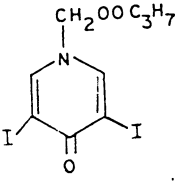
Iopanoic Acid, B.P.

Iopanoic Acid Tablets, B.P., U.S.P.

PROPYLIODONE

Nomenclature : 3,5-Diiodo-4-oxo-1-(4H)-pyridineacetic acid propyl ester.

Brand Names : Propiodone; Dionosil.



Propyliodone, m.p. 186-187°, is the propyl ester of 3,5-di-iodo-4-pyridone-N-acetic acid. It occurs as a white; almost odourless,

crystalline powder which is practically insoluble in water; slightly soluble in alcohol and in chloroform, very slightly soluble in ether. It is kept in airtight containers and protected from light.

Hydrolysis by means of boiling sodium hydroxide solution and subsequent acidification yields the butyric acid. It is used as a sterile aqueous or oil suspension for instillation into trachea prior to bronchography.

Uses : Propyliodone is used as a diagnostic aid (radiopaque medium) for the examination of the bronchial tract.

Propyliodone may give rise to transient pyrexia, sometimes associated with malaise and aching of the joints. In few cases dyspnoea, transient lobar collapse and allergic reactions may also occur.

Official

Propyliodone, B.P.

Propyliodone Suspension, B.P.

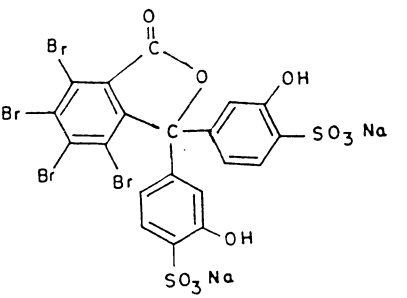
Propyliodone Oily Suspension, B.P.

SULPHOBROMOPHTHALEIN SODIUM

Nomenclature : 3,3'-(4,5,6,7-Tetrabromo-3-oxy-1(3H)-isobenzofuranylidene) bis [6-hydroxybenzenesulfonic acid] disodium salt.

Brand Names : Bromosulphophthalein; BSP; SBP; Sulphobromophthal Sodium; Sulphobromophthalein; Disodium phenoltetrabromophthalein sulfonate; Hepartest; Bromthalein; Bromsulphalein sodium; Brom-Tetragnost.

Sulphobromophthalein sodium is a phthalein derivative used as a dye in tests of liver function. It is prepared by dissolving phthalic anhydride in fuming sulphuric acid, followed by bromination with iodine as a catalyst. The tetrabromophthalic anhydride is then condensed with phenol and the resulting tetrabromophenolphthalein is sulphonated and converted to the disodium salt.



It occurs as a white, bitter, odourless, crystalline, hygroscopic powder; soluble in water; practically insoluble in alcohol and in acetone. The presence of sulphonic acid groups into the compound decreases the toxicity and increases the water solubility. The compound is injected intravenously and the amount remaining in the blood after a certain time interval is determined colourimetrically. The rate at which the dye is removed from the blood is a measure of the hepatic function.

Uses : Sulphobromophthalein sodium is used as a diagnostic agent for testing the functional capacity of the liver. The test is usually performed in the morning after the patient has taken a fat-free breakfast. No food must be given during the test. The concentration of the dye in the bloodstream is measured at the end of 1 hour and at regular time intervals thereafter to determine the rate of clearance.

Allergic-type reactions have been reported in patients given sulphobromphthalein. Inadvertent subcutaneous infiltration may cause irritation and necrosis.

Official

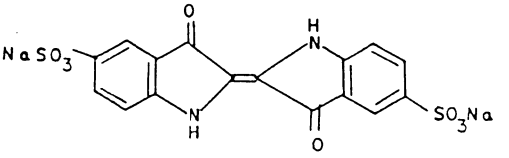
Sulphobromophthalein Sodium, B.P., I.P.

Solphobromophthalein Sodium Injection I.P., U.S.P.

INDIGOTIN DISULPHONATE SODIUM (INDIGO CARMINE)

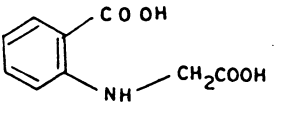
Nomenclature : 2-(1,3-Dihydro-3-oxo-5-sulfo-2H-indol-2-ylidene) -2,3-dihydro-3-oxo-1H-indole-5-sulfonic acid disodium salt; Disodium 5,5'-indigotin disulphonate.

Brand Names : Sodium indigotin disulphonate; Soluble indigo blue; Indigotine; Acid Blue 74; CI. Acid Blue 74; C.I. Food Blue 1; FD&C Blue No-2. C.I. 73015, Blue X; Ceruleinum.



Indigo carmine is the sodium salt of a disulphonic acid derived from indigo. Indigo is a natural blue dye which has been obtained from the indigo plant (*Indigofera tinctoria* Linn; Leguminosae). It can be prepared by condensing two molecules

of phenylglycine-O-carboxylic acid and then sulphonating the product.



Indigo carmine is a purplish-blue powder or blue granules with a coppery lustre. It is soluble in water (1 in 100); slightly soluble in alcohol; practically insoluble in most other organic solvent. Its solutions have a blue or bluish-purple colour. It is also marketed as a paste with water, the dye contents varying according to specification or requirement of the user. The colour is due to resonance associated with the chromophore O=C—C=C-C=O which is discharged by alkaline reducing agents and by oxidizing agents like nitric acid, chlorates, etc.

Indigo carmine is very sensitive to light and the colour of the aqueous solution fades on standing. Its solutions may be sterilized by autoclaving.

Uses : Indigo carmine is used as a dye for testing renal (kidney) function; to locate the ureteral orifices; in colouring nylon surgical sutures; as a reagent for the detection of nitrate, chlorate, and in testing milk. It has also been used as a marker dye to aid urological and other procedures; as a food colour and as a blue dye in medicinal preparations. Normally, it appears in urine in 10 minutes, and about 10 per cent of it is eliminated during the first hour.

Indigo carmine may cause nausea, vomiting, hypertension and bradycardia, and sometimes allergic reactions such as skin rash, prutitus and bronchoconstriction.

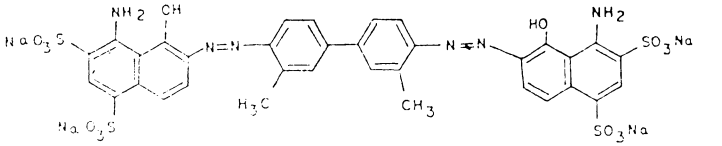
Official

Indigo Carmine, I.P.

Indigotindisulfonate Sodium Injection, U.S.P.

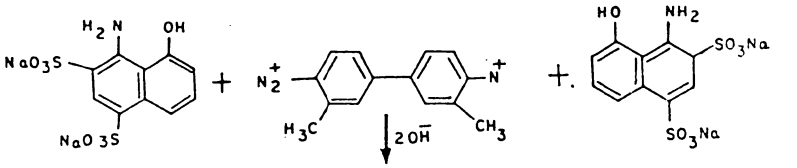
EVANS BLUE

Nomenclature : 6, 6'-[(3,3'-Dimethyl [1, 1'-biphenyl]-4-4'-diyl) bis (azo)] bis [4-amino-5-hydroxy-1, 3-naphthalenedisulfonic acid] tetrasodium salt.



Brand Names : C.I. Direct Blue 53; C.I. 23860; T-1824; Azovan Blue.

Evans blue is an azo-dye of diagnostic value and is prepared by coupling tetrazotized o-tolidine with 2 moles of Chicago acid (8-amino-1-hydroxy-5,7-naphthalenedisulphonic acid) in alkaline solution.



Evans blue

Evans blue is green, bluish-green or brown, odourless powder. It is very soluble in water; very slightly soluble in alcohol; practically insoluble in carbon tetrachloride, chloroform and ether; at pH 10 the colour is changed. It is destroyed by strong oxidizing and reducing agents and precipitated from saturated solution of neutral salts. It is rather stable in aqueous solution, and may be autoclaved at 15 lbs pressure for 30 minutes. The aqueous solutions are quite stable and may be autoclaved. Saline solutions are less stable and should not be autoclaved.

In body Evans dye combines firmly with the plasma albumin. The colour developed is directly proportional to its concentration.

Uses : Evans dye is used for the determination of blood (or plasma) volume. A quantitative amount of the dye is injected intravenously. After a suitable interval a sample of blood is taken, and the dye in the plasma is determined colorimetrically. The dye does not escape into the extracellular fluid and is only slowly excreted via the kidneys.

Official

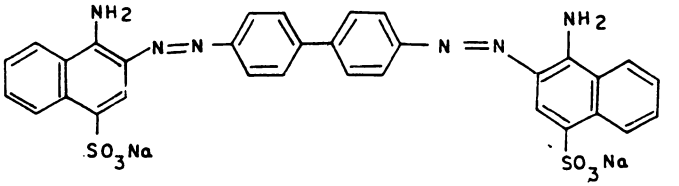
Evans Blue, I.P.

Evans Blue Injection U.S.P.

CONGO RED

Nomenclature : 3, 3'-[[1,1'-Biphenyl]-4,4'-diylbis (azo)] bis [4-amino-1-naphthalenesulfonic acid] disodium salt.

Brand Names : C.I. Direct Red 28; C.I. 22120.

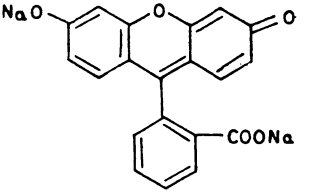


Congo red is a reddish-brown powder which is soluble in water and ethanol; very slightly soluble in acetone; practically insoluble in ether.

Uses : Congo red is used as a stain in the diagnosis of amyloid disease (amyloidosis); as addition to culture media; reagent for bitter-almond water; dye; for estimating free mineral acids and for detecting and estimating free hydrochloric acid in gastric contents.

FLUORESCEIN SODIUM

Nomenclature : 3', 6'-Dihydroxyspiro [isobenzofuran-1(3H), 9'-[9H] xanthen]-3-one disodium salt.



Brand Names : Soluble fluorescein; Resorcinol Phthalein sodium; Uranin(e); Uranine yellow; D&C yellow No.8; C.I. Acid yellow 73; C.I. No. 45350; Funduscein; Resorcinolphthalein sodium; Soluble fluorescein.

Fluorescein is a dye of the phthalein group. It is prepared by condensing phthalic anhydride with resorcinol by melting the two substances together in the presence of anhydrous zinc chloride or other suitable condensing agent.

Fluorescein occurs as red, sparingly soluble crystals. It dissolves freely in aqueous sodium hydroxide, forming a sodium salt. Fluorescein sodium is a disodium salt which occurs as an orange-red, odourless, hygroscopic powder.

It is soluble in water with yellow-red colour and intense yellowish-green fluorescence. The fluorescence disappears when the solution is made acidic and re-appears when the solution is again made neutral or alkaline. It is kept in airtight containers and protected from light.

Uses : Sodium fluorescein is used as an ophthalmologic diagnostic agent for detecting corneal lesions and foreign bodies. It is used as an aid to the fitting of hard contact lenses and to differentiate

healthy tissues from diseased or damaged tissues.

The intravenous injection of fluorescein sodium may produce nausea and vomiting. Allergic reactions may consist of urticaria. The skin and urine may be coloured yellow but that is transient. Patients may also experience an unpleasant taste.

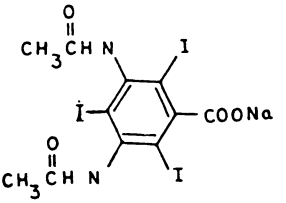
Official

Fluorescein Sodium Ophthalmic Strips, U.S.P.

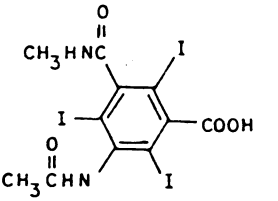
Fluorescein Sodium, B.P., I.P.

Fluorescein Injection. U.S.P.

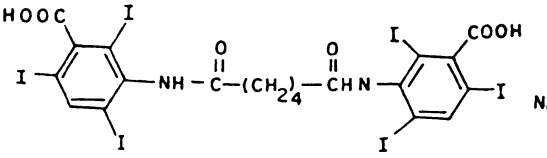
Miscellaneous Agents



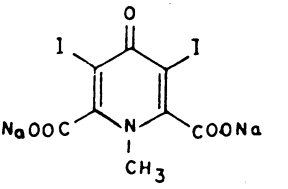
Sodium Diatrizoate



Iothalamic Acid



Iodipamide



Iodoxyl

Official

Iothalmic Acid, B.P

Meglumine Iothalamate Injection, B.P.

Sodium Iothalamate Injection, B.P.

Iodipamide Meglumine Injection, B.P.

Sodium Diatrizoate, B.P.

Sodium Diatrizoate Injection, B.P.

Iodoxyl, I.P.

Iodoxyl Injection, I.P.

31

ANTICONVULSANT DRUGS

Epilepsy is a chronic central nervous system disorder in which brief episodes of seizures appear with or without the loss of consciousness. Epileptic seizures are spontaneous, recurrent, chronic and paroxysmal with a discontinuity of symptoms and wide interval between seizures. There may be other symptoms such as convulsive movements of arms or legs, increased muscle tone, causing locked jaw, followed by decreased muscle tone, frothing at the mouth, the eye-ball moving upwards. An attack of epilepsy may occur at any time and it is usually difficult to predict its onset. However, some patients get a warning signal (aura) in the form of flashes of light or sounds.

Anticonvulsant drugs are used to prevent and control epileptic seizures. An epileptic seizure has been defined as a paroxysmal discharge of cerebral neurones accompanied by a clinical phenomenon apparent to the patient or to an observer. Epilepsy is a condition characterized by a recurrence of such seizures. Thus, epilepsy is a disease which arises due to the disorders of central nervous system.

There are two useful drugs which would depress the motor cortex (prevent convulsions) and the sensory cortex (produce sleep). The bromides, phenobarbital, and diphenylhydantoin have been used to control seizures. They demonstrate that sedation may be dissociated from anticonvulsant activity in the various types of epilepsy. Each type of epilepsy may be distinguished by clinical and electroencephalographic manners, and each shows different results with various classes of anticonvulsant drugs.

Epileptic seizures are classified into *generalized* and *partial* seizures. The generalized seizures are further sub-divided as follows :

1. **Grand mal (Tonic-clonic) :** Sudden loss of consciousness followed by general muscle spasms lasting for an average of 2 to 5 minutes. The frequency and the severity of attacks are different.
2. **Petit mal (Abences) :** When there is sudden, brief loss of consciousness with minor movements of the head, the eyes and the extremities, lasting for about 5 to 10 seconds, it is known as petit mal. The patient is immediately alert, and ready to continue normal activity. There may be many episodes in a day. The highest incidence of petit mal is found in children.

The partial (focal, local) seizures are concerned with motor, sensory or automatic symptoms and those of complex symptoms (psychomotor seizures).

In psychomotor seizures automatic, patterned movements lasting from 2 to 3 minutes occur. Amnesia is common and general. There is no remaining of memory of the incident. This state is sometimes confused with psychotic behaviour.

Barbiturates, hydantoins, oxazolidinediones, succinimides and some other compounds are used as anticonvulsant drugs. The drugs acting as selective depressants of convulsant activity have a common structural feature, except primidone.

The choice of antiepileptic agent for the treatment of epilepsy is determined by the type of seizure. For grand mal seizures and partial seizures, phenytoin, carbamazepine, or valproic acid is generally used with phenobarbitone or primidone as alternatives. For petil mal usually ethosuximide or valproic acid are used. Clonazepam, ethosuximide or valproic acid are employed to treat myoclonic seizures. In general, therapy with a single antiepileptic agent is preferred unless seizures of a mixed type are present.

BARBITURATES

Barbiturates are cyclic ureides derived from malonic acids. These are the early drugs used to prevent *epileptic seizures.* Structurally they are derivatives of hexahydropyrimidine. Barbituric acid itself can be prepared by condensing urea with the acid chloride of malonic acid or with ethyl malonate in the presence of sodium ethoxide. (page 165)

Phenobarbital, mephobarbital and metharbital are important barbiturates which show selective anticonvulsant activity and used in symptomatic treatment of epilepsy.

PHENOBARBITONE



Phenobarbital is prepared by condensing benzyl cyanide with ethyl carbamate (page 169).

Phenobarbital, m.p. 174-178°, occurs as colourless crystals or a white odourless crystalline powder. It is very less soluble in water (1in 1000); sparingly soluble in chloroform; soluble in alcohol (1 in 10), ether and aqueous solutions of alkali carbonates, hydroxodes and ammonia. A saturated solution has a pH of about 5.

Phenobarbital sodium is a white, odourless, hygroscopic powder, granules, or flakes which is soluble in water and alcohol; practically insoluble in chloroform and ether.

Uses : Phenobarbital is used as an antiepileptic agent to control grand mal and partial seizures. It has anticonvulsant, hypnotic and sedative properties.

Adverse effects of barbiturates include respiratory depression, sedation and allergic reactions.

Official

Phenobarbitone, B.P.

Phenobarbitone Sodium, B.P., I.P.

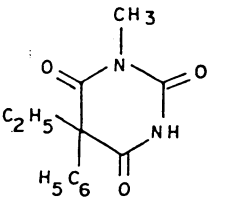
Phenobarbitone Tablets/Capsules, B.P.

Phenobarbital Sodium Tablets/Injection, U.S.P.

Sterile Phenobarbital Sodium, U.S.P.

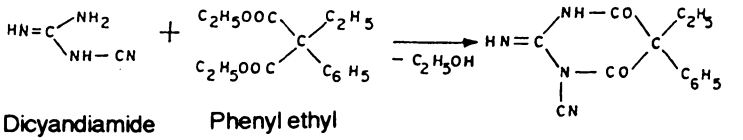
MEPHOBARBITAL

Nomenclature : 5-Ethyl-1-methyl-5-phenyl-2,4,6-(1H, 3H, 5H) pyrimidinetrione; N-Methylethylphenyl-barbituric acid.

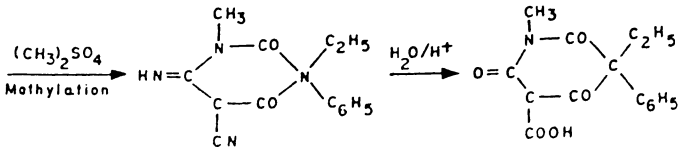


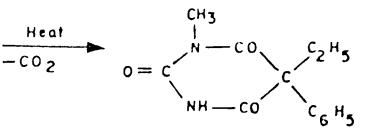
Brand Names : Phemitone; Prominal; Mebaral; Isonal.

It is N-methyl derivative of phenobarbitone. It is prepared from phenyl ethyl malonic ester and dicyandiamide as follows:



Dicyandiamide Phenyl ethyl malonic acid



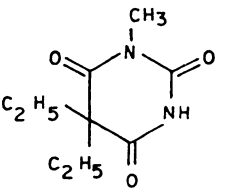


Mephobarbital

Mephobarbital, m.p. 176°, occurs as odourless, colourless crystals or a white crystalline powder. It is practically insoluble in water; very slightly soluble in dehydrated alcohol; slightly soluble in chloroform and ether. It is sedative and anticonvulsant and used as an antiepileptic agent similarly to phenobarbitone.

METHARBITAL

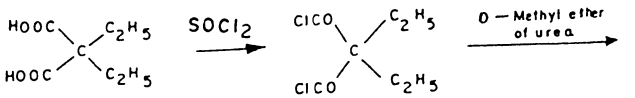
Nomenclature : 5, 5-Diethyl-1-methyl-2,4,6-(1H, 3H, 5H)-pyrimi-dinetrione.



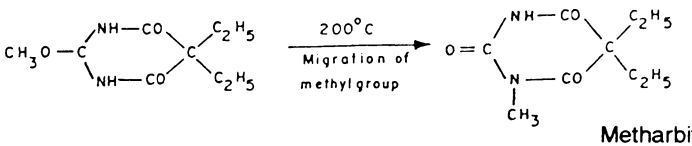
Brand Name : Gemonil.

Metharbital is prepared starting from diethylmalonic acid and thionyl chloride.

Metharbital, m.p. 155°, is a white crystalline powder with a faint aromatic odour. It is soluble in water, alcohol and ether. A saturated solution in water has a pH of about 6. It is stored in airtight containers.



Diethylmalonic acid O-Methylether of urea



Metharbital

Metharbitone is an antiepileptic agent with general properties similar to those of phenobarbitone. It is demethylated in the liver to barbitone. The usual initial dose is 100 mg one to three times daily.

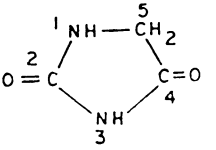
The anticonvulsant activity of the barbiturates is not related to the sedation action. The three anticonvulsant barbiturates show a high degree of effectiveness in grand mal only and not useful in petit mal and psychomotor epilepsy.

Official

Metharbital Tablets, U.S.P.

HYDANTOINS

Hydantoin is a diketo-derivative of tetrahydroimidazole (imidazolidine). It is related in structure to the barbiturates as:

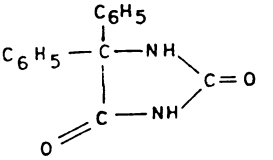


Nivanol was the first hydantoin introduced as a hypnotic and anticonvulsant in 1914. The hydantoins are most effective against grand mal and ineffective against petil mal. Diphenylhydantoin, mephenytoin and ethotoin are the hydantoins generally used as anticonvulsant.

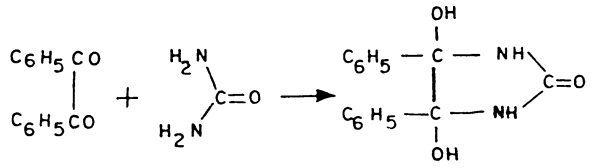
DIPHENYLHYDANTION

Nomenclature : 5, 5-Diphenylhydantoin.

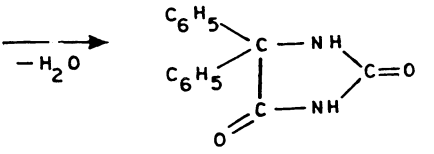
Brand Names : Phenytoin; Dilantin; Diphentoin; Difhydan; Dihycon; Di-Hydan; Di-Lan; Dilabid; EKKO; Hydantol, Lehydan; Zentropil.



Diphenylhydantoin is prepared by condensing benzil with urea to yield heterocyclic pinacol which on rearrangement produces diphenylhydantoin.

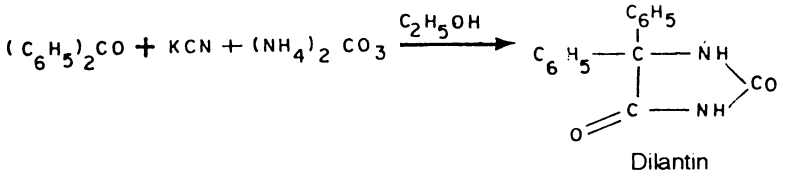


Benzil Urea



Dilantin

Diphenylhydantoin is also produced when a mixture of diphenyl ketone, potassium cyanide and ammonium carbonate is heated in 50% alcohol (Bucherer reaction) :



Dilantin

Diphenylhydantoin, m.p. 295-298°, is a white, odourless, crystalline powder. It is very slightly soluble in water; slightly soluble in chloroform and ether; soluble in alcohol.

DIPHENYLHYDANTOIN SODIUM

Brand Nemes : Phenytoin sodium; Dephenin; Phenytoin soluble; Di-Len; Danten; Citrullamon; Antisacer; Alepsin; Epanutin; Derizene; Eptoin; Hidantal; Minetoin; Diphentoin; Phenhydon (Inj); Tacosal; Thilophenyt; Solantoin; Solantyl.

Diphenylhydantoin sodium is a white, odourless, slightly hygroscopic crystalline powder which on exposure to air absorbs carbon dioxide with the liberation of phenytoin. It is soluble in water, the solution showing some turbidity due to partial hydrolysis and absorption of carbon dioxide; also soluble in alcohol; practically insoluble in chloroform and ether. It is stored in airtight containers.

Uses : Diphenylhydantoin is an antiepileptic agent used to control grand mal, partial seizures, and prophylactic control of seizures developed after neurosurgery.

Side-effects include nausea, vomiting, constipation, ataxia, slurred speech, diplopia, nystagmus and mental confusion.

Official

Sterile Phenytoin Sodium, U.S.P.

Phenytoin Sodium Injection, U.S.P.

Phenytoin Oral Suspension U.S.P.

Phenytoin Sodium, B.P., I.P.

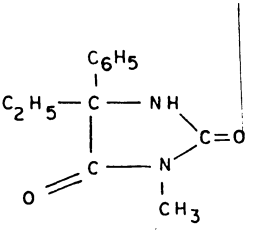
Phenytoin Capsules/Injection, B.P.

Phenytoin Tablets, I.P., U.S.P.

Prompt Phenytoin Sodium Capsules, U.S.P.

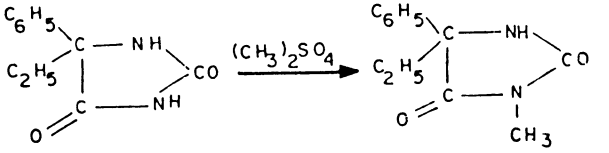
MEPHENYTOIN

Nomenclature : 5-Ethyl-3-methyl-5-phenyl-2,4-imidazolidine-dione.



Brand Names : Methyl hydantoin; 3-Ethylnirvanol; Methoin; Insulton; Insulton; Mesontoin; Mesantoin; Phenantoin; Sedantoinal; Gerot-Epilan; Sacerno; Hydental; Nesantoin.

Mephenytoin is prepared by methylating phenylethyl-hydantoin directly with dimethyl sulphate.



Mephenytoin, m.p. 136-137°, is a crystalline compound which is insoluble in water. It forms a water soluble sodium salt which has an alkaline reaction.

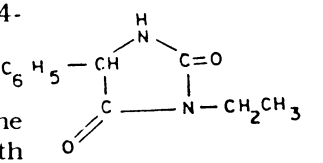
Uses : Mephenytoin is an anticonvulsant with little or no sedative effect. It is used primarily for the control of grand mal seizures. In conjunction with other anticonvulsants it is used to control psychomotor and jacksonian seizures.

Official

Mephenytoin Tablets, U.S.P.

ETHOTOIN

Nomenclature : 3-Ethyl-5-phenyl-2,4-imidazolidinedione.



Brand Name : Peganone.

Ethotoin is prepared by heating the potassium salt of 5-phenylhydantoin with

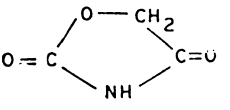
ethyl bromide in alcohol at 100° in a sealed tube. It occurs as prism-type crystals from water, m.p. 94°. It is sparingly soluble in cold water, more soluble in hot water; freely soluble in alcohol, ether, benzene, and dilute aqueous solutions of alkali hydroxides.

Uses : Ethotoin is used as an anticonvulsant for the control of grand mal epilepsy. Adverse reactions include blood dyscrasias, skin rash, ataxia, and gum hypertrophy. The drug may be used alone, but it is most frequently used in combination with other anticonvulsants.

OXAZOLIDINEDIONES

The diketo-derivatives of tetrahydroxazole (the oxazolidinediones) are oxygen analogues of the hydantoins, and, like the hydantoins many of them have anti-convulsant properties.

The oxazolidinediones are effective in the treatment of petit mal. They are uneffective against grand mal but are used in conjunction with other drugs in the treatment of mixed types of seizures, such as combined petit mal and grand mal epilepsy.



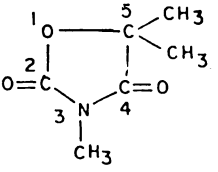
2, 4-Oxazolidinedione

TRIMETHADIONE

Nomenclature : 3, 5-Trimethyl-2,4-oxazolidinedione.

Brand Names : Troxidone; Absentol; Tridione; Trimedal; Petidon; Epidone; Ptimal.

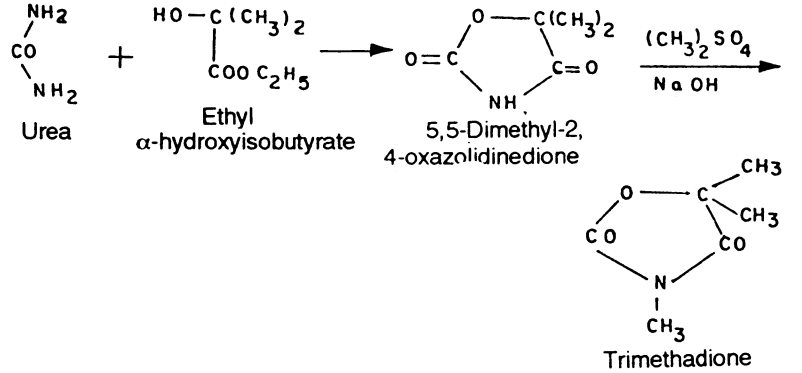
Trimethadione is prepared by condensing urea with an ester of α-hydroxyisobutyric acid in the presence of sodium ethoxide. The 5,5-dimethyl compound so formed is then methylated in the nitrogen atmosphere by means of methyl sulphate and dilute sodium hydroxide solution.



Trimethadione, m.p. 46-47°, is a colourless or white granular crystalline substance with a slightly camphoraceous odour. It is soluble in water, alcohol, chloroform and ether. It is stored in airtight containers and protected from light. The pH of a 5% solution is about 6.0.

Uses : Trimethadione is an antiepileptic agent used in the treatment of petit mal seizures. Because of its potential toxicity

it is given only to patients unresponsive to other treatment.



Common side effects of trimethadione therapy are drowsiness, photophobia, hemeralopia, nausea, vomiting, gastric distress, abdominal pain, weight loss, hiccups, malaise, insomnia, vertigo, headache, alopecia, etc.

Official

Troxidone. B.P.. I.P.

Troxidone Capsules, B.P., I.P.

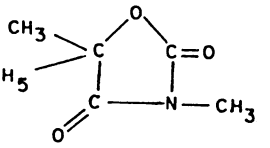
Trimethadione Capsules/Tablets, U.S.P.

Trimethadione Oral Suspension, U.S.P.

PARAMETHADIONE

Nomenclature : 5-Ethyl-3, 5-dimethyl-2,4-oxazolidinedione; 3, 5-Dimethyl-5-ethyloxazolidine-2,4-dione.

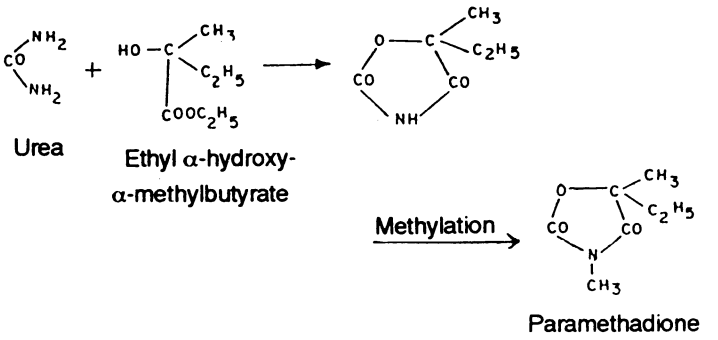
Brand Name : Paradione.



Paramethadione is a white, odourless, hygroscopic powder, granules, or flakes. It is soluble in water and alcohol; practically insoluble in chloroform and ether. A 10% solution in water has a pH of 9.2 to 10.2.

Paramethadione is a homologue of trimethadione and has an ethyl group in place of one of the methyl groups at the 5-position. It is prepared by treating urea with ethyl α-hydroxy-α-methylbutyrate.

Uses : Paramethadione is an antiepileptic agent with general properties similar to those of trimethadione.



Official

Paramethadione, I.P.

Paramethadione Capsules, U.S.P.

Paramethadione Oral Suspension, U.S.P.

SUCCINIMIDES

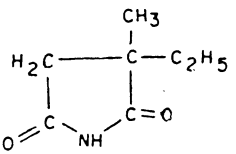
Substituted succinimides are used to treat petit mal seizures. These succinimides are prepared by reaction of the derivative of succinic acid with ammonia or an alkyl amine. The succinimides are less potent than the oxazolidinediones and exhibit significant side effects. These drugs are moderately effective in the control of petit mal seizures but are ineffective against grand mal. They are taken orally.

ETHOSUXIMIDE

Nomenclature : 3-Ethyl-3-methyl-2, 5-pyrrolidinedione.

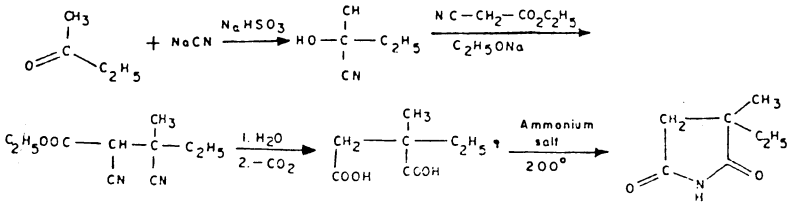
Brand Names : Atysmal; Capitus; Emeside; Epileo Petilmal; Ethymal; Mesentol; Pemal; Peptinimid; Petinimid; Petnidan; Pyknolepsinum; Simatin; Succimal; Suxilep; Suximal; Suxinutin; Thilopemal; Zarontin.

Ethosuximide is synthesized from ethyl methyl ketone by the following route.



Ethosuximide, m.p. 64-65°, is considered as a 2, 5-pyrrolidinedione. The hydrogen atom of the imide group is acidic and can be replaced by metals or alkyl groups. It is freely soluble in water, alcohol, chloroform and ether. It condenses with resorcinol in

the presence of concentrated sulphuric acid to yield a phthalein-like compound. Its sodium salt has a bright green fluorescence. It is stored in airtight containers.



Ethosuximide

Uses : Ethosuximide is effective in pure petit mal but less effective in mixed petit mal.

Gastro-intestinal side-effects including nausea, vomiting, anorexia, gastric upset and abdominal pain occur with ethosuximide.

Official

Ethosuximide, B.P.

Ethosuximide Capsules, B.P., U.S.P.

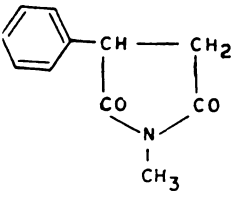
Ethosuximide Elixier, B.P.

PHENOSUXIMIDE

Nomenclature : N-Methyl-2-phenylsuccinimide.

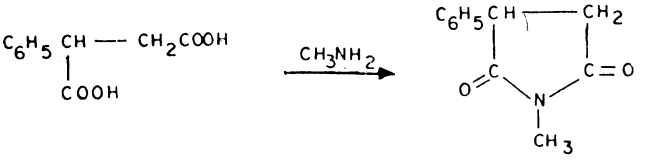
Brand Nemes : Milontin; Lifene; Succitimal; Mirontin.

Phenosuximide is prepared by reaction of the derivative of succinic acid with ammonia or an alkyl amine.



Phenosuximide, m.p. 71-73°, is a white to off-white, odourless, crystalline powder. It is soluble in water, alcohol, chloroform and ether; stored in airtight containers. Aqueous solutions are fairly stable at pH 2-8, but hydrolysis sets in under more alkaline conditions.

Uses : Phenosuximide is an antiepileptic agent with general properties similar to those of ethosuximide, but it is reported to be less effective. It is given in usual doses of 0.5 to 1 g two or three times daily by mouth.



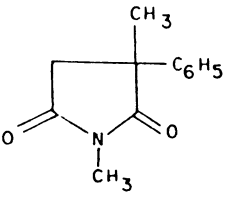
α-Phenylsuccinic acid Phenosuximide

METHSUXIMIDE

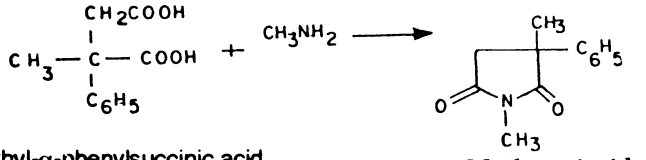
Nomenclature: 1, 3-Dimethyl-3-phenyl-2, 5-pyrrolidinedione.

Brand Names : Mesuximide; Celontin; Petinutin;

Methsuximide, is prepared by the action of methylamine on α-methyl-α-phenylsuccinic acid.



Methsuximide, m.p. 52-53°, is a white to greyish-white crystalline compound; odourless or with slight odour. It is soluble in water, alcohol, chloroform and ether. It is stored in airtight containers.



α-Methyl-α-phenylsuccinic acid Methsuximide

Uses : Methsuximide is an antiepileptic agent with general properties similar to those of ethosuximide. The side effects include psychic disturbances, heptic disfunction and bone marrow aplasia.

Miscellanceous

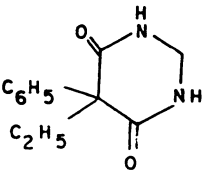
Some compounds of miscellaneous structures are used as anticonvulsant agents. These drugs are primidone, phenacemide and carbamazepine.

PRIMIDONE

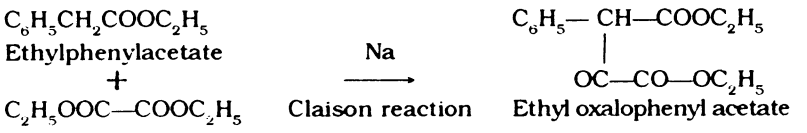
Nomenclature : 5-Ethyldihydro-5-phenyl-4,6-(1H,5H)-pyrimidinedione; 5-Ethyl-5-phenyl-hexahydropyrimidine-4,6-dione; 5-Phenyl-5-ethylhexahydropyrimidine-4,6-dione.

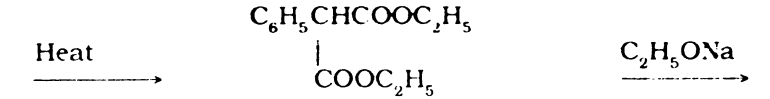
Brand Names : Lepsiral; Liskantin; Mylepsin; Mylepsinum; Mysoline; Primaclone; Primoline; Resimatil; Sertan.

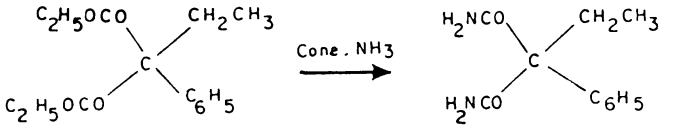
Primidone is a diketone derived from hexahydropyrimidine. The chemical nature of primidone is similar to that of a cyclic diamide, and it has none of the acidic character of barbituric acid and the barbiturates, which have -CO- and not $-CH_2-$ between the two nitrogen atoms. It is prepared from phenobarbitone by electrolytic reduction.



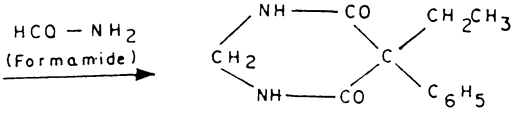
Primidone is also prepared from diethyl ethylphenylmalonate which is converted into the amide by the action of concentrated ammonia. The amide on heating under reflux with formamide yields primidone.







Ethyl ethylphenyl malonate — Ethylphenyl malonamide



Primidone, m.p. 281-282°, is white, odourless, tasteless, crystalline powder. It is soluble in water (1 in 2000) and alcohol (1 in 200); very slightly soluble or practically insoluble in most organic solvents.

Uses : Primidone is an anticonvulsant agent used chiefly to control epileptiform seizures, i.e. grand mal and partial (focal) seizures.

The side-effects caused by primidone include drowsiness, ataxia, nausea, vomiting, vertigo, irritability, headache, visual disturbances, and weakness, and sometimes skin eruptions.

Official

Primidone, B.P., I.P.

Primidone Mixture, B.P.

Primidone Tablets, B.P., I.P., U.S.P.

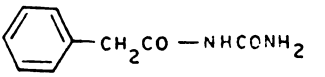
Primidone Oral Suspension, B.P., U.S.P.

PHENACEMIDE

Nomenclature : N-(Aminocarbonyl) benzene acetamide.

Brand Names : Phenylacetylurea; Epiclase; Pharcetur; Phenurone; Phetyl ureum.

Phenacemide is prepared by the action of aqueous ammonia on phenacetylurethan or by the action of phenacetyl chloride on urea. It occurs as an odourless, white, fine crystalline powder, m.p. 212-216°. It is very slightly soluble in water, alcohol, chloroform and ether; slightly soluble in acetone and methyl alcohol. It is stored in airtight containers.



Uses : Phenacemide is an acetylurea antiepileptic agent used in the treatment of epilepsy, especially in the psychomotor type of seizure. Due to its potential toxicity it should be employed only in patients whose seizures are impossible to control with other recognized antiepileptics.

Severe adverse effects reported with phenacemide include personality changes, blood disorders including aplastic anaemia, and liver and kidney damage.

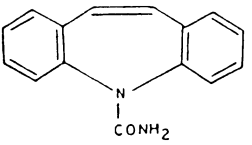
Official

Phenacemide Tablets, U.S.P.

CARBAMAZEPINE

Nomenclature : 5H-Dibenz [b,f] azepine-5-carboxamide; 5-Carbamoyl-5H-dibenz [b,f] azepine.

Brand Names : G 32883; Biston; Finlepsin; Stazepine; Tegretal; Tegretol; Telesmin; Timonil.



Carbamazepine possesses the dibenzazepine ring system of the psychotherapeutic drug imipramine. It occurs as white crystalline powder, m.p. 190-193°. It is practically insoluble in water and ether; sparingly soluble in alcohol; soluble in chloroform (1 in 10); soluble in acetone. It is stored in airtight containers.

Uses : Carbamazepine is an antiepileptic agent used to control grand mal and partial seizures; and to treat trigeminal neuralgia.

Official

Carbamazepine. B.P., I.P.

Carbamazepine Tablets. B.P., I.P., U.S.P.

32

CARDIAC GLYCOSIDES

The plant steroids possessing the property of stimulating the unsufficient heart muscles are known as cardiac glycosides or C_{23}- glycosides. They possess bile acid-like steroidal carbon framework (tetracyclic 10,13-dimethyl-cyclopentanoperhydrophenanthrene) with twenty three carbon atoms. These steroids occur as glycosides with sugars attached at the C-3 atom of the steroid nucleus. The steroid aglycones or genins are of two types:

1. **Cardenolides :** These glycosides are found more abundantly in nature. They are C_{23} steroids having a 17β-side chain as an α,β-unsaturated 5-membered lactone ring. Digitoxigenin, gitoxigenin, digoxigenin and ouabagenin are the cardenolides. *Digitalis purpurea, D. lanata* and Strophanthus are the herbal drugs which contain cardenolides.
2. **Bufadienolides :** The bufadienolides are C_{24} homologs of cardenolides and possess double bond containing 6-membered lactone ring at the C-17 position. The compounds are less widely distributed in nature than are the cardenolides. They are found in some Liliaceae and Ranunculaceae and in the toad venoms. Therapeutically they are little used as cardiac drugs due to their low therapeutic index and producing side-effects.

Both cardenolides and bufadienolides possess the C/D ring junction in *cis*-configuration. For maximum cardiac activity, the aglycone should possess an α,β-unsaturated lactone ring that is attached β at the 17-position of the steroidal skeleton. If the glycoside is cleaved, the aglycone retains cardiac activity;

however, the sugar portion of the glycoside helps to dissolve the molecule which is important in its absorption and distribution in the body. Oxygen substitution on the steroid nucleus also influences the distribution of glycosides. If there are excess number of hydroxyl groups on the molecule, the onset of action and the subsequent dissipation from the body will be more rapid.

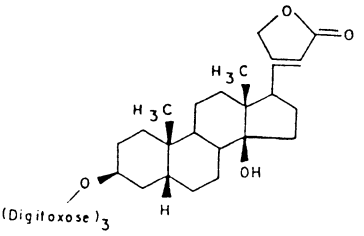
In all the known biologically active cardiac glycosides the sugar residues are present in the pyranoside form and are joined in a β-glucoside linkage to the axial C_3-β-OH of the aglycone.

Cardiac glycosides have the ability to increase the force of systolic contraction. Due to increasing contractility, ventricle becomes more empty and a shortening in the length of systole takes place. Thus, the heart has more time to rest between contractions. Cardiac output and circulation are increased and the heart rate is decreased. When rapid digitalisation is required, digoxin or ouabain may be given by intravenous injection.

DIGITOXIN

Nomenclature : 3-[0-2,6-Dideoxy-β-D-ribo-hexopyranosyl) (1→4)-0-2,6-dideoxy-β-D-ribo-hexopyranosyl-(1→4)-2,6-dideoxy-β-D-ribo-hexopyranosyl) oxy]-14-hydroxycard-20 (22)-enolide.

Brand Names : Digitalin; Crystalline; Digitophyllin; Asthenthilo; Cardigin; Carditoxin; Cristapurat; Crystodigin; Digilong; Digimerck; Digimed; Ditaven; Digisidin; Lanatoxin; Mono-Glycocard; Myodigin; Purodigin; Purpurid; Tardigal; Unidigin.



Digitoxin is a cardiotonic glycoside obtained from *Digitalis purpurea, D. lanata* and other suitable species of *Digitalis* (Fam. Scrophulariaceae). It is extracted from the dried leaves with 50 per cent alcohol. Ten kilo leaves yield about 6 grams pure digitoxin. Acid hydrolysis of digitoxin yields one mole of digitoxigenin and 3 moles of digitoxose. The sugar residue is attached to the hydroxyl group at C-3 of the aglycone.

Digitoxin, m.p. 256-257°, is a white or pale buff-coloured, odourless, microcrystalline powder. It is practically insoluble in water; soluble in alcohol and chloroform; slightly soluble in methyl alcohol and ether; freely soluble in a mixture of equal

volumes of chloroform and methanol. It is kept in airtight containers at a temperature not exceeding 15° and protected from light.

Digitoxin is absorbed rapidly and nearly completely when given by mouth. It is 1,000 times as active as digitalis leaf. It is the most potent of the digitalis glycoside and is the most cumulative in action. The onset of its action is slower than that of the other cardiac glycosides. Its effects may be evident in about 2 hours after oral administration.

Uses : Digitoxin is a cardiotonic that incrcases the tone of cardiac muscle and thus causes the heart to empty more effectively. Usual initial dose for rapid digitalization is 800 μg, followed by 200 μg at 6 to 8 hour intervals for 2 to 3 doses.

Adverse effects of digitoxin and other cardiac glycosides include nausea, vomiting, anorexia, diarrhoea and abdominal pain. Certain neurological effects are also common symptoms of digitoxin overdosage.

Official

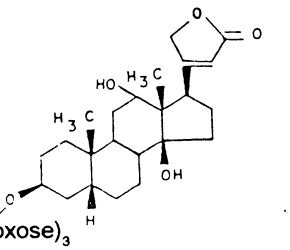
Digitoxin, B.P., I.P.

Digitoxin Injection/Tablets, B.P., I.P., U.S.P.

DIGOXIN

Nomenclature : 3-[(0-2,6-Dideoxy-β-D-ribo-hexopyranosyl-(1→4)-0-2,6-dideoxy-β-D-ribo-Hexopyranosyl-(1→4)-2,6-dideoxy-β-D-ribo-hexopyranosyl)oxy]-12,14-dihydroxycard-20,(22)-enolide.

Brand Names : Cordioxil; Davoxin; Digacin; Dilanacin; Dixina; Dynamos; Lanacordin; Lanicor; Lanoxin; Lenoxin; Rougoxin; Vanoxin.



Digoxin is a cardiotonic glycoside obtained from the leaves of *D. lanata* or *D. orientalis* (Fam. Scrophulariaceae). Acid hydrolysis of digitoxin yields 1 mole of digoxigenin and 3 moles of digitoxose. The sugar residue is attached to the hydroxyl group at C-3 of the aglycone.

Digoxin, m.p. 230-265° (decomp), occurs as odourless, colourless, or white crystals or a white powder.

It is practically insoluble in water, acetone, ether, ethyl acetate; slightly soluble in chloroform and in alcohol; freely soluble in a mixture of equal volumes of chloroform and methanol and in pyridine.

Digitoxin is less cumulative and its duration of action is shorter than that of digitoxin.

Uses : Digoxin is used in the treatment of congestive heart failure and cardiac tachyarrhythmia. In cardiac failure, the increased force of myocardial contraction results in increased cardiac output.

When given by mouth, digoxin may take effect within 2 hours and the maximum effect may be reached in about 6 hours.

The side-effects of digoxin are similar to those of digitoxin.

Official

Digoxin, B.P., I.P.

Digoxin Injection B.P., U.S.P.

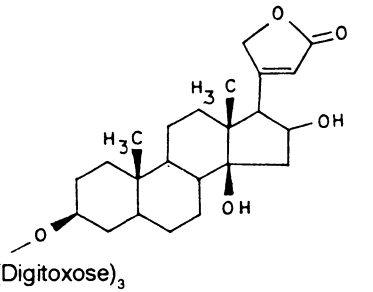
Digoxin Tablets, B.P., I.P., U.S.P

Paediatric Digoxin Elixer, B.P., U.S.P.

Paediatric Digoxin Injection, B.P.

GITOXIN

Nomenclature : 3-[(0-2,6-Dideoxy -β-D-ribo-hexopyranosyl-(1→4)-0-2,6-dideoxy-β-D-ribo-hexopyranosyl-(1→4)-2,6-dideoxy-β-D-ribohexopyranosyl) oxy] 14,16-dihydroxy-card-20 (22)-enolide.



Brand Names : Anhydrogitalin; Bigitalin; Pseudogitoxin.

Gitoxin is a secondary glycoside obtained mainly from *Digitalis purpurea* and *D. lanata* (Scrophulariaceae). It is a by-product of digitoxin production. On acid hydrolysis it yields 1 mole of gitoxigenin and 3 moles of digitoxose.

Gitoxin, m.p. 285° (decomp), is a colourless crystalline compound. It is insoluble in chloroform, ethyl acetate and

acetone, but dissolves in a mixture of chloroform and alcohol or in pyridine or in dilute alcohol. It is very poorly absorbed and used as a cardiotonic agent.

ACETYLDIGITOXIN

Brand Name : Acylanid.

Acetyldigitoxin is obtained by enzymatic hydrolysis of lanatoside A. It is composed of the aglycone digitoxigenin and 3 molecules of digitoxose, to one of which an acetyl group is attached. Acetyldigitoxin-α differs from acetyldigitoxin-β in the position of the acetyl group. The β-form is obtained either by splitting off the glucose residue from lanatoside-A by means of enzymes, or by extraction from the leaves of *Digitalis ferruginea* (Fam. Scrophulariacae).

Acetyldigitoxin, m.p. 217-221°, is a white microcrystalline hygroscopic powder which is slightly soluble in chloroform and water but is more liposoluble. Alcoholic or hydroalcoholic solutions slowly lose the acetyl group by hydrolysis.

Acetyldigitoxin is absorbed equally when taken orally. It is less toxic and more safe than digitoxin. It is dissipated twice as fast as digitoxin.

Uses: Acetyldigitoxin is a cardiotonic agent.

ACETYLDIGOXIN

Brand Names : α-Form: Lanatilin; Decardil; Dioxanin; Sandolanid.

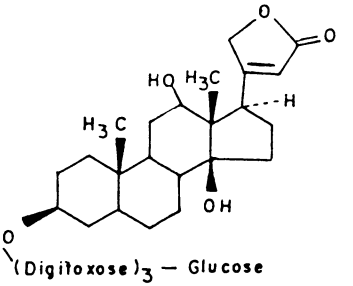
β-Form : Novodigal; Agolanid; Kardiamed.

Acetyldigoxin, obtained from *Digitalis lanata*, is digoxin containing an acetyl group at C_4 of the terminal digitoxose residue. α-Form, m.p. 225°(decomp), is a crystalline compound which is very sparingly soluble in ethyl acetate. β-Form, m.p. 240° (decomp), is more soluble in ethyl acetate than the α-form. It is more absorbed and more tolerated than digoxin.

LANATOSIDE-C

Nomenclature : 3β-[(O-β-D-Glucopyranosyl - (1→4) - 0-3-acetyl-2, 6-dideoxy-β-D-*ribo* - hexopyranosyl - (1→4) - 0-2,6-dideoxy-β-D-*ribo* - hexopyranosyl - (1→4)-0-2,6-dideoxy-β-D-*ribo*-hexopyranosyl) - 12β, 14-dihydroxy - 5β,14β-card-20 (22)-enolide.

Brand Names : Allocor; Ceglunat; Digilanide C; Celadigal; Cedilanid-D; Lanimerck; Cetosanol; Desacetyl-Lanatoside C.



Lanatoside is a glycoside obtained from the leaves of *Digitalis lanata* (Scrophulariaceae). It occurs as odourless, white or yellowish, hygroscopic crystals or crystalline powder, m.p. 248-250° (decomp). It is practically insoluble in water, chloroform and ether; soluble in methyl alcohol. It is stored in airtight, glass containers at a temperature not exceeding 10° and protected from light.

Alcoholic and hydroalcoholic solutions are slowly deacetylated upon standing.

Lanatoside-C is less cumulative, and its duration of action is shorter than that of digitoxin. It is poorly absorbed from the gastro-intestinal tract.

Uses : The action, uses and side-effects of lanatoside-C are similar to those of digoxin.

Official

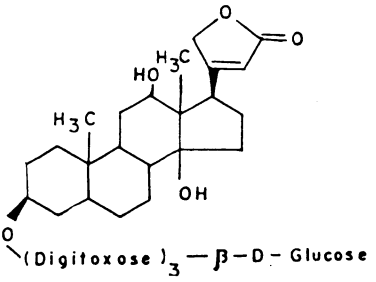
Lanotoside-C, I.P.

Lanotoside-C Tablets, I.P.

DESLANOSIDE

Nomenclature : 3β-[(O-β-D-Glucopyranosyl - (1→4)-0,2,6-dideoxy-β-D-*ribo*-hexopyranosyl - (1→4) - 0-2,6-dideoxy-β-D-*ribo*-hexopyranosyl(1→4) - 2,6-dideoxy-β-D-*ribo*-hexopyranosyl)-oxy] - 12β, 14-dihydroxy - 5β,14β-card-20(22) - enolide.

Brand Names : Deacetyllanatoside C; Desacetyllanatoside C; Deacetyldigilanide C; Purpurea glycoside C; Cedilamid-D; Desace; Desaci; Lanimerck (ampules).



Deslanoside is prepared by alkaline deacetylation of lanatoside C. It occurs as odourless, white, crystalline powder, m.p. 265-268° (decomp). It is very slightly soluble

in water, chloroform and alcohol; slightly soluble in methanol; practically insoluble in ether. It is hygroscopic, absorbing about 7% of moisture from air and is highly potent.

Uses : Deslanoside is a cardiotonic agent. It acts rapidly, i.e., in 10 to 30 minutes, has a quick dissipation rate with a wide margin of safety and low toxicity and is well tolerated.

Official

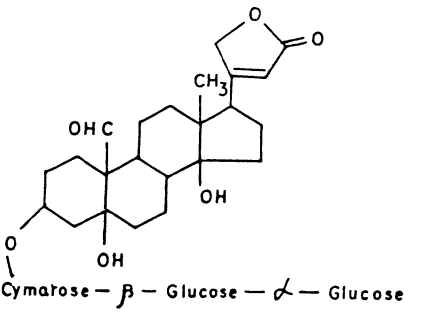
Deslanoside, B.P.

Deslanoside Injection, B.P., U.S.P.

STROPHANTHIN

Brand Names : K-Strophanthin; K-Strophanthoside; Combetin; Eustrophinum; Kombetin. Strophanthin-K; Estrofantina.

Strophanthin is a glycoside or a mixture of glycosides obtained from *Strophanthus kombe* (Fam. Apocynaceae). The 90 per cent of the cardio-active constituents are present as K-strophanthoside which contains α-glucose (19%), β-glucose (19%), cymarose (15%), and strophanthidin (47%).



Strophanthin is a white or yellowish powder containing about 10% of water, which it does not lose entirely without decomposition. It is stable in air, but is affected by light. It is soluble in water and in dilute alcohol; less soluble in absolute alcohol; nearly insoluble in chloroform, ether and benzene. Aqueous solutions are neutral to litmus.

Uses : Strophanthin is used as a cardiotonic and adiministered intravenously in emergencies for its cardiac effects.

OUABAIN

Nomenclature : 3-[(6-Deoxy-α-L-mannopyranosyl) oxy] 1,5, 11a, 14, 19-pentahydroxycard-20 (22) enolide.

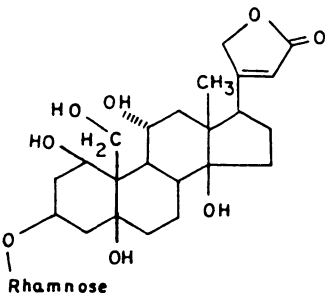
Brand Names : G-Strophanthin; Gratus strophanthin; Acocantherin; Gratibain; Astrobain; Purostrophan; Strophoperm; Strodival.

Ouabain is a glycoside of ouabagenin and rhamnose. It is obtained from the seeds of *Strophanthus gratus*. It also occurs in *Acokanthera ouabaio* (Fam. Apocynaceae). It is extremely poisonous.

Ouabain, m.p. 190° (decomp), occurs as a white, odourless, crystalline powder which gives up its water of crystallization at 130°. It is stable in air, but is affected by light.

It is soluble in water, alcohol and dioxane; slightly soluble in ether, chloroform and ethyl acetate. Aqueous solutions are neutral to litmus.

Uses : Ouabain is a cardiotonic agent. It is absorbed slowly and irregularly from the alimentary canal. It is used intravenously for its cardiac effects in emergencies.



Official

Ouabain, I.P.

Ouabain Injection, I.P.

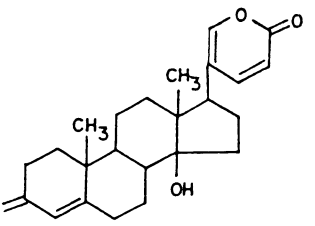
SCILLAREN

Scillaren is a mixture of the natural glycosides, scillaren A and scillaren-B, occurring in fresh squill, *Urginea maritima* (Fam. Liliaceae) in about 2 parts of A and 1 part of B. It occurs as a white or yellowish white, odourless, granular, very bitter powder. It is very slightly soluble in water; soluble in alcohol and methanol; practically insoluble in ether and chloroform.

Acid hydrolysis gives the disaccharide called scillabiose, which is composed of rhamnose and glucose.

The cardiac action of the scillarens is essentially identical to that of digitalis. The squill glycosides produce copious diuresis and are often used when digitalis and strophanthin fail to act.

Scillaren B is a water-soluble mixture of glucosides remaining after extraction of scillaren A. It is an amorphous, granular powder, possessing a very bitter taste. It is freely soluble in water; soluble in alcohol and in methanol. It is more water soluble and more active than scillaren A.



33

ANTI-ARRHYTHMIC DRUGS

In a normal person the heart functions in a rhythmic manner. In heart disease or due to toxic effects of some drugs this normal rhythm is disturbed and this condition is generally called 'arrhythmia'. Arrhythmias could be due to a defect in the impulse generation or due to abnormal propagation of impulse. Antiarrhythmic drugs are used to correct cardiac arrhythmias. Antifibrillatory drugs are compounds which prevent the development of atrial or ventricular fibrillation.

Anti-arrhythmic agents (formerly described as cardiac depressant) are divided broadly into two categories.

1. That act on venticular arrhythmias, e.g. lignocaine, and
2. That act on supraventricular arrhythmias, e.g. verapamil.

According to the mode of action anti-arrhythmic agents are classified as :

Class I : Includes drugs which directly interfere depolarization of the cardiac membrane by blocking the fast inward current of sodium into cardiac cells; they also have local anaesthetic properties, for example quinidine, lignocaine.

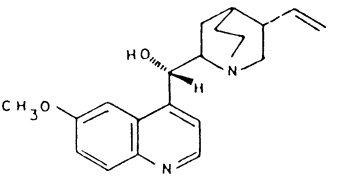
Class II : Includes drugs with antisympathetic properties, e.g. propranolol and bretylium.

Class III : Includes drugs that prolong the duration of the cardiac action potential, such as amidodarone.

Class IV : Includes drugs that block the slow inward calcium current, e.g., verapamil.

Quinidine and procainamide are the most effective drugs to treat cardiac rate and rhythm. Some other drugs are procaine, quinacrine, quinine, papaverine, digitalis preparation, etc.

Quinidine (Brand Names : Pitayine; β- Quinine), m.p. 174-175°, is a dextrorotatory stereoisomer of quinine present in cinchona bark to the extent of 0.25-3.0%. The molecule contains two nitrogens — the side chain nitrogen is more basic. It forms two series of salts.



Quinidine Sulphate (Brand Names : Quinidine bisulphate, Kiditard; Kinichron; Kinidin; Kinidrin; Quiniduran). This salt crystallizes from water as the dihydrate to yield needle-like, white crystals. It has bitter taste and darkens on exposure to light. It is slightly soluble in water; soluble in boiling water, alcohol and chloroform; practically insoluble in acetone and the ether. It is stored in well-closed containers and protected from light.

Commercial quinidine sulphate may contain up to 20 per cent of dihydroquinidine sulphate, which has a greater antifibrillating action than quinidine, but is more toxic.

Quinidine Gluconate (Brand Names : Gluconic acid quinidine salt; Duraquin; Dura-Tab; Gluquinate; Quinaglute), m.p. 175-177°, is a white odourless powder. It is freely soluble in water; slightly soluble in alcohol. The aqueous solutions are stable. It is protected from light.

Quinidine Polygalacturonate (Brand Names : Cardioquin; Galactoquin; Naticardina; Sineflutter), m.p. 180° (decomp), is an amorphous powder. This is produced by reacting quinidine and polygalacturonic acid in a hydroalcoholic medium. It contains the equivalent of nearly 60 per cent quinidine. Anhydrous product is insoluble in methanol, alcohol, chloroform, ether, acetone, dioxane; soluble in 40% methanol or ethanol; 12% in water at 25°. It affords controlled and more uniform absorption through the mucosa than quinidine sulphate.

Uses : Quinidine is an anti-arrhythmic agent. It also has antimuscarinic and alpha-adrenergic blocking properties.

Quinidine and its salts cause both cardiac and extracardiac adverse effects. They commonly cause gastro-intestinal irritation with nausea, vomiting and diarrhoea. Other side effects are

cinchonism, tinnitus, impaired hearing, visual disturbances, headache, confusion, vertigo, and hypotension.

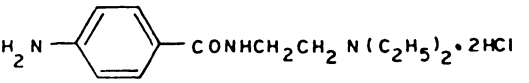
Official

Quinidine Gluconate Injection, U.S.P.
Quinidine Sulfate Capsules/Tablets, U.S.P.
Quinidine Sulfate Extended-release Tablets, U.S.P.

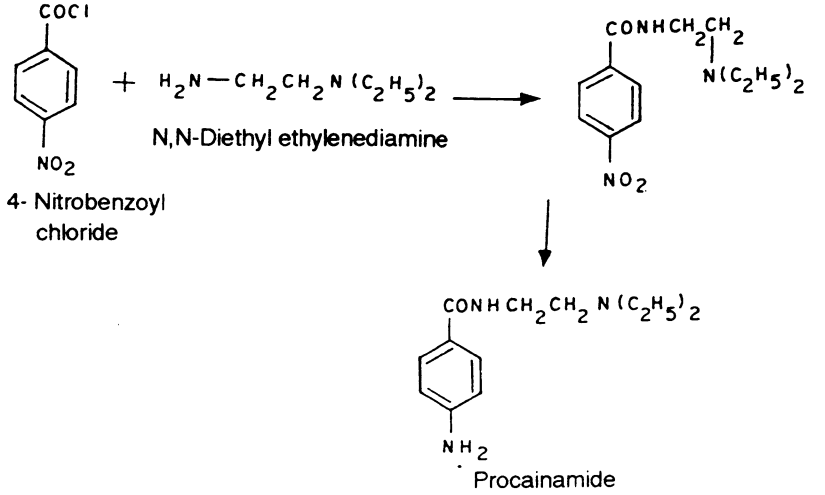
PROCAINAMIDE HYDROCHLORIDE

Nomenclature : 4-Amino-N[2-(diethylamine) ethyl] benzamide monohydrochloride.

Brand Names : Procainamide hydrochloride; Amidoprocain; Novocamid; Novocainamid; Procamide; Procan-SR; Procapan; Procardyl; Promide; Pronestyl hydrochloride; Supicaine amide hydrochloride.



Procainamide is prepared by condensing 4-nitrobenzoyl chloride with N,N-diethylethylenediamine, and then reducing the nitro-group.



Procainamide hydrochloride m.p. 165-169°, is a white to tan coloured, odourless, hygroscopic, crystalline powder. It is freely soluble in water; soluble in alcohol; slightly soluble in chloroform; very sparingly soluble in benzene and ether. The pH

of a 10 per cent solution is 5.5. Commercially available aqueous solutions are preserved with 0.9 per cent benzyl alcohol and 0.09 per cent of sodium bisulfite. The drug is stored in airtight containers.

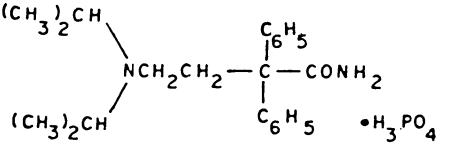
Uses : Procainamide is cardiac depressant used for the acute control of arrhythmias to maintain sinus rhythm after cardioversion of atrial fibrillation, to treat arrhythmias and extrasystoles and correct cardiac arrhythmias during anaesthesia.

Cardiac effects, hypersensitivity, anorexia, nausea, vomiting, bitter taste, and diarrhoea are the common side effects of procainamide therapy.

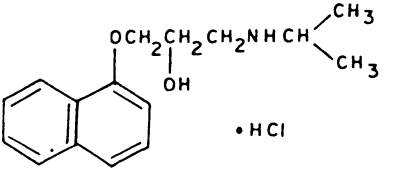
Official

Procainamide Hydrochloride Capsules/Injection, U.S.P.
Procainamide Tablets/Injection, B.P.

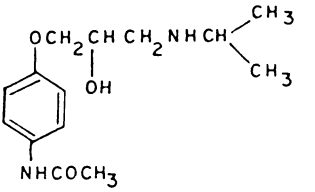
Miscellaneous Agents



Disopyramide phosphate



Propranolol Hydrochloride



Practolol

34

ANTI-HYPERTENSIVE AGENTS

Hypertension is a disease characterized by abnormally high blood pressure. Hypertension may be primary for which the exact cause is not known or secondary which may be due to renal, endocrine or vascular lesions. It may give rise to degenerate changes on cerebral, coronary, renal and retinal tissues. Antihypertensive drugs are used to treat hypertension.

Blood pressure is expressed in terms of the arterial systolic and diastolic pressure. A normal adult blood pressure is a systolic pressure equal to or below 140 mm Hg (18.7 KPa) together with a diastolic pressure equal to or below 90 mm Hg (12.0 KPa). The blood pressure depends on two important factors - (1) force of contraction and rate of beating of heart, and (2) resistance of blood flow caused by inner diameter of the blood vessels. Besides these, the viscosity (thickness) and volume of blood may also affect the blood pressure. Emotional trauma or excitement, physical excerise or exertion increase the heart rate which experienced in the form of palpitation, resulting in a rise of blood pressure. This is generally for a short period and does not require any treatment. The dangerous form of high blood pressure is due to narrowing of the lumen of the blood vessels and must be treated immediately. Normal blood pressure of a person may vary from person to person depending on age, sex, heredity, nutrition, body weight, etc.

The antihypertensive agents discussed here include Rauwolfia alkaloids, the Veratrum alkaloids, and an unclassified group.

RAUWOLFIA ALKALOIDS

Synonyms : Chotachand, Rauwolfia; Rauwolfia serpentina; Raudixin; Rauserpa; Rauvel.

Rauwolfia is the powdered whole root of *Rauwolfia serpentina* (Apocynaceae). It contains not less than 0.15 per cent of reserpine-rescinnamine group alkaloids calculated as reserpine. This is a small shrub native to the Orient from India to Sumatra. It contains many indole alkaloids, e.g., reserpine, resespinine, yohimbine, ajmaline, serpentine and respentinine. The most active as hypotensive agents being the ester alkaloids, reserpine and rescinnamine. The drug is stored at 15° to 30° in a dry place.

Rauwolfia powder is a light-tan to light-brown powder, sparingly soluble in alcohol and only slightly soluble in water. It contains the total alkaloids, reserpine being about 50 per cent of the total activity. Extracts are sold under trade names, such as Austrawolf, Egalin, Gendon, Hiwolfia, Koglucoid, Ralfen, Raucolyt, Raudixin, Raulfin, Raurixin, Rauserpol, Rautensine, Rauverid, Rauviloid, Ra-Valeas, Rauwoldin, Rawotal, Rivadescine, Roxinil, Sarpagan, Serpina, Wolfin.

Uses : Rauwolfia is used as an antihypertensive agent.

Official

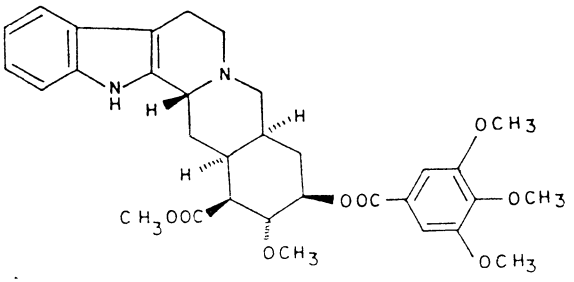
Powdered Rauwolfia Serpertina, U.S.P.

Rauwolfia Serpertina Tablets, U.S.P.

RESERPINE

Nomenclature : 11,17-Dimethoxy-18-[(3,4,5-trimethoxybenzoyl) oxy] yohimban-16-carboxylic acid methyl ester.

Brand Names : Alserin; Austrapine; Crystoserpine; Eskaserp; Hiserpia; Orticalm; Quiescin; Rau-red; Reserpex; Reserpoid; Rivasin; Roxinoid; Sandril; Sedaraupin; Serfin; Serolfia; Serpanray; Serpasil; Serpasol; Serpate; Serpen; Serpine; Serpiloid.



Reserpine is an alkaloid obtained from the roots of certain species of *Rauwolfia* (Apocynaceae) mainly *Rauwolfia serpentina* and *R. vomitoria*, or by synthesis. It occurs as odourless, small, white or pale buff to slightly yellow coloured crystals or crystalline powder, m.p. 264-265° (decomp). It is very sparingly soluble in water; freely soluble in chloroform, methylene chloride, glacial acetic acid; soluble in benzene and ethyl acetate; slightly soluble in acetone, methanol, alcohol, ether and in aqueous solutions of acetic and citric acids. Upon standing most solutions acquire a yellow colour and pronounced fluorescence, especially after the addition of acid or upon exposure to light. It is stored in airtight containers and protected from light. Storage of solutions in daylight causes epimerization at C-3 to form 3-isoreserpine. In daylight, oxidation also takes place and 3-dehydroreserpine is formed. It is green in solution but, as the oxidative process progresses, the colour disappears and, finally, a strongly orange colour appears.

Uses : Reserpine is an antihypertensive agent used in the treatment of hypertension, as sedative in anxiety states and to treat Raynaud's syndrome.

Side-effects commonly include nasal congestion, CNS symptoms including depression, drowsiness, lethargy, nightmares, gastro-intestinal disturbances and respiratory distress.

Official

Reserpine, B.P., I.P.

Reserpine Injection, I.P., U.S.P.

Reserpine Tablets, B.P., I.P., U.S.P.

Reserpine Elixir, U.S.P.

Reserpine and Hydrochlorothiazide Tablets, U.S.P.

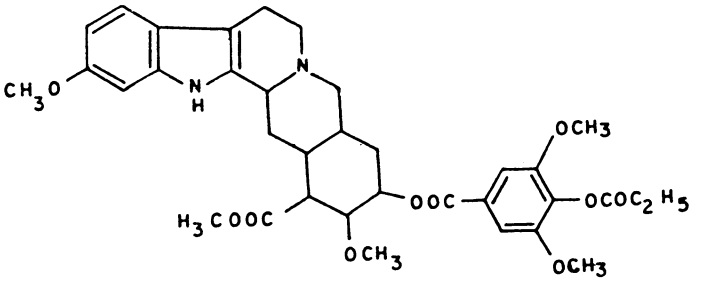
SYROSINGOPINE

Nomenclature : 18-[[4-[(Ethoxycarbonyl) oxy]-3,5-dimethoxybenzoyl] oxy]-11, 17-dimethoxyyohimban-16-carboxylic acid methyl ester.

Brand Names : Su-3118; Isotense; Londomin; Seniramin; Singorerp; Siringina; Raunova.

Syrosingopine, m.p. 175-179°, is closely related to reserpine, except esterification of the hydroxyl group at C-18. It is less toxic

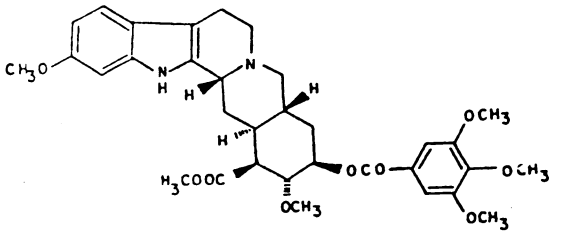
and less potent than reserpine and possesses nearly the same therapeutical value. It is effective in the control of some cases of mild hypotension and with other hypotensive agents to treat severe hypertension.



DESERPIDINE

Nomenclature : 17α-Methoxy-18β -[(3,4,5-trimethoxybenzoyl) oxy]-3β, 20α-yohimban-16β-carboxylic acid methyl ester.

Brand Names : Recanescine; Raunormine; Harmonyl.



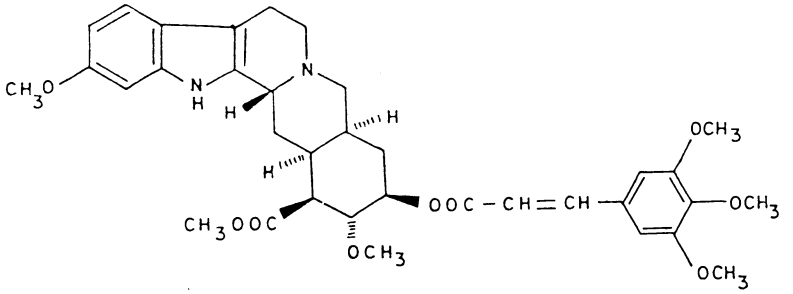
Deserpidine is an ester alkaloid isolated from the root of *Rauwolfia canescens*. It differs from reserpine only in the absence of a methoxyl group at C-11. It is a crystalline compound, m.p. 228-232°. It has a more rapid onset of action than reserpine.

Uses : Deserpidine has properties and uses similar to those described under reserpine.

RESCINNAMINE

Brand Names : Reserpinine; Anaprel; Apoterin; Cartric; Cinnaloid; Scinnamina; Rescaloia; Rescisan; Moderil.

Rescinnamine is the 3,4,5-trimethoxycinnamic acid ester of methyl reserpate. It differs from reserpine only in the acid used to esterify the hydroxyl group at C-18. It is practically insoluble in water; moderately soluble in methanol, benzene, chloroform and other organic solvents. It is an antihypertensive agent.



VERATRUM ALKALOIDS

Veratrum alkaloids are found in roots and rhizomes of *Veratrum viride* and *Veratrum album.* The alkaloids have a complex polycyclic skeleton containing amino groups. The free alkaloids are soluble in organic solvents but practically insoluble in water. Their salts are water soluble and stable at room temperature to light and air in solution.

Veratrum viride : Brand Names : American hellebore; Green hellebore; American veratrum; Indian poke.

It is the dried rhizome and roots of *Veratrum viride* (Fam. Liliaceae) found in North America. It contains the alkaloids jervine, pseudojervine; rubijervine; cevadine; germitrine; germidine; veratralbine and veratroidine. It is used as an antihypertensive agent.

The mixture of alkaloids from *V. viride* is known as **Alkavervir.** It is a light-yellow powder; practically insoluble in water but freely soluble in alcohol. It is given orally or by injection.

The mixture of alkaloids from *V. viride* used as the tannate and the acetate salts is known as **Cruptenamine.** The acetate salts are more water- soluble and are used in parenteral solutions. Cryptenamine tannates are a tan powder, slightly soluble in water but highly soluble in alcohol.

Protoveratrines A and B (Brand Name : Veralba). It is a mixture of two alkaloids isolated from *V. album.* The mixture is slightly bitter, white crystalline powder which is stable in light and air and in solution of pH 4 to 6 but readily destroyed in basic and alcoholic solution. The mixture is used to control hypertension.

Protoveratrine A and B Maleates (Brand Names : Provell maleate; Puroverin (e), Veralba) is the mixture of maleate salts of 2- alkaloids obtained from *V. album.* It is a white to light-tan powder, freely soluble in alcohol or water; m.p. 210-222°; practically insoluble in ether and petroleum ether.

Protoveratrine A (Brand Names : Pro-Amid; Protalba), is a purified alkaloid from the rhizome of *V. Album.* m.p. 267-269°. It is soluble in chloroform, pyridine and hot alcohol.

UNCLASSIFIED ANTIHYPERTENSIVE AGENTS

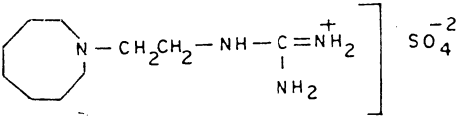
GUANETHIDINE SULPHATE (Page - 248)

Nomenclature : [(Octahydro-2-azocinyl) methyl] guanidine sulphate.

Brand Names : Ismelin; Iporal; Isobarin; Guethine.

Guanethidine sulphate, m.p. 276-281° (decomp), is a white, odourless, crystalline powder which is freely soluble in water; practically insoluble in alcohol, chloroform and ether.

Uses : Guanethidine is an antihypertensive agent. The common side-effects are hypotension, diarrhoea, dizziness, syncope, muscle weakness and lassitude.



Official

Guanethidine Monosulphate, B.P.

Guanethidine Tablets, B.P., I.P.

Guanethidine Monosulfate Tablets, U.S.P.

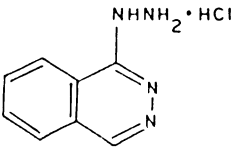
Guanethidine Sulfate Tablets, U.S.P.

HYDRALAZINE HYDROCHLORIDE

Nomenclature : 1 (2H)-Phthalazinone hydrazone.

Brand Names : 1-Hydrazinophthalazine HCl; Ciba-5968 HCl Praparat 5968 HCl; C-5968 HCl; Hipoftalin HCl; Hypophthalin; Apresoline; Lopress.

Hydralazine hydrochloride, m.p. 273° (decomp), is a yellow crystalline substance which is soluble in water and alcohol; very slightly soluble in ether; pH of a 2% aqueous solution is 3.5 to 4.5.



Hydralazine is used to treat hypertension. It has action on the smooth muscle of the vascular walls with a decrease in peripheral resistance to blood flow. This results in an increased blood flow through the peripheral blood vessels.

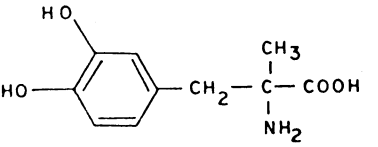
Official

Hydralazine Injection/Tablets, B.P.

Hydralazine Hydrochloride Injection/Tablets U.S.P.

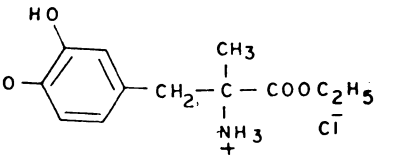
Hydralazine hydrochloride, B.P., I.P.

METHYLDOPA (Page - 247)



Methyldopa is a colourless or a white to yellowish-white, odourless, fine powder which may contain friable lumps; m.p. ~ 300 (decomp). It is slightly soluble in water and alcohol; practically insoluble in chloroform and ether; dissolves in dilute mineral acids. It is kept in well-closed containers and protected from light.

Methyldopate Hydrochloride (Brand Names : Aldomet Ester Hydrochloride) is a zwitter ion and is not soluble enough for parenteral use. It is soluble in water to the extent of 10-300 mg/ml at pH 2-7. It may be stabilized with sodium bisulphite or disodium EDTA. It is a white, odourless, crystalline powder which is slightly soluble in chloroform; practically insoluble in ether.



Uses : Methyldopa and its derivatives are antihypertensive agents.

The common side effects include depression, psychic effects, nightmares, nausea, dryness of the mouth, headache, dizziness, oedema and disorders of sexual function.

Official

Methyldopate Hydrochloride, B.P.

Methyldopate Injection, I.P.

Methyldopa Tablets, B.P., I.P., U.S.P.

Methyldopa Oral Suspension, U.S.P.

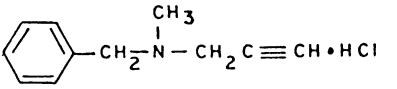
Methyldopa and Chlorothiazide Tablets, U.S.P.

Methyldopa and Hydrochlorothiazide Tablets, U.S.P.

PARGYLINE HYDROCHLORIDE

Nomenclature : N-Methyl-N-2-propynylbenzenemethanamine; N-Benzyl-N-methyl-2-propynylamine.

Brand Names : MO-911; A-19120; Eudatin HCl; Eutonyl; Supirdyl HCl.



Pargyline hydrochloride, m.p. 154-155°, is a white crystalline powder with a slight odour. Sublimation occurs when kept at high temperatures. It is readily soluble in water; soluble in alcohol and acetone; aqueous solutions are unstable. It is stored in airtight containers.

Uses : Pargyline hydrochloride is a monoamine oxidase inhibitor which is used to treat hypertension.

The main side-effects are orthostatic hypotension and attacks of dizziness; others are drowsiness, headache, weakness, fatigue, dryness of mouth, constipation, oedema and gastro-intestinal disturbances.

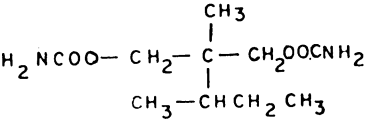
Official

Pargyline Hydrochloride Tablets, U.S.P.

MEBUTAMATE

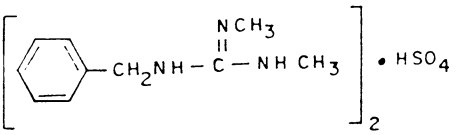
Nomenclature : 2-Methyl-2-(1-methylpropyl)-1,3-propanediol dicarbomate.

Brand Names : W-583; Capla; Butatensin; Carbuten; Dormate; Mebutina; Prean; Sigmafon; Vallence; Mega; No-Press; Axiten; Ipotensivo.

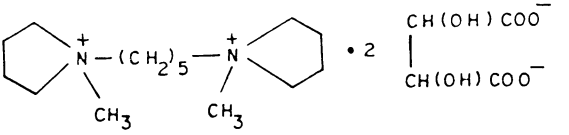


Mebutamate, m.p. 77-79°, is a carbamate which is a bitter, white crystalline powder; slightly soluble in water and freely in alcohol. It is used to treat mild hypertension. The main side effects are drowsiness, nausea, vomiting, diarrhoea, weakness, etc.

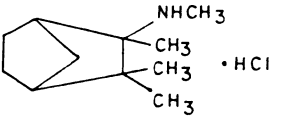
Miscellaneous Agents



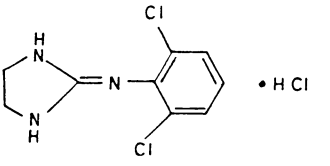
Bethanidine Sulphate



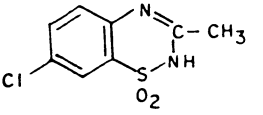
Pentolinium Tartrate



Mecamylamine Hydrochloride



Clonidine Hydrochloride



Diazoxide

35

VITAMINS

Vitamins are organic compounds required by the body in small amounts for normal growth, various metabolic processes and maintenance of life in animals, including man. They do not provide energy and are not utitized as building units of the body. As metabolic regulators, vitamins act as redox agents, e.g., vitamins A,C,E,K, and niacin; they act as coenzymes or enzyme activators, e.g., vitamins B_1, B_2, B_6, B_{12} and D; they also act as nuclear agents, e.g., biotin, folic acid. Some vitamins combine two or more of these activities. Vitamins are not synthesized in the body, or are synthesized in small quantities. When the natural supply of vitamins is lacking due to inadequate diet and increased requirements such as during pregnancy, then a number of deficiency diseases occur. Thus, vitamins are used clinically for the prevention and treatment of specific vitamin deficiency states. Excessive intakes of most water-soluble vitamins have little effect due to their rapid excretion in urine, but excessive intakes of fat-soluble vitamins accumulate in the body and are potentially dangerous.

Vitamins are obtained from a number of sources, both plant and animals. They are usually isolated, concentrated, and purified for use as drugs. Many vitamins are now synthesized. Some animals and birds can synthesize some of the vitamins and provitamins, such as vitamin C and 7-dehydrocholesterol.

Vitamins are classified according to their solubility in water and fats, e.g.

1. Water-soluble vitamins-B_1, B_2, B_6, B_{12}, C, nicotinic acid, folic acid, pentothenic acid, biotin, inositol and p-aminobenzoic acid, and
2. Fat-soluble vitamins- A, D, E and K.

WATER SOLUBLE VITAMINS

Water-soluble vitamins are essential constituents of enzyme systems, and are present in plant and animal cells where active metabolic processes are taking place. Many of these vitamins cannot be stored in the body and must therefore be regularly supplied in some form; vitamin B_{12} is an exception.

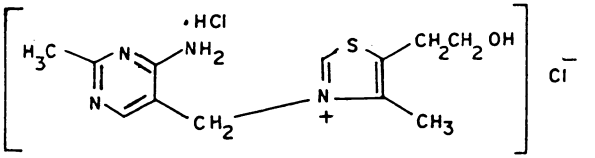
Vitamin B Complex

Vitamin B complex is found abundantly in yeast, cereal seed embryos, eggs, meat and milk. The structures of at least 12 recognized compounds are present in "B complex".

THIAMINE HYDROCHLORIDE

Nomenclature : 3-[(4-Amino-2-methyl-5-pyrimidinyl) methyl]-5-(2-hydroxyethyl)-4-methylthiazolium chloride monohydrochloride.

Brand Names: Vitamin B_1; Bedome; Begiolan; Benerva; Bequin; Berin; Betabion; Betalin S; Betaxin; Bethiazine; Bevitex; Bewon; Biuno; Bivatin; Bivita; Clotiamina; Metabolin; Thiadoxine; Thiavit; Tiamidon; Tiaminal; Vitaneuron.



Thiamine hydrochloride is a colourless crystalline powder with a faint characteristic thiazole odour; m.p. 248° (decomp). It is soluble in water and glycerol; practically insoluble in chloroform, ether and benzene. On exposure to air, the vitamin absorbs an amount of water forming a hydrate. The article of commerce contains about 4% water which is removable by drying at 100°. In the dry form the vitamin is stable, and heating at 100° for 24 hours does not diminish its potency. In aqueous solution it can be sterilized at 110°, but if the pH of the solution is above 5.5, it is destroyed rapidly.

One gram of crystalline vitamin B_1 hydrochloride is equivalent to 333,00 I.U. The vitamin is destroyed by alkalies and alkaline drugs such as phenobarbital sodium and by oxidizing and reducing agents. It is preciptated by tannins and by reagents which precipitate alkaloids. It is kept in airtight nonmetallic containers and protected from light.

Thiamine mononitrate, thiamine nicotinate or vitamin B_1 mononitrate is similar to thiamine hydrochloride in therapeutic use and dose.

Uses : Thiamine is an essential coenzyme for carbohydrate metabolism. Thiamine deficiency produces beriberi which is characterized by cardiac failure, oedema, polyneuritis, muscular atrophy, cardio- and vascular changes. Thiamine is used in the treatment and prevention of thiamine deficiency.

Official

Thiamine Hydrochloride Elixir/Injection/Tablets, U.S.P.

Thiamine Hydrochloride, B.P., I.P.

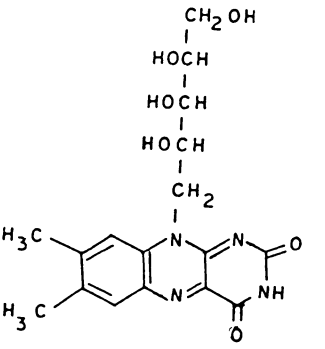
Thiamine Hydrochlorde Injection/Tablets, B.P., I.P.

Thiamine Mononitrate, I.P.

RIBOFLAVIN

Nomenclature : 7,8-Dimethyl-10(D-ribo-2,3,4,5-tetrahydroxy-pentyl) isoalloxazine; 7,8-Dimethyl-10-ribitylisoalloxazine.

Brand Names : Vitamin B_2; Lactoflavine; Vitamin G; Beflavine; Flavaxin; Ribipca.



Riboflavin was first identified in milk and due to its yellow colour, it was known as "lactochrome". It occurs naturally in the free form or in various chemical complexes with protein, phosphoric acid, adenine, or nucleic acid. This nutritional factor is found in milk, eggs, malted barley, liver, kidney, heart and leafy vegetables. The richest natural source is yeast. It occurs in the free form only in the retina of the eye, in whey and in urine.

Riboflavin, m.p. 278-282° (decomp), is a yellow to orange yellow crystalline powder with a slight odour. It is very soluble in water and dilute alkali solutions; practically insoluble in alcohol, acetone, chloroform, and ether. A saturated solution in water has a pH of about 7.0. Although sensitive to alkalies, riboflavin is stable to mineral acids in dark. At 27° the decomposition of acidic solutions was observed to take place. It is stored in airtight containers and protected from light. In the

presence of alkali, it deteriorates rapidly; the decomposition being accelerated by light.

Riboflavin Phosphate (Brand Names : Cytoflav; Cofeavinase; Alloxazine mononucleotide). It is a fine yellow to orange-yellow, odourless, crystalline hygroscopic powder; soluble in water; very slightly soluble in alcohol; practically insoluble in chloroform and ether.

Methylol Riboflavin (Brand Names : Hyflavin) is a mixture of methylol derivatives of riboflavin formed by treating formaldehyde with riboflavin in an alkaline solution. The number of methylol groups attached in the ribityl moiety varies from 1 to 3. It possesses the activity of riboflavin and is recommended for parenteral therapy.

Uses : Riboflavin is essential for the utilization of energy from food. Riboflavin deficiency leads aribоflavinosis characterized by cheilosis, angular stomatitis, and seborrheic accumulations of the nose. Burning of eyes, photophobia and corneal vascularisation are other symptoms.

Official

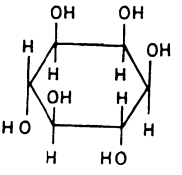
Riboflavine, B.P.. I.P.

Riboflavine Injection/Tablets, I.P., U.S.P.

Riboflavine Sodium Phosphate, B.P.

INOSITOL

Brand Names : *myo*-Inositol; *meso*-Inositol; i-Inasitol; Cyclohexanehexol; Cyclohexitol; Meat sugar; Inosite; Mesoinosite; Phaseomannite; Dambose; Nucite; Bios I; Rat antispectacled eye factor.



Inositol is widely distributed in plants and animals. It is prepared from natural sources, such as corn steep liquors. Among nine possible stereisomers, seven forms are optically inactive or meso. Two optically active forms, the racemic form, and several *cis, trans*-isomers, occur naturally.

Inositol, m.p. 225-227°, is a white, crystalline powder and is soluble in water and dilute alcohol; slightly soluble in alcohol, in usual organic solvents and in fixed oils.

Inositol occurs in cereal grains, citrus fruits, other plant parts, yeast molds, eggs, blood, milk, liver, brain, kidney, heart

muscle and other sources. The concentration of inositol in leaves reaches a maximum shortly before the fruit ripens.

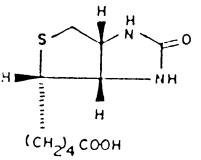
Inositol is found free and combined in nature. The natural product, phytic acid, is inositol hexaphosphate. Inositol, a lipotropic, has been used in the treatment of lipid metabolic disorders and diabetes mellitus.

Lyxoflavine : It is the L-lyxose analogue of riboflavin isolated from human myocardium. It is yellow to orange crystalline substance, mp 283-284° (decomp); sparingly soluble in water; even less soluble in alcohol; freely soluble with decomposition in alkaline aqueous solution. It is a growth promoting agent in foodstuffs.

BIOTIN

Nomenclature : Hexahydro-2-oxo-1H-thieno [3,4-d] imidazole -4-pentanoic acid.

Brand Names : Vitamin H; Coenzyme R; Bios II; Bioepiderm; Anti-Egg white injury Factor; S/Skin Factor.



Biotin is the growth factor present in minute amounts in every living cells. It plays an indispensable role in numerous naturally occurring carboxylation reactions. It occurs mainly bound to proteins or polypeptides. The richest sources are liver, kidney, pancreas, yeast and milk. The biotin content of cancerous tumors is higher than that of normal tissue. Biotin combines with the proteinaceous substance, avidin, in egg-white and becomes inactive.

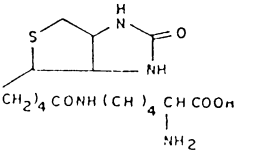
Biotin, m.p. 232-233°, is a white, crystalline powder which is very slightly soluble in water and in alcohol; insoluble in other common organic solvents; more soluble in hot water and in dilute alkali. The pure compound is stable to air and temperature; moderately acid and neutral solutions are stable for several months; alkaline solutions are less stable. Aqueous solutions are very susceptible to mold grouth.

Biotin functions as a carboxylation cofactor. Its deficiency in mammals develops only when raw egg white is added to the biotin-deficient diet. Certain cases of baldness in men are caused by seborrheic conditions and can be improved by biotin.

BIOCYTIN

Nomenclature : N^{16}-[5-Hexahydro-2-oxo-1H-thieno [3, 4-d] imidazol-4-yl] -1-oxopentyl] - L-lysine.

Brand Names: Biotin complex of yeast.

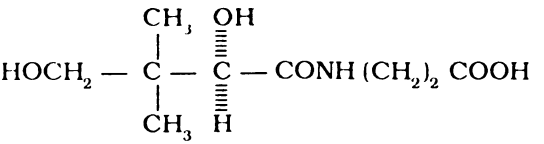


Biocytin, m.p. 241-243°, is a naturally occurring complex of biotin. It contains 65.6 per cent of biotin. It is freely soluble in water, glacial acetic acid, less soluble in alcohol; practically insoluble in acetone and most other organic solvents. On acid hydrolysis, it yelds biotin and L-lysine.

PANTOTHENIC ACID

Nomenclature : (R)-N-(2,4-Dihydroxy-3,3-dimethyl-1-oxobutyl)-β-alanine.

Brand Names : Chick antidermatitis factor, Vitamin B_3.



Pantothenic acid, an unstable, viscous oil, extremely hygroscopic, is a factor in the vitamin B complex that is necessary for the proper gowth of animals. It is dextrorotatory and is usually marketed as the calcium salt, calcium D (+)— pantothenate. Pantothenic acid occurs every where in animal and plant tissues. The richest common sources are liver, yeast, cereal brans, leafy vegetables diary products and eggs. It may be prepared by the direct condensation of β-alanine with lactone of pantoic acid. It is easily destroyed by acids, bases and heat. The vitamin is freely soluble in water, ethyl acetate, dioxane, glacial acetic acid; moderately soluble in ether, and amyl alcohol; practically insoluble in benzene and chloroform. One gram of pantothenic acid equals to 70,000-75,000 chick units.

Calcium Pantothenate (Brand Names : Calpanate; Galamila; Pantholin).

Calcium pantothenate, m.p. 195-196° (decomp), occurs as white, odourless, slightly hygroscopic powder. It is soluble in water and glycerol; practically insoluble in alcohol, chloroform and ether; reasonably stable to air and light. Rate of hydrolysis

is a function of pH and is catalyzed by the presence of eletrolytes. Solutions are not stable to autoclaving, and sterilization by filtration is necessary.

Uses : Pantothenic acid is a vitamin B substance. It is a component of co-enzyme A which is essential in the metabolism of carbohydrate, fat, and protein.

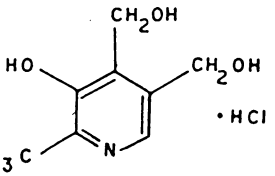
Official

Calcium Pantothenate Tablets, U.S.P.

PYRIDOXINE HYDROCHLORIDE

Nomenclature : 5-Hydroxy-6-methyl-3,4-pyridinedimethanol hydrochloride.

Brand Names : Pyridoxol hydrochloride, Vitamin B_6 hydrochloride; Adermine hydrochloride; Hexabione hydrochloride; Hexabetalin; Hexavibex; Pyridipca; Pyridox; Becilan; Benadon; Hexermin; Compoviton 6; Hexobion.



Pyridoxine hydrochloride is one of the vitamins of the B_6 complex. It is present in many foodstuffs; especially good sources are yeast, liver and cereals. It occurs as a white, odourless, crystalline powder which is soluble in water and alcohol; practically insoluble in chloroform and ether. A 5 per cent solution in water has a pH of 2.4 to 3.0. Acidic aqueous solutions are stable and may be heated for 30 minutes at 120° without decomposition.

Uses : Pyridoxine is involved in amino acid metabolism, but is also involved in carbohydate and fat metabolism. It is used in the treatment and prevention of pyridoxine deficiency states.

Official

Pyridoxine Hydrochloride, B.P., I.P.

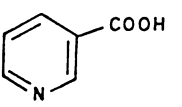
Pyridoxine Tablets, I.P.

Pyridoxine Hydrochloride Injection/Tablets, U.S.P.

NIACIN

Nomenclature : 3-Pyridenecarboxylic acid; Pyridine β-carboxylic acid.

Brand Names : Nicotinic acid; P.P. factor; Pellagra preventive factor; Antipellagra vitamin; Nicacid; Nicagin; Nicobid; Niconacid; Nico-span; Nicotene; Nicotinipca; Nicyl; Akotin; Daskil; Tinic; Nicolar; Wampocap.



Nicotine occurs in minute amounts in all living cells; appreciable amounts are found in liver, yeast, milk, adrenal glands, white meat, alfalfa, legumes, whole cereals, corn, etc. Whole wheat flour contains about 60 μg/g of nicotinic acid. It can be prepared by oxidation of nicotine with nitric acid or by oxidation of β-substituted pyridines. Nicotinic acid, m.p. 236-237°, is a white, odourless, crystalline powder. It is nonhygroscopic and stable in air; sublimes without decomposition. It is freely soluble in water; soluble in hot alcohol and in dilute aqueous solution of alkali hydroxides and carbonates; very slightly soluble in chloroform; practically insoluble in ether. It is stored in well-closed containers and protected from light.

Official

Nicotinic Acid, B.P., I.P.

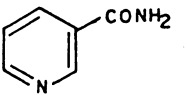
Nicotinic Acid Tablets, B.P., U.S.P., I.P.

Niacin Injection, U.S.P.

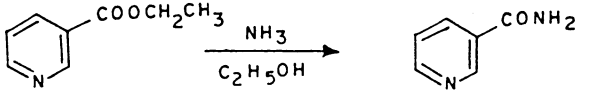
NICOTINAMIDE

Nomenclature : 3-Pyridinecarboxylic acid amide; Pyridine-3-carboxamide.

Brand Names : Niacinamide; Nicotinic acid amide; Nicotyl amide; Vitamin PP. Nicamindon; Nicotilamide; Pelonin amide; Benicol; Aminicotin; Vi-Nicotyl; Dipegyl; Amide PP; Nicofort; Niozymin; Pelmine.



Nicotinamide is prepared by the amidation of esters of nicotinic acid or by passing ammonia gas into nicotinic acid at 320° C.



Ethyl Nicotinate Nicotinamide

Nicotinamide is a white crystalline powder, odourless or with a faint characteristic odour. It is soluble in water and alcohol; slightly soluble in chloroform and ether; stored in airtight containers and protected from light.

Uses : Nicotinic acid and nicotinamide are coenzymes involved in electron transfer reactions in the respiratory chain. Its deficiency leads to the development of pellagra which is characterized by skin lesions with hyperpigmentation and hyperkeratinisation. Other symptoms include diarrhoea, abdominal pain, glossitis, stomatitis, loss of appetite, headache, lethargy and mental and neurological disturbances. Nicotinic acid and nicotinamide are used in the treatment and prevention of nicotinic acid deficiency.

Adverse effects with high doses of nicotinic acid include dryness of the skin, pruritus, hyperpigmentation, abdominal cramps, diarrhoea, nausea, vomiting, anorexia, peptic ulcer, amblyopia, jaundice, decrease in glucose tolerance, hyperglycaemia, and hyperuricaemia.

Official

Nicotinamide, B.P., I.P.

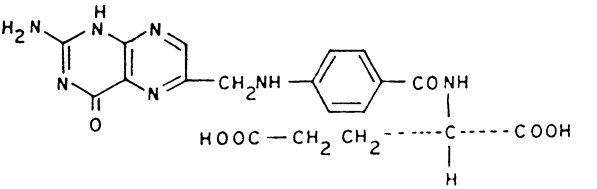
Nicotinamide Injection/Tablets, I.P., U.S.P.

Nicotinate, B.P.

FOLIC ACID

Nomenclature : N-[4-[2-amino-1,4-dihydro-4-oxo-6-pteridinyl) methyl] amino] benzoyl]-L-glutamic acid.

Brand Names : PGA. Liver *Lactobacillus casei* factor; Vitamin BC; Vitamin M; Folsäure; Cytofol; Folacin; Foldine; Folaemin; Foliamin; Folicet; Folipac; Folettes; Folsan; Folvite; Incafolic; Millafol.



Folic acid is a hematopoietic vitamin present in free or combined with one or more additional molecules of L (+)— glutamic acid in liver, kidney, mushrooms, spinach, yeast,

green leaves, and grasses. It is the active principle required for the growth of a *Streptococcus lactis* under specific conditions.

Folic acid is a yellow to orange brown, odourless, crystalline powder. it is practically insoluble in water and most organic solvents.

It darkens and chars from about 250°. Injectable solutions are prepared by dissolving folic acid in normal sodium bicarbonate solution or by preparing solutions of the sodium or methylglucamine salt. A suspension of 1 g folic acid in 10 ml water has a pH of 4.0 -4.8. Aqueous solutions of folic acid or its sodium salt are stable to air. Folic acid in the dry state or in very dilute solutions is decomposed readily by sunlight or ultraviolet light. Folic acid in foods is destroyed more readily by cooking than are the other water soluble vitamins. It is kept in well-closed containers and protected from light.

Uses : Folic acid is a member of the vitamin B group. Folic acid is reduced in the body to tetrahydrofolate, which is a co-enzyme for the synthesis of DNA. Its deficiency produces megaloblastic anaemia.

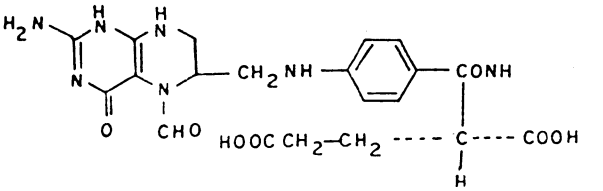
Official

Folic Acid, B.P., I.P.
Folic Acid Tablets, B.P., I.P., U.S.P.
Folic Acid Injection, U.S.P.

FOLINIC ACID —SF

Nomenclature : N-[4-[[(2-Amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl) methyl] amino] benzoyl] glutamic acid.

Brand Names : CF; Citrovorum factor; NSC-3590; Leucovorin.



Folinic acid is an intermediate product of the metabolism of folic acid; the active form into which that acid is converted in the body, ascorbic acid being a necessary factor in the conversion process. Folinic acid and not folic acid is the natural factor in digests of liver and that folic acid arises from folinic acid. Folinic

acid can be prepared from folic acid by formylation, reduction and autoclaving or the action of dilute alkali. It also can be prepared by the formylation of tetrahydrofolic acid.

Folinic acid occurs as crystalline material, m.p. 240-250°. It is sparingly soluble in water; pH of saturated aqueous solution is 2.8-3.0 at which pH partial decomposition takes place. It is more stable at neutral or mildly alkaline pH.

Calcium Folinate (Brand names : Calcium Leucovorin; NS-3590; Leucovorin calcium) is a yellowish-white or yellow, odourless powder. It is very soluble in water; practically insoluble in alcohol; protected from light.

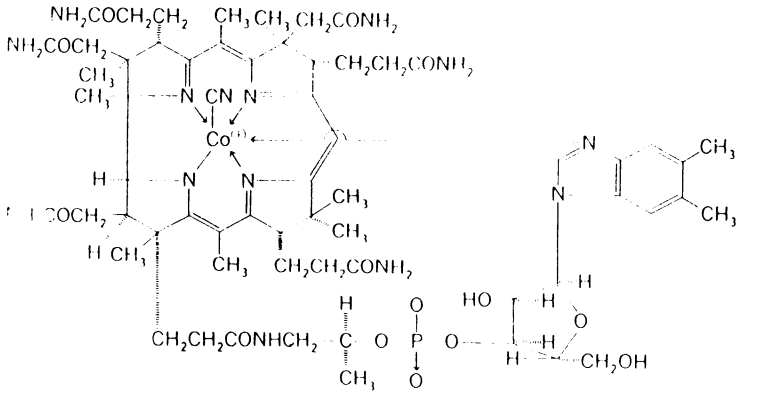
Uses : Folinic acid is used as an antidote to folic acid antagonists, such as methotrexate. It is effective in the treatment of megaloblastic anaemia.

Official

Leucovorin Calcium Injection, U.S.P.

CYANOCOBALAMIN

Brand Names : Cobamamide; Cobamamidum; Coenzyme B_{12}; DBC; Dibenzcozamide; Dimebenzcozamide; Vitamin B_{12} coenzyme; Actimide; Ademide; Anabasi; Betarin; Calomide; Cobalion; Cobaltamin S; Cobanzyme; Cobazymase; Dolonevran; Enzicoba; heraclene; Hi-Fresmin; Hycobal; Indusil; Ripresil; Sabalamin; Xobaline.



Vitamin B_{12} is the name generally used for a group of related cobalt-containing compounds, also known as cobalamins, of which cyanocobalmine and hydroxycobalamin are the principal

forms. This coenzyme is the metabolically active form of vitamin B_{12}. It is isolated from a culture of *Propionibacterium shermanii*. The co-enzyme differs from vitamin B_{12} by the presence of a 5'-deoxyadenosyl group in the axial ligand occupied by the cyanide in the vitamin. Cyanocobalamin may occur as several vitamers (B_{12}a, B_{12} b, B_{12}c. B_{12}d) which are designated as cobalamines.

The macro-ring system devoid of peripheral substituents and found in vitamin B_{12} is named corrin, and its derivatives are corrinoids that contain central cobalt atom when found in nature. When the corrin ring contains the peripheral group, it is called cobyrinic acid.

Cyanocobalamin is a dark red crystalline or amorphous powder. In the anhydrous form it is very hygroscopic and when exposed to air it may absorb about 12 % of water. It is soluble in water; sparingly soluble in alcohol; practically insoluble in acetone, chloroform and ether. It is highly sensitive to light, to cyanide and moderately sensitive to acid. Solutions are most stable at pH 6-7 stored in dark. Heating of acid or alkaline solutions produces slow inactivation. It is stored in airtight containers and protected from light.

Uses : Vitamin B_{12} is a hematopoietic vitamin which acts as coenzymes in synthesis of nucleic acid, proteins, lipids and in other metabolic pathways. Its deficiency causes metabolic disorders, megaloblastic anaemias and neurological damage. Allergic hypersensitivity reactions have been observed by vitamin B_{12} therapy.

Official

Cyanocobalamin, B.P., I.P.

Cyanocobalamin Injection, B.P., U.S.P., I.P.

Hydroxocobalamin, B.P., I.P.

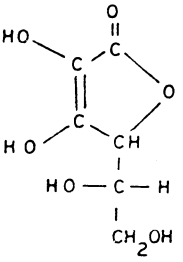
Hydroxocobalamin Injection, B.P., I.P., U.S.P.

ASCORBIC ACID

Nomenclature : 3-Oxo-L-gulofuranolactone; L-3- Ketothreo-hexuronic acid lactone.

Brand Names : Vitamin C, Cevitamic acid; Cebid; Cebion; Cantaxin; Cevalin; Cevatine; Cevimin; Cevitex; Cewin; Cipca; Cebicure; C-Vimin; Cevitamin; Testascorbic; Allercorb; Cecon; Ce-Vi-Sol; Ascorin; Ascorteal; Cegiolan; Adenex; Ascorvit; Cevex;

Lemascorb; Ciamin; Hybrin; Vitacee; Cantan; Catavin C; Celin; Cenetone; Cescorbat; Cereon; Cergona; Cetamican; Cetamid; Planavit C; Colascor; Concemin; Duoscorb; Scorbacid; Davitamon C; Proscorbin; Redoxon; Scrobu-C; Ribena; Vicelat; Vitacin; Vitacimin; Vitascorbol; Xitix; Cevitan; Laroscorbine.

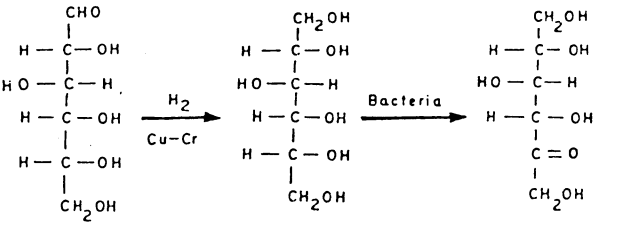


Ascorbic acid is widely distributed in the plants and animal kingdom. Good sources are citrus fruits, hip berries, acerola, fresh tea leaves, peppers, paprikas, tomatoes, rose hips, blackberries, green English walnuts, West Indian cherries and other sources. It is formed rapidly in germinating seeds and apparently reaches a high concentration in rapidly growing stem or root tips, green leaves and seeds.

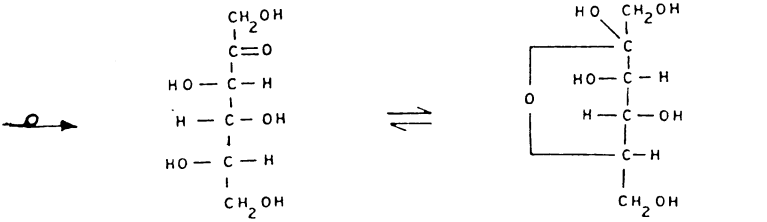
Although ascorbic acid occurs in relatively large quantities in some plants, fruits and other natural sources, its isolation is tedious, and difficult. Ascorbic acid is now manufactured from D-glucose via microbiological oxidation to a keto-acid, which is catalytically reduced to L-idonic acid. This is converted to 2-oxo-L-gulonic acid in the presence of bacteria which is esterified with methanol. The ester is then isomerized and cyclized to L-ascorbic acid.

The natural ascorbic acid is of L-series, though it is dextro-rotatory. It undergoes reversible oxidation and reduction in the organism which owe its antiscorbutic activity. Its name ascorbic acid was given because it exhibited acid properties (sour taste) and would cure scurvy. The enolic group imparts acidity to the molecule and it can form salts. Vitamin C shows marked reducing properties but it does not produce colour with Schiffs base. It is quantitatively oxidized in aqueous solution by iodine or by 2,6-dichlorophenolindophenol and the oxidation process is reversible. Ascorbic acid is the least stable of all vitamins.

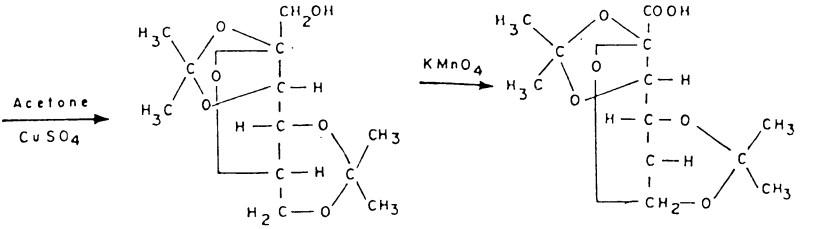
Ascorbic acid, m.p. 190-192°, occurs as odourless, colourless or slightly yellow crystals or crystalline powder with pleasant, sharp acidic taste. It is soluble in water and alcohol; practically insoluble in chloroform, benzene, oils, fats, ether and petrol. It is stable in air when dried. In impure preparations and in many natural products the vitamin oxidizes on exposure to air and light. It possesses relatively strong reducing power, and decolourizes many dyes. Aqueous solutions are rapidly oxidized by air and the reaction is accelerated by alkalies, iron and copper. It produces colour with ferric chloride and precipitated with basic lead acetate. It is kept in well-closed containers and protected from light.



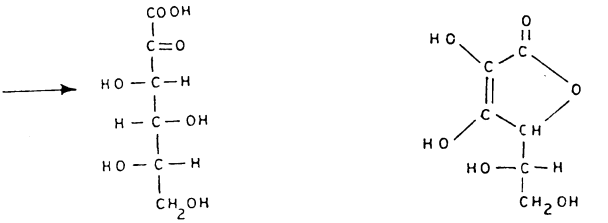
D-Glucose D-Sorbitol L-Sorbose



L-Sorbose L-Sorbose (Furanose form)



Diacetone Sorbose Diacetone Sorburonic Acid



2-Keto-L- Gulonic Acid L-Ascorbic Acid

Sodium Ascorbate (Brand Names : E 301; Monosodium L-ascorbate; Vitamin C sodium; Ascorbin; Sodascorbate; Natrascorb; Cenolate; Ascorbicin; Cebitate), m.p. 218° (decomp), is prepared by treating aqueous ascorbic acid solution with an equivalent amount of sodium bicarbonate. After cessation of effervescence the sodium ascorbate is precipitated by the addition isopropanol.

Sodium ascorbate occurs as white or very faintly yellow, odourless crystals or crystalline powder. It gradually darkens on exposure to air. It is soluble in water; very slightly soluble in alcohol; insoluble in chloroform and ether. A 10% solution in water has a pH of 7 to 8. Aqueous solutions are quickly oxidized by air at pH 6.0. It is stored in airtight containers and protected from light.

Uses : Ascorbic acid is essential for the synthesis of collagen and intercellular material. Its deficiency leads scurvy which is characterized by capillary fragility, bleeding, anaemias, cartilage and bone lesions and slow healing of wounds.

Ascorbic acid is used to treat scurvy and cold, to acidify urine, as antioxidants in pharmaceutical and food industries.

Large doses of Vitamin C causes diarrhoea and other gastro-intestinal disturbances.

Official

Ascorbic Acid, B.P., I.P., U.S.P.

Ascorbic Acid Injection, I.P., U.S.P.

Ascorbic Acid Tablets, B.P., I.P., U.S.P.

Ascorbic Acid Oral Solution, U.S.P.

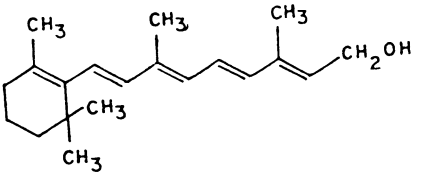
FAT SOLUBLE VITAMINS

VITAMIN A

Nomenclature : 3,7-Dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,4,6,8- nonatetraen -1-ol.

Brand Names : Anti-infective vitamin; Lard-factor; Axerophthol; Biosterol; Oleovitamin A; Ophthalamin; Vitamin A_1; Vitamin A alcohol; Acon; Afaxin; Agiolan; Alphalin; Anatola; Aoral; Apexol; Apostavit; Atav; Avibon; Avita; Avitol; Axerol; "Dohyfral" A; Epiteliol; Neo-A-Let; Prepalin; Testavol; Voflol; Vi-Alpha; Vitpex; Vogan; Vogan-Neu.

Vitamin A occurs in the animal organism and not in plants. Carotenoids are converted into vitamin A by the liver. It is extracted from fish liver oils where it occurs mostly in esterified form.



A suitable form of retinol (vitamin A alcohol) consists of esters of edible fatty acids, principally acetic and palmitic acid. It is a light yellow to red oil which may solidify on cooling. It is practically odourless or with a mild fishy odour, but no rancid odour or taste.

Pure vitamin A, m.p. 62-64°, occurs as pale yellow plates or crystals and is insoluble in water but soluble in alcohol, fixed oils and usual organic solvents. It is unstable in the presence of light and oxygen and in oxidized fats and oils. Ultraviolet light inactivates vitamin A and its solutions which exhibit a characteristic green fluorescence. The free alcohol is sensitive to air-oxidation, but oil solutions of it are quite stable. Esters of vitamin A are more stable to oxidation. In solid form, it may be dispersible in water. The vitamin is stored in airtight containers and protected from light.

Uses : Vitamin A is essential for growth, for the development and maintenance of epithelial tissues, and for vision. Its deficiency causes night blindness and changes in the skin and mucous membranes. Vitamin A is used to treat night blindness and skin disorders including acne and psoriasis.

Intake of excessive amounts of vitamin A leads toxicity, known as hypervitaminosis which is characterized by fatigue, irritability, anorexia, loss of weight, vomiting and other gastro-intestinal disorders, fever, skin changes, alopecia, dry hair, cracking and bleeding of lips, anaemia, headache, pain in bones and joints, etc.

Official

Vitamin A Capsules, U.S.P.

Cod-liver Oil, B.P.

Concentrated Vitamin A Solution, I. P.

Concentrated Vitamin A and D Solution, I.P.

Halibut-oil, B.P.

Shark-liver oil, I.P.

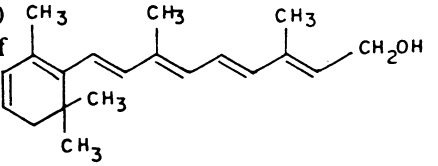
Synthetic Vitamin A Concentrate, B.P.

Vitamin A, I.P.

Vitamin A Ester Concentrate (Natural), B.P.

Vitamin A_2 (Brand Names : Retinol 2; 3,4-Didehydroretinol; Dehydroretinol); all *trans*, m.p. 17-19°; 13-cis, m.p. 73-74°, is found in marine fishes of the family Labridae and in turtles. It exhibits chemical, physical and biological properties identical to vitamin A

Vitamin A_2 has about 40 per cent of the bioactivity of crystalline vitamin A.



VITAMIN D

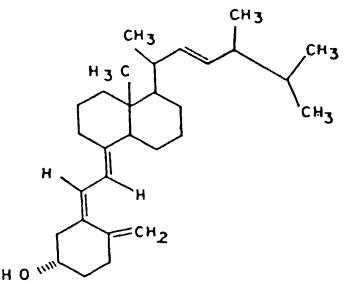
The term vitamin D is used for a range of closely related sterol compounds which possess the property of preventing or curing rickets. These include alfa calcidol, calcifediol, calcitriol, cholecalciferol, dihydrotachysterol and ergocalciferol.

VITAMIN D_2

Nomenclature : 9,10-Secoergosta -5,7,10 (9), 22-tetraen-3-ol.

Brand Names : Calciferol; Ergocalciferol; Oleovitamin D_2; Activated ergosterol; Viosterol; Drisdol; D-Tracetten; Divit urto; Ostelin; Condol; Ergorone; Davitin; Metadee; Mina D_2; Mulsiferol; Mykostin; Radsterin; Shock-Ferol; Dee-Ron; Decaps; Deltalin; De-Rat concentrate; Deratol; Hi-Deratol; Detalup; Diactol; Doral; Vio-D; Ertron; Infron; Radiostol; Sterogyl; Fortodyl.

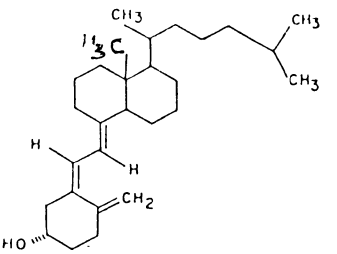
Vitamin D_2 is formed by exposing ergosterol to ultraviolet irradiation or other energy. It may be prepared from ergosterol by UV irradiation in a suitable solvent. It occurs as a white, odourless, crystalline compound that is soluble in fats, alcohol and usual organic solvents, but is insoluble in water, m.p. 115-118°. It is oxidized slowly in oils by oxygen of the air. It is an antirachitic vitamin.



VITAMIN D_3

Nomenclature : 9,10-Secocholesta-5,7,10 (19)-trien-3-ol.

Brand Names : Activated 7-dehydrocholesterol; Oleovitamin D_3; Cholecalciferol; Colecalciferol; CC; Duphafral D_3 1000; Delsterol; Deparal; Ebivit; Micro-Dee; Neo Dohyfral D_3; Provitina; Ricketon; Trivitan, D_3 -Vicotrat; Vi-De-3-hydrosol; Vigantol; Vigorsan.



Vitamin D_3 is the naturally occurring form of vitamin D. It is produced from 7-dehydrocholestrol, a sterol present in mammalian skin, by ultraviolet irradiation. It mediates intestinal calcium absorption, bone calcium metabolism and probably muscle activity.

Vitamin D_3, m.p. 84-85°, is a white, odourless crystalline compound which is sensitive to air and light. It is practically insoluble in water; freely soluble in alcohol, acetone, chloroform and ether; soluble in fixed oil. Solutions in volatile solvents are unstable and should be used immediately. It is oxidized and inactivated by moist air within few days. It is an antirachitic vitamin.

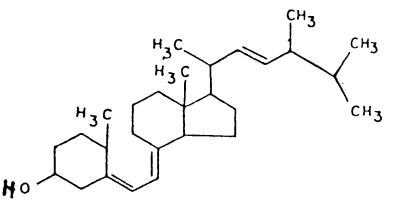
Vitamin D_3 is stored at a temperature of 2 to 8° in hermetically sealed containers in which the air has been replaced by an inert gas. The contents of an opened container should be used immediately. It is protected from light.

DIHYDROTACHYSTEROL

Nomenclature : 9,10-Secoergosta -5,7,22-trien-3-β-ol.

Brand Names : Dichystrolum; Anti-tetany substance 10; AT 10; Antitanil; Calcamine; Dygratyl; Dihydral; Hytakerol; Parterol; Tachyrol.

Chemical reduction of 3,5-dinitro-4-methylbenzoic acid ester of tachysterol with sodium and alcohol followed by saponification produces dihydrotachysterol which is purified by crystallization.



Dihydrotachysterol, m.p. 125-127°, occurs as colourless or white crystals or crystalline powder. It is soluble in alcohol; freely soluble in chloroform; sparingly soluble in vegetable oils and practically insoluble in water. It has slight antirachitic activity. It causes an increase of the calcium concentration in the blood. It is used in infantile tetany and postoperative tetany. It is stored at a temperature not exceeding 15° in hermetically sealed glass containers in which the air has been replaced by an inert gas. It is protected from light.

Uses : Vitamin D is involved in the regulation of calcium and phosphate and bone formation. Its deficiency leads a syndrome characterized by lacking of calcium and phosphate and bone softening and bone pain. Vitamin D is used in the treatment and prevention of vitamin D deficiency states.

Excessive intake of vitamin D increases calcium concentration in plasma causing anorexia, nausea, vomiting, constipation, abdominal pain, muscle weakness, mental disturbances, polydipsia, polyurea, bone pain, renal calculi, cardiac arrhythmias and coma.

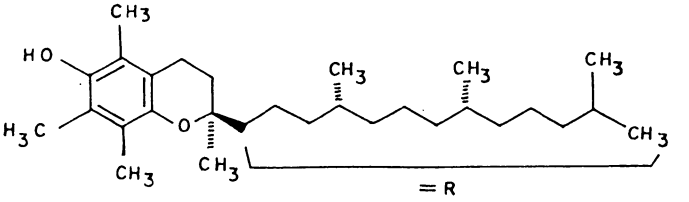
Official

Cholecalciferol, B.P.
Cod-liver Oil, B.P.
Concentrated Vitamin D Solution, I.P.
Dihydrotachysterol, B.P.
Dilute Shark-liver Oil, I.P.
Ergocalciferol, B.P.
Calciferol Injection/Oral Solution/Tablets, B.P.
High Strength Calciferol Tablets, B.P.
Halibut-liver Oil, B.P.
Shark-liver Oil with Vitamin D,I.P.
Vitamins A and D Capsules, I.P.
Dihydrotachysterol Tablets/Capsules/Oral Solution, U.S.P.
Calcifediol Capsules, U.S.P.
Ergocalciferol Capsules/Oral Solution/Tablets, U.S.P.

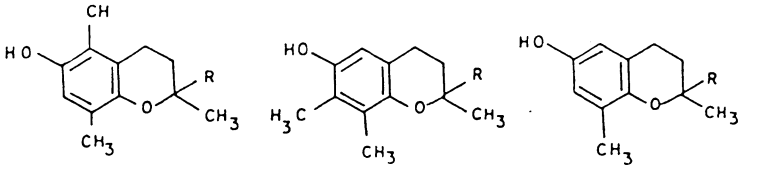
VITAMIN E

Nomenclature : 3,4-Dihydro-2,5,7,8-tetramethyl -2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6-ol.

Brand Names : α-Tocopherol; 5,7,8-Trimethyltocol; Antisterility Vitamin; Eprolin-S; Epsilan; Ephynal; Syntopherol; E-Vimin; Evipherol; Etavit; Phytogermine; Esorb; Profecundin; Tokopharm; Viteolin; Vascuals; Covitol; Evion.



α- Tocopherol



β-Tocopherol γ-Tocopherol δ-Tocopherol

Vitamin E, m.p. 2-4°, b.p. 200-220°, contains various forms of α-tocopherol. It is present in highest concentrations (0.1-0.3%) in wheat germ, corn, sunflower seed, rape seed, soyabean oils, alfalfa and lettuce. Natural α-tocopherol is usually found with β-and γ-tocopherols. It is a clear, slightly greenish-yellow, odourless, viscous oily liquid. It is practically insoluble in water; freely soluble in alcohol, acetone, chloroform, ether and fixed oils. They are stable to heat in the absence of oxygen, stable to strong acids and visible light, but unstable to UV light, alkalies and oxidation. The tocopherols are antioxidants, but they are destroyed by rancid fats. The esters of the tocopherols are more stable than the free alcohols. Vitamin E is slowly oxidized by atmospheric oxygen, rapidly by ferric and silver salts.

Uses : Vitamin E acts as an antioxidant for certain fats and is involved in metabolic reactions. Its deficiency leads to neurological syndromes.

Large doses may cause diarrhoea, abdominal pain, fatigue and weakness. Contact dermititis has occurred following topical application.

Official

Alpha Tocopheryl Acetale, B.P.

Vitamin E Capsules, U.S.P.

Vitamin E Preparation, U.S.P.

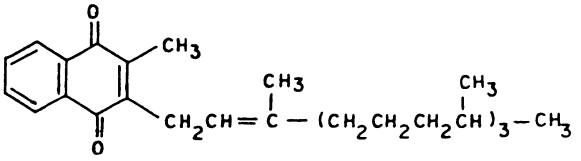
VITAMIN K

The term vitamin K is used for a range of naphthoquinone compounds which are necessary for the biosynthesis of blood clotting factors. These include acetomenaphthone, menadiol, menadione, menatetrenone and phytomenadione.

VITAMIN K_1

Nomenclature : 2-Methyl-3-(3,7,11,15-tetramethyl-2-hexadecenyl) -1,4-naphthalenedione.

Brand Names : 3-Phytylmenadione; Phytomenadione; Phytonadione; Phylloquinone; Antihemorrhagic vitamin; K-ject; Konakion; Mephyton; Mono-kay.



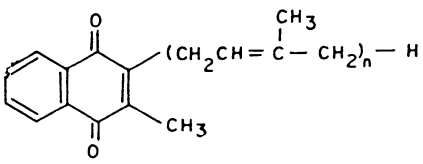
Vitamin K_1 occurs naturally as the *trans* isomer. It was first isolated from alfalfa and is widely distributed in higher green plants. It is a clear, deep yellow to amber, very viscous, odourless oil which is stable in air but decomposes on exposure to light.

It is practically insoluble in water; soluble in alcohol, freely soluble in chloroform, ether, and fixed oil. Vitamin K_1 is stable to air and moisture, but decomposed in sunlight. It is unaffected by dilute acids, but is destroyed by solutions of alkali hydroxides and by reducing agents.

It is stored in airtight containers and protected from light.

VITAMIN K_2

Nomenclature : 2-Methyl-3-*all trans*-polyprenyl-1,4-naphthoquinones.



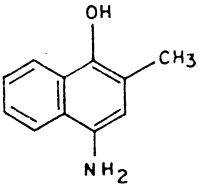
Brand Names : Menaquinones.

Vitamin K_2 are antihaemorrhagic vitamins possessing

side chains varying in length from C_5 to C_{65} which have been isolated from gram-positive bacteria, anaerobic and facultative nonphotosynthetic gram-negative bacteria and photosynthetic bacteria and from putrefied fish meal. Vitamin K_2 is a yellow, crystalline solid.

VITAMIN K_5

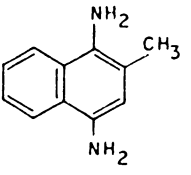
Nomenclature ; 4-Amino-2-methyl-1-naphthalenol; 4-Amino-2-methyl-1-naphthol.



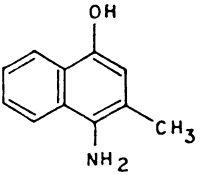
It is prepared from 2-methyl naphthalene or from menadione.

Its hydrochloride, m.p. 280-282° (decomp), is freely soluble in water; slightly soluble in alcohol and insoluble in ether. It turns pink to dark violet on exposure to air and light. It is an antihaemorrhagic vitamin .

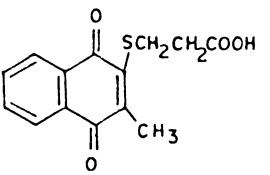
Other vitamin K compounds are given hereunder.



Vitamin K_6



Vitamin K_7



Vitamin K_8

Uses : Vitamin K is an essential cofactor in hepatic synthesis of prothrombin and other blood clotting factors. Vitamin K deficiency leads to a state in which the clotting time of the blood is prolonged and spontaneous bleeding can occur.

Official

Acetomenadione, I.P.

Acetomenadione Tablets, I.P.

Menadione, I.P., B.P.

Manadione Sodium Bisulphite, I.P.

Menadione Sodium Bisulphite Injection, I.P.

Menadione Sodium Diphosphate Injection/Tablets, U.S.P.

Phytomenadione, B.P.

Phytomentadione Injection/Tablets, B.P.

Manadiol Phosphate Tablets, B.P.

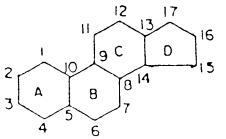
36

STEROIDAL DRUGS

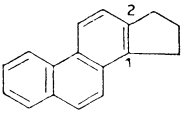
Steroids in general are tetracyclic compounds characterized by the presence of a perhydro-1,2-cyclopentenophenanthrene ring system. The three cyclohexane rings are designated as A,B,C and the cyclopentane ring is the D-ring. These are colourless crystalline compounds and widely distributed in animals and plants. All the steroids give, among other products, Diel's hydrocarbon on dehydration with selenium at 360°C. They possess an alcoholic group; may be saturated (plant sterols) and unsaturated (animal and many plant sterols); they occur free or esters of the higher fatty acids. Mammalian endocrine glands have been the source of several hundred naturally occurring steroids, many with biochemical, clinical or therapeutic significance.

On the basis of their sources, sterols are classified as :

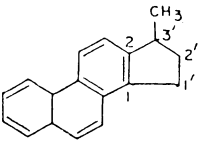
1. *Zoosterol*, which have been isolated from animals, e.g. cholesterol, cholestanol, coprostanol.
2. *Phytosterol*, which are obtained from plant sources, e.g. sitosterol, stigmasterol, and
3. *Mycosterol*, which are obtained from yeast and fungi, e.g. ergosterol.



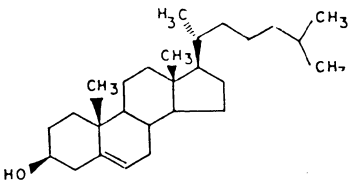
Steroid Skeleton



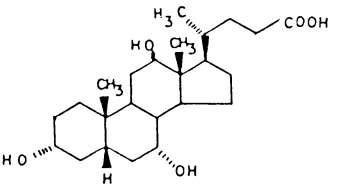
Perhydro-1,2-cyclopenteno-phenanthrene nucleus



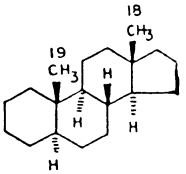
Diels Hydrocarbon



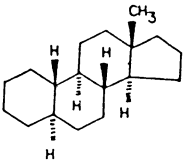
Cholesterol



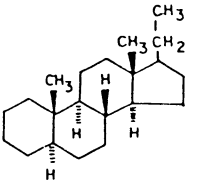
Cholic acid



5α-Androstane



5α-Estrane



5α-Pregnane

Androstane is the simple parent hydrocarbon containing 19 carbons. The male sex hormone testosterone is derived from androstane. The oestrogenic hormone oestradiol is a derivative of estrane which possesses 18 carbons.

Steroidal drugs act as hormones. The hormones are the internal secretion of the endocrine (ductless) glands required for the specific physiological function(s). These are brought to the organ where required by blood streams.

The progestational hormone progesterone and adrenocortical hormones are the derivatives of pregnane.

Steroid sex hormones are produced in gonads, ovaries, testes, adrenal cortex and the placenta. They influence the development and maintenance of the reproductive organs. There are three main types of sex hormones.

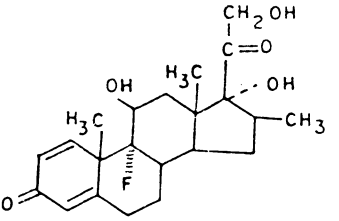
Androgens have distinct roles in male sex physiology. The oestrogens and progesterone influence the female sex physiology.

The adrenal cortex synthesizes three types of steroids-the glucocorticoids, mineralocorticoids and sex corticoids (e.g. oestrogens and androgens). The glucocorticoids, namely cortisone and hydrocortisone, have their action on gluconeogenesis, glycogen deposition and protein and calcium metabolism. The mineralocorticoids (e.g. deoxycortone and aldosterene) have their action on electrolyte and water metabolism causing sodium and fluid retention and potassium excretion.

BETAMETHASONE

Nomenclature : 7-Fluoro-11,17,21-trihydroxy-16-methylpregna-1, 4-diene-3, 20-dione.

Brand Names : Betadexamethasone; Flubenisolone; β-Methasone; Sch 4831; NSC-39470; Beta-Corlan; Becort; Betasolon; Betnelan; Betnesol tablets; Celestan; Celestene; Celestone; Visubeta.



Betamethasone, m.p. 231-234° (decomp), is a white to creamy-white, odourless powder. It is practically insoluble in water; soluble in alcohol and chloroform. It is kept in airtight containers and protected from light.

Betamethasone acetate (Brand Name: Betafluorene), m.p. 196-201° and 205-208°, is a white to creamy white odourless powder. It is slightly soluble in water, more in alcohol and chloroform; freely soluble in acetone.

It is kept in airtight containers.

Betamethasone Benzoate (Brand Names : W 5975; Behen; Benisone; Flurobate; Parbetan, Uticort), mp 225-228°, is a white, odourless powder which is practically insoluble in water; soluble in alcohol, chloroform and methyl alcohol. It is kept in airtight containers.

Betamethasone Dipropionate (Brand Names : Sch 11460, Diproderm; Diprophos; Diprosone; Rinderon-DP), mp 170-179°, is a white or creamy-white, odourless powder. It is practically insoluble in water; sparingly soluble in alcohol; freely soluble in acetone and chloroform.

Betamethasone Valerate (Brand Names : Bedermin; Betnesol-V; Betneval; Betnovate; Bextasol; Celestan-V; Celestoderm-V; Dermosol, Dermovaleas; Ecoval 70; Hormezon; Valisone), m.p. 183-184°, is a white to creamy white, odourless powder. It is

practically insoluble in water; soluble in alcohol, chloroform and ether; freely soluble in acetone. It is kept in airtight containers and protected from light.

Uses : Betamethasone is a glucocorticoid used as anti-inflammatory and immunosuppressant glucocorticoid agent.

The side-effects of betamethasone therapy in large doses are gluconeogenesis, the action on tissue repair and healing, and inhibitory effect on the secretion of corticotrophin by pituitary gland. Disturbance of electrolyte balance is also observed. Other adverse effects include amenorrhoea, hyperhidrosis, mental disturbances, intracranial hypertension, acute pancreatitis and aseptic necrosis of bone.

Official

Betamethasone, B.P., I.P.

Betamethasone Tablets, B.P., I.P.

Betamethasone Sodium Phosphate, B.P., I.P.

Betamethasone Sodium Phosphate Injection/Tablets, B.P., I.P.

Betamethasone Valerate, B.P.

Betamethasone Syrup/Tablets/Cream, U.S.P.

Betamethasone Valerate Topical Aerosol, U.S.P.

Betamethasone Dipropionate Topical Aerosol, U.S.P.

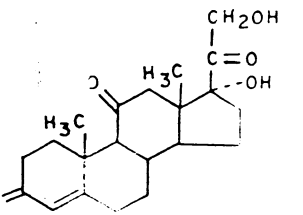
Betamethasone Benzoate Gel, U.S.P.

Betamethasone Valerate Ointment/Lotion/Cream, U.S.P.

CORTISONE

Nomenclature : 17 α, 21-Dihydroxy-4-pregnene-3,11,20-trione; 17-Hydroxy-11-dehydrocorticosterone.

Brand Names : Kendall's Compound E; Wintersteiner's Compound F; Reichstein's Substance Fa; KE; Incortin; Cortone; Cortadren; Scheroson; Corlin; Cortogen; Adreson.



Cortisone may be prepared by partial or total synthesis starting from ergosterol, progesterone and sapogenins.

Cortisone, m.p. 220-224°, occurs as platelets. It is fairly soluble in cold methanol, ethanol, acetone; much less soluble in ether, benzene, chloroform; slightly soluble in water. It gives orange-red solution with

intense green fluorescence in concentrated sulphuric acid. It is used primarily as the 21-acetate due to its increased stability.

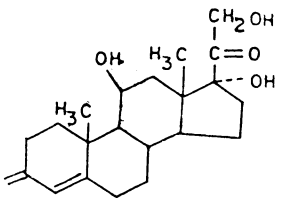
Cortisone Acetate (Brand Names : Cortistab; Cortelan; Cortisyl artriona; Compound E acetate; Cortogen acetate), mp 235-238°, is a white, odourless, crystalline powder. It is practically insoluble in water; soluble in alcohol, acetone, chloroform and dioxane; slightly soluble in ether and methyl alcohol. It reduces ammonical silver nitrate solution at room temperature. Solution in sulphuric acid gives a yellow solution without fluorescence. It is kept in well-closed containers and protected from light.

Uses : The uses, properties and adverse effects of cortisone and its acetate are the same as described under betamethasone. Cortisone acetate has been used in the treatment of many allergic and inflammatory disorders. It is given in the treatment of rheumatoid arthritis including gouty arthritis, ulcerative colitis, regional enteritis, nephrotic syndrome, scleroderma dermatomyositis, psoriasis, periarteritis nodosa, pulmonary granulomatosis and alcoholism.

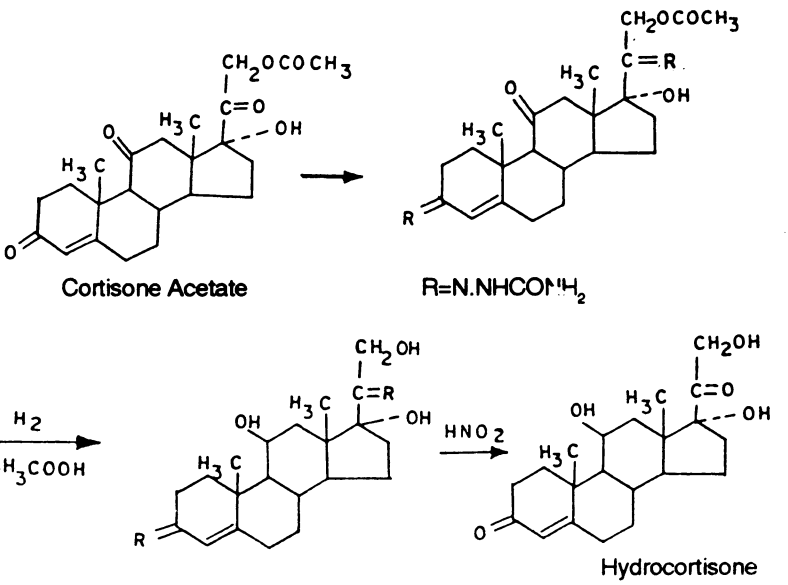
HYDROCORTISONE

Nomenclature : 11,17,21- Trihydroxypregn-4-en-3, 20-dione.

Brand Names : 17-Hydroxycorticosterone; Hydrocortisone free alcohol; Anti-inflammatory hormone; Ala-cort; Cleiton; Cremesone; Cobadex; Cort-Dome; Cortef; Cortifoam; Cortril; Dermacort; Dermolate; Dermolen; Dome-Cort; Efcorbin; Efcorlin; EF-cortelan. Efcortelin; Eye-Cort; Epicort; Ficortril; Genacort (Lotion); Hidro-Colisona; HVB; Hydro-Adreson; Hydrocort; Hydrocortisyl; Hydrocortone; Incortin-H; Kendall's compound F; Lubricort; Meusicort; Maintasone; Reichstein's substance M; Scheroson F; Sigmacort; Texacort; Protocort; Rectoid.



Hydrocortisone is the major hormone secreted by the adrenal cortex; cortisone is converted in large amount into hydrocortisone *in vivo*. Hydrocortisone may be obtained from cortisone acetate by conversion to the 3,20- disemicarbazone, followed by reduction of the 11-keto group with simultaneous removal of the acetyl group in the presence of potassium borohydride in aqueous tetrahydrofuran. Semicarbazone groups are removed by treating the compound with nitrous acid.



Hydrocortisone is the main product when adrenocorticotropin (ACTH) is perfused through isolated beef adrenal glands or ACTH is administered in patients with hyperfunctioning adrenal cortical tumors or corticosterone is perfused through adrenal glands. Hydrocortisone, m.p. 217-220°, is a white, odourless, bitter-tasting crystalline powder. It is practically insoluble in water; slightly soluble in ether; soluble in acetone, alcohol and methanol; freely soluble in chloroform. It is soluble in concentrated sulphuric acid with intense green fluorescence. Its stability properties are identical to those of cortisone.

Hydrocortisone Acetate (Brand Names : Cortisol acetate; 17-Hydroxycorticosterone 21-acetate; Cormol HC; Cortaid; Cortes; Epifoam; Hydrocortisat; Hydrocortone acetate; Lanacort; Litraderm; Pabracort; Biocortar). m.p. 223° (decomp), is an odourless, white, somewhat hygroscopic, tasteless, crystalline powder. It is practically insoluble in water, soluble in alcohol and chloroform; very soluble in dimethyl sulphoxide, pH of aqueous suspension in water is in between 5.5 to 7.5. It is soluble in concentrated sulphuric acid showing yellowish-green fluorescence. It is kept in well-closed containers and protected from light.

Hydrocortisone 21-Sodium Succinate (Brand Names : A-hydro Cort; Solu-Cortef; Corlan; EF-Cortelan Soluble; Hycorace; Buccalsone; Solu-Glyc; Intracort; Nordicort; Suxizon 300), m.p.

169-173°, is a white, odourless, hygroscopic, amorphous solid. It is very soluble in water and alcohol; very slightly soluble in acetone; practically insoluble in acetone. The ampuled dry material may be stored for an indefinite length of time. Solutions may be kept under refrigeration for 3 to 5 days. The compound is kept in airtight containers and protected from light.

Uses : Hydrocortisone is a glucocorticoid used in the treatment of all conditions of corticosteroid therapy. Although hydrocortisone is structurally related to cortisone, but there are quite significant difference in potencies.

The onset of hydrocortisone and improvement in cases of rheumatoid arthritis are rapid in comparison with cortisone acetate.

Adverse effects of hydrocortisone are the same as described for betamethasone.

Official

Cortisone Acetate, I.P., B.P.

Cortisone Tablets/Injection, B.P.. I.P.

Cortisone Acetate Tablets, U.S.P.

Sterile Cortisone Acetate Suspension, U.S.P.

Hydrocortisone Acetate, I.P., B.P.

Hydrocortisone Acetate Injection, I.P.

Hydrocortisone Hydrogen Succinate, B.P.

Hydrocortisone Sodium Phosphate, B.P.

Hydrocortisone Cream, B.P.

Hydrocortisone Acetate Cream, B.P.

Hydrocortisone Acetate Clioquinol Cream, B.P.

Hydrocortisone and Neomycin Cream, B.P.

Hydrocortisone Acetate and Neomycin Eye ointment/Ear Drops/ Eye Drops, B.P.

Hydrocortisone Acetate Injection, B.P.

Hydrocortisone Sodium Phosphate Injection, B.P.

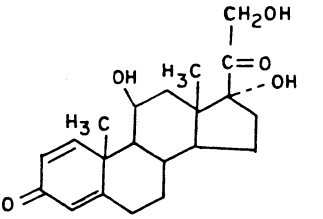
Hydrocortisone Sodium Succinate Injection, B.P.

Hydrocortisone Ointment, B.P.

PREDNISOLONE

Nomenclature : 11,17, 21-Trihydroxypregna-1,4-diene-3,20-dione.

Brand Names : Metacortandralone; Delta F; Delta-Stab; Δ^1 Dehydrocortisol; Δ^1-Hydrocortisone; Hydroretrocortine; Decaprednil; Meticortelone; Ultracortene-H; Precortilon; Precortisyl; Precortancyl; Cortalone; Predniretard; Prednilíderm; Solone; Prednicen; Dicortol; Hydeltra; Delta-Cortef; Paracortol; Deltisolone; Codelcortone; Hydrodeltisone; Prenolone; Hydrodeltalone; Sterolone; Sterane; Prednelan; Decortin H; Deltacortril; Scherisolon; Di-Adreson-F; Hostacortin H; Predonine; Nisolone; Ropredlone; Flamasone.



Prednisolone is 1,2-dehydro derivative of hydrocortisone which is prepared microbiologically in one step from the parent steroid, hydrocortisone. This is approximately three times as active as the natural hormones, as glucocorticoids and anti-inflammatory agents.

Prednisolone, m.p. 240-241° (decomp), is an odourless, white, crystalline, hygroscopic powder which is very slightly soluble in water; soluble in alcohol, acetone, chloroform, dioxane and methyl alcohol. It is kept in well-closed containers and protected from light.

Prednisolone acetate, m.p. 237-239° (decomp), is an odourless, white, crystalline powder which is practically insoluble in water; soluble in alcohol; slightly soluble in acetone and chloroform.

Other salts or derivatives of prednisolone are prednisolone butyl acetate, prednisolone sodium phosphate, prednisolone succinate, prednisolone hexanoate; prednisolone pivalate; prednisolone sodium metasulphobenzoate, prednisolone steaglate, prednisolone tebutate, methyl prednisolone N.F. and methylprednisolone sodium succinate.

Uses : Prednisolone is a glucocorticoid used as anti-inflammatory agent. The side-effects of prednisolone are similar to those of betamethazone.

Official

Prednisolone, B.P., I.P.

Prednisolone Tablets, B.P., I.P., U.S.P.

Prednisolone Acetate, I.P.

Prednisolone Pivalate, I.P., U.S.P.

Prednisolane Pivalate Injection, B.P.

Prednisolone Sodium Phosphate Injection, B.P.

Prednisolone Sodium Phosphate Injection, B.P., U.S.P.

Sterile Prednisolone Acetate Suspension, U.S.P.

Prednisolone Sodium Succinate for Injection, U.S.P.

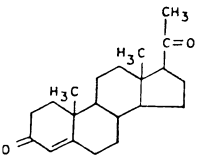
Sterile Prednisoline Tebutate Suspension, U.S.P.

Prednisolone Cream, U.S.P.

PROGESTERONE

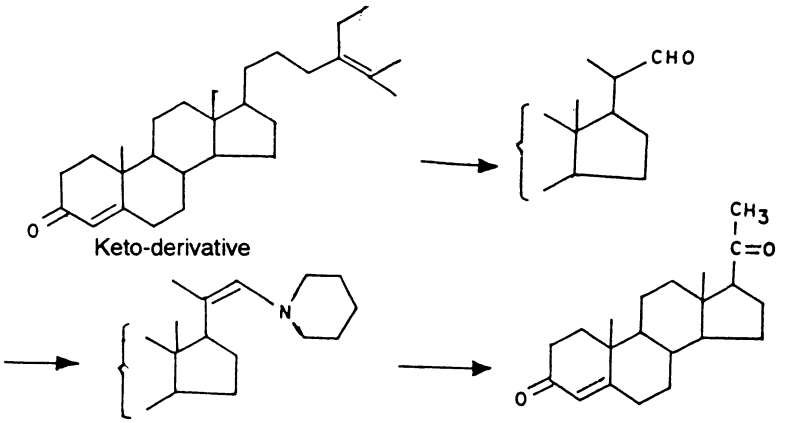
Nomenclature : Pregn-4-ene-3,20-dione; Δ^4-Pregnene-3,20-dione.

Brand Names : Corpus luteum hormone; Luteohormone; Corlutina; Gestone; Lutidon; Progekan; Corlutin; Corluvite; Fologenon; Gestormone; Hormoluton; Hormoflaveine; Lucorteum sol; Luteol; Luteovis; Lutex; Lutocyclin M; Lutoform; Lutogyl (Inj); Gestron; Prolidon (Inj); Percutacrine Luteinique; Primolut; Syngesterone; Flavolutan; Lipo-Lutin; Luteogan; Lutocylin; Luteodyn; Luteosan; Lutren; Lutromone; Nolutron; Progestin; Progesterol; Progestone; Prolutone; Cyclogest; Progestasert.



Progesterone is the natural progestational hormone concerned with the preparation for and maintenance of pregnancy. It is found in the pregnancy urine of woman, cows, mares and monkeys. It can be synthesized from many different starting materials such as ergosterol, cholesterol, saponins and stigmasterol. It is an active principle of the corpus luteum, secreted during the latter half of the menstrual cycle. If pregnancy ensues, secretion continues. It exerts an antiovulatory effect when administered during days 5 to 25 of the normal menstrual cycle.

The shortest commercial preparative route is from stigmasterol which is obtained from soybean oil. The stigmasterol is oxidized by Oppenauer oxidation to the corresponding ketone, with rearrangement of the cyclic double bond. Selective ozonolysis of the side-chain double bond forms a ketoaldehyde, which is converted to an enamine dichromate oxidation of which furnishes progesterone.



Progesterone

Progesterone exists in two crystalline forms of equal physiologic activity and which are readily interconverted. The α-form, m.p. 127-131°, and β-form, m.p. 121°, are orthorhombic.

Progesterone occurs as a white, crystalline powder that is colourless and stable in air. It is insoluble in water, soluble in alocohol and acetone and sparingly soluble in vegetable oils. Progesterone is sensitive to alkalies and to light. It should be stored in tight, light resistant containers. It is excreted chiefly as the reduction product pregnandiol. It is administered intramuscularly in order to obtain the maximum effect.

Uses : Progesterone suppreses uterine motility, acts to prepare the uterus to receive the fertilized ovum and is responsible for the development of breasts. It is used in many menstrual disorders and irregularities such as dysmenorrhoea, dysfunctional uterine bleeding, in the treatment of endometriosis and for the management of the post and premenstrual syndrome.

The side effects of progesterone may include gastro-intestinal disturbances, acne, fluid retention or oedema, weight gain, allergic skin rashes, mental depression, breast changes and altered menstrual cycles.

Official

Progesterone, B.P.

Progesterone Injection, B.P., U.S.P.

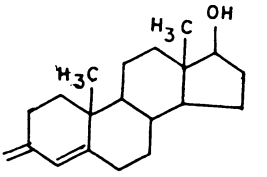
Progesterone Intrauterine Contraceptive System, U.S.P.

Sterile Progesterone Suspension, U.S.P.

TESTOSTERONE

Nomenclature : 17β-Hydroxyandrost-4-en-3-one; Δ^4-Androsten-17β-ol-3-one.

Brand Names : Geno-cristaux Gremy; Malestrone (amps); Orquisteron; Percutacrine Androgenique; Virosterone; Virormone; Testryl; Testrone; Homosteron; Oreton-F; Teslen; Primotest; Primoteston; Sustanon; Mertestate; Testobase.



Testosterone is the principal androgenic hormone of the testes, produced by the interstitial cells. It is isolated in minute amounts from testes, especially bull testes. About 90 to 270 mg are present in a ton of testes. It controls the development and maintenance of the male sex organs and male sex characters. There is no natural source rich enough from which testosterone can be prepared. However, it is synthesized on commercial scale from the androgenic excretory products found in stallion urine, cholesterol and sapogenins such as diosgenin and sarsasapogenin. The important intermediate dehydroandrosterone is efficiently transformed into testosterone by a microbial process. Testosterone is only weakly active orally. Testosterone propionate, acetate, cypionate, decanoate, enanthate, isocaproate, heptanoate, cyclopentane-propionate, undecanoate and phenylpropionate are all used in medicine.

Testosterone, m.p. 155°, is a white or creamy-white, odourless, crystals or crystalline powder. It is practically insoluble in water; soluble in alcohol, chloroform, dioxane, vegetable oils and ether; slightly soluble in ethyl oleate. It is protected from light.

In underdeveloped or adolescent males, testosterone increases the size of the scortum, phallus, seminal vesicles, and prostate; libido and sexual activity may also be increased.

Testosterone also produces systemic effects, such as an increased retention of nitrogen, calcium, sodium, potassium, chloride, and phosphate. This leads to an increase in skeletal weight, water retention, and increased growth of bone. The skin becomes more vascular and erythropoiesis is increased.

Uses : Testosterone is an androgen used as replacement therapy in male hypogonadal disorders and in adolescent males with delayed puberty. It is usually used as a subcutaneous implant

in a dose of 200 to 600 mg. Testosterone esters have been used in postmenopaual breast carcinoma and in osteoporosis.

The side-effects of testosterone include increase in nitrogen retention and skeletal weight, oedema, increased vascularity of the skin, hypercalcaemia and increased growth of the bone.

Official

Testosterone, B.P.

Testosterone Implants, B.P.

Testosterone Pellets, U.S.P.

Testosterene Phenylpropionate, B.P.

Testosterone Phenylpropionate Injection, B.P.

Sterile Testosterone Suspension, U.S.P.

Testosterone Propionate, B.P., I.P.

Testosterone Propionate Injection, B.P., U.S.P.

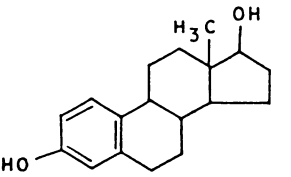
Testosterone Enanthate Injection, U.S.P.

Testosterone Cypionate Injection, U.S.P.

OESTRADIOL

Nomenclature : Estra-1,3,5-(10) -triene-3,17-diol.

Brand Names : Estradiol; Dihydrofollicular hormone; Dihydroxyestrin; Compudose 365; Dihydromenformon; Dimenformon; Diogyn; Femestral; Gynergon; Gynoestryl; Lamdiol; Macrodiol; Ovahormon; Ovasterol; Ovocyclin; Perlatanol; Primofol; Profoliol; Progynon-DH.



Oestradiol, an important and potent female sex hormone, contains ring A aromatic; the methyl group attached to C-10 is absent and the 3-hydroxyl group is phenolic. Naturally, it is formed by the ovary, placenta, testis and possibly by the adrenal cortex. It has been isolated from follicular liquor of sow ovaries (6 mg per ton) and from pregnancy urine of mares. It can be prepared by reduction of oestrone. Esters of oestradiol are absorbed more slowly than oestradiol.

Oestradiol, m.p. 173-179°, occurs as white or creamy-white, odourless, hygroscopic crystalline powder. It is practically insoluble in water; soluble in alcohol, chloroform, ether, acetone, dioxane and solutions of alkali hydroxides; sparingly soluble in

vegetable oils. It is stored in airtight containers and protected from light.

Oestradiol benzoate, cypionate, dipropionate, enanthate, hexahydrobenzoate, undecanoate and valerate are all used as drugs.

Uses : Oestradiol takes part in the development and maintenance of the female sex organs, secondary sex organs i.e. vagina, the fallopian tubes and uterus; the development of breasts, and genital tract and the distribution of hairs. It is used in deficiency states of menopausal syndrome, for the treatment of metastatic prostate cancer and breast cancer of postmenopausal women, for the suppression of lactation.

The side-effects of oestradiol therapy include sodium retention and oedema, nitrogen retention and weight gain, tenderness of the breasts, gynaecomastia in the male, alteration of liver function, jaundice, depression, headache and dizziness.

Official

Oestradiol Benzoate, B.P., I.P.

Oestradiol Benzoate Injection, B.P.

Oestradiol Dipropionate, I.P.

Sterile Estradiol Suspension, U.S.P.

Estradiol Cypionate Injection, U.S.P.

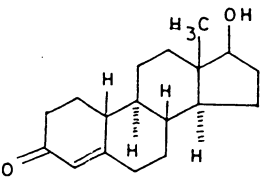
Estradiol Valerate Injection, U.S.P.

Estradiol Pellets/Tablets/Vaginal Cream, U.S.P.

NANDROLONE

Nomenclature : 17β-(1-Oxopropoxy) estr-4-en-3-one; 17-Hydroxyestr-4-en-3-one; 4-Estren-17β-ol-3-one; 19-Nortestosterone.

Brand Names : Norybol-19; Nortesto.



Nandrolone is prepared from alkyl ethers of estradiol. It occurs as crystalline substance, m.p. 112° and 124°; soluble in alcohol, ether and chloroform.

Nandrolone cyclohexylpropionate, benzoate, decanoate, hemisuccinate, laurate and phenylpropionate are all used as medicine.

Nandrolone Decanoate (Brand Names : Nandrolone laurate Deca-Durabol; Deca-Hybolin; Laurabolin V), m.p. 32-35°, is a white to creamy-white crystalline powder which is odourless or with a faint characteristic odour. It is practically insoluble in water; soluble in alcohol and acetone; freely soluble in chloroform, ether, fixed oils, and esters. It is stored at 2° to 10° in an atmosphere of nitrogen.

Uses : Nandrolone has anabolic and androgenic properties. Nandrolone cyclohexylpropionate and nandrolone laurate have been used in veterinary medicine.

The side-effects are similar to those of testosterone.

Official

Nandrolone Decanoate, B.P.

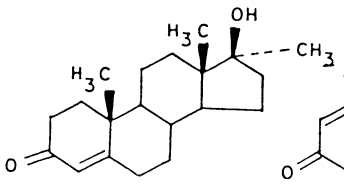
Nandrolone Decanoate Injection, B.P., U.S.P.

Nandrolone Phenylpropionate, B.P.

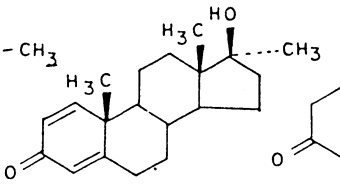
Nandrolone Phenylpropionate Injection, B.P.

Nandrolone Phenpropionate Injection, U.S.P.

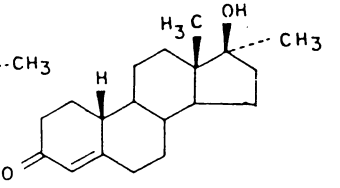
Miscellaneus Agents



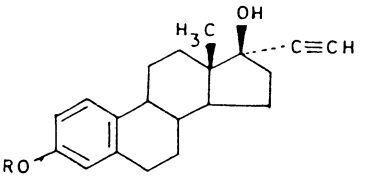
Methyltestosterone



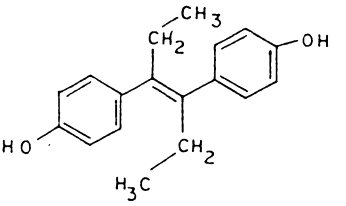
Methandienone



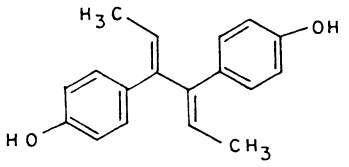
Norethandrolone



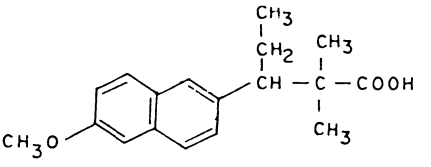
Ethinyloestradiol (R=H);Mestranol (R=CH_3)



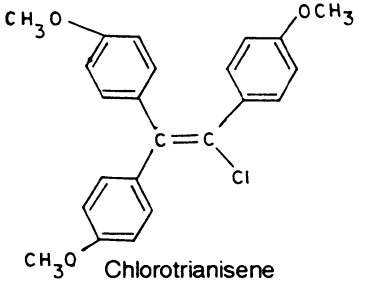
Stilboestrol



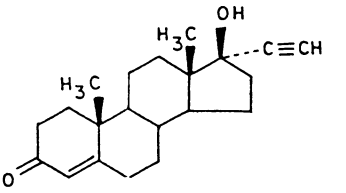
Dienoestrol



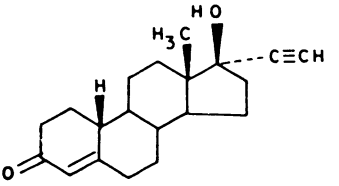
Methallenoestril



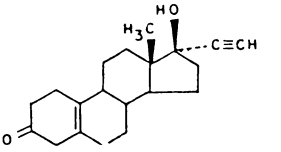
Chlorotrianisene



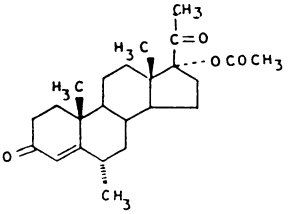
Ethisterone



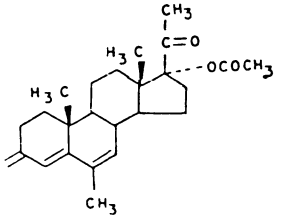
Norethisterone



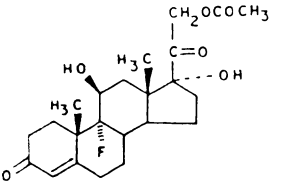
Norethynodrel



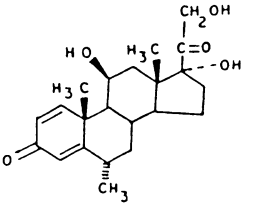
Medroxyprogesterone Acetate



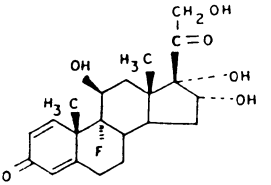
Megestrol Acetate



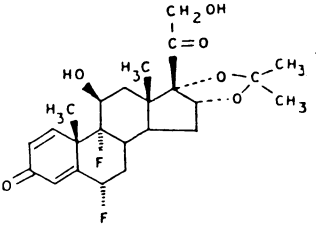
Fludrocortisone Acetate



Methylprednisolone



Triamcinolone



Flucinolone Acetonide

37

ANTINEOPLASTIC AGENTS

The chemotherapeutic agents which are used to treat cancer are called antineoplastic agents. Cancer is a tumour produced due to abnormal growth of some cells. It is not clear how cancer is caused. Generally cancer is produced by heavy smoking, constant physical irritation of any tissue of the body, chewing of tobacco, exposure to x-rays, ultraviolet rays and other ionizing radiation and by viruses.

Antineoplastic agents, also known as cytotoxic agents, are used to treat malignant disease when surgery or radiotherapy is not possible or remained ineffective. They are used as an adjunct to surgery or radiotherapy and in the treatment of leukaemia. Direct contact of cytotoxic agents may cause irritation of the skin, eyes and mucous membranes.

The two main types of antineoplastic drugs are the alkylating agents and the antimetabolites. Nitrogen mustards, ethyleneimine compounds and alkyl sulphonates are the main alkylating agents. The antimetabolites include some enzymes.

Majority of antineoplastic agents act by interfering with cell division. No cytotoxic agent has complete tumor selectivity and most will damage all rapidly dividing cells. Major adverse effects include bone marrow depression, alopecia, nausea, vomiting, stomatitis, dysphagia and diarrhoea. Hepatotoxicity, metabolic abnormalities, urinary tract, cardiac and nervous system toxicities are also reported with these drugs. Menstrual irregularities and premature menopause occur with long-term use of alkylating agents.

Combinations of antineoplastics are superior to single drug therapy leading to higher response rates and increased

duration of remissions. Improved response may be due to use of agents which work by different mechanisms.

ACTINOMYCINS

Actinomycins are the antibiotics first isolated from a culture of *Streptomyces antibioticus* by Waksman and Tishler in 1942. Now many naturally occurring actinomycins have been isolated from various genera of the actinomycetes. Actinomycins possess potent antitumor and cytotoxic effects and show bacteriostatic activity against gram-positive bacteria.

The actinomycins are yellow or red peptide-containing derivatives of phenoxazine. The chromophore of the molecule is 2-amino-4,6-dimethyl-3-oxophenoxazine-1, 9-dicarboxylic acid.

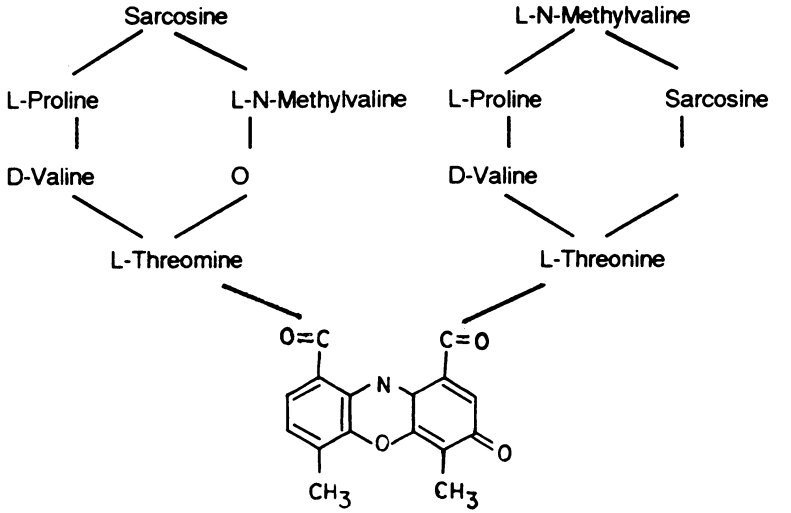
Actinomycin C is a mixture of actinomycin D (10%), actinomycin C_2 (45%) and actinomycin C_3 (45%). In actinomycin C series, the only variations that occur are in the two D-valine components. Actinomycin C_3 contains two D-alloisoleucine components in place of the two D-valine components. The structure of actinomycin C_2 contains one D-valine component and one D-alloisoleucine component. Changes in other subgroups give other series of actinomycines. For example, in the actinomycin X series, changes in the L-proline component occur. In the actinomycin E series, changes in the L-N-methylvaline component occur. In the actinomycin F series, additional sarcosine components are present in subgroup 3 substituted for proline components.

In addition to the naturally occurring amino acids found in C series, other amino acids may be present into the actinomycin molecule. Some actinomycins have been prepared by synthetic methods.

The cytotoxic effect of actinomycins is due to an inhibition of protein synthesis. They bind reversibly to the guanidine moiety of DNA.

Actinomycin F_1 (Brand Names : Actinomycin KS4; KS4) is an antibiotic produced by cultures of actinomycin C-elaborating strains of Streptomyces. It is considered to be a derivative of actinomycin C_2. Amino acid analysis indicates that the prolines present in actinomycin C_2 are substituted by sarcosine in actinomycin F_1. It is used as antineoplastic agent.

Dectinomycin (Brand Names : Actinomycin D; Meractinomycin; Actinomycin A_{IV}; Actinomycin IV/C_1/I_1/ X_1; NSC 3053; Cosmegen).



Dactinomycin is an antibiotic substance belonging to the actinomycin complex and produced by several *Streptomyces* species such as *S. Chrysomallus and S.,antibioticus.* The component amino acids in the cyclic peptides attached to carbon atom 1 and to carbon atom 9 are identical in nature and arrangement.

Dactinomycin is a bright, red, somewhat hygroscopic crystalline powder, m.p. 241-243° (decomp). It is soluble in water; freely soluble in alcohol; very slightly soluble in ether. It is stored at a temperature not exceeding 40° in air-tight containers and protected from light. Dilute solutions are very sensitive to light.

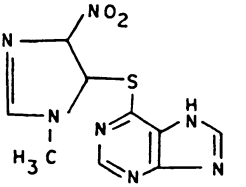
Uses : Dactinomycin is a highly toxic antibiotic with antineoplastic and immunosuppressant properties. It inhibits the proliferation of cells by forming a stable complex. It is used in the treatment of Wilms' tumour, rhabdomyosarcoma, tumors of the uterus and testis, in Ewing's sarcoma, osteogenic sarcoma, Kaposi's sarcoma and other solid tumors.

Adverse effects include toxicity, anorexia, nausea, vomiting, allergic reactions and local irritant effects, bone-marrow depression, anaemia and bleeding.

Official

Dactinomycin for Injection, U.S.P.

AZATHIOPRINE



Nomenclature : 6-[(1-Methyl-4-nitro-1H-imidazol-5-yl) thio]1H-purine.

Brand Names: Azothioprine; BW 57-322; NSC-39084; Azanin; Imuran; Imurel.

Azathioprine occurs as pale yellow odourless crystals or powder. It is practically insoluble in water, alcohol and chloroform; sparingly soluble in dilute mineral acids; dissolves in dilute solutions of alkali hydroxides. Solutions of azathioprine sodium for injection have a pH of 9.8 to 11.0; they are prepared by dissolving in Water for Injections, immediately before use. The drug is stored in airtight containers and protected from light.

Uses : Azathioprine is an immunosuppressant and antineoplastic agent. It is used in the treatment of leukaemia and mainly as an immunosuppressant for facilitating the survival of organ and tissue transplants. It is also used in lupus erythematosus, rheumatoid arthritis, renal disorders, chronic active hepatitis and some severe skin disorders.

The side-effects include depression of the bone marrow, gastro-intestinal disorders, joint pains, rashes, drug fever, liver damage, and pancreatitis. Solutions for injection are irritant.

Official

Azathioprine Sodium for Injection; U.S.P.

Azathioprine Tablets, B.P., U.S.P

BUSULPHAN

Nomenclature : 1,4-Butanediol dimethanesulfonate; 1,4-Bis (methanesulfonoxy) butane.

Brand Names : Methanesulphonic acid tetramethylene ester; CB-2041; GT 41; Misulban; Mitosan; Myleran; Myelosan; Myeleukon; Myelolukon; Sulfabutin; Meilucin.

$$CH_3—SO_2—O(CH_2)_4—O—SO_2—CH_3$$

Busulphan is tetramethylene di-(methanesulphonate). It is prepared from methanesulphonyl chloride and 1,4-butanediol.

$$HO—(CH_2)_4—OH + 2\ CH_3\ SO_3H \longrightarrow CH_3—SO_2—O(CH_2)_4—O—SO_2—CH_3$$

Busulphan, m.p. 114-118°, is a white crystalline powder. It is sparingly soluble in water, but dissolves slowly as hydrolysis takes place; soluble in alcohol and acetone. It is stored in airtight containers and protected from light.

Uses : Busulphan is an antineoplastic agent and has depressant action on bone marrow. It is used in the palliative treatment of chronic granulocytic leukaemia.

The most important side-effects of busulphan in high dosage are leukopenia, thrombocytopenia and haemorrhage symptoms.

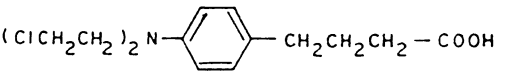
Official

Busulfan Tablets, B.P., U.S.P.

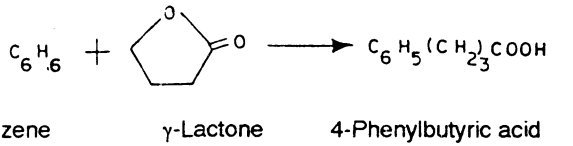
CHLORAMBUCIL

Nomenclature : 4-[Bis (2-chloroethyl) amino] benzenebutanoic acid; 4-[b-Bis-(2-chloroethyl) amino) phenyl] butyric acid.

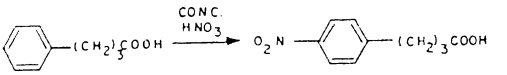
Brand Names : CB 1348; Amboclorin; Leukeran.

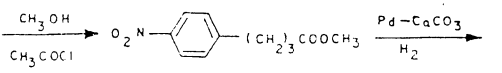


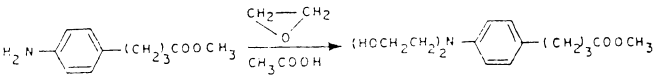
Chlorambucil is a nitrogen mustard which is synthesized from 4-phenylbutyric acid. The 4-phenylbutyric acid is prepared from benzene and γ-butyrolactone by heating with aluminium chloride, followed by acidification with concentrated hydrochloric acid.

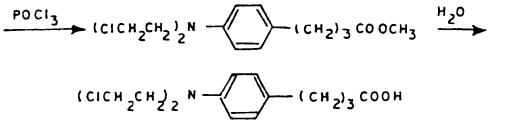


Benzene γ-Lactone 4-Phenylbutyric acid









Chlorambucil

Chlorambucil, m.p. 64-66°, is a white or off-white crystalline or granular powder. It is practically insoluble in water; soluble in alcohol, acetone, chloroform and dilute solutions of alkali hydroxides. It is stored in airtight containers and protected from light.

Uses : Chlorambucil is an antineoplastic agent and is most valuable in lymphocytes. It is used in the treatment of chronic lymphocytic leukaemia, Hodgkin's disease, in carcinoma of the breast, ovary and testes.

The side-effects include bone-marrow depression, gastro-intestinal disorders, hepatotoxicity, skin rashes, central neurotoxicity, including seizures, interstitial pneumonia and pulmonary fibrosis.

Official

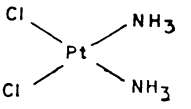
Chlorambucil Tablets, B.P., U.S.P.

CISPLATIN

Nomenclature : Diamminedichloroplatinum; cis-Diamminedi-chloroplatinum.

Brand Names : *cis*-Platinum II; *cis*-DDP; CACP; CPDC; DDP; NSC-119875; Cisplatyl; Neoplatin; Platinex; Platinol.

The antineoplastic agent cisplatin is a platinum-containing complex.



It occurs as deep yellow solid, m.p. 270° (decomp). It is insoluble in most common solvent and is changed to *trans*-form in aqueous solution. Aqueous solutions are stable for 24 hours at room temperature. It is not necessary to prepare a solution immediately before use provided it was protected from light.

Uses : Cisplatin is used in the treatment of metastatic tumours of testes, ovary and bladder.

Severe nausea and vomiting occur in most patients during treatment with cisplatin. Serious toxic effects on kidney, bone marrow, and ears have been reported.

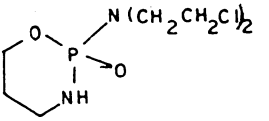
Official

Cisplatin for Injection, U.S.P.

CYCLOPHOSPHAMIDE

Nomenclature ; N,N-Bis (2-chloroethyl) tetrahydro-2H-1,3,2-oxazaphosphorin-2-amine 2-oxide.

Brand Names : Cyclophosphane; Cytophosphane; B 518; Cytoxan; Endoxan; Procytox; Sendoxan.



Cyclophosphamide, m.p. 41-45°, is a fine, white crystalline powder. It liquefies upon loss of its water of crystallization. It is soluble in water, alcohol, benzene, ethylene glycol, carbon tetrachloride, dioxane; sparingly soluble in ether and acetone.

Uses: Cyclophosphamide is an antineoplastic agent which has marked immunosuppressant properties. It is used in the treatment of a variety of malignant diseases including Burkitt's lymphoma, Hodgkin's disease, leukaemia, myeloma and mycosis fungoides. It is also used in the treatment of various solid tumours such as tumours of the breast, cervix, lung and ovary.

Leucopenia, urinary complications, alopecia, hyper pigmentation of skin, gastro-intestinal disorders, hepatotoxicity, disturbance of carbohydrate metabolism and secretion of antidiuretic hormone, etc, are some side-effects of cyclophosphamide therapy.

Official

Cyclophosphamide for Injection, U.S.P.

Cyclophosphamide Injection, B.P.

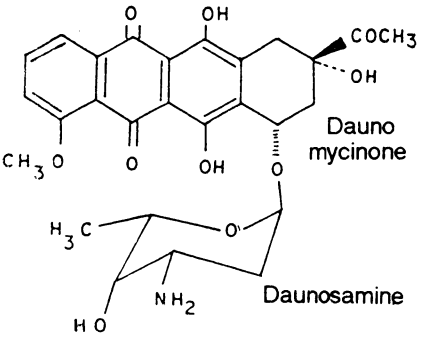
Cyclophosphamide Tablets, B.P., U.S.P.

DAUNORUBICIN

Nomenclature : 8-[Acetyl-10-(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl) oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-1-methoxy-5-12-naphthacenedione.

Brand Names : Daunomycin; Leukaemomycin C; Rubido-mycin; Cerubidin.

Daunorubicin is a glycoside formed by a tetracyclic aglycone, daunomycinone (C_{21} H_{18} O_8) and an amino sugar, daunosamine (C_6 $H_{13}NO$). It is an antineoplastic anthracycline antibiotic produced by *Streptomyces coeruleorubidus or S. peucetitus.*



Daunorubicin Hydrochloride (Brand Names : Cerubidine; Daunoblastina; Ondena), m.p. 188-190° (decomp), occurs as thin red needles. It is soluble in water, methanol, aqueous alcohols; practically insoluble in chloroform, ether and benzene. Colour of aqueous solution changes from pink at acid pH to blue at alkaline pH.

Uses : Daunorubicin is an antineoplastic antibiotic agent. Its hydrochloride is given in association with vincristine and prednisone in acute lymphoblastic leukaemia.

Cardiotoxicity is more likely when the total dose of daunorubicin exceeds 500 mg in adults.

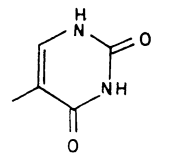
Official

Daunorubicin Hydrochloride for Injection, U.S.P.

FLUOROURACIL

Nomenclature : 5-Fluoro-2,4-(1H, 3H) -pyrimidinedione; 2,4-Dioxo-5-fluoropyrimidine.

Brand Names : Ro 2-9757; NSC 19893; Adrucil; 5-Fu; Arumel; Efudex; Efudix; Fluril; Fluracil; Fluoroplex; Fluro uracil; Timazin.



Fluorouracil, a pyrimidine analogue, m.p. 282-283° (decomp), is a white, odourless, crystalline powder. It is sparingly soluble in water; slightly soluble in alcohol; practically insoluble in chloroform and ether. A 1 per cent solution has a pH of 4.3 to 5.3.

Uses : Fluorouracil is an antineoplastic agent which is used in malignant neoplasms, especially those of the gastro-intestinal tract, breast, liver, genito-urinary system, and pancreas.

The main adverse effects of fluorouracil are on the bone marrow and the gastro-intestinal tract. Leucopenia, stomatitis, gastro-intestinal ulceration, bleeding and severe diarrhoea are signs that treatment should be stopped.

Official

Fluorouracil Cream, B.P., U.S.P.

Fluorouracil Injection, B.P., U.S.P.

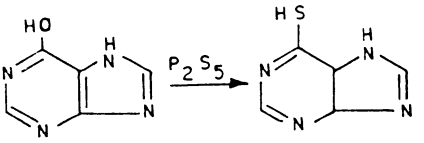
Fluorouracil Topical Solution, U.S.P.

MERCAPTOPURINE

Nomenclature : 6-Purinethiol; 6-Mercaptopurine.

Brand Names : 6-MP; Leukerin; Mercaleukin; Purinethol; NSC-755; Purinethiol; WR -2785.

Mercaptopurine, a 6-thiol analogue of adenine, is prepared by the action of phosphorus pentasulphide on hypoxanthine.



Mercaptopurine

Mercaptopurine, m.p. 313-314° (decomp), is a yellow, odourless, crystalline powder. It is practically insoluble in water, acetone and ether; slightly soluble in alcohol; soluble in hot alcohol and in solutions of alkali hydroxides; slightly soluble in M sulphuric acid. It is stored in air-tight containers and protected from light.

Mercaptopurine acts as an antimetabolite for adenine in the synthesis of nucleotides by living cells. It is thought to act by entering leukaemic blood cells and interfering with their function. It is metabolized in the body to 6-thiouric acid. After the intracellular conversion of mercaptopurine to active nucleotides, it interferes with nucleic acid synthesis.

Uses : Mercaptopurine is an antineoplastic agent which acts as an antimetabolite. It also has immunosuppressant properties. It is used, usually with other agents, in the treatment of leukaemia and various auto-immune disorders.

The side-effects of mercaptopurine include bone-marrow depression, hypoplasia and hepatotoxicity.

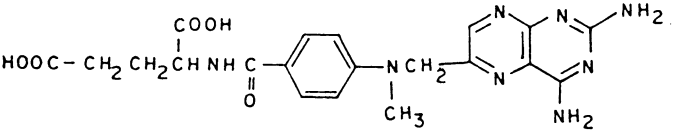
Official

Mercaptopurine Tablets, B.P., U.S.P.

METHOTREXATE

Nomenclature : N-[4-[(2,4-Diamino-6-pteridinyl) methyl] methylamino] benzoyl] -L-glutamin acid.

Brand Names : Methylaminopterin; Amethopterin; MTX; CL-14377; Emtexate; NSC-740 A-Methopterin; WR-19039; Methotrexatum.



Methotrexate is a closely related compound with folic acid (pteridine derivative). It is a yellow to orange-brown crystalline powder, m.p. 185-204° (decomp). It is practically insoluble in water, alcohol, chloroform and ether; dissolves in solutions of mineral acids and in dilute solutions of alkali hydroxides and carbonates with decomposition. It is placed in air-tight containers and protected from light. Within the cell it is reduced to dihydrofolic and then tetrahydrofolic acid.

Uses : Methotrexate is an antineoplastic agent which acts as an antimetabolite of folic acid. It also has immunosuppressant properties. It is used to treat leukaemia, different cancerous diseases and psoriasis.

Early signs of toxicity with methotrexate include leucopenia, anaemia, thrombocytopenia, ulceration of mouth and gastro-intestinal effects.

Official

Methotrexate Injection, B.P.

Methotrexate Sodium Injection, U.S.P.

Methotrexate Tablets, B.P., U.S.P.

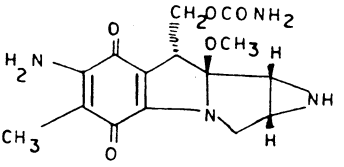
MITOMYCIN

Nomenclature : 6-Amino-1,1a,2,8,8a,8b-hexahydro-8-hydroxymethyl-8a-methoxy-5-methylazirino (2',3', : 3,4)-pyrrolo [1,2-a] indole-4,7- dione carbomate.

Brand Names : Mitomycin C; Mitomycine C; NSC-26980; Mutamycin, Mitocin-C; MMC; Ametycine

Mitomycin, m.p. 360°, is an antineoplastic antibiotic produced by the growth of *Streptomyces verticillatus* or

Streptomyces caespitosus. It occurs as a blue-violet crystalline powder. It is soluble in water, acetone, methyl alcohol, butyl acetate, and cyclohexanone. A 0.5% solution in water has a pH of 6 to 8. It is slightly soluble in benzene, carbon tetrachloride, ether; practically insoluble in petroleum ether. It is stored in airtight containers and protected from light.



Unlike most other antibiotics, it is activated *in vivo* to a bifunctional or trifunctional alkylating agent. After activation it binds preferentially to the guanine and cytosine moieties of DNA, leading to cross-linking of DNA, thus inhibiting DNA synthesis and function. Mitomycin C contains three groups that can damage cells; the quinone that can participate in free radical reactions generating superoxides, and aziridinyl and urethane functions that can take part in DNA alkylation. Activation of mitomycin proceeds by means of reduction of the quinone and loss of a methoxy group. This is followed by alkylation of DNA with the formation of interested cross links, resulting in inhibition of DNA synthesis, DNA fragmentation and cell death.

Mitomycin disappears rapidly from the blood after intravenous injection. It is widely distributed and metabolized mainly in the liver. Following normal doses about 10% of a dose is excreted unchanged in the urine; small amounts are also present in bile and faeces.

Uses : Mitomycin is a highly toxic antibiotic with antineoplastic properties. It is used, with other antineoplastic agents, in the palliative treatment of gastric, colon, breast and pancreatic adenocarcinomas as well as certain head, bladder, rectum, lung, cervix and neck tumours and chronic myelogenous leukaemia.

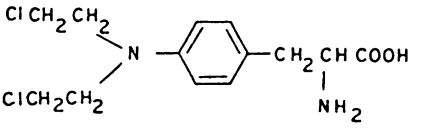
It is also used as a bladder instillation. The short duration of response (1 to 3 months) and the toxicity causing myelosuppression has limited the use of mitomycin as a single agent. It is commonly used with other drugs for the treatment of gastric adenocarcinomas.

The main adverse effect of mitomycin is delayed cumulative bone-marrow suppression. Other side-effects include renal damage, pulmonary reactions, gastro-intestinal toxicity, dermatitis, alopecia, fever and malaise.

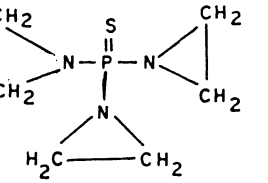
Official

Mitomycin for Injection, U.S.P.

Miscellaneous Agents



Melphalan



Thiotepa

Official

Melphalan, B.P.

Melphalan Injection, B.P.

Melphalan Tablets, B.P.

Thiotepa, B.P.

Thiotepa Injection, B.P.

GLOSSARY OF MEDICAL TERMS

Abortifacient : A drug or agent inducing expulsion of a fetus.

Abscess : A localized collection of pus.

Aching : Suffering from an ache or pain.

Acidosis : Decrease of alkali and increase in acid contents in bodily fluid.

Acrocyanosis : A condition occurring in young women, in which there is persistent blueness of hands, feet, nose and ear.

Actinomycosis : A fungal disease caused by Actinomyces.

Addiction : Habitual; compulsive use of narcotics.

Addison's disease : A deficiency disease of adrenal cortex (lack of aldosterone and cortisol).

Adjuvant : A supporting thereby to help in promotion the action of main treatment; assist or aid .

Adrenergic blocking : The sites in the body on which adrenaline and comparable stimulants of the sympathetic system act.

Adrenolytic : A substance that antagonises the action of adrenaline or noradrenaline.

Agonist : A substance that initiates a response by acting on a specific receptor.

Agranulocytosis : Marked reduction or absence of granulocytes. It usually results from bone marrow depression.

Akinesia : Loss or impairment of voluntary movement; immobility.

Akinetic : Without movement.

Alcoholism : A condition of mind and body produced by taking alcohol.

Alkalosis : Excess of alkali or reduction of acid in the body.

Alopecia : Baldness; falling of hairs.

Amaenia : A deficiency of haemoglobin due to lack of red blood cells.

Amblyopia : Defective vision for which no recognizable cause exists in any part of the eye.

Amebicide (Amoebicide) : An agent fatal to amoebas, especially to *Entamoeba histolytica.*

Amenorrhoea : Absence of menses; Absence of the menstrual flow during the time of life at which it should occur.

Amnesia : Partial or complete loss of memory.

Amoebiasis : Dysentery caused by an amoeba *Entamoeba histolytica.*

Amyloidosis : A condition in which deposits of complex protein, known as amyloid, are found in various parts of the body; waxy disease.

Anaemia : A condition of inadequate red blood carpulses or haemoglobin in the blood.

Anaerobic : Relating to a bacteria having the power to live without air.

Anaesthesia : A state characterized by loss of sensation.

Anaesthetics : Drugs and other measures which produce insensibility to external impressions.

Analgesia : Loss of pain sensation; analgesic; drugs causing temporary loss of the sense.

Anaphylaxis : A hypersensitive state of the body to a foreign protein.

Angia pectoris : Heart stroke; severe constricting pain on the chest due to ischaemia of the heart muscle, usually caused by coronary disease.

Anginal pain : Pain due to swellings of the throat or other cause of difficulty in breathing.

Angiogenesis : An allergic disorder, characterized by development of oedematous area of skin mucous membranes or vicera.

Angio-oedema : Swelling of vessel; vascular swelling.

Ankylosing spondylitis : Arthritis of the spine, resembling rheumatoid arthritis; immobilizing of one or more vertebrae due to inflammation.

Ankylosis : Stiffening or fixation of a joint.

Anorexia : Loss of appetite for food; diminished appetite.

Anorexia nervosa : A personality disorder manifested by extreme aversion to food.

Anovulatory : Not accompanied by production of and discharge of an ovum.

Antacid ; A substance that neutralizes acidity.

Antagonist : Something opposing or resisting the action of another.

Anthrax : A very serious disease occurring in sheep and cattle and persons dealing them.

Antiadrnergic : Inhibiting, counteracting, or modifying adrenergic action.

Antiamoebic : A drug or agent active in the treatment of infection with amoebas.

Antiarrhythmic : Preventing or effecting against arrhythmia.

Antibacterial : An agent that prevents or hinders the growth of or destroy bacteria.

Antibiotic : An antibacterial agent derived from micro-organisms, such as penicillin, streptomycin, etc.

Anticoagulants : Drugs which prevent coagulation of the blood.

Anticonvulsant : A therapeutic agent that prevents or arrests convulsions.

Antidepressant : Any drug used for the treatment of depression.

Antidote : Remedies which neutralize the effects of poisons.

Antiemetic : Preventing or arresting vomiting; drug for controlling nausea and vomiting.

Antiepileptic : Suppressing or controlling epileptic seizures; anticonvulsant.

Antifungal : Any agent useful in treating infections caused by fungi; suppressing or destroying fungi; effective against infections by fungi.

Antihistamic : Relating to drugs which antagonize the action of histamine.

Antihistamine : Drugs which antagonize the action of histamine.

antihypertensive : Counteracting high blood pressure; an agent that reduces high blood pressure.

Antihypotensive : Drugs used to treat lower blood pressure.

Anti-infective : Counteracting infection.

Antimetabolite : A group of drugs used to treat certain forms of malignant disease; Agent which is a competitive inhibitor of a natural endogenous substrate of enzyme.

Antimuscarinic : Drugs used to treat effects of a poisonous alkaloid obtained from certain mushrooms, as *Amanita muscaria*.

Antineoplastic : Inhibiting the development of neoplasms.

Antiparkinsonian : Alleviating the symptoms of parkinsonism.

Antipruritic : A medical agent that relieves or prevents itching.

Antipsychotic : Agents used to cure psycotic disorders.

Antipyretic : Drugs used to reduce temperature in fever.

Antirachitic : An agent for the prevention or cure of rickets.

Antiseptic : Drugs which prevent putrefaction.

Antiserotonin : Inhibiting or modifying serotonin activity.

Antispasmodic : Relieving or preventing convulsions or spasmodic pains.

Antitrichomonal : Inhibiting a genus of flagellate protozoa found in the intestines of man.

Antitussive : Agents that prevents or relieve cough.

Anxiety : A feeling of apprehension, worry, uneasiness, or dread especially of future.

Aplasia : Absence or defective development of a tissue or organ.

Aplastic : Incomplete development or structures as in aplastic anaemia.

Apnoea : Transitory cessation of breathing.

Aribоflavinosis : A state produced by a deficiency of riboflavine in the diet.

Arrhythmia : Abnormal rhythm of the heart.

Arthralgia : Pain in joint.

Arthritis : Inflammation of joint.

Articular : Relating to a joint.

Ascites : An accumulation of serous fluid in the peritoneal cavity.

Asepsis : Absence of microorganisms; prevention of sepsis

Aspergillosis : A disease caused by invasion of the lung by the fungus, *Aspergillus fumigatus*.

Asthma : Breathing problem accompanied by wheezing caused by a spasm of the bronchial tube or by swelling of mucous membrances; paroxysmal attack of difficulty in breathing.

Astringent : Agent that has a constricting or binding effect.

Asymptomatic : Symptomless; exhibiting no symptoms.

Ataxia : Loss of power of governing movements, though the power necessary to make the movements is still present.

Atrophy : A decrease in size of an organ or tissue.

Auditory acuity : Quick sensibility of the organ of hearing.

Auricular fibrillation : Rapid irregular twitching of the muscular wall of cardiac atria.

Azospermia : Absence of spermatozoa in the semen.

Bactericide : An agent that destroys bacteria, but not necessarily their spores.

Bacteriostatic : Relating to the growth of bacteria, a process of bringing bacteria by preventing their nourishment and growth.

Balantidiasis : A form of dysentery caused by a protozoa known as *Balantidium coli*, a common parasite in pigs.

Blastomycosis : Any disease caused by yeast like fungi, especially species of Blastomyces.

Blood pressure : The pressure exerted by the blood on the vessel walls.

Bradycardia : Slowness of the heart beat .

Bradykinesia : Extreme slowness in movement.

Bradypnea : Slow or laboured breathing.

Bronchial : Relating to bronchi and bronchial tubes.

Bronchitis : Inflammation of mucous membrane of the bronchial tubes.

Bronchodilator : An agent which dilates the bronchi.

Bronchoconstrictor : Any substance which decreases the caliber of the pulmonary air passages.

Bronchospasm : Temporary narrowing of the bronchi due to violent, involuntary constriction of the smooth muscle of the bronchi.

Brucellosis : A long continued fever which occurs on shores and islands of the Mediterranean; Malta fever; Undulant fever; Mediterranean fever; Rock fever.

Buerger's diseasee : An inflammatory disease involving the blood-vessels of the limbs, thromboangitis obliterans.

Burkitt's lymphoma : A malignant lymphoma of children, typically involving the retroperitoneal area and the mandible, but sparing the peripheral lymph nodes, bone marrow, and spleen.

Candidiasis : Disease or infection caused by *Candida* species.

Carcinoma : A malignant new growth derived from epithelial and glandular tissue; cancer.

Cardiothoracis : Pertaining to the heart and thorax.

Cardioversion : The condition of heart being turned or placed away from its normal position.

Catalepsy : A state of sustained immobility.

Chancroid : A soft or non-syphilitic venereal sore caused by a micro-organism known as *Haemophilus ducreyi.*

Cheilosis : An eczematous condition of the lips developed due to deficiency of vitamin B complex in diet.

Chemotherapy : Use of chemical agent to arrest the progress of disease in the body; drugs used in bacterial diseases including cancer.

Chlamydial infection : Infection due to a genus of micro-organism responsible for non-specific urethritis, ornithosis, psittacosis and trachoma.

Cholera : An acute infectious disease characterized by severe intestinal disturbances.

Cholinergic : Relating to the basic compound choline which is essential to the function of liver.

Cholinesterase : Any enzyme found in blood and in various other tissues that catalyzes hydrolysis of choline esters.

Choriocarcinoma : Malignant tumour of chorionic tissue.

Chorion : The outermost foetal membrane.

Congestion : The presence of an abnormal amount of blood in the vessels of a part.

Congestive : Relating to congestion.

Congestive heart failure : Inability of heart to maintain cardiac output.

Conjuctiva : The delicate transparent membrane which lines the inner surface of the eyelids.

Conjunctivities : Inflammation of the conjunctive tissues.

Constipation : A condition in which the bowels are opened incompletely, or with difficulty.

Convulsion : Rapidly alternating contractions and relaxation of the muscles violent agitation or disturbance; a violent spasm.

Corneal : Relating to the clear membrane in front of the eye through which light passes to it.

Corneal lesions : Disease of eye.

Corticotrophin : Adrenocorticotrophic hormone (ACTH) of the pituitary gland.

Cough : A sudden indrawing of air with glottis wide open.

Cryptococcal : Relating to a genus of yeast *Cryptococcus neoformans.*

Cryptococcosis : A rare disease due to infection with a yeast known as *Cryptococcus neoformans.*

Crystalluria : The excretion of crystalline materials in the urine; appearance of crystals in urine.

Cushing's disease : Disorder due to elevated levels of plasma corticoids.

Cutaneous : Belonging to the skin.

Cyanosis : A condition of blueness seen particularly about the face and extremities and the blood is not properly oxygenated in the lungs.

Cycloplegia : Paralysis of accommodation, loss of power in the ciliary muscle of the eye.

Cytotoxic : Any substance which is toxic to cells. Generally applied to anticancer agents; destructive to cell.

Debilitate : To produce weakness of tonicity in functions or organs of body.

Decongestant : Relief of congestion.

Delirium : Abnormal mental condition based on illusions or hallucinations. A state of prevented consciousness in which an irregular discharge of nervous energy goes on causing incoherent talk, delusion and ill-regulated muscular action.

Dementia : A general mental deterioration due to organic or psychological factors.

Demulcent : A substance which exerts a soothing or protective influence upon the surface of alimentary canal or mucous membranes or skin.

Depression : Mental depression; a psychiatric state representing diminution of activity.

Dermatologic : Relating to the science of the skin and its diseases.

Dermatomyositis : A disease of unknown origin, characterized by erythema of the skin and wasting of the muscles.

Dermatophyte : A fungus pathogenic for the skin; a fungal parasite which grows in or on the skin.

Dermatoses : Any disease of the skin.

Dermititis : Inflammation of the skin.

Diabetes insipidus : Excessive urination caused by inadequate secretion of vasopressin, the antidiuretic hormone.

Diabetes mellitus : A disorder of carbohydrate metabolism, characterized by excess sugar in blood and passage of sugar in urine resulting from inadequate production or utilization of insulin.

Diaphoretic : Perspiration promoting remedies.

Diarrhoea : Looseness of bowels; abnormal frequent loosened discharge from the bowels.

Diastolic blood pressure : The point of least pressure in the arterial vascular system.

Dilatation : Expansion of an organ, orifice or vessel.

Diluent : Watery fluid of a non-irritating nature which are given to increase the amount of perspiration or of urine.

Diphtheria : An acute infectious disease accompanied by a membranous exudation on a mucous surface, generally on the tonsils and back of the throat.

Diplopia : Double vision.

Disinfectant : The process of rendering harmless persons, articles, rooms, etc, which are liable to communicable diseases.

Distension : Swelling, dilation; expansion.

Diuresis : Excretion of urine in large volumes.

Diuretic : Promoting the excretion of urine; an agent that increases the amount of urine.

Dizziness : A sensation of whirling or feeling tendeney to fall.

Dracontiasis (Dracunculiasis) : Infection with the nematode *Dracunculus medinensis;* characterized by ulcers of the feet and legs.

Drowsiness : Sleepy condition.

Dyscrasias : A diseased constitution.

Dysentery : An infectious disease with a local lesion in the form of inflammation and ulceration of lower portion of the bowels; frequent watery stool often with blood and mucous.

Dysfunction : Abnormal functioning of any organ or part.

Dysmenorrhoea : Painful menstruation.

Dyspepsia : Indigestion.

Dysphagia : Difficulty in swallowing.

Dyspnoea : Difficulty in breathing; shortness of breath.

Dysuria : Difficulty or pain in urination.

Eclampsia : Convulsions arising in pregnancy.

Effusion : Escape of fluid into a part.

Electroence phalography : Recording of a regular, rhythmical change of electrical potential in the brain due to the rhythmic discharge of energy by nerve cells.

Electrolytic : Retating to electrolysis or a substance whose solutions are capable of conducting electric current.

Embolism : Plugging of a small blood vessel by a transported clot, vegetation, bacteria or other foreign material.

Embolus : An abnormal particle circulating in the blood stream, as an air bubble or blood clot.

Emergence reactions : Reaction rising out from a fluid or other surrounding substances.

Emphysema : The presence of air in the interstices of the connective tissues of a part.

Endocarditis : Inflammation of the smooth membrane lining the heart.

Endogenous : Originating or produced within the organism or one of its parts.

Endometriosis : A condition in which the cells lining the interior of the uterus is found in other parts of the body.

Endometrium : The mucous membrane comprising the inner layer of the uterine wall.

Endoscopy : Examination of the interior of a canal or hollow viscus.

Enterococcus : A Streptococcus usually found in the intestine.

Enterohepatic : Relating to infections, often fatal, disease affecting the intestines and liver of various wild birds, turkeys and chicken.

Enuresis : Involuntary passage of urine, usually occurring at night or during sleep.

Eosinophilia : Increased eosinophils in the blood.

Epigastric : The abdominal region lying directly over the stomach.

Epilepsy : A disease of the brain due to abnormal electrical discharge.

Epileptic seizure : A nervous attack characterized by sudden loss of consciousness, attended with convulsions.

Episode : A parenthetic addition; an incident in the course of a series of events.

Erysipelias : A disease characterized by diffuse inflammation of the skin, or of sub-cutaneous cellular tissue, attended with fever.

Erythem : Reddening of the skin.

Erythema multiforma : An allergic skin eruption.

Erythematosus : Relating to reddening of the skin (erythema).

Erythrocytic : Relating to red blood carpuscles.

Eunuchoidism : A state in which testes fail to function.

Euphorbia : A feeling of well-being.

Ewing's sarcoma : A malignant tumour of bone whose parenchyma consists of cells resembling endothelial or reticulum cells.

Excipient : Inert substance added to a prescription.

Excitability : Capable of being excited; ability to react to stimulus or to be aroused to activity by a stimulus.

Exfoliate dermatitis : Skin disease causing to separate in scales or splitting into scales.

Exocrine : Secretion of glands reaching an epithelial surface either directly or through duct.

Exoerythrocytic : Outside of erythrocytes.

Exophthalmos : Protrusion of the eyeballs.

Extracellular : Ourtside of a cell or cells.

Extrapulmonary : Outside of the pulmonary vein. Applied to other descending motor pathways.

Extrapyramidal : Outside of the pyramidal tracts.

Extrasystoles : Premature contraction of one or more of the chambers of the heart.

Extremity : The extreme or terminal point.

Falciparum malaria : A severe form of malaria caused by *Plasmodium falciparum* characterized by pyroxysms occurring at irregular intervals.

Fibrillation : Rapid contraction of muscles; abnormal action of the heart muscles.

Fibrosis : An increment in fibrous connective tissues.

Filaria : Parasitic, thread like worm causing elephantiasis.

Flare : A flush or spreading area of redness.

Flatulence : A collection of gas in the stomach or intestine.

Fragility : Brittleness.

Friedlander's bacillus : A microorganism known as *Klebsiella pneumoniae.*

Frostbite : The condition resulting from the action of extreme cold; Frostnip.

Fungicide : Any substance that has a destructive action upon fungi.

Fungistatic : Having an inhibiting action upon the growth of fungi.

Gametocyticide : Agents affecting gamete producing cells.

Gangrene : Death of a part of the body; a necrosis or death of tissue usually due to deficient or absence of blood supply.

Gastric : Relating to stomach.

Gustritis : Inflammation of the stomach.

Gastroenteritis : Inflammation of the mucous membrane of both stomach and intestine.

Genitourinary : Consisting of kidney, ureter, bladder and genital organs.

Germicidal : A substance that destroys germs.

Germicide : An agent which is destructive to germs or microbes.

Giardiasis : A condition caused by a parasite organism known as *Giardia lamblia* which is found in stomach. The symptoms include explosive diarrhoea, abdominal pain and nausea.

Giddiness (Vertigo) : A condition in which the affected person loses the power of balancing himself, and has a false sensation.

Glaucoma : A disease of eye after the age of 50 years.

Glomerular : Relating to a compact cluster, as of capillary blood vessels; a cyme condensed into a headlike cluster.

Glossitis : Inflammation of tongue.

Gluconeogenesis : Formation of glycogen from noncarbohydrate sources such as amino acid or fatty acid.

Glucosuria : The urinary excretion of glucose.

Glycosuria : The urinary excretion of carbohydrates.

Goitre : Enlargement of thyroid gland.

Gonorrhoea : An inflammatory disease affecting the mucous membrane of urethra in males and that of vagina in the female.

Gout : A constitutional disorder connected with excess of uric acid in the blood and inflammation of joints and morbid changes in organs.

Granuloma : A tumour formed of granulation tissue.

Granulocytic : A white blood cell whose cytoplasm contains granules.

Granulomatosis : A disease characterized by multiple granulomas.

Gynaecomastia : Excessive development of male mammary glands.

Haematoma : A swelling filled with blood.

Haematological : Branch of medical science devoted to the study of diseases of the blood.

Haematopoiesis (Haemopoiesis) : The process of formation of development of various types of blood cells.

Haematuria : Blood in the urine.

Haemolysis : Disintegration of elements in the blood.

Haemorrhage : Escape of blood from the vessels which naturally contain it; bleeding.

Haemorrhoids (Piles) : It consist of a varicose and often inflammed condition of the veins about the lower end of the bowel.

Haemostasis : Arrest of bleeding.

Haemostatic : Arresting the flow of blood within the vessels; arresting haemorrhage.

Hallucination : Errors in perception, affecting some sense organs.

Hay fever : An allergic condition of the mucous membrane of the eye, nose and air passages.

Hematopoietic : A process relating to the formation of blood cells.

Hemeralopia : Day blindness.

Hemolytic : The condition caused by the destruction of red blood cells and the resultant escape of haemoglobin.

Hepatic : Relating to liver.

Hepatitis : Inflammation of the liver.

Hepatotoxicity : Liver toxicity.

Hiccups : A spasmodic indrawing of air to the lungs, ending with a click, due to sudden closure of the local cords.

Hodgkin's disease : A condition in which the lymphatic glands undergo a progressive enlargement.

Hypercalcaemia : Abnormally low levels of calcium in the circulating blood.

Hyperglycaemic : Relating to abnormally high concentration of glucose in circulating blood.

Hyperglycaemic : Relating to abnormally high concentration of glucose in circulating blood.

Hyperglycemia (Hyperglycinaemia) : A hereditary metabolic disorder, reported only in males, resulting in abnormally high glycine levels in the blood.

Hyperidrosis (Hyperhidrosis) : Excessive sweating.

Hyperinsulinism : A condition resulting from an excessive secretion of insulin by the islets of Langerhans resulting hypoglycaemia.

Hyperkinesis : Excessive motility; excessive muscular activity.

Hypernatraemia : Sodium in blood.

Hyperpyrexia : An excessive degree of fever.

Hypersensitive : Abnormal sensitivity to a stimulus of any kind.

Hypertensive : Rise in blood pressure.

Hyperthyroidism : Excessive activity of thyroid gland.

Hypertonic : Having a greater degree of tension.

Hypertrophy : The increase in size which takes place in an organ, as the result of an increased amount of work demanded of it by the bodily economy.

Hyperuricaemia : Abnormal amount of uric acid in the blood.

Hyperventilation : Abnormally rapid, deep breathing; overbreathing usually due to anxiety.

Hypnotics : Measures including drugs which produce sleep.

Hypocalaemia : Abnormally low levels of calcium in the circulating blood; low concentration of calcium.

Hypochloremia : A condition of blood in which its content of calcium is below normal.

Hypoglycaemia : An abnormally high concentration of glucose in the circulating blood.

Hypogonadal (Hypogonadism) : Inadequate gonadal function; defective internal scerections of gonads.

Hypokalaemia : The presence of an abnormally small concentration of potassium ions in the circulating blood.

Hypomagnesaemia : Abnormally low level of megnesium in the blood.

Hypoplasia : Excessive smallness of an organ or part, arising from imperfect development; excessive formation of cells.

Hypoproteinemia : Decrease in amount of protein in blood.

Hypoprothrombinaemia : Deficiency of prothrombin in the blood which retards its clotting ability.

Hypotension : Low arterial blood pressure.

Hypotensive : Denoting low blood pressure; unusual low blood pressure.

Hypothermia : Fall in the body temperature.

Hypothyroidism : A condition due to deminution or absence of the secretion of the thyroid hormones.

Hypoxia : Diminished amount of oxygen in tissues.

Idopathic : A disease to indicate that their cause is unknown.

Ileus : Severe colic due to obstruction of the bowels.

Immunosuppressant : Agent suppressing immunity.

Impairment : Loss of function or activity.

Impotence : Inability to perform the sexual act.

Inanimate : Not alive.

Inco-ordination : Irregularity of movements produced either by loss of the sensation or by defects in the muscles themselves or their nerves.

Indomethacin : A drug used in the treatment of gout and rheumatoid arthritis.

Infection : Multiplication of microorganisms in the body.

Infertility : Failure to reproduce.

Inflammation : Reaction of living tissue to injury, infection or irritation, characterized by pain, swelling, redness and heat.

Influenza : An acute viral infection of the upper respiratory tract, characterized by a sudden onset of fever, aches and pains.

Ingestion : Administration into stomach by oral route.

Insecticide : An agent used to kill insects.

Insomnia : Wakefulness : inability to sleep.

Intoxication : Poisoning.

Intracranial : Structures and diseases contained or rising within the head.

Intraocular : Within the eyeball.

Intrinsic : Inherent, belong to a part.

Iritis : Inflammation of iris.

Irritability : The state of being irritable; the attribute of organisms and protoplasm to become aroused to distinctive action following a certain stimulus.

Ischaemia : Reduced blood supply.

Jacksonian seizure : Recurrent focal seizures.

Jaundice : A liver disease leading to increased bilirubin level in the blood.

Kaposi's sarcoma : Multiple idiopathic hamorrhagic sarcoma.

Ketonaemia : The presence of recognizable concentration of ketones in the plasma.

Ketouria : Enhanced urinary excretion of ketone bodies.

Labour : Delivery; Childbirth; the process of expulsion of a foetus from the uterus at the normal termination of pregnancy.

Lacrimal : Arrangement attached to the eye for moistening and cleansing the front of this organ.

Lacrymation : Tears; weeping; lacrimal glands.

Lactation : Secretion of milk in breast after childbirth.

Larvacide : Destructive to larvae.

Laryngeal spasm (Largngospasm) : A sudden, abnormal muscular contraction of larynx.

Larynx : The organ of voice.

Lassitude : Weariness; exhaustion.

Laxative : A mixed act of evacuation of faeces.

Legionnaires : An infective disease of lungs.

Leprosy : A chronic disease which affects particularly the skin, mucous membrane, and nerves.

Leptospirosis : A disease caused by the infection with leptospira.

Lethargy : Sluggishness; pathologic drowsiness.

Leucopenia : A condition in which the white blood carpuscles of the blood are greatly reduced in numbers.

Leukaemia : A malignant state wherein an increase of abnormal leucocytes in the blood is seen.

Libido : Sexual desire.

Lipotropic : Tending to produce the utilization of fat and thus prevent excessive fat deposits in the hair.

Lozenges : A small tablet containing drugs mixed with sugar. gum, glycerine-jelly or fruit-paste.

Luminal amoebicide : Amoebic dysentery pertaining to a lumen.

Lupus : A group of skin diseases of intractable character.

Lyme disease : A disease caused by a bacterium transmitted to human beings by the bite of a deer tick, *Ixodes ricinus.*

Lymphoblastic leukaemia : Leukaemia of an immature cell which becomes a lymphocyte.

Lymphocytic : Relating to a variety of white blood corpuscle produced in the lymphoid tissues and lymphatic glands of the body.

Lymphogranuloma inguinale : A venereal disease caused by a virus in which glands in the groin enlarge.

Lymphoma : Various abnormally proliferative, probably neoplastic diseases of the lymphoid tissues.

Lymphosarcoma : A malignant tumour arising from lymphatic tissues.

Lypolysis : Decomposition of fat.

Lypotropic : An arrangment of the ions in the order of their behaviour.

Lysis : Dissolution; destruction.

Malabsorption : It includes a multiplicity of diseases, all of which are characterized by faulty absorption from the intestine of essential food stuffs such as fat, vitamins and mineral salts.

Malaise : Discomfort; Uneasiness.

Malignant : Resistant to treatment, occurring in severe form, and frequently fatal.

Mania : Madness; mental disease characterized by undue elation of mood and psychomotor excitation.

Mastitis : Inflammation of the breast.

Megaloblastic anaemia : Caused by vitamin B_{12} or folic acid deficiency in diet.

Melanin : A block pigment found in hair and skin.

Meningitis : Inflammation of the membranes of the brain or spinal cord.

Meningococcal (Neisserial) : Relating to a group, or genus, of rounded bacteria that occurs in pairs.

Menopause : The cessation of menstruation.

Menopausal syndrome : Syndrome relating to the cessation of menstruation.

Methemoglobinemia : Concerned with a brownish compound formed by combination of oxygen and haemoglobin in the blood; the presence of the oxidized form of haemoglobin in the urine.

Methotrexate : An antimetabolite which is proving of value in the treatment of choriocarcinoma.

Microbe : One-celled organism, e.g., bacteria, germs.

Micturition : The act of passing urine.

Migraine : A form of throbbing headache, generally unilateral associated with nausea or vomiting and visual disturbances.

Miosis : Excessive contraction of the pupil.

Motor cortex : Motor area.

Mould : A multicellular fungal growth.

Mucocutaneous : Relating to an area where mucous membrane and the skin come together, as in nose, mouth, vagina and anus.

Mucus : A clear, viscid secretion of the mucous membranes.

Multiforme : Having many forms, shapes, kinds or appearance.

Myalgia : Muscular pain.

Myasthenia gravis : A disorder characterized by marked weakness in the voluntary muscles; an autoimmune disease.

Mycoplasmal : Relating to a genus of micro-organisms which differ from bacteria in that they lack a rigid cell wall.

Mycosis fungoides : Diseases caused by the presence of fungi.

Mycotic : Relating to contraction of the pupil; an agent that causes the pupil to contract.

Mydriasis : Abnormal dilation of the pupil of the eye.

Mydriatics : drugs causing unusual dilation of the pupil, e.g. atropine, cocaine.

Myeloma : A tumour composed of cells derived from haemopoietic tissue of the bone marrow; a malignant disease of the bone marrow.

Myocardial (Coronary thrombosis) : The acute, dramatic manifestation of ischaemic heart disease; relating to the middle layer of the heart.

Mycardium : Heart muscle.

Narcosis : Unconsciousness produced by a drug; general and nonspecific reversible depression of neuronal excitability.

Nasal : Relating to nose.

Nausea : Feeling of vomiting; sea sickness.

Necrolysis : Dissolution or disintegration of dead tissue.

Necrosis : Localized death of tissues.

Nematode : Belonging to the phyllum, Nematoda, of thin, unsegmented, cylindrical, parasitic worms, whose hosts may be domestic plants, animals or man.

Neonatal : New born.

Neoplasm : New growth; an abnormal growth of tissues; tumour.

Neoplastic : Relating to abnormal growth of tissues or tumour.

Nephritis : Inflammation of the kidney.

Nephrotoxic : Any substance which inhibits or prevents the function of kidney.

Neuralgia : Pain of a severe, throbbing or stabbing character in the course or distribution of a nerve.

Neuritis : Inflammation of a nerve.

Neurodermatitis : A skin disorder characterized by localized, often symmetrical, patches of pruritic dermatitis with lichenification.

Neuroleptic : Drugs acting on nervous systems particularly antipsychotic drugs.

Neuromuscular : Pertaining to both nerves and muscles.

Neuropathy : Any disease affecting neurons.

Neuropenia : A reduction in the number of neutrophil leucocytes per cubic millimeter of circulating blood to a figure below that found in health.

Neurotoxic : Poisonous to nerves or to nerve tissue such as the brain.

Nightmare : A fearful or terrifying dream causing intense anxiety and feeling of oppression and helplessners.

Nostrilis : One of the two apparatus of the nose which give passage to air.

Numbness : Without physical sensation or feeling.

Nystagmus : Involuntary and jerky movement of eye balls.

Obesity : Fatness; fatty; an increase of body weight due to accumulation of fat.

Occlusion : The act of closing or the state of being closed.

Oedema : Swelling; an abnormal accumulation of fluid beneath the skin or in cavities of the body (dropsy).

Oesophageal ulceration : Ulcer of oesophagus.

Ophthalmic : Relating to eye.

Orthopaedic : Relating to the medical especially concerned with preservation, restoration, and development of forms and functions of the extermites, spine and associated structures.

Orthostatic : Pertaining to, or caused by, standing upright.

Osteogenic sarcoma : A malignent tumor composed of anaplastic cells of mesenchymal derivation.

Osteomylitis : Inflammation of the bone marrow or the bone.

Osteoporosis : Increased porosity of the bone.

Otitis : Inflammation of the ear.

Ototoxicity : Having a toxic action upon the ear.

Palliative : Treatment of incurable disease.

Pallid cyanosis : A bluish -purple discolouration of the mucous membranes and skin on the globus pallidus due to the

presence of excessive amounts of reduced haemoglobin in capillaries.

Palpitation : Rapid heart beat; any heart action that produces a disagreeable awareness in a patient.

Pancreatitis : Relating to the gland pancreas situated near the stomach.

Paraesthesis : Any abnormality of sensation.

Paralysis : Loss of muscular power due to interference with the nervous system.

Paralytic : Relating to loss of muscular power.

Parkinsonism : A degenerative syndrome of mask-like face, tremors, difficulty in changing gait.

Parturition : Labour, act of delivering a child; childbirth.

Pathogenic organisms : Disease producing living agents.

Peptic : Relating to pepsin.

Periasteritis nodosa : A disease of unknown origin in which prolonged fever and obscure symptoms are associated with local areas of inflammation along the arteries.

Perioral : Surrounding the mouth; circumoral.

Peripheral neuritis : Inflammation of peripheral neuron.

Peristalsis : Worm-like movement by which the stomach and bowels propel their contents.

Peritoneum : A membrane which lines to abdominal and pelvic cavities and covers the organs contained in them; peritoneal; peritonitis.

Peritonitis : Inflammation of peritoneum.

Pharmacopoeia : A compendia containing monographs of therapeutic agents, standards for their strenghths and purity and directions for making preparations.

Phlebitis : Inflammation of a vein.

Photophobia : Inability to expose the eye to light.

Photosensitivity : Sensitivity to light.

Pilo-erection : Erection of hair.

Pinta : A disease of the skin characterized by dsychromic changes and hyperkeratosis in patches of the skin, caused by the spirochete *Treponema carateum.*

Pityriasis alba : A form of chronic eczema which occurs mainly in children.

Plague : An infectious epidermic disease common to man.

Plasticizer : Any material which makes a substance plastic, giving its flexibility, stretchability and softness.

Plasmodia : Minute protoplasmic cells, particularly to those which cause malaria.

Pleura : A membrane which forms a covering for one lung.

Pneumococcal : Relating to a bacterium, *Diplococcus pneumonia*, causing pneumonia and other infections diseases.

Pneumonia : Infection of lungs with production of alveolar exudate.

Polydipsia : Excessive thirst.

Polyneuritis : Simultaneous inflammation of a large number of the spinal nerve.

Polyurea : Excretion of excessive amount of urine.

Porphyria : An inborn (hereditory) error in porphyrin metabolism.

Postmenopaual : Occurring after the menopause.

Postoperative : Occurring after an operation; following closely upon an operation.

Potentiate : To intensify the effect of a drug.

Premedicant : The administration of drugs before induction of anaesthesia; any drug administered for this purpose.

Pressor : Producing increased blood pressure.

Priapism : Persistent erection of the penis, usually unaccompanied by sexual desire, as seen in leukemia, with urinary calculi, and in spinal cord lesions.

Proliferation : Production of multiplication of parts, as in budding or cell divisions.

Prophylactically : Defending from or warding off disease.

Prophylaxia : Treatment or action adopted with the view of warding off disease.

Prophylaxis : Prevention of a disease.

Proteinuria : A condition in which proteins are found in the urine.

Protoplasmic : Relating to viscid, translucent, glue-like material containing fine granules.

Pruritus : Itching; an uncomfortable sensation due to irritation of a peripheral sensory nerve.

Pseudomonas : A bacterial genus; gram-negative mobile rods found in water and decomposing vegetable matter. Some of them are pathogenic to plants and animals.

Psittacosis : A contagious infection of parrots caused by a micro-organism known as *Chlamydia psittaci.*

Psoriasis : A chronic disease of the skin in which raised, rough, reddened areas appear, covered with fine silvery scales.

Psychic disorder : Mental disorders.

Psychiatry : The medical science dealing with the mental and emotional disorders.

Psychomotor : Relating to the mental origin of muscular movement; relating to the production of voluntary movements.

Psychosedative : Quieting function or activity of mental part.

Psychosis : Severe disorder of the mind.

Psychotic : A psychotic individual; pertaining to psychosis.

Pulmonary embolism : The occlusion of a blood vessel by an embolus in lungs.

Purgative : A drug causing evacuation of faces rapidly.

Purpurea : A disease characterized by the occurrence of purple coloured spots upon the surface of the body.

Pyrexia : Fever; elevation of temperature above the normal.

Pyrogen : A substance capable of producing fever (pyrexia).

Q fever : An actute infectious disease of world-wide distribution due to the *Coxiella burneti:* characterized by sudden onset of fever, malaise, headache, and interstitial pneumonitis.

Rash : Skin eruption; urticaria.

Raynaud's syndrome : A condition in which the circulation becomes suddenly obstructed in outlying parts of the body; paroxysmal spasm of the digital arteries producing pallor or cyanosis of fingers or toes and occasionally resulting in gangrene.

Receptor : A proteineous site on nerve membrane on which neurotransmitters and drugs act to produce stimuli.

Refractory : Resistant to treatment.

Regional enteritis : Regional inflammation of the intestine.

Reiter's disease : A condition characterized by arthritis, urethritis and conjunctivities.

Renal : Relating to kidney.

Renal calculi : A stone-like mass sometimes formed in the kidney.

Rhabdomyo sarcoma : A malignant tumour, usually involving the muscles of the extremities or torso, composed of anaplastic striated muscle cells.

Rheumatism : A group of diseases concerning infection affections of the fibrous textures of joints, muscles and other parts.

Rhinitis : Inflammation of the nasal mucous membrane.

Rickettsial infection : Infection due to a group of micro-organisms which are intermediate between bacteria and virus.

Rigidity : Stiffness, fixed, inflexible.

Rocky Mountain Spotted fever : A fever of the typhus group first reported in the Rocky Mountain states of U.S.A.

Rubefacient : An agent which causes a reddening of the skin.

Salivation : The process or action of salivating: an excessive flow of saliva.

Saluretic : Facilitating the renal excretion of sodium and chloride ions.

Sarcoma : A tumour, usually highly malignant, formed by proliferation of mesodermal cells.

Scab : A crust formed by coagulation of blood, pus, serum, or a combination of these, on the surface of an ulcer, erosion or wound.

Scabies : An eruption due to *Sarcoptes scabiei* var. *hominis*.

Scarlet fever : An acute infectious disease, characterized by high fever, sore throat and diffuse red rash on the skin due to infection with a haemolytic streptococcus.

Schizontocide : A substance destructive to schizonts.

Schizophrenia : Forms of psychosis in which there is a cleavage of the mental function, a group of mental illness characterized by disorganization of the patient's personality.

Sciatica : Neuralgia of the sciatic nerve, felt at the back of thigh.

Scleroderma : Thickening of the skin caused by swelling and thickening of fibrous tissue, with eventual atrophy of the epidermis.

Seborrhoeic : A group of disease of skin in which the sebaceous or oil forming glands are at fault.

Sedative : Calming; an agent that quiets nervous exitement; drug which soothe over excitement of nervous system; an agent which reduces functional activity.

Seizure : An attack; the sudden onset of a disease or of certain symptoms, such as convulsions.

Sensory cortex : Any area of the cerebral cortex associated with the perception of sensation.

Sepsis : The presence of various pus-forming and other pathogenic organisms, or their toxins, in the blood or tissues.

Septicaemia : Systemic disease caused by the multiplication of microorganisms in the circulating blood.

Sequelae : Symptoms or effects which are liable to follow certain diseases.

Serotonin : A crystalline substance, normally found in certain blood, brain, and intestinal cells of mammals, that cause muscle contraction and vasoconstriction.

Serous : Relating to or producing serum; a substance having watery consistency.

Sialorrhoea : Salivation.

Side-effects : Any physiological response other than the desired one for which the drug is administered.

Sinus : A hollow or cavity.

Sinusitis : Inflammation of the lining membrane of any sinus, especially of one of the prenasal sinuses.

Spasm : An involuntary and painful contraction of a muscle of a hollow organ with a muscular wall.

Spermicidal : Destructive to spermatozoa.

Spermicide : An agent destructive to spermatozoa.

Splenomegaly : Enlargement of the spleen.

Spondylitis : Inflammation of one or more of the vertebrae.

Sprains : Injuries in the neighbourhood of joints, consisting usually in tearing of a ligament with effusion of blood.

Staggering gait : The lurching , drunken gait seen in acute alcoholism, or other central nervous system intoxication.

Staphylococci : A bacterium which under the microscope appears in small masses like bunches of grapes.

Steatorrhoea : Any condition characterized by the passing of stool containing an excess of fat.

Stenosis : A narrowing of any canal; narrowing of one of the cardiac valves.

Stevens-Johnson Syndrome : Type of severe allergic response as produced by drugs like sulphonamides.

Stomatitis : Generalized inflammation of the mouth.

Streptococcal infection : Infection due to a variety of bacterium which under microscope has much the appearance of a string of beads.

Stuffiness : Substance or matter indefinitely.

Stupor : Lethargy, unconsciousness; loss of consciousness.

Subcutaneous : Anything pertaining to the loose cellular tissue beneath the skin.

Sublingual : Beneath the tongue.

Sympathomimetic : Drugs which produce an effect comparable to those produced by stimulation of the sympathetic nervous system.

Symptomatic : Relating to symptoms (s).

Syncope : Fainting; a sudden fall of blood pressure ; failure of the cardiac systole resulting loss of consciousness and cerebral anaemia.

Syndrome : The aggregate of signs and symptoms associated with any morbid process.

Syphilis : A contagious disease of slow development having sore at the site of infection.

Tachycardia : Rapid beating of the heart; rapid pulse rate.

Tetanus : A disorder of the nervous system consisting in a greatly increased excitability of the spinal cord.

Therapeutics : The science and art of healing. A scientific account of the treatment of diseases.

Thrombocytopenia : Decrease in number of platelets in circulating blood; a disease characterized by marked absence of platelets in the blood.

Thrombolysis : Destruction or dissolution of a clot of blood formed during life within the heart or blood vessels.

Thrombophlebitis : The development of venous thrombi in the presence of inflammatory changes in the vessel wall; inflammation of the veins with clot formation.

Thrombosis : A clot in a blood vessel or in one of the cavities of the heart; a universal harmless habit in infancy.

Thrombotic : Relating to the function of thrombus; the presence of a thrombus.

Thrombus : A clot of blood formed during life within the heart or blood vessels.

Thyrotoxicosis : A condition due to excessive production of thyroid gland hormone.

Tingling : To have a sensation of slight stings; the feeling of a slight, sharp, and sudden thrill, as of pain.

Tinnitus : A noise in the ears without any external cause; ringing sound in the ears.

Tonicclonic : Relating to vocal accent, pronounciation or speaking.

Tonsillitis : Inflammation of the tonsils.

Topically : Relating to a detinite place or locality.

Toxicology : The science dealing with poisons.

Trachoma : Contagious inflammation affecting conjuctiva, cornea and eyelids; a chronic, persistent and severe form of conjunctivities rampant amid the dirt and poverty of tropics and sub-tropics.

Tranquilizer : A drug which induces a mental state free from agitation and anxiety.

Trauma : A wound or injury, especially produced by external force; disorders due to wounds or injuries.

Tremor : Trembling; shaking; involuntary movement due to alternating contractions of opposing muscles occurring physiologically or pathologically.

Tremulousness : Characterized by trembling, as from fear, nervousness, or weakness.

Treponemal infection : Infection due to a genus of spirochaetal microorganisms which consist of slender spirals and progress by means of bending movements.

Trichomoniasis : A disease caused by infection with *Trichomonas vaginalis.*

Trigeminal : Relating to the fifth cranial or trigeminus nerve.

Tubercle bacilli : Microorganism that causes tuberculosis.

Tuberculoid : Resembling tuberculosis, or a tubercle; any skin lesion which is the result of infection with the tubercle bacillus.

Tuberculosis : A disease of lungs due to the presence of *Mycobacterium tuberculosis.*

Tuberculostatic : Inhibiting the growth of tubercle bacilli.

Tularaemia : A disease of rodents such as rabbits and rats, caused by the bacillus, *Francisella tularense.*

Tumour : A swelling; a mass of abnormal tissues.

Tympany : Tympanites; a tympanitic percussion note.

Typhoid fever : An infectious fever caused by *Salmonella typhi* organism.

Typhus fever : An infective disease caused by micro organisms of the genus Rickettsia.

Ulcer : A lesion on the surface of the skin or a mucous surface.

Ulceration : Formation of an ulcer.

Uremia : A condition resulting from the retention in the blood of waste products that should normally be eliminated in the urine.

Urethra : The tube which leads from the bladder to the exterior. and by which the urine is voided.

Urethritis : Inflammation of the urethra.

Uricosuric : Enhanced renal excretion of uric acid.

Urticaria : An allergic skin eruption; formation of itch wheels.

Uveitis : Inflammation of the uvea.

Vasculitis : Inflammation of a blood vessel.

Vaginitis : Inflammation of the vagina.

Vascular : Relating to or containing blood vessels.

Vascularisation : The process of tissues becoming vascular, the formation and extension of vascular capillaries within and into tissues.

Vasicant : An agent that produces a blister.

V- colour : Changeable in colour.

Vasocontriction : Narrowing of the blood vessels.

Vasodilation : Dilation of blood vessels.

Vasodilator : Substances that cause dilations of the blood vessels.

Vasomotor : Causing dilation or constriction of the blood vessels; denoting the nerves which have this action.

Vector : A carrier of disease.

Ventricular arrhythmia : Absence of rhythm of ventricle.

Vertigo : A condition in which the affected person loses the power of balancing himself.

Vestibular : Pertaining to vestibule; particularly pertaining to the vestibule part of the eighth cranial nerve, connected with equilibrium.

Viruside : An agent active against viral infection.

Vomiting : The expulsion of the stomach contents through mouth.

Whipple's disease : A generalized disease characterized by infiltration of the intestinal wall and lymphatics.

Wilm's tumour : Kidney tumour, a hereditary malignancy.

Yaws (Framboesia; Pian) : A disease of the tropics; consisting in the appearance of small tumours covered with yellow crusts, scattered over the surface of the body.

Xerophthalmia : Extreme dryness of conjunction which loses its luster and becomes skin like in appearance from lack of intrinsic secretion.

EXAMINATION QUESTION PAPERS

PHARMACEUTICAL CHEMISTRY-II
(ORGANIC CHEMISTRY)

This Page is Intentionally Left Blank

UNIVERSITY OF DELHI, DELHI.

D. PHARM 1992 (ANNUAL)

1. What are pharmaceutical aids? Give an account of preservatives, antioxidants colouring and flavouring agents.

2. Write chemical structure and uses of any eight of the following :
   (i) Sodium lauryl sulphate (ii) Ascorbic acid (iii) Carbimazole (iv) Thyroxine (v) Vitamin K (vi) Prednisolone (vii) Nalorphine (viii) Sodium cromoglycate (ix) Clofibrate (x) Mersalyl acid.

3. What do you know about steroids in general ? Give an account of androgens, oestrogens and progestogens.

4. What do you know about diagnostic agents and drugs used to test the organ function ? Write a general account giving suitable examples wherever necessary.

5. Write short notes on any ***two*** of the following :
   (i) Thyroid and antithyroid drugs. (ii) Coagulants and anticoagulant drugs (iii) C.N.S. stimulants.

6. What are cardiovascular drugs? Give a classification of them along with the names of drugs of each category. Write an account of vasodilators.

7. Give an account of the drugs used as cholinergic and anticholinesterase agents.

8. Write the name and structure of a drug possessing the following characteristic features : (Attempt any *eight)* :
   (i) An antimalarial having 1,3-diazine nucleus (ii) A sulphone used as antileprotic drug (iii) An anti-inflammatory agent having pyrazolidinedione 3,5 ring (iv) An antianxiety drug derivative of benzodiazepine nucleus (v) An alkaloid with tropane nucleus having local anaesthetic action (vi) An

adrenergic drug derivative of catecholamine (vii) An antihistaminic agent derivative of ethylenediamine (viii) An antirachitic vitamin derivative of sterols (ix) A cationic surface active agent used as anti-infective agent (x) A hypoglycaemic agent derivative of biguanides.

D. PHARM. 1991 (ANNUAL)

1. (a) Write the formulae of the following organic groups :
   (i) Acetamido (ii) Carbamoyl (iii) Formyl (iv) Guanidino (v) Mercapto (vi) Methyl sulphonyl (vii) Sulphamoyl (viii) Sulphanilamido.
   (b) Write the structure of the following basic rings :
   (i) Pyrrole (ii) Pyrazole (iii) Pyridine (iv) Oxazole (v) Thiazole (vi) Indole (vii) Purine (viii) Quinoline.

2. What are antibiotics? Describe briefly chloramphenicol and tetracyclines.

3. (a) Define hypnotics and sedatives. What is the difference between these?
   (b) Write short note on Barbiturates.

4. Write short notes on any ***two*** of the following :
   (i) Tricyclic antidepressant drugs (ii) Anti-infective agents (iii) Analgesics.

5. Write chemical structure and uses of any ***eight*** of the following :
   (i) Thiopentone sodium (ii) Paracetamol (iii) Pethidine (iv) Atropine (v) Acetyl Salicylic Acid (vi) Acetazolamide (vii) Chlorpropamide (viii) Indomethacin (ix) Ascorbic acid (x) Sulphacetamide.

6. (a) Fill in the blanks :
   (i) Vitamin ..... is a cobalt containing substance.
   (ii) Diazepam is used as a .....
   (iii) Chloroquine is used in the treatment of .....
   (iv) Dapsone is mainly used for the treatment of .....
   (v) Propranolol is prescribed for .....
   (vi) Ascorbic Acid is given for the treatment of .....
   (vii) Benzyl Benzoate is used topically in the treatment of .....

(viii) Frusamide is used as a .....
(ix) Metronidazole is given for .....
(x) Penicillin is an anti ..... agent.

(b) Name three sulphonamides. How do these act ?

7. (a) Name B Complex Vitamins. Give structure of two of these Vitamins.
(b) What are antispasmodic drugs. Name two such drugs.

8. Write short notes on any ***two*** of the following :
(i) Trimethoprim (ii) Caffeine (iii) Petridine.

D. PHARM 1991 (SUPPLEMENTARY)

1. (a) Write the formulae of the following organic groups:
(i) Acetyl (ii) Benzamide (iii) Carboxy (iv) Ethynyl (v) Glycyl (vi) Methyl thio (vii) Tosyl (viii) Vinyl.
(b) Write the structure of the following rings :
(i) Thiophene (ii) Imidazole (iii) Piperazine (iv) Barbituric acid (v) Quinoline (vi) Phenothiazine (vii) Xanthine (viii) Tropane

2. What are general anaesthetics? Give an account of them.

3. Define analgesics, antipyretics and anti-inflammatory drugs (non steroidal). Classify them according to their chemical moiety. Give details of indolyl and aryl acetic acid' derivatives.

4. What are antispasmodic and antiulcer drugs? Give an account of the chemistry of synthetic cholinergic blocking agents.

5. Explain the importance of coagulant and anticoagulants. Give an account of them.

6. Write short notes on any ***two*** of the following :
(i) Sulphonamides (ii) Antianginal agents (iii) Disinfectants and antiseptic anti-infective agents.

7. Write chemical structures and uses of any ***eight*** of the following :
(i) Procaine (ii) Diazepam (iii) Diphenhydramine (iv) Morphine (v) Thyroxine (vi) Ascorbic acid (vii) Quinine (viii) Frusemide (ix) Phenobarbitone (x) Hydrochlorthiazide.

8. (a) Complete the following sentences :
   (a) Morphine is used mainly as .....
   (b) Pheneramine maleate is used in the treatment of .....
   (c) The chemical name of paracetamol is .....
   (d) Warfarine is an .....
   (e) Adrenaline is a .....
   (f) Salbutamol is used in .....
   (g) Caffeine is a ..... derivative.
   (h) Tetracycline is a ..... spectrum antibiotic.
   (i) Chloroquine is a ..... derivative.
   (j) ..... is popularly known as aspirin.

   (b) Name any ***three*** commonly used diureties ?

D. PHARM 1990 (ANNUAL)

1. What are local anaesthetics? Give a detailed account of ester type local anaesthetic drugs.
2. Write a detailed note on hypoglycemic agents.
3. What are vitamins? Write a detailed note on water soluble vitamins.
4. Write short notes on any ***two*** of the following :
   (a) Antimalarial drugs (b) Antiamoebic drugs (c) Antibiotics used for treating urinary tract infections.
5. Write chemical structures and uses of any ***eight*** of the following :
   (a) Paracetamol (b) Methyl salicylate (c) Pheniramine maleate (d) Diazepam (e) Phenobarbitone (f) Menadione (g) Methyldopa (h) Metronidazole (i) Isoniazid (j) Chlorambucil
6. What do you know about diagnostic agents? Write a detailed note on these agents.
7. Write a detailed note on hypnotics and sedatives. Give suitable examples with chemical structures
8. Complete the following sentences :
   (a) Aspirin gradually hydrolyses in contact with moisture .....

(b) Benzocaine is ethyl .....
(c) Piperazine is effective against .....
(d) Paraaminosalicylic acid is used in the treatment .....
(e) Adrenaline is stored in .....
(f) Heparin is an .....
(g) Amaranth is used as .....
(h) Ampicillin is active against .....

B. PHARM I YEAR, 1992 (ANNUAL) SECTION B

1. Write the structure, properties and uses of any ***four*** of the following :
   (a) Sulphacetamide (b) Caffeine (c) Diphenhydramine hydrochloride (d) Aspirin (e) Procaine.

2. (a) Give the structure, uses and pharmaceutical preparations of any ***two*** sulpha drugs.
   (b) Discuss 8-amino quinolines as antimalarial agents.

3. (a) Give an account of water-soluble vitamins.
   (b) What are hypoglycemic agents? Give structure and dosage forms of any ***two*** of them.

4. Write short notes on any ***two*** of the following :
   (a) Diuretics (b) Anticoagulants (c) CNS depressants (d) Pharmaceutical preservatives.

B. PHARM I YEAR, 1991 (ANNUAL) SECTION B

1. Write the structure, properties, uses and dosage forms of any **four** of the following :
   (a) Aspirin (b) Tolbutamide (c) Amphetamine (d) Dapsone (e) Acetazolamide (f) Procaine (g) Acetamenaphthone.

2. (a) What are hypnotics and sedatives ? Give the structure, uses and dosage forms of any ***Three*** of them.
   (b) Give an account of 8-amino quinoline antimalarials.

3. (a) What are local anaesthetics? Give the structure, uses and dosage forms of any ***two*** of them.
   (b) Give an account of Antihypertensive agents.

4. Write short notes on any ***Three*** of the following :
   (a) Antibiotics (b) Medicinal dyes (c) Adrenergic agents (d) Lipid-soluble vitamins.

B. PHARM. I YEAR, 1991 (SUPPLEMENTARY) SECTION B

1. Write the structure, properties, uses and dosage forms of any ***Four*** of the following :
   (a) Paracetamol (b) Chlorpropamide (c) Caffeine (d) Methyl dopa (e) Chloroceresol (f) Benzocaine.

2. (a) What are diuretics ? Give the structure, uses and dosage forms of any ***Two*** of them.
   (b) Give an account of Antimalarials.

3. (a) What are nonsteroidal anti-inflammatory agents ? Give the structure, uses and dosage forms of any ***Two*** of them.
   (b) Give an account of Anti-infective agents.

4. Write short notes on any ***Three*** of the following :
   (a) General anaesthetics (b) Anticoagulants (c) Water-soluble vitamins (d) Cholinergic agents.

B. PHARM. I YEAR, 1990 (ANNUAL) SECTION B

1. Write the structure, properties and pharmaceutical dosage forms of any ***Five*** compounds of the following :
   (i) Chloroamphenicol (ii) Paracetamol (iii) Nitrofurazone (iv) Trimethoprim (v) Nikethamide (vi) Ephedrine (vii)Frusemide (viii) Methyl salicylate

2. Write notes on the following :
   (i) Sulphonamides OR 8-amino-quinoline antimalarials
   (ii) Antitubercular Antibiotics OR Autonomic blocking agents
   (iii) Skeletal Muscle relaxants OR Antithyroid Drugs

3. What are local-anti-infective agents ? Give their chemical classification and write the name,properties and pharmaceutical applications of atleast two componds of each chemical class.

4. (a) Give an account of Nonsteriodal anti-inflammatory agents OR Adrenergic agents.

   (b) Write brief account on handling and storage of radio-pharmaceuticals.

B. PHARM I YEAR, 1990 (SUPPLEMENTARY) SECTION B

1. Write the structure, general properties, class of drug and uses of any ***Five*** of the following :

   (i) Crystal Violet (ii) Dapsone (iii) Isonicotinic Acid Hydrazide (iv) Paraldehyde (v) Aspirin (vi) Saccharine Sodium (vii) Sulphadiazine (viii) Glyceryl trinitrate.

2. Write notes on the following :

   (i) Penicillins *Or* Narcotic analgesic (ii) Sex hormones *Or* vitamin B Complex (iii) Antiarrhythmic Agents *Or* Antihistaminic agents.

3. Give an account of the following :

   (i) Cholinergic Agents *Or* Hypoglycaemic agents (ii) General Anaestheitcs *Or* C.N.S. Stimulants

4. What are 'diuretics' ? Give their chemical and pharmacological classification and name at least two examples of each chemical class and write their properties and dosage forms.

BOARD OF TECHNICAL EDUCATION, DELHI

D. PHARM II YEAR, FEB. 1994.

1. (a) Explain different solubility terms as used in I.P

   (b) Write the structure of the following rings and groups :

   (i) Guanidino (ii) Sulphamoyl (iii) Methyl sulphonyl (iv) Indoline (v) Isoquinoline (vi) Acridine (vii) Propyl (viii) Formyl.

2. What are anti-ulcer drugs? Give an account of these.

3. What are allergens? How they elicit allergic reactions? Briefly give an account of histamine antiagonists.

4. Write the chemical structure, category/sub-category and medicinal uses of any ***eight*** of the following :
   (i) Salbutamol (ii) Frusemide (iii) Amphetamine (iv) Homatropine (v) Chlorpromazine (vi) Clofibrate (vii) Phenytoin (viii) Methandienone (ix) Nicotinic acid (x) Vanillin.

5. What are general anaesthetics ? Classify them and describe these briefly.

6. Write notes on any ***two*** of the following :
   (i) Narcotic antagonist (ii) Skeletal muscle relaxants (iii) Anti-anxiety drugs.

7. What do you know of hypoglycaemic agents? Give a suitable account of them.

8. What are antibiotics? Classify them according to their biogenesis, alongwith the names of antibiotics of each class. Give an account of penicillins and tetracyclines.

D. PHARM. II YEAR, JUNE 1993.

1. (a) Write the formula of the following group :
   (i) Benzamido (ii) Carbamoyl (iii) Acetamido (iv) Ethynyl (v) Formyl (vi) Mercapto (vii) Chloromethyl (viii) Propyl.

   (b) Write the structure of the following ;
   (i) Indole (ii) Isoxazole (iii) Piperazine (iv) Pyrazole (v) Pyrimidine (vi) Phenothiazine (vii) Acridine (viii) Thiazole.

2. What is histamine and what are its various sources? Classify antihistamines and give the structure of one compound of each subclass.

3. What are local anaesthetics? Classify them and give a brief account of any amide type of local anaesthetic agent.

4. Give a brief account of hypnotics and sedatives other than the barbiturates.

5. What do you understand by cholinergic and anticholinesterase agents?

   Write the structure and uses of two of these drugs.

6. Give the structure and use of any ***Eight*** of the following :

   (i) Chloroxylenol (ii) Dapsone (iii) Trimethoprim (iv) Aspirin (v) Thiopentone sodium (vi) Propranolol (vii) Chloroquin (viii) Methyldopa (ix) Sulphamethoxale (x) Oxyphen butazone.

7. Write any essay on antibiotics.

   Give names of four antibiotics and their main uses.

8. Write short notes on any ***Two*** of the following ;

   (i) Diagnostic agents. (ii) Antianginal drugs (iii) Antimalarials.

D. PHARM. II YEAR, JANUARY 1993.

1. What are antimalarial drugs? Name the alkaloid which has antimalarial action and give its source. Name antimalarial drugs which have quinoline nucleus.

2. Write the structure, properties and uses of the following :
   (a) Noradrenaline (b) Methyl salicylate (c) Urea (d) Nicotinamide.

3. What is the source of insulin? Why insulin cannot be given orally? Name some hypoglycaemic agents which can be given orally.

4. Write the physical properties, storage conditions and uses of the following :
   (a) Vitamin A (b) Cholecalciferol (c) Phytomenadione (d) Thiamine hydrochloride (e) Folic acid.

5. (a) What are Xanthine derivatives? Give examples of some Xanthine derivatives which are used medicinally.
   (b) Give an account of antihypertensive agents.

6. What is a steroidal drug? What are the different classes of drugs which have steroid nucleus? Give an account of any one of the class of steroidal drugs.

7. Write notes on :
   (a) Antithyroid drugs (b) Anticoagulants.

8. Give the physical characteristic, solubility and official formulations of the following :

   (a) Acetyl Salicylic Acid (b) Mepyramine maleate (c) Chlorpheniramine maleate (d) Promethazine hydrochloride (e) Sodium Cromoglycate (f) Ampicillin (g) Paracetamol (h) Phenylbutazone.

D. PHARM II YEAR, MAY-JUNE 1992.

1. (a) Draw the structures of the following heterocyclic systems and number the different positions in each

   (i) Phenothiazine (ii) Indole (iii) Isoquinoline (iv) Benzimidazole

   (b) Write the structure of the following

   (i) Pyridine (ii) Piperazine (iii) Thiazol (iv) Peperidine (v) Furan (vi) Pyrimidine (vii) Imidazole (viii) Pyrazole.

2. What are local anaesthetics? Give a brief account of the ester type local anaesthetics agents. Name the local anaesthetic which is an alkaloid.

3. In which diseased conditions the use of diuretics is recommended? Name a diuretic each possessing the following structural characteristics :

   (i) Phenoxyacetic acid (ii) Sulphamoyl group (iii) Sterioid nucleus (iv) Pteridine heterocycle (v) An amide

   Write the physical properties and solululity in water of each drug.

4. What are adrenergic drugs? What are their therapeutic uses? Give the structure of adrenaline. Write an account of adrenergic drugs which have catechol nucleus.

5. Write the structures, properties and medicinal uses of the followeing :

   (a) Aspirin (b) Nikethamide (c) Pracetamol (d) Chlorocresol

6. Write short notes on

   (a) Digitalis glycosides (b) Vasodilators

7. What do you understand by the term vitamin? Give an account of fat soluble vitamins and their physiological role.

8. Write the structure of sulphanilamide? How is it related to p-aminobenzoic acid. Give a brief account of sulphonamides and their uses.

JAMIA HAMDARD, NEW DELHI.

D. PHARM. 1994 (ANNUAL)

1. Solve any three of the following :
   (a) Give the structures and method of numbering of the following heterocyclic systems *(any four)* :
   (i) Quinoline (ii) Imidazole (iii) Pyridine (iv) Acridine (v) Pyrimidine (vi) Indole.
   (b) Give structures of the following *(any three)* :
   (i) Chloramphenical (ii) Antipyrine (iii) Chloroquine (iv) Paracetanol.
   (c) Match the following *(any five)* :

(i) Heparin	(1) Sex hormone
(ii) Fusicid acid	(2) Anticoagulants
(iii) Digitoxin	(3) Antimalarials
(iv) Primaquine	(4) Antibiotics
(v) Acetylcholine chloride	(5) Cardiovascular agent
(vi) Progesterone	(6) Cholinergic agent

   (d) Write a note on antiseptic anti-infective agents.
   (e) What is a major hormone secreted by adrenal medula? Give its pharmacological actions, structure and storage conditions.
2. (a) What is the physiological role of histamine? Mention different drugs used under each class of antihistaminic agents.
   (b) Give structure, chemical name, storage conditions and official preparations of any two antihistamines of aminoalkyl-ether class.
3. (a) Define vitamin. Give examples of oil soluble vitamins. Give official preparations of vitamins obtained from fish liver oil.
   (b) Name six vitamins belonging to B-complex group. Draw structure of vitamin used in beriberi.
4. Write short notes on any ***two*** of the following :
   (a) Official anti-thyroid drugs
   (b) Surface active agents
   (c) Diagnostic agents

5. What are Diuretics ? How will you classify them ? Give the properties, storage conditions and uses of three nonmercurial diuretics.

6. Give the structure, chemical properties, stability, storage conditions and uses of the following (any ***four***) :

   (a) Mepacrine (b) Ephedrine (c) Phenindione (d) Testosterone (e) Lignocaine (f) Methadone.

7. Answer any three of the following :

   (a) Draw the structure of sulphanilamide and dapsone. Mention their uses.

   (b) Define hypoglycaemic agents. Name the hypoglycamic agents drived from biguanides with their structures.

   (c) What are anti-inflammatory agents? Give an account of non-steroidal anti-inflammatory agents with suitable examples.

   (d) Write a short account of pethidine and analogues.

D. PHARM. 1993 (ANNUAL)

1. What are local anaesthetics? Give a detailed account of amide type of local anaesthetics.

2. (a) Write structure of the following :

   (i) Isoxazole (ii) Quinoline (iii) Imidazoline (iv) Phenanthrene (v) Xanthine (vi) Thiazole (vii) Acridine (viii) Phenothiazine (ix) Barbituric acid (x) Pyridazine.

   (b) Explain what do you understand by different solubility terms used in the pharmacopoeia ?

3. What do you know of adrenergic drugs? Give an account with suitable examples.

4. What are antihistaminic agents? Classify them, give structure and uses of at least one drug of each category.

5. Write short notes on any two of the following :

   (a) Steroids (b) Fat soluble vitamins (c) Hypoglycaemic agents.

6. What are antibiotics? Explain and give the structure of antibiotics which are derivatives of amino acids.

7. Write the structure, category/sub-category and uses of any ***Eight*** of the following :
   (i) Thymol (ii) Cetrimide (iii) Sulphaguanidine (iv) Trimethoprim (v) Nitrazepam (vi) Acetylcholine (vii) Clofibrate (viii) Ibuprofen (ix) Tolbutamide (x) Quinine.

D. PHARM. 1992 (ANNUAL)

1. Write this structure, pharmacological category and properties of the following (only ***six***) :
   (i) Chloroxylenol (ii) Dapsone (iii) Trimethoprim (iv) Nikethomide (v) Nitrazepam (vi) Chlorpromazine (vii) Orcipemaline (viii) Clofibrate.
2. What are cardiovascular agents ? Classify them and give the names of various drugs of each class/subclass. Give an account of B-blockers.
3. What are hypoglycaemic agents ? Give an account of them.
4. Write the structure and chemical name of the following drugs :
   (i) Trichloroethylene (ii) Paracetamol (iii) Procaine (iv) Methylphenobarbitone (v) Paraldehyde (vi) Caffeine (vii) Methyl salicylate (viii) Phenytain.
5. Write notes on :
   (i) Sulphonamides (ii) Antispasmodic and anti-ulcer drugs.
6. Define hypnotics and sedatives. What is the difference between them? Give an account of them.
7. Identify the heterocyclic ring and other groups present in the following drugs (any ***six***) :
   (i) Morphine (ii) Papaverine (iii) Chloroquine (iv) Propylthiouracil (v) Oestradiol (vi) Amphetamine (vii) Methylnicotinate (viii) Dicoumarol.

D. PARM. 1991 (ANNUAL)

1. Write the structures of the following :
   (a) A cholinergic alkaloid
   (b) An agent used for the treatment of leprosy

(c) An adrenergic noncatecholamine
(d) A sulphonamide diuretic agent
(e) A sulphonamide antidiabetic agent
(f) A 9-aminoacridine used as antimalarial
(g) A component of viramin B complex
(h) A nonsteroidal oestrogenic compund.

2. (a) Write the physical properties and uses of :
(i) Vitamin B_1 (ii) Glyceryl trinitrate (iii) Benzyl alcohol (iv) Paraldehyde

(b) Answer the following :
(i) Name a barbitutate having anticonvulsant activity
(ii) Name an alkaloid having CNS stimulant activity
(iii) Name a psychotropic phenothiazine.
(iv) Name an alkaloid having local anaesthetic activity.

3. (a) Write the uses and route of administration of the following:
(i) Streptomycin sulphate (ii) Piperazine citrate (iii) Sodium bromoglycate (iv) Lignocaine Hydrochloride

(b) Which drugs may be used in the following clinical conditions ; 2 each
(i) Hay fever (ii) Nasal congestion (iii) Pernicieous anaemia (iv) Arterial or venous thrombosis.

4. What are the different classes of cardiovascular drugs. Describe various antihypertensive agents in detail.

5. (a) Write a note on the role of vitamins on our body and their medicinal significance
(b) Describe various radio-opaque media as diagnostic agents.

6. Give a chemical classification of antihistamines with structures of each class.

7. (a) Discuss the medicinal significance of cholinergies and anticholinergic drugs.
(b) Write a note on antidepressant drugs.

D. PHARM. 1990 (SUPPLEMENTARY)

1. What are antibiotics? How can they be classified on chemical basis? Describe medicinally important tetracyclines.
2. (a) In what type of indications are adrenergic drugs used ? Describe giving suitable examples.
   (b) Write down the uses and official preparations of various anticholinesterases.
3. Write down the uses, official preparations and storage conditions for the following in brief :
   (a) Diethyl ether (b) Paracetamol (c) Ascorbic acid (d) Streptomycin sulphate.
4. Write short notes on :
   (a) Sulphonomides as diuretic drugs (b) Antihypertensive agents.
5. What are the major classes of steroids used for therapeutic purposes? Describe the medicinal inportance of glucocorticoids.
6. Describe ;
   (a) Anticonvulsant drugs (b) Antidepressant drugs.
7. Give the structures, official preparation and uses of the following :
   (a) P-Aminosalicylic acid (b) Chloroquine (c) Salbutamol (d) Ibuprofen.
8. Write structural formulae and brief uses of the following :
   (a) Methyldopa (b) Progesterone (c) Frusemide (d) Phenytoin (e) Saccharin (f) Lignocain (g) Phenobarbitone (h) Primaquine.

B. PHARM -I YEAR,1993 (ANNUAL) SECTION B

1. What are diuretics? Give an account of various classes of diuretics with suitable exmples.
2. Write notes on any ***three*** of the following :
   (i) Vasodilators (ii) Progestogens (iii) Sulphonamides (iv) Antihypertensives (v) Anticonvulsants.
3. Discuss different types of the antimalarial drugs. Give suitable examples.

4. Write the structures and uses of any six of the following :
   (i) Betamethasone (ii) Paracetamol (iii) Diazepam (iv) Testosterone (v) Pethidine (vi) Indomethacin (vii) Chlorpromazine, (viii) Phenytoin.

5. Write an account of anti-infective agents.

B. PHARM. I YEAR, 1992 (ANNUAL) SECTION B

1. Write the structures, pharmacological category and properties of the following.
   (i) Stilbestrol (ii) Thiomersal (iii) Sulphathiazole (iv) Trimethoprim (v) Carbamazepine (vi) Methacholine (vii) Propranolol (viii) Carbimazole.

2. Write notes on :
   (i) Antihypertensive drugs (ii) Anti-infective agents (iii) C.N.S. Stimulants.

3. What is histamine? How is it produced in the body ? What are its various manifestations? Give a classification of antihistamines along with the names of drugs of each class. Describe one drug of each class.
   (a) Classify antibiotics and write names of antibiotics belonging to each class. Write the structure of tetracyclines.
   (b) Classify hypoglycaemic agents giving the names of agents of each class. Describe the structure of insulin and its various official preparations.
   (c) Classify nonsteroidal analgesics, antipyretics and anti-inflammatory drugs, giving the names of agents of each class. Give the structure of ibuprofen, analgin and oxyphenbutazone.

B. PHARM. I YEAR, 1991 (ANNUAL) SECTION B

1. Write the structure and uses of the following compounds each.
   (a) Halothane (b) Glyceryl trinitrate (c) Metronidazole (d) Pentobarbitone (e) Methyldopa (f) amphetamine (g) Antazoline (h) Carbachol

2. How allergic conditions can be treated ? Classify antihistamines with suitable examples. Describe two drugs of the class giving structures, physical properties and storage conditions.

3. (a) Classify cardiovascular drugs. Describe various cardiotonics.
   (b) What are anti-infective agents. Give a chemical classification with suitable examples.

4. (a) What are hypnotics and sedatives. Describe various barbituric acid derivatives.
   (b) Write a detailed note or antifungal agents.

B. PHARM. I YEAR, 1990 (SUPPLEMENTARY) SECTION B

1. (a) Write the structures of the following :
   (i) Primaquine (ii) Phenobarbitone (iii) Amphetamine (iv) Tolbutamide
   (b) Describe ***two*** anticogulants used orally.

2. Write short notes on.
   (a) Non-steroidal anti-inflammatory agents (b) Non-catecholamine sympathomimetic agents.

3. How antibiotics are classified on chemical basis. Give an account of orally active penicillins.

4. (a) Answer the following :
   (i) Salbutamol belongs to which class of adrenergic drugs.
   (ii) Give two examples of 4-aminoquinoline derivatives used as antimalarial drugs.
   (iii) Enumerate various water soluble vitamins
   (iv) Give two examples of tricyclic antidepressants.
   (b) Describe gaseous general anaesthetics.

5. (a) Describe in brief the role of oestrogens and progestilins as antifertility agents.
   (b) Write the structure of two antihypertensive agents and their medicinal significance.

BOARD OF TECHNICAL EDUCATION, HARYANA

DIP. PHARM. II YEAR, JULY 1993

1. (a) What are adrenergic drugs? Describe in detail giving suitable examples.
   (b) Write a short note on anticonvulsant drugs.
2. Attempt any ***two*** of the following :
   (a) Explain your understanding about the use of D.L. descriptor, (R)-(S) notations, and (Z)-(E) isomerism.
   (b) What are pharmaceutical aids? Give a general account of preservatives and antioxidants.
   (c) Classify vitamins. Write chemical name, structure and uses of one vitamin.
3. Write down the uses, official preparations and storage conditions of any ***four*** of the following :
   (a) Ethyl alcohol, (b) Diethyl ether. (c) Chloroform. (d) Glycerol (e) Chloramphenicol.
4. What are sulfonamides ? Describe different classes of sulfonamides with suitable examples with their official preparations and uses.
5. Attempt any ***two*** of the following :
   (a) Describe various broad spectrum antibiotics with their uses and side effects.
   (b) Give an account of oral contraceptives.
   (c) Describe the phenomenon of blood coagulations ? What different drugs are used as coagulants ?
6. (a) Give a general account of antimalarial drugs.
   (b) Discuss with suitable examples various drugs used as hypoglycaemic agents.
7. (a) What are antihistamine drugs. Mention different types of drugs used as antihistaminics.
   (b) Write an account on surface active agents giving suitable examples.
8. Write down the structural formula and medicinal uses of any ***eight*** of the following :
   (a) Paracetamol. (b) Progesterone (c) Thiopental sodium (d) Procaine (d) Phenytoin sodium (f) Codeine (g) Ethambutol (h) Leptazol (i) Methyldopa (j) Oxytetracycline.

DIP PHARM II YEAR, JULY 1992

1. (a) What are adrenergic drugs. Describe in detail giving suitable examples.
   (b) Write a short note on anticonvulsant drugs.

2. Attempt any ***two*** of the following.
   (a) Explain your understanding about the use of D.L. descriptors, (R)-(S) notations, and (Z)-(E) isomerism.
   (b) What are pharmaceutcal aids ? Give a general account of preservatives and antioxidants.
   (c) Classify vitamins. Write chemical name, structure and uses of one vitamin.

3. Write down the uses, official preparations and storage conditions of any ***four*** of the following.
   (a) Ethyl alcohol. (b) Diethyl ether (c) Chloroform (d) glycerol (e) Chloramphenicol.

4. What are sulfonamides. Describe different classes of sulfonamides with suitable examples with their official preparations and uses.

5. Attempt any ***two*** of the following :
   (a) Describe various broad spectrum antibiotics with their uses and side effects.
   (b) Give an account of oral contraceptives.
   (c) Describe the phenomenon of blood coagulation? What different drugs are used as coagulants ?

6. (a) Give a general account of antimalarial drugs.
   (b) Discuss with suitable examples various drugs used as hypoglycaemic agents.

7. (a) What are antihistaminic drugs? Mention different types of drugs used as antihistaminics.
   (b) Write an account on surface active agents giving suitable examples.

8. Write down the structural formula and medicinal uses of any ***eight*** of the following.
   (a) Paracetamol (b) Progesterone (c) Thiopental sodium (d) Procaine (e) Phenytoin sodium (f) Codeine. (g) Ethambutol (h) Leptazol (i) Methyldopa (j) Oxytetracyline.

DIP PHARMACY II YEAR, NOV. 1991.

1. Write the structure and uses of the following :
   (a) A short acting barbiturate (b) A phenothiazine derivative. (c) An 8-aminoquinoline (d) A constituent of vitamin B complex (e) A non-catecholamine (f) An alkaloid (g) INH (h) A progestational agent.
2. Write notes on :
   (a) Organic pharmaceutical aids (b) Antifungal agents
3. What are the different classes of cardiovascular drugs. Describe antihypertensive agents in detail.
4. Describe the uses, storage conditions and pharmaceutical preparations of the following :
   (a) Acetylsalicylic acid (b) Salbutamol (c) Insulin (d) Vitamin A.
5. (a) Describe various antitubercular drugs.
   (b) What are diagnostic agents? Describe various radio-opaques in detail.
6. How do you differentiate between local and general anaesthetics. Describe various medicinal agents used for local and general anaesthesia.
7. What are cholinergic drugs. How do they differ from cholinesterase inhibitors. Describe both types of agents with their medicinal significance.
8. What are broad spectrum antibiotics. Classify various antibiotics on chemical basis describing their medicinal importance in comparison to one another.

DIP. PHARMACY II YEAR, AUGUST 1991.

1. Write down the structural formula and medicinal uses of any ***eight*** of the followings :
   (a) Tolbutamide (b) Trimethoprim (c) Ibuprofen (d) Adrenaline (e) Clonidine Hydrochloride (f) Chlorthiazide (g) Methyl Salicylate (h) Warfarin Sodium (i) Thiamine Hydrochloride (j) Chloramphenicol Palmitate.
2. Write down the uses, official preparations and storage conditions of any three of the following :
   (a) Methyl Choline (b) Ethyl Chloride (c) Riboflavin (d) Analgin.

3. Define and classify cardiovascular drugs with suitable examples. Write structures, properties and specific uses of any ***three*** drugs belonging to different categories.

4. What are antibiotics ? Write mode of actions of any ***three*** antibiotics. Write a detailed note on semisynthetic penicillins.

5. Write structures, chemical names and uses of any ***four*** of the following :

   (a) Aspirin (b) Paracetamol (c) Frusemide (d) Methyl DOPA (e) Barbitone Sodium (f) Ascorbic Acid.

6. (a) Write a detailed note on biological importance of vitamins.

   (b) Comment on physical state (a solid or liquid) and solubilities of any ***four*** of the following vitamins :

   (a) Tocopherols (b) Cyanocobalamin (c) Vitamin A_1 (d) Folic acid (e) Pantothenol (f) Vitamin K.

7. Write short notes on any ***three*** of the followings :

   (a) Antihistamic agents (b) Pharmaceutical Aids. (c) Diagnostic agent (d) Non opiate analgesics (e) Non steroid anti-inflammatory agent.

8. (a) Discuss the various stages of anaesthesia. Classify general anaesthetics with suitable examples and representation structures.

   (b) Write common names and structures of any four of the following :

   (i) p-Amino-N-(2-diethyl amino ethyl) benzamide hydrochloride.
   (ii) 1,3,7-Trimethyl xanthine.
   (iii) Bis (4-amino phenyl) sulphone.
   (iv) 1-(4 hydroxy-3-hydroxyphenyl) 2-butyl amino ethanol.
   (v) p-Acetamido phenol.
   (vi) (-) 2-Methylamino-1-phenyl-propan-o1.

DIP PHARMACY II YEAR, NOV 1990.

1. Write chemical name, structures and uses of any ***five*** of the following :

   (a) Ephedrine (b) Anatazoline (c) Pentobarbitone (d) Metranidazole (e) Amphetamine (f) LEVO DOPA (g) Glyceryl trinitrate (h) Halothane.

2. How will you treat the manifestation produced by Histamine? Classify the drugs with suitable examples. Give the structures, physical properties, specific uses and storage conditions of any two drugs.
3. Define hypnosis and sedation. Describe the barbiturate type drugs used as sedative and hypnotics.

   (a) Oral hypoglycaemic agents (b) Antifungal agents (c) Colinergic drugs (d) Ointment Bases.
5. Enumerate the mode of actions of diuretics. Write structures, properties and official preparations of important diuretics.
6. Write notes on :

   (a) antithyroid drugs (b) Chemical contraceptives.
7. Write structures, physical properties and official preparations of any four of the followings :

   (a) Tetracycline (b) Ibuprofen (c) Analgin (d) Sodium Cromoglycollate (e) Ampicillin trihydrate.
8. Write detailed notes on any ***two*** of the followings :

   (a) Antihypertensive agent (b) Sympathomimetic amines. (c) Coagulants and Anticoagulants.

DIP. PHARMACY II YEAR, MAY 1990.

1. Describe different sulphonamides and sulphonyl ureas used as diuretic and antidiabetic drugs. Write down their official preparetions.
2. Describe three of the followings in brief;

   (i) General anaesthetics (ii) Antitubercular drugs. (iii) Steroidal contraceptive agents (iv) Diagnostic agent.
3. Attempt any ***two*** of the following :
   (i) What are the indications for the use of adrenergic agents. Describe in detail giving suitable examples.
   (ii) Write down the uses and official preparations of various anticholinesterases.
   (iii) Classify antimalarials. Describe one compound of each class giving the structure and side effects.
4. What are psychoactive drugs. Describe different classes of psychoactive agents with suitable examples.
5. Write the uses, official preparations and storage conditions of any ***three*** of the following :

   (i) Diethyl ether (ii) Aspirin (iii) Streptomycin sulphate (iv) Ascorbic acid.

6. Describe the ailments in which antihistaminic agents are used. Mention various antihistamines with their official preparations.

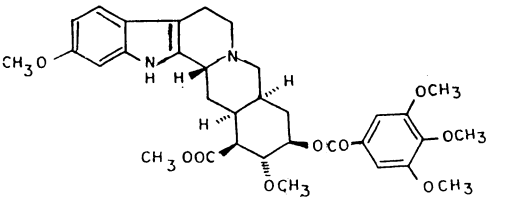
7. (i) What are analgesics? How do they differ from narcotic analgesics? Describe in brief two important analgesics.
   (ii) Write a short note on antithyroid drugs.
   (iii) Describe various tetracyclines listing their uses and side effects.

8. Write down the structural formula and medicinal uses of any ***seven*** of the following :
   (i) Phenobarbitone (ii) Isoniazid (iii) Metronidazole (iv) Progesterone (v) Tolbutamide (vi) Phenindione (vii) Frusemide (viii) Methyldopa (ix) Phenytoin.

UNIVERSITY OF RAJASTHAN, JAIPUR

DIP. PHARMACY II YEAR, NOVEMBER 1986

1. (a) Give the method of numbering and structure of (any ***two***):
   (i) Thiophene (ii) Pyraxole (iii) Barbituric acid
   (b) Draw the structure of (any ***two***)
   (i) 1-(2, 4-Dihydroxyphenyl) -2-methylaminoethanol (ii) 1,3,7-Trimethyl xanthine (iii) 4,5-Dichlorobenzene-1,3-disulphonamide
   (c) Write the structure of a drug which has following nucleus (any ***two***)
   (i) Quinoline (ii) Furan (iii) Phenothiazine
   (d) Give the structures of (any ***two***)
   (i) Mepacrine (ii) Dapsone (iii) Cortisone
   (e) Describe the skeletal structure, peripheral groups and linkage in the following structure:



2. (a) What are the uses of nitrofurazone and chlorocresol or thymol? Give the strucutre and chemical name of nitrofurazone.
   (b) Answer any ***one*** of the following :
      (i) Define antiarrhythmic agents. Give structure and properties of one such drug.
      (ii) Give the properties, uses and official preparations of niacinimide
   (c) Give the names of three colouring, flavouring and sweetening agents used in pharmaceutical preparations.
   (d) Attempt any ***one*** of the following :
      (i) Give the sugar part and aglycone part of digoxin and ouabain.
      (ii) Enumerate the drugs that reduce blood pressure.

3. Attempt any ***four*** of the following :
   (a) Give the structure and chemical names of amphetamine and ephedrine.
   (b) Mention the official preparations of three cholinergic agents.
   (c) What do you know about diagnostic agents? How will you classify them ? Enumerate general properties and uses of florescein.
   (d) Define the term coagulants and anticoagulants. Give the properties and uses of warfarin or thrombin.
   (e) Give the official preparations of insulin. What are it uses?
   (f) Name antithyroid drugs. Give their structure and properties.

4. Answer any ***four*** of the following :
   (a) Classify general anaesthetics. Give one example of each class.
   (b) What are barbiturates ? Where are they used ? Give their official preparations.
   (c) Write the properties, storage conditions and uses of the following (any ***two***):
      (i) Benzocaine (ii) Lignocaine hydrochloride (iii) Procaine hydrochloride
   (d) Give chemical names of xanthine derivatives. Which of these is a potent CNS stimulant?

(e) Write the structures and uses of the following (any ***two***)
(i) Paraldehyde (ii) Phenytoin sodium (iii) Ethosuximide

5. Attempt any ***four*** of the following :
   (a) Give the properties, stability, storage conditions and uses of neomycin or griseofulvin.
   (b) What do you know about antibiotics in general ? Write basic structure, storage conditions and official forms of penicillins.
   (e) Name the sulphonamides used as diuretics. Give their properties and uses.
   (f) Give official formulations and stability of vit B-1.

6. Solve any ***four*** of the following :
   (a) Give a general account of diuretics. Mention examples of different types of diuretics.
   (b) Mention the chemical names, storage conditions and official preparations of antihistamines of aminoalkyl ether class.
   (c) Name one analgesic each possessing the following chemical features (any ***two***) :
   (i) An alkaloid (ii) A ketone (iii) A piperidine
   (d) Enumerate the general properties, uses and trade names of market preparations of any three antipyretics.
   (e) What are anti-inflammatory agents? Give brief account of non-steroidal anti-inflammatory agents with suitable examples.
   (f) Justify "The antihistamines agents are generally used in form of salt".

DIP. PHARMACY II YEAR, APRIL-MAY 1987

1. (a) Give the method of numbering and structure of (any ***two***)
   (i) Tetrazole (ii) Isoxazolidine (iii) Phenothiazine
   (b) Draw the structure of (any ***two***)
   (i) 3,5,5-Trimethyloxazolidine 2,4 dion (ii) Ethyl-1-methyl-5-phenyl barbituric acid, (iii) 4, 5-dichloro benzene-1, 3-disulphonamide.
   (c) Explain the following terms and drugs used for its treatment (any ***two***) :
   (i) Vasoconstriction (ii) Inflammation (iii) Gout

(d) Fill in the blanks in the following sentences :

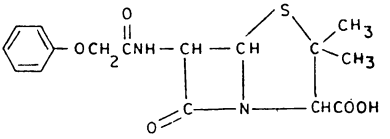
(i) The solutions of adrenaline should contain ..... as an antioxidant.

(ii) Isoniazid is useful in the treatment of .....

(iii) aminophylline is the salt of theophylline with .....

(iv) Aspirin gradually hydrolyses in contact with moisture to .....

(e) Describe the skeletal structure, peripheral groups and linkage in following structure :



2. (a) Draw steroid skeleton. Mention two steroidal drugs from androstane, estrane and pregnane. Give the properties and uses of cortisone.

(b) Under which class following diagnostic agents are covered? Give their properties, storage and stability conditions (any two):

(i) Diodone (ii) Methylene blue (iii) Iodised oil.

(c) What are pharmaceutical aids? Give a general account of suspending and emulsifying agents.

(d) Write the properties, storage, stability conditions and uses of the following (any ***two***):

(i) Methyl salicylate (ii) Betamethasone (iii) Propylthiouracil (iv) Dimethyl sulphoxide.

3. Solve any ***four*** of the following :

(a) give structure and uses of dapsone. Name the sulphonamides used in the treatment of intestinal infections.

(b) Write a short note on nicotinic acid or ascorbic acid.

(c) Classify antimalarials. Give properties, uses and official preparations of chloroquine.

(d) Give the dosage forms and official preparations of :

(i) Primaquine (ii) Sulphadiazine (iii) Cyanocobalamine

(e) What are penicillins? Where are they used? Give their official preparations.

4. Answer any ***four*** of the following :

   (a) Mention the drugs under central nervous system stimulants.

   (b) Draw the structure of paraldehyde. Give its properties, stability, sterilisation and storage conditions.

   (c) Mention the local anaesthetics obtained from plants. State the properties, uses and official form of procaine.

   (d) Name a general anaesthetic each possessing the following chemical/physical features :

   (i) Barbiturate (ii) Ether (iii) Halogenated hydrocarbon.

   (e) Classify anticonvulsant drugs on chemical basis. Give example from each class.

5. Attempt any ***four*** of the following :

   (a) What is major hormone secreted by adrenal medulla ? Give its pharmacological actions, storage and stability conditions.

   (b) Give a brief account of the drugs used as oral hypoglycaemic.

   (c) What is the source of acetylcholine ? Give its official dosage forms and storage conditions.

   (d) Write short note on (any ***two***):

   (i) Oxytoxin (ii) Ester-type local anaesthetics (iii) Digitalis glycosides.

6. Solve any ***four*** of the following :

   (a) Define anti-inflammatory agents. Name important official preparations of indomethacin.

   (b) Give the structure, properties, uses and official preparations of acetazolamide.

   (c) What is the physiological role of histamine? Mention the potent drugs used under each class of antihistamine agents.

   (d) How will you classify antipyretics? Draw the structure of :

   (i) Aspirin (ii) Paracetamol and (iii) Phenacetin.

   Give their storage and stability conditions.

(e) Define analgesics. Give an account of morphine and related compounds. Name important synthetic analgesics.

DIP. PHARMACY II YEAR, NOVERMBER 1987

1. (a) Give the method of numbering and structure of (any ***two***) :

   (i) Isoquinoline (ii) Piperidine (iii) Thiazole

   (b) Draw the structure of (any ***two***) :

   (i) 1-Acetamido -4-ethyne benzene (ii) 10-(3-Dimethylamino-2-methylpropyl) phenothiazine. (iii) N,N-Dimethyl-3-phenyl-3-pyrid 2^1-Y^1 propylamine.

   (c) Explain the following terms and drugs used for its treatment (any ***two***) :

   (i) Asthma (ii) Diarrhoea (iii) Margraine

   (d) Fill in the blanks in the following sentences :

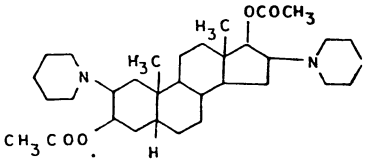
   (i) Cardiac glycosides are used in the treatment of.....

   (ii) Methyldopa is administered in .....

   (iii) Cyanocobalmin is effective in the treatment of.....

   (iv) Diphenhydramine hydrochloride is used as .....

   (e) Describe the skeletal structure, peripheral groups and linkage in the following structure :



2. (a) Name hormones which are derivatives of androstane, estrane and pregnane. Give the properties and uses of two of them.

   (b) What are the requirements of a satisfactory radio-paque materials? What are major side effects? Give properties and uses of iodoxyl.

   (c) Describe the physical characters of different agents used in ointment bases. Give a short account of preservatives and antioxidants.

   (d) Write the properties, storage conditions and uses of the following (any ***two***) :

   Sodium lauryl sulphate (ii) Carbimazole (iii) Propylene glycol (iv) Prednisolone.

3. Attempt any ***four*** of the following :
   (a) Give the structure, properties and uses of amphetamine.
   (b) Write short note on (any ***two***) :
   (i) Lipid-lowering agents (ii) Antipsychotic drugs (iii) Thyroxine.
   (c) Mention different preparations of insulin. Give the properties, uses and official form of modern hypoglycaemic agents.
   (d) Give the phenomenon of blood clotting. What is the role of heparin? Mention the different official forms of heparin.
   (e) What is acetylcholine ? Under which category it comes? Give its properties, stability, storage conditions and uses.

4. Solve any ***four*** of the following :
   (a) Classify diuretics on chemical and pharmacological basis. Which of these is a potent diuretic agent ?
   (b) What are anti-inflammatory agents ? Give an account of non-steroidal anti-inflammatory agents with suitable examples.
   (c) Give the structure, properties, stability, storage conditions and uses of oxyphenbutazone.

5. Answer any ***four*** of the following :
   (a) Under which chemical and pharmacological class caffeine belongs? Give its properties, uses and official preparations.
   (b) Draw the structure of barbituric acid. Give the properties, stability and storage conditions of paraldehyde.
   (c) State two anticonvulsant drugs of the hydantoins and barbiturates class. How do they differ structurally?
   (d) Give an account of general anaesthetics. Mention examples of different types of anaesthetics.
   (e) What are the natural sources of local anaesthetics? Enlist the agents which are in the class of amides.

6. Attempt any ***four*** of the following :
   (a) What do you know of sulphonamides? Writea note on long-acting sulphonamides.
   (b) State the uses, properties and official forms of Vitamin A.

(c) What do you know about antibiotics ? Write an account on antibiotics derived from sugars.

(d) How will you classify anti-malarials on chemical basis? Give properties and uses of primaquine.

(e) Write the properties, storage conditions and official preparations of the following (any ***two***) :

(i) Chloroquine (ii) Dapsone (iii) Thiamine.

DIP. PHARMACY II YEAR, APRIL/MAY 1988

1. (a) Give the method of numbering and structure of (any ***two***)

1. Imidazole 2. barbituric acid 3. Indole

(b) Draw the structure of (any ***two***) :

1. 5-Ethyl-5-(1-methyl butyl) 2-thiobarbiturate.
2. 1,3,7-Trimethyl xanthine
3. 1-(3,4-Dihydroxyphenyl)-2-methyl amino ethanol.

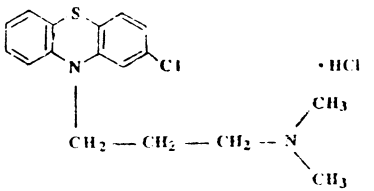
(c) **Write the structure of a drug which has following nucleus (any *two*) :**

1. Pyrroliline 2. Pyridine 3. Acridine

(d) **Give the structures of (any *two*) :**

1. Diazepam 2. Benzocaine 3. Methylene blue

(e) **Identify and describe the skeletal structure, peripheral groups and linkage in the following structure :**



2. Attempt any ***four*** of the following :

(a) What are local anaesthetic agents? Give structure and uses of lignocaine.

(b) Classify non-steroidal anti-inflammatory, analgesics and antipyretics with examples.

(c) Mention chemical name, structure and uses of frusemide.

(d) Define the term 'diagnostic agents'. Mention three

drugs used to test organ function. Draw the structure of iodoxyl.

(e) What do you know about female sex hormones ? Draw the structure of progesterone and give uses.

(f) What are organic pharmaceutical acids? Describe the role of preservatives and antioxidants in it. Draw the structure of propyl gallate.

3. Attempt any ***four*** of the following :

(a) Define the coagulants and anticoagulants. Mention stability and storage conditions and uses of Heparin.

(b) Give properties, uses and official preparations of Reserpine.

(c) In what pharmaceutical formulations the following drugs are used :

1. Ephedrine 2. Promethazine 3. Phenytoin.

(d) What are sulphonamides? Describe the structure activity of sulphonamides with reference to sulphadiazine.

(e) What do you know about cardiac glycosides? Mention the sugar and aglycone part of digitoxin, digoxin and ouabain.

(f) Define antipyretics. Give the structure, properties and uses of Paracetamol.

4. Attempt any ***four*** of the following :

(a) Define hypoglycaemic agents. Name the hypoglycaemic agents derived from sulphonyl urea. Give the structure of Phenformin HCl.

(b) Give structure, uses and official preparations of Methadone.

(c) Give structure, properties and official preparations of an antibiotic used in typhoid fever.

(d) Classify antihistamines giving one example from each class. Draw the structure of Histamine.

(e) Name six vitamins belonging to B-complex group. Draw the structure of vitamin used in 'pellagra'.

(f) Mention the general anaesthetic given by intravenous route. Draw its structure and give its properties.

5. Attempt any ***four*** of the following :
   (a) What do you know about Quinine and its salts. Give their uses.
   (b) Give chemical name, structure and properties of Methyl dopa.
   (c) What are anti-infective agents? Classify antiseptics and disinfectants giving examples.
   (d) What do you know about hypnotic and sedatives? Give structure, chemical name and official preparations of chloral hydrate.
   (e) How do Aspirin and Methyl Salicylate differ structurally ? Give their uses.
   (f) What are surface active agents? Give properties and uses of sodium lauryl sulphate.

6. Attempt any ***four*** of the following :
   (a) Name two thyroid hormones. Give structure, properties and uses of propyl thiouracil.
   (b) Define and classify diuretics giving examples.
   (c) Give the structure and chemical name and uses of Ephedrine.
   (d) Mention the narcotic analgesic containing piperidine ring. Give its structure, properties and official preparations.
   (e) Mention the sources, deficiency symptoms, uses and official preparations of vitamin A.
   (f) List out the antibiotics derived from sugar. Draw the basic skeleton of Tetracyclines. Give the uses of Tetracyclines.

BOARD OF TECHNICAL EDUCATION, RAJASTHAN

DIPLOMA IN PHARMACY EXAMINATION, 1992

1. (a) Define the following terms used in the pharmacopoeia under solubility description and storage :
   (i) Freely soluble; (ii) Sparingly soluble; (iii) Practically insoluble; (iv) Cool; (v) Warm; (vi) Storage under non-specific conditions.
   (b) Write down the structure along with numbering of any four of the following :

(ii) Thiophene; (ii) Oxazolidine; (iii) Pyradazine; (iv) Quinazoline; (v) Acridine; (vi) Barbituric Acid.

(c) Write structure, chemical names and uses of any ***three*** of the following :

(i) Chloroxylenol; (ii) Nitrofurazone; (iii) Iodoxyl; (iv) Methylparaben; (v) Vanillin.

2. Define, classify and enumerate steroidal drugs. Write structure, nomenclature, physical properties, stability, storage and official preparations (dosage forms) of important Oestrogens.

3. (a) Give structure, nomenclature, dosage forms and uses and any ***four*** of the following :

(i) Halothane; (ii) Proguanil; (iii) Nikethamide; (iv) Thiopentone; (v) Chlorpromazine; (vi) Carbamazepine.

(b) Write a brief account on the chemistry and applications of dyes used for medicinal purposes.

4. (a) Define and classify any ***two*** of the following agents enumerating (giving names) all such drugs belonging to each class :

(i) Diuretics; (ii) Local anaesthetics; (iii) Cardiovascular drugs.

(b) Write a brief chemical account on Fat Soluble Vitamins.

(c) What do you understand about Benzodiazepines ? Write structure of two such drugs.

5. (a) Write structure and nomenclature of any ***three*** of the following :

(i) Pilocarpine; (ii) Salbutamol; (iii) Acetonenaphthone; (iv) Ibuprofen; (v) Prednisolone.

(b) Write storage of any ***four*** of the following :

(i) Heparin; (ii) Oxytocin; (iii) Paraldehyde; (iv) Levallorphan; (iv) Riboflavin; (v) Methadone.

(c) In what type of dosage forms (official preparations) the following drugs are used ?

(i) Betamethasone; (ii) Paracetamol; (iii) Clofibrate; (iv) Chloroquine (v) Adrenaline; (vi) Physostigmine.

6. (a) Write short notes with sufficient emphasis on chemical aspects on any ***two*** of the following :

(i) Insulin and insulin preparations; (ii) Tetracyclines; (iii) Sulphonamides used in the intestinal infections.

(b) Differentiate the following pairs of drugs by giving their structures and main uses :

(i) Phentolamine and Phentolinium; (ii) Digoxin and Digitoxin.

DIPLOMA IN PHARMACY EXAMINATION, 1991

1. (a) Define the following terms used in the Pharmacopoeia under solubility description and storage:

Very soluble, Soluble, Very slightly soluble, Cold, Room Temperature, Excessive Heat.

(b) Write down the structure alongwith numbering of any ***four*** of the following :

Furan, Isoxazolidine, Pyrazine, Isoindoline, Hydantoin, Morpholine.

(c) Write structure, chemical names and uses of any ***three*** of the following :

Thymol, Cetrimide, Diodone, Chlorbutol, Saccharin.

2. Define, classify and enumerate Cardiovascular Drugs. Write structure, nomenclature, physical properties, stability, storage and official preparations (dosage forms) of Antiarrhythmic drugs.

3. (a) Give structure, nomenclature, dosage forms and uses of any ***four*** of the following :

Trichloroethylene, Pyrimethamine, Caffiene, Phenobarbitone, Chlorodiazepoxide, Phenytoin.

(b) Write a brief account on the chemistry of ointment bases.

4. (a) Define and classify any ***two*** of the following agents enumerating (giving names) all such drugs belonging to each class:

Adrenergic Agents, Antihistaminics, Nonsteroidal anti-inflammatory drugs.

(b) Write a brief chemical account on water-soluble vitamins.

(c) What do you understand about Phenothiazines? Write structures of two such drugs.

5. (a) Write structure and nomenclature of any ***three*** of the following :

Neostigmine, Hydrochlorthiazide, Warfarin sodium, Procaine, Indomethacin.

(b) Write storage of any ***four*** of the following :

Thrombin, Insulin, Formaldehyde, Nalorphine, Acetazolamide, Ergocalciferol.

(c) In what types of dosage forms (official preparations) the following drugs are used :

Propylthiouracil, Morphine, Aminophylline, Amodiaquine, Thyroxine, Gentamycin.

6. (a) Write short notes with sufficient emphasis on chemical aspects on any ***two*** of the following :

Oral Hypoglycaemic Agents, Co-trimoxazole, Anti-tubercular antibiotics.

(b) Differentiate the following pairs of drugs by giving their structures and main uses :

Carbamazepine and Carbimazole; Methyltestosterone and Methandienone.

BOARD OF TECHNICAL EDUCATION, PUNJAB

D. PHARM. FINAL JAN. 1993

1. (a) Write ***true*** or ***false*** against each of the following:

(i) Thiopentenone is general anaesthetic.
(ii) Propyl gallat is used as antioxidant.
(iii) Aldosterone is gluco-corticoid hormone.
(iv) Methylene blue is used in the treatment of cyanide poisoning.
(v) Benzyl alcohol is antifungal agent.
(vi) Paracetamol is phenolic analgesic.
(vii) Scurvy is due to the deficiency of Vit. K
(viii) Phenolphthaline has luxative property.

(b) Complete the following sentences :

(i) Adrenaline is stored in .....
(ii) ..... is the richest source of Vit. B. Complex.
(iii) Isoniazid is useful in the treatment of .....
(iv) Chemical name of aspirin is ....
(v) Paracetamol has..... taste and is ..... in water.
(vi) Streptomycin is used in the treatment of .....
(vii) .... is adevergic drug having catechol nucleus.

(viii) ..... is antimalarial drug obtained from natural source.

2. Give the structure, physical properties, class of drug and storage conditions of the following :
   (a) Primaquine (b) Nicotinic acid (c) Amphetamine (d) Thymal.
3. (a) Name any ***two*** anticonvulsant drugs. Write their preparation and Pharmaceutical properties.
   (b) Give the properties and dosage forms of any two heterocyclic non barbituratic hypnotic sedatives.
4. Write short notes on any ***two*** of the following :
   (a) Colouring and flavouring agents (b) Adrenergic drugs (c) Orally active hypoglycaemic agents.
5. What are Vitamins? Classify and illustrate your answer with suitable examples. Add a note on water soluble vitamins.
6. Write structure, chemical name, class of drug and properties of the following :
   (a) Aspirin (b) Promethazine hydrochloride (c) Dizepam (d) Lignocaine.
7. Describe briefly :
   (a) Vasodialators (b) Adrenocortico hormones.
8. Mention class of drug, properties and storage conditions of the following :
   (a) Phenindione (b) Nitrofurazone (c) Methyl dopa (d) Carbachol.

D. PHARM. FINAL, JAN. 1992.

1. Define diuretics. Classify them giving one example of each class with structural formulae, chemical name and the uses.
2. Give the uses and storage conditions of the following.
   (1) Sulfadiazine (2) Acetyl-choline (3) Digitoxin (4) Chlorpromazine (5) Anaesthetic Ether (6) Tolazoline (7) Ascorbic Acid and (8) Morphine
3. What are anti-inflammatory agents? give an account of non-steroidal anti-inflammatory agents with suitable examples.

4. What are cardiovascular agents? Classify them. Discuss in detail any one type.

5. Name the vitamins belonging to vitamin B complex group. Give a brief description of the important members. Write chemical name and structure of one of them.

6. Write notes on
   (a) Oestrogens & Progestogens. (b) Anticoagulants.

7. What do you know about diagnostic agents ? Write a general account.

8. Write briefly on
   (1) Coagulants (2) Haemostatics (3) Orally active hypoglycaemic agents and vitamin D.

D. PHARM FINAL, JULY 1992.

1. Give the structural formulae and uses of any five of the following :
   (i) Caffeine (ii) Diazepam (iii) Troxidone (iv) Primidone (v) Pethidine Hydrochloride (vi) Phenobarbitone (vii) Benzocaine (viii) Aspirin

2. Give an account of the drugs as used cholinergic and anticholinesterase agents.

3. What do you know about disinfectants and antiseptics in general ? Give in detail phenols and related substances used as disinfectants.

4. Write notes on :
   (a) Thyroid and antithyroid drugs. (b) Diuretics.

5. Write the structural formulae and number the different positions of the following :
   (1) Hydantoin (2) Acridine (3) Isoquinoline (4) Indole (5) Isoxazolidine (6) Pyrazine (7) Quinazoline (8) Piperidine

6. What are antimalarials? Give their classification.
   Name the drugs giving their structural formulae, properties and uses of the class of 4-amino quinolines.

7. Give the storage conditions and uses of the following :
   (a) Adrenaline (b) Insulin (c) thyroxine (d) Methyl salicylate (e) Vitamin B_{12} (f) Chloramphenicol (g) Paracetamol (h) Phenazone.

8. What do you know about antibiotics ? Write in detail about penicillin.

MAHARSHI DAYANAND UNIVERSITY, ROHTAK.

D. PHARM II YEAR, 1992 (SUPPLEMENTARY)

1. What are Antimalarial drugs? Discuss their chemical nature, sources and uses.
2. Give a detailed account of Narcotic analgesics.
3. Give the chemical structure, category and uses of any ***eight*** of the following :
   (a) Chloramphenicol. (b) Bemegride. (c) Ephedrine. (d) Physostigmine (e) Frusemide. (f) Reserpine. (g) Talbutamide. (h) Lignocaine. (i) Carbimazole (j) Analgin.
4. Classify drugs acting on C.N.S. Write an account of C.N.S. stimulants.
5. What do you know of Histamine and Antihistamine agents? Describe, in detail, one drug of each subcategory.
6. Write brief notes on :
   (a) Anticoagulants. (b) Antidepressant drugs.
7. Describe Cholinergic blocking agents. Give a brief account of them.

DIPLOMA IN PHARMACY (PART II-A) EXAMINATION, 1992 (ANNUAL)

1. What are antibiotics? Classify them. Write down names, chemical structures and uses of at least ***five*** important antibiotic drugs.
2. What are cardiovascular agents? Classify them giving the names of agents of each class. Discuss giving chemical structure of one drug from each sub-category.
3. Give the chemical structure and uses of any ***eight*** of the following :
   (i) Sulphaguanidine; (ii) Quninine ; (iii) Theophylline; (iv)

Diazepam; (v) Neostigmine; (vi) Cocaine; (vii) Mepyramine maleate; (viii) Morphine; (ix) Papaverine; (x) Testosterone.

4. Write the name and structure, the category it belongs to, of the drugs possessing the following features. (Attempt any ***eight***) :
   (i) A none-ureide nonbarbiturate hypnotic and sedative drug;
   (ii) An anticonvulsant having hydantoin nucleus;
   (iii) A MAO inhibitor anti-depressant drug;
   (iv) A synthetic C.N.S. stimulant having pyridine nucleus;
   (v) An alkaloid having cholinergic activity;
   (vi) An adrenergic drug with 2-imidazoline as the basic ring;
   (vii) A carbonic anhydrase inhibitor diuretic drug having thiadiazole nucleus;
   (viii) A biguanide synthetic hypoglycaemic agent ;
   (ix) An antithyroid drug having thiouracil nucleus;
   (x) An antimalarial derivative of 4-aminoquinoline.

5. What are diagnostic agents? Describe the various drugs to test the organ function.

6. Write brief notes on :
   (i) Ganglion blocking agents;
   (ii) Intravenous general anaesthetics.

7. Define and classify psychoactive drugs giving the names of compound of each class. Give a detailed account of antianxiety drugs.

SECOND DIPLOMA IN PHARMACY SUPPLEMENTARY, 1993.

1. Give the structure, category/sub-category of any ***eight*** of the following :
   (i) Chloramphenicol; (ii) Benzocaine; (iii) Chlortniazide; (iv) Frusemide; (v) Ephedrine; (vi) Nalorphine; (vii) Atropine; (viii) Clofibrate; (ix) Acetazolamide; (x) Tolbutamide.

2. Write a brief account on any ***two*** of the following :
   (i) Diagnostic agents; (ii) Autonomic Blocking agents; (iii) Narcotic antagonists.

3. Give a detailed account of thyroid and anti-thyroid drugs.
4. Classify antimalarials giving the names of drugs of each class. Describe in detail one drug of each class.
5. What are antihistaminic drugs? Classify them and give the names of drugs of each category. Give a detailed account of one drug of each category.
6. Write notes on the following :
   (i) Hypoglycaemic agents; (ii) Antidepressants;
7. Write the structure, category/sub-category and properties of any ***eight*** of the following :
   (i) Chlordiazepoxide; (ii) Pholcodine; (iii) Lignocaine; (iv) Guanethidine; (v) Nicoumalone; (vi) Sulphacetamide; (vii) Chlortetracycline; (viii) Spironolactone; (ix) Phytomenadione;

INDEX

Acetazolamide 244
Acetylcholine chloride 227
Acetyldigitoxin 333
Acetyldigoxin 333
Achromycin 107
Acriflavin 21
Actinomycins 388
Acyctic ureides 167
Adrenaline 208
Adrenergic antagonists 218
Adrenergic drugs 208
Amethocaine 193
Amidopyrine 298
Aminacrine hydrochloride 32
p-Aminosalicylic acid 54
Amitriptyline 195
Amodiaquine 142
Amodiaquine hydrochloride 143
Amphoteracin 131
Ampicillin 89, 95
Ampicillin Sodium 96
Ampicillin trihydrate 97
Amylobarbitone 177
Anaesthetics 170,187
Analeptics 202
Analgesics 280
Analgin 289
5α-Androstone 273
Antazoline hydrochloride 279
Anthelmintic drugs 66
Antiamoebic drugs 66
Antiarrhythmic drugs 337
Antibiotics 81
Anticoagulants 262
Antidepressant drugs 314
Antifungal agents 126
Antihistaminic agents 269
Antihypertensive agents 341
Anti-inflammatory agents 294
Antileprotic drugs 46
Antimalarial drugs 134
Antimony sodium tartrate 80
Antineoplastic agents 387
Antipyretics 19, 280
Antiseptics 19
Antithyroid, 289
Antitubercular drugs 52
Ascorbic acid 361
Aspirin 287, 298
Atropine 230
Aureomycin 107
Azathioprine 389

Barbiturates 165, 315
Bendrofluazide 244
Benzalkonium Chloride 21
Benzathine penicillin 94
Benzocaine 191
Benzthiazide 240
Benztropine mesylate 234
Benzylpenicillin 90
Benzylpenicillin potassium 92
Benzylpenicillin sodium 91
Bephenium hydroxynaphthoate 80
Betamethasone 374
Betamethasone benzoate 374
Betamethasone Dipropionate 374
Betamethasone Valerate 374
Bethanidine Sulphate 349
Biocytin 355
Biotin 354
Biperiden 236

Bishydroxycoumarin 265
Brilliant Green 32
Bupivacaine 194
Busulphan 390
Butobarbitone 170

Caffeine 204
Calcium aminosalicylate 57
Calcium folinate 360
Calcium pantothenate 355
Carbachol chloride 227
Carbamazepine 328
Carbenicillin 99
Carbenicillin sodium 99
Carbinazole 304
Cardiac glycosides 32
Cardiovascular drugs 245
Cephalexin 118
Cephaloridine 119
Cephalosporins 84, 117
Cephalothin 120
Cephamycins 84
Cetrimide 23
Cetylpyridinium Chloride 32
Ciniofon 72
Chlorambucil 391
Chloramine 33
Chloramphenicol 122
Chlorhexidine hydrochloride 33
Chlordiazepoxide 158
Chlordiazepoxide hydrochloride 159
Chlorocresol 23
Chlorpromazine 152
Chlorpromazine hydrochloride 153
Chloroquine 139
Chloroquine Phosphate 140
Chloroquine sulphate 140
Chlorothiazide 238
Chlorotrianisene 386
Chloroxylenol 24
Chlorpheniramine 277
Chlorpheniramine maleate 277
Chlothalidone 244
7- Chlortetracycline 107
Chlortetracycline hydrochloride 112
Chlorthalidone 244
Cholesterol 373
Cholic acid 373
Cholinergic antagonists 229
Cholinergic drugs 221
Choline theophyllinate 244
Cinchona alkaloids 135
Cinnamaldehyde 50
Cisplatin 392
Classification 4
Clavulanic acid 84
Clofazimine 47
Clofibrate 249
Clonidine hydrochloride 349
Cloxacillin 89, 98
Cloxacillin sodium 98
Coagulants 262
Cocaine 192
Codeine 284
Congo red 311
Coramine 206
Cortisone 375
Cortisine acetate 376
Co-trimoxazole 42
Cyanocobalamin 360
Cyclobarbitone 171
Cyclobarbitone calcium 172
Cyclomethylcaine 193
Cyclopenthiazide 244
Cyclophosphamide 393
Cyproheptadine 274
Cyproheptadine hyodrochloride 274
Cyclopropane 180
Cycloserine 63

Dapsone 47, 50
Daunorubicin 393
Daunorubicin hydrochloride 394
DEC 79
Demeclocycline 107, 115
6-Deoxy-5-oxytetracycline 107
Dequalinium chloride 33
Deserprdine 344
Deslanoside 334
6-Desmethyl-6-deoxy- 5- hydroxy-6-methylene tetracycline 107
Dextroamphetamine sulphate 207
Dextromoramide 293

Dextropropoxyphene 290
Dextropropoxyphene hydrochloride 291
Diagnostic agents 305
Diazepam 160
Diazoxide 349
Dibromopropanidine isothionate 33
Dichlorophenamide 244
Dichlorphene 80
Dicloxacillin 89
Dictinomycin 388
Diels hydrocarbon 373
Dienoestrol 385
Diethylcorbamazine 79
Diethyl ether 181
Digitoxin 330
Digoxin 331
Dihydropenicillin F 90
Dihydrotachysterol 367
Di-iodohydroxyquinoline 71
Diloxamide furoate 73
Diphenyhydramine 272
Diphenylhydantion 318
Diphenylhydantoin sodium 319
Diphenylpyraline hydrochloride 278
Dipipanone 293
Disinfectants 19
Disopyramide phosphate 340
Dithranol 133
Diuretic drugs 237
Domiphen bromide 33
Dothiepin hydrochloride 201
Doxepin hydrochloride 201
Doxycycline 107, 116
Doxycycline hydrochloride 117

Ecothiopate iodide 228
Edrophonium chloride 228
Emetine 67
Ephedrine 215
Erythromycin 104
5α-Estrane
Ethacrynic acid 243
Ethambutol 60
Ether peroxide 182
Ethinyloestradiol 385
Ethionamide 62
Ethisterone 386
Ethosuximide 323
Ethotoin 320
Ethyl isonicotinate
Ethyl nitrite 254
Evans blue 310

Fat soluble vitamins 364
Fenfluramine 217
Fentanyl 293
Flucinoline acetonide 386
Fludrocortisone acetate 386
Flufenamic acid 298
Fluoresccin sodium 312
Fluorouracil 394
Folic acid 358
Folinic acid SF 359
Formaldehyde 25
Formaldehyde solution 27
Formalin 27
Furosemide 237

General anaesthetics 178
Gentamycin 100
Gntamycin sulphate 101
Gitoxin 332
Glibenclamide 258
Glutethimide 172
Glyceryl trinitrate 246
Griseofulvin 121
Guanidine 37
Guanethidine 248
Guanethidine sulphate 346

Haloperidol 156
Halothane 179
Hamycin 132
Heparin 262
Heparin calcium 263
Heparin sodium 263
Hexachlorophene 27
Hexylresorcinol 80
Histamine 269, 270
Homatropine 233
Hydantoins 318
Hydralazine hydrochloride 346
Hydrochlorothiazide 239

Hydrocortisone 376
Hydrocortisine acetate 377
Hydrocortisine 21-sodium succinate 377
Hyoscine 231
Hypnotics 165
Hypoglycemic agents 252

Ibuprofen 297
Imidazole 203
Imipramine hydrochloride 198
Indigo carmine 309
Indigotin disulphonate sodium 309
Indomethacin 294
Inositol 353
Insulin 252
Insulin Injection 255
Insulin zine sulphate 255
Iodipamide 313
Iodochlorhydroxyquin 69
Iothalamic acid 313
Iopanoic acid 306
Isoniazid 53
Isoprenaline 211
Isoxsuprine 251

Lanatoside C 333
Levaclophan 293
Levorphanol 293
Lignocaine 187
Liquified phenol 30
Local anaesthetics 187
Lorazopam 161
Lyxoflavine 354

Mannitol 242
Mebendazole 78
Mebutamate 348
Mecamylamine hydrochloride 349
Meclozine hydrochloride 279
Medroxyprogesterone acetate 386
Mefenamic acid 298
Megestrol acetate 386
Melphalan 398
Menadione 264
Mepacrine hydrochloride 148
Mephentermine 217
Mephenytoin 320
Mephobarbital 316
Meprobamate 161
Mepyramine 275
Mercaptopurine 395
Mersalyl acid 244
Mestranol 385
Metformin 259
Methacholine chloride 228
Methacycline 107
Methacycline hydrochloride 114
Methadone hydrochloride 286
Methallenoestril 385
Methandienone 177, 385
Methaqualine 177
Metharbital 317
Methicillin 89
Methohexital sodium 183
Methsuximide 325
Methotrexate 396
Methoxamine hydrochloride 217
Methsuximide 325
Methylamphetamine 217
Methsuximide 325
Methylamphetamine 217
Methyldopa 247, 347
Methyldopate hydrochloride 347
Methylol riboflavin 353
Methyl prednisolone 386
Methyl solicylate 298
Methyltestosterone 385
Methyprylon 174
Metronidazole 68
Miconazole nitrate 133
Minocycline 107
Mitomycin 396
Morphine 280
Morphine hydrochloride 282
Morphine sulphate 282

Nafcillin 89
Nalorphine 293
Nandrolone 384
Naphazoline nitrate 217
Neomycin 102
Neomycin sulphate 103
Neostigmine 222
Niacin 356
Nicoumalone 26

Nicotinamide 357
Nitrazepam 172
Nitrofurantoin 31
Nitrofurazone 33
Nomenclature 5
Norcardicins 84
Noradrenaline 210
Norethandrolone 385
Norethisterone 386
Norethynodrel 386
Nortryptyline 197
Nystatin 130

Octaphonium chloride 33
Oestradiol 383
Orciprenaline 217
Ouabain 335
Oxacillin 89
Oxazepam 160
Oxazolidinediones 321
Oxypertine 158
Oxyphenbutazone 296
5-Oxytetracydine 107
Oxytetracycline hydrochloride 113

Pamaquine 141
Pantothenic acid 355
Paracetomol 289
Paraformaldehyde 26
Paraldehyde 175
Paramethadione 322
Pargyline hydrochloride 348
Paromomycin 74
PAS 54
Penaldic acid 88
D-Penicillamine 88
Penicilloic acid 88
Penicillin F 90
Penicillin G 89
Penicillin K 90
Penicillin O 90
Penicillins 82
Penici''in V 89
Penicillin X 90
D- Penillic acid 88
Penilloaldehyde 88
Penilloic acid 88
Pentazocine 292
Pentobarbitone sodium 177
Pentolinium tartrate 349
Perphenazine 163
Pethidine 283
Pethidine hydrochloride 283
Pharmacopoeia 2
Phenacemide 327
Phenacetin 298
Phenalzine 199
Phenethicillin 89
Phenformin 258
Phenindamine tartrate 279
Phenindione 268
Pheniramine 276
Phenobarbitone 168, 316
Phenobarbitone sodium 177
Phenol 28
Phenosuximide 324
Phenoxybenzamine hydrochloride 251
Phenoxymethyl penicillin 93
Phenoxymethyl penicillin potassium 93
Phensuximide phentolamine mesylate 251
Phenylbutazone 295
Phenylephrine hydrochloride 212
Phthalylsulfathiazole 39
Physiostigmine 226
Pillaromycin A, 107
Pilocarpine 225
Piperazine 75
Piperazine adipate 76
Piperazine calcum edathamil 77
Piperazine citrate 77
Practalol 220, 340
Pralidoxime chloride 224
Prednisolone 378
Prilocaine 193
Primaquine 144
Primaquine phosphate 145
Primidone 326
Procainamide hydrochloride 339
Procaine hydrochloride 189
Prochlorperazine 153
Prochlorperazine dimaleate 154
Proflavine 20
Progestene 380

Proguanil hydrochloride 146
Proinsulin 255
Promethazine 273
Promethazine hydrochloride 273
Propanidid 186
Propantheline bromide 234
Propicillin 89
Propionic acid 126
Propranolol hydrochloride 219, 340
Propyliodone 307
Propylthiouracil 304
Protoveratrines A and B 345
Protoveratrine A and B maleats 345
Protriptyline hydrochloride 201
Proxymetacaeme 193
Pseudoephedrine 216
Purine pyrimidine and related heterocyclic compounds 202
Pyrazinamide 64
Pyridostigmine bromide 223
Pyridoxine hydrochloride 356
Pyrimethamine 147
Pyrimidine 203

Quinacrine hydrochloride 148
Quinalbarbitone sodium 177
Quinidine 250
Quinidine gluconate 338
Quinidine polygalacturonate 338
Quinidine sulphate 338
Quinine 137
Quinine sulphate 138

Rauwolfia alkaloids 342
Rescinnamine 344
Reserpine 251, 342
Riboflavin 352
Rifampicin 59
Rolitetracycline 107, 112

Salbutamol 214
Scillaren 336
Secobarbital sodium 177
Sodium aminosalicylate 56
Sodium ascorbate 364
Sodium cephalothin 121
Sodium diatrizoate 279, 313
Sodium levothyroxine 300
Sodium propionate 127
Sodium sulfacetamide 44
Solanaceous alkaloids 229
Solapsone 50
Spironolactone 244
Stability 12
Steroidal drugs 372
Stibophen 80
Stilboestrol 385
Storage conditions 12
Streptomycin 57
Streptomycin sulphate 58
Strophanthin 335
Succinylsulfathizole 39
Sulfacetamide 43
Sulfadiazine 35
Sulfadimethoxine 40
Sulfafurazole 45
Sulfaguanidine 36
Sulfamethoxazole 41
Sulfamethoxy pyzidazine 41
Sulfapyridine 45
Sulphobromophthalein sodium. 308
Sulphonamides 34
Syrosingopine 343

Terramycin 107
Terbutaline sulphate 215
Testosterone 382
Tetrachloroethylene 80
Tetracyclines 106
Tetracycline 107,110
Tetracycline hydrochloride 110
Theobromine 203
Theoclic acid 278
Theophylline 203
Thiabendazole 80
Thiacetazone 61
Thiambutosine 49
Thiamersal 32
Thiamine hydrochloride 351
Thiopental sodium 184

Thiotepa 398
Thiothixene 155
Thiombin 264
Thymol 32
Thymoxamine hydrochloride 251
Thyroxine 299
Tolazoline 218
Tolazoline hydrochloride 251
Tolbutamide 257
Tolnaftate 129
Tranquillizers 150
Tranylcypromine sulphate 200
Triamcinolone 386
Triamterene 244
Trichloroethylene 185
Trichlofos sodium 176
Trifluoperazine 154
Trimethadione 321
Trimethoprim 148
Trimipramine maleate 201
Tripelennamine hydrochloride 278
Triperidol 157
Triprolidine hydrochloride 278
Tropicamide 235

Undecylenic acid 128
Urea 240
Uric acid 203

Veratrum alkaloids 345
Veratrum viride 345
Viprynium embonate 80
Vitamins 350
Vitamin A 364
Vitamin B Complex 351
Vitamin C 361
Vitamin D 366
Vitamin D_2 366
Vitamin D_3 367
Vitamin E 368
Vitamin K 370
Vitamin K_1 370
Vitamin K_2 370
Vitamin K_3 371

Warfarin 266
Warfarin sodium 267
Water soluble vitamins 351

Xanthine 203

Zinc undecylenate 128

CBS OUTSTANDING BOOKS

Biopharmaceutics & Pharmacokinetics....Kulkarni
Pharmacology for MBBS, BDS & Other Exams....Bhatia, M.S.
Chemistry of Natural Products (in 2 Vols.) ....Kar, Ashutosh
Clinical Pharmacology Review ....Saif, S.R.
Concepts of Biochemistry (Physiotherapy & Pharmacy) ....Singh, S.P.
Cooper & Gunn's Dispensing for Pharmaceutical Students, 12/e ....Carter
Cooper & Gunn's Tutorial Pharmacy, 6th ed....Carter
Dictionary of Pharmacy....Jarald
Drug Store & Business Management....Mohd. Ali / Gupta
Essentials of Pharmaceutical Biochemistry ....Harbans Lal
Experimental Pharmaceutical Chemistry, 2nd ed. ....Siddiqui
Experimental Pharmacology....Pillai, K.K.
Experimental Pharmacology for Undergraduate Students....Garg / Arya
Handbook of Health Education & Community Pharmacy ....Gupta, A.K.
Handbook of Drug Store & Business Management....Gupta, A.K.
Health Education & Community Pharmacy....Parmar, N.S.
Hospital & Clinical Pharmacy ....Mohd. Ali / Siddiqui
Instrumental Methods of Analysis, 7th ed....Willard, M.H.
Introduction to Organic Mass Spectrometry....Siddiqui, Anees A.
Introduction to Pharmaceutics (Vol. I), 3rd ed....Gupta, A.K.
Introduction to Pharmaceutics (Vol. II), 4th ed....Gupta, A.K.
Advances in Controlled & Novel Drug Delivery ....Jain, N.K.
Advances in Liposomal Therapeutics....Vyas, S.P. / Dixit, V.
Advances in Pharmaceutical Biotechnology ....Vyas / Kumar
Health Education & Community Pharmacy ....Jain, N.K.
Medical Pharmacology....Sengupta
Medical Pharmacology, 3rd ed....Udaykumar, P.
Nanocolloidal Carriers....Vyas, S.P.
Organic Spectroscopy (N.M.R., I.R., Mass and UV) ....Dewan, S.K.
Pharmaceutical Biochemistry ....Vyas / Kohli
Pharmaceutical Biotechnology ....Vyas, S.P.
Pharmaceutical Product Development, 2nd ed. ....Jain, N.K.
CBS Quick Medical Examination Review Series:
Pharmacology, 15th ed....Bhatia, M.S.
CBS Quick Text Revision Series:
Important Text for Viva / MCQs: Pharmacology ....Bhatia, M.S.



CBS Publishers & Distributors Pvt. Ltd.
4819/XI, 24 Ansari Road, Daryaganj, New Delhi - 110 002 (India)
E-mail: cbspubs@airtelmail.in; delhi@cbspd.com • www.cbspd.com
New Delhi · Bengaluru · Chennai · Kochi · Kolkata · Mumbai
Hyderabad · Nagpur · Patna · Pune · Vijayawada