CBS Confident Pharmacy Series

Fourth Edition

Pharmaceutics

for First Year Diploma in Pharmacy

Course Code: **ER20-11T**

According to the latest syllabus prescribed by Pharmacy Council of India under Regulation 7 of the Education Regulations, 2020, for Diploma in Pharmacy course, implemented with strict compliance from 2021–2022 academic session.



VN Raje

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Salient Features

- ❏ Lucid and easy language
- ❏ To the point answers
- ❏ Remembering the concepts in the simplest way
- ❏ Infusing confidence in the reader to appear in the board examinations

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Preface

This edition of book builds self-confidence in students which will help them to get success in the examinations. The book has been written to meet the requirements of students of Diploma in Pharmacy (D Pharm) in accordance with the new revised syllabus ER-2020 prescribed by Pharmacy Council of India.

This book is small and humble effort has been put in for compiling necessary information on the subject. An attempt has been made to demystify and simplify the basic concepts for the students of pharmacy and to enable them get an evergreen success in MSBTE examinations.

The salient features of the present book are:

- Lucid and easy language
- To the point answers
- Remembering facts in the simplest way and
- Infusing confidence in the reader to appear in the board examinations.

Hence the series is named

CBS Confident Pharmacy Series

I am confident that this book will be useful to both the students and the teachers of Diploma in Pharmacy as well as the candidates desiring to succeed in competitive examinations for better job opportunities in pharmacy profession such as hospital pharmacists in PHCs, civil hospitals, etc.

Raje Vijay N

to

my beloved family

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I am also thankful to Shri Satish Kumar Jain, Chairman and Managing Director, and Shri Shantanu Sarkar, General Manager, Mumbai Branch, CBS Publishers & Distributors Pvt Ltd, for their sustained efforts and keen interest in the publication of this book.

I wish all my beloved students to have a great success in the board examinations.

Raje Vijay N

Syllabus

(Strictly Based as per New ER2020)

Pharmaceutics

1. • History of the profession of Pharmacy in India in relation to Pharmacy education, industry, pharmacy practice, and various professional associations.
   • Pharmacy as a career.
   • Pharmacopoeia: Introduction to IP, BP, USP, NF and Extra Pharmacopoeia. Salient features of Indian Pharmacopoeia.
2. **Packaging materials:** Types, selection criteria, advantages and disadvantages of glass, plastic, metal, rubber as packaging materials.
3. **Pharmaceutical aids:** Organoleptic (Colouring,flavouring, and sweetening) agents.

   Preservatives: Definition, types with examples and uses.
4. **Unit operations:** Definition, objectives/applications, principles, construction and workings of:

   Size reduction: hammer mill and ball mill.

   Size separation: Classification powder according to IP, Cyclone separator, Sieves and standards of sieves.

   Mixing: Double cone blender, Turbine mixer, Triple roller mill and Silverson mixer homogenizer.

   Filtration: Theory of filtration, membrane filter and sintered glass filter.

   Drying: working of fluidized bed dryer and process of freeze drying.

   Extraction: Definition, Classification, method and applications.
5. **Tablets:** Coated and uncoated, various modified tablets (sustained release, extended-release, fast dissolving, double layered).

   Capsules: Hard and soft gelatine capsules.

   Liquid oral preparations: Solution, syrup, elixir, emulsion, suspension, dry powder for reconstitution.

Topical preparations: Ointments, creams, pastes, gels, liniments and lotions, suppositories and pessaries.

Nasal preparations, Ear preparations.

Powders and granules: Insufflations, dusting powders, effervescent powders and effervescent granules.

Sterile formulations: Injectables, eye drops and eye ointments.

Immunological products: Sera, vaccines, toxoids and their manufacturing methods.

6. **Basic structure, layout, sections and activities of pharmaceutical manufacturing plants.**

   Quality control and quality assurance: Definition and concepts of quality control and quality assurance, current good manufacturing practice (cGMP), Introduction to concept of calibration and validation.

7. **Novel drug delivery systems:** Introduction, Classification with examples, advantages and challenges.

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CHAPTER 1

History of Pharmacy Profession in India

1 Explain the "History of Pharmacy Profession in India".

☞ **History of Pharmacy Profession in India:**

- The first time in India, a chemist shop was opened in about 1811 by Mr Bathgate, who came to India with East India Company in Calcutta. After one hundred years (i.e. in 1910), this firm started manufacture of tinctures and spirits.
- Bengal Chemical and Pharmaceutical Works, a small factory was started in Calcutta in 1901, by Acharya Prafulla Chandra Ray.
- In 1903, under the leadership of Prof. TK Gajjar, a small factory at Parel was started, which led to the development of other pharmaceutical units, the Alembic Chemical Works Ltd, at Baroda.
- India has a long history of pharmacy when the sources of drugs were vegetables, animals and minerals origin before 19th century.
- Initially most of the medicines were being imported from abroad mainly from UK, France, and Germany.
- There was no control on the drugs and therefore, anything under the name of drug could be made, sold or imported.
- As there was no restriction on the import of drugs and also quality of drugs, many adulterated and spurious drugs have got entry in India.
- As a result, the Indian market got flooded with inferior, standard and even harmful drugs.
- To that effect sir Haroon Zaffer moved a resolution on 9th March 1927 in the Council of State, recommending the Governor-General to take immediate steps to control the quality and standard of drugs.

- To have a comprehensive legislation, the Indian Government appointed a "Drug Enquiry Committee" under the chairmanship of Lt. Col. RN Chopra, in 1931 (DEC or Chopra Committee)
- The DEC was asked to make enquiries in the said matter and then to make recommendations for smooth control of manufacture, import, distribution, and sale of drugs in the interest of public health.
- The "Import of Drugs Bill" was introduced in 1937 in legislative assembly, to control import of drugs.
- This bill did not contain any provision about the manufacture, sale and distribution of drugs.
- Thus "The Drug Bill" was introduced in 1940, in the legislative assembly and Drugs and Cosmetics Act, 1940, came into force.
- Presently, Drugs and Cosmetics Act, 1940, covers the provisions relating to Drugs and Cosmetics, Ayurvedic, Siddha and Unani drugs.
- The central government has made a number of rules for the manufacture, distribution and sale of drugs and cosmetics in India entitled "The Drugs and Cosmetics Rules, 1945".
- With the achievement of independence in 1947, the following acts were passed in respect with the recommendations of DEC.
    (a) The Pharmacy Act, 1948 was passed with the object to regulate the profession of pharmacy in India.
    (b) The Drugs and Magic Remedies Act, 1954 was passed to control certain types of advertisements related to drugs and to prohibit certain kinds of advertisements related to magic remedies.
    (c) The Medicinal and Toilet Preparations (excise duties) Act, 1955 was passed providing for the levy and collection of duties of excise on medicinal and toilet preparations containing alcohol, opium, Indian hemp or other narcotic drugs and narcotics.
- There are also some other Act, which directly or indirectly related to manufacture, distribution and sale of drugs and pharmaceuticals in India.

1. Essential Commodity Act, 1955.
2. Drugs Price Control Order, 1987, 1995

3. NDPS Act, 1985
4. Prevention of Food Adulteration Act, 1954 and Rules.
5. The Industry (Development and Regulation) Act, 1951.

2 Write a note on "Pharmacy as a career".

☞ Pharmacy as a career

- Pharmacy is an ancient profession dedicated to development and dispensing of drugs to provide healthcare in every aspect.
- Several developed and developing countries have given recognition to pharmacy as a major component in providing total healthcare to the society.
- Today pharmacy is regarded as a prestigious profession in India.
- Prof. Mahadeva Lal Schroff (Prof. ML Schroff) is known as "Father of Indian Pharmacy Education" as he has given right direction to pharmacy education in India.
- A pharmacist plays an important role in the healthcare team to dispense the medications to the patients and ensures that these drugs are used in the safest and most effective way.
- Pharmacist mainly has following career opportunities in the following areas:
  (a) Pharmaceutical industry.
  (b) Pharmacy practice area.
  (c) Academics.
  (d) Regulatory (government service)
  (e) Clinical research.

(a) Pharmacist in the pharmaceutical industry:

- In India, pharmaceutical industry is one of the most developed, advanced and largest industries.
- It provides million of job opportunities and assists in the healthcare service of the country by providing drugs to the patients.
- Pharmacists have a promising career in different sectors of the pharmaceutical industries like production, packaging, quality control, quality assurance, sales and marketing, regulatory affairs and research and development.

(b) Pharmacy in practice area:

- Pharmacist is the link between doctor, nurse and the patients and hence, considered as vital component of healthcare system in order to provide patient welfare.
- The best career for the pharmacists right from diploma pharmacist to the postgraduate pharmacist is the retail and wholesale pharmacy.
- Pharmacists are responsible for the hospital activities related to health are system including medicine selection, inventory control and storage of medicine, dispensing of medicines, patient counseling, health promotion, and participating in the national health programmes.
- Hence, hospital pharmacist is very bright career for the pharmacists.
- Clinical pharmacy is also another area where pharmacists play a significant role in patient care.

(c) Pharmacy in academics:

- Pharmacists also have very bright career in the academics.
- They can start their career in educational institutes as assistant professor, associate professor, and professor.
- They may involve in research work individually or as a collaborative work.
- Now-a-days as number of education institutes are increasing, there is a good demand of pharmacists in the education institutes of pharmacy.

(d) Pharmacy in regulatory area:

- Drug industry is growing with high pace which requires the controlling and regulating the quality of products as per the regulatory requirements of India as well as foreign countries.
- This created job opportunities for a pharmacist in the regulatory department of the company.
- Government posts like Drug Inspector, Assistant Drug Commissioner and Drug Commissioner at state level and drug controller at national level are open for regulating production, quality, marketing, import and export of the drugs.

(e) Pharmacy in clinical research:
- Clinical research is a very promising area for many job opportunities for pharmacists.
- Contract research organizations offer various opportunities for pharmacists in clinical research which undertake the following services:
  (i) Clinical studies from phase I to phase II.
  (ii) Development of protocol.
  (iii) Case report from review to designing.
  (iv) Report writing.
  (v) Monitoring.
  (vi) Quality assurance and data management.
  (vii) Conduction of bioavailability studies.
  (viii) Data management of global clinical trials.

3 Describe/Write a note on "Pharmacy Education in India".

☞ Pharmacy Education in India:

- In India, Pharmacy Education has traditionally been focused on industry and product development.
- The various courses framed under pharmacy education involves DPharm, BPharm, MPharm, Pharm D, PhD, etc.
- The first college in India was Madras Medical College established in 1835 where professional training was given to students for treating patients with drugs.
- The first pharmacy college in Asia was started in Goa in 1842 by the Portuguese.
- The first two years professional course "Chemist and Druggist Diploma" was started in Madras Medical College in 1874.
- Mahadeva Lal Schroff "The Father of Pharmacy Education" in India has started 03 years industry-oriented BPharm course at Banaras Hindu University, Varanasi in 1932.
- The first MPharm Program was introduced in 1940 at BHU.
- In 1945, 'Doctor of philosophy' (PhD in pharmacy) program was introduced at BHU.

- The Pharmacy Act, 1948 provided a minimum standard of educational qualification for pharmacy practice to regulate the practice education and profession of pharmacy.
- Under PCI regulation 2014 the BPharm and MPharm curriculum was made uniform throughout the nation.
- To train the graduate pharmacist to provide clinical-oriented services, the MPharm Program in pharmacy practice was introduced at JSS College of Pharmacy at Mysore (1996) and at Ooty (1997).
- The present education regulation for DPharm is ER 2020.
- Pharmacy education in India has been developing fastly because of rapid industrialization of pharmaceutical sector, privatization and economic growth.
- The pharmacy education in India is regulated by the 'Pharmacy Council of India' under the 'Pharmacy Act, 1948'.
- The pharmacists registration is decentralized and the respective state pharmacy councils are responsible for registration of pharmacists in the states.

4 Write a note on "Pharmacy Practice in India".

☞ The Pharmacy Practice In India:

- The healthcare system in India is going through dramatic changes due to growth in the demand for healthcare and patient needs.
- The educational and professional responsibilities of pharmacists are being constantly changing.
- The pharmacy practice is the discipline of pharmacy, which involves developing the professional role of pharmacists.
- Good pharmacy practice requires pharmacy activities like compounding and dispensing of medications and modern services related to healthcare, including clinical services, medication monitoring, drug safety, and efficacy and drug information services.
- Pharmacy practice course provides instructions in the technical procedures for preparing and dispensing drugs in the hospitals and retail settings under the supervision of registered pharmacists.

- The pharmacy, practice in India was marked by the 'Chemist and Druggist' Program in 1870 to train students to gain skills in pharmacy practice.
- The profession of pharmacy practice has evolved through following stages:
  (a) **Traditional Era:** It was the period from early 20th century, where the pharmacists were involved in the formulation, dispensing and study of medicinal properties of natural products of animal, plant and mineral origins.
  (b) **Scientific Era:** It began after World War II. In this period, pharmaceutical industries were emerged and drugs were made by pharmacists in factories.
  (c) **Clinical Era:** This era began in second half of 20th century. During this period pharmacists were educated in the area of clinical pharmacy to establish study of ADME of the drugs within the body.
  (d) **Industrialization Era:** In India, the development of manufacturing pharmacy began in 20th century, which was followed by mass production of medicines.
  (e) **Pharmaceutical Care Era:** It involves expanded role of pharmacist that is from supply of medications to achieve positive outcomes with the prescribed drugs.

5 State/Enlist different Professional Associations of Pharmacy in India (Pharmaceutical Associations in India).

☞ Pharmaceutical Associations in India:

The various pharmaceutical associations are working with the aims and objectives:

1. To Promote Drug Research in all its branches including the manufacture of Drugs in India.
2. To Promote Research and Development of New Drugs in the Country.
3. To enhance the better understanding of Indian products amongst the medical profession.
4. To work for the welfare of every citizen in India.

The number of Pharmaceutical Associations In India are:

- Bengal Chemists and Druggists Association.
- Pharmaceutical Society of India.
- Banaras Hindu University "(BHU) Pharmaceutical Society".
- Indian Pharmaceutical Association (IPA) in 1936.
- Allied Manufacturers and Distributors Association Ltd, Mumbai.
- Indian Pharmaceutical Congress Association (IPCA).
- Indian Pharmacy Graduates Association (IPGA).
- Indian Hospitals Pharmacists Association (IHPA).
- Association of Pharmaceutical Teachers of India (APTI).
- Organization of Pharmaceutical Producers of India (OPPI).
- Common wealth Pharmaceutical Association (CPA)
- All India Organization of Chemist and Druggist (AIOCD).
- Indian Drug Manufacturers Association (IDMA).
- All India Cosmetics Manufacturers Association.
- Bulk Drugs Manufacturers Association.
- Association of Community Pharmacists of India.
- Indian Association of Colleges of Pharmacy (IACP).

6 Define the terms. (a) Pharmacy, (b) Pharmacists.

☞ **(a) Pharmacy:**

Pharmacy is an art and science of compounding, and dispensing of medications.

(b) Pharmacists:

Pharmacists are the healthcare professionals who practice in pharmacy, the field of heatlh sciences focusing on safe and effective use of medication.

7 Fill in the blanks:

1. **Hippocrates** is the father of medicine.
2. The first pharmacy shop was opened in **Bagdad**.
3. Government of India appointed a Drug Enquiry Committee under the chairmanship of **Col. R.N. Chopra** in 1931.

4. **Prof. M.L. Shroff** is the Father of Indian Pharmacy Education in India.
5. The Bengal Chemical and Pharmaceutical Works, Calcutta was established by **Acharya PC Ray**.
6. The first chemist shop was opened by **Scotch Bathgate** at Calcutta in 1811.
7. In 1842, in India **Portuguese** started Pharmacy Education by providing a certificate course in **Goa**.
8. The Pharmacy Council of India (PCI) was established in **1949**.
9. The Pharmacy Act was established in **1948**.
10. The current Education Regulation framed by PCI is known as **ER 2020**.

CHAPTER 2

Introduction to Pharmacopoeia

1 What is pharmacopoeia?/Define pharmacopoeia.

☞ **Pharmacopoeia**

Pharmacopoeia is the official book of standards published by respective governments containing the list of drugs, pharmaceuticals, their formulae, identification, standardisation, dose, uses, etc.

The word pharmacopoeia is derived from two Greek words:
'Pharmacon' means 'drug'
'Poeio' means 'To make'.

2 What is object/need/purpose and scope of pharmacopoeia?

☞ Pharmacopoeias are published or needed:
(i) To ensure uniformity in composition of drug.
(ii) To ensure purity of drug.
(iii) To ensure potency of drug.
(iv) To study official preparations of drugs.
(v) To refer procedures for testing of drugs.

3 Why "there is no world pharmacopoeia" published?

☞ There is no single book like world pharmacopoeia because:
(i) Pharmacopoeia is a book of standards published by respective government.
(ii) The drugs or the standards which are used in different parts of the world are different.

4 Give the list of official or standard books/pharmacopoeias published by WHO.

☞ 1. Indian Pharmacopoeia (IP).
2. British Pharmacopoeia (BP).

3. International Pharmacopoeia.
4. United States Pharmacopoeia (USP).
5. British Pharmaceutical Codex (BPC).
6. National Formulary (NF) of India.
7. Merk index.
8. European Pharmacopoeia.
9. Indian Pharmaceutical Codex.

5 What are the contents of pharmacopoeia? Define 'monograph'.

☞ Indian pharmacopoeia contains:

(a) Monograph

(i) Main title
(ii) Synonym
(iii) Chemical formula
(iv) Category
(v) Dose
(vi) Description
(vii) Solubility
(viii) Standards
(ix) Identification
(x) Test for purity

(b) Appendices

Monograph

It means detail study of drug with reference to title, synonym, preparation, storage, category, official preparations, etc.

6 Describe the "history of Indian pharmacopoeia".

☞
- The government of India in 1944 directed the "Drug Technical Advisory Board" to list the drugs which are not published in British pharmacopoeia.
- To that effect government of India published "Indian pharmacopoeial list" in 1946.
- In 1948, Dr BN Ghosh prepared the first edition of Indian pharmacopoeia.
- First edition of pharmacopoeia was published in 1955 and was in Latin.
- Second edition of IP was published in 1966.
- Second edition of IP was prepared under the chairmanship of Dr Mukharji and its supplements were published in 1975.
- Third edition of IP was published in 1985.

- Third edition of IP was published in two volumes, namely Volume I and Volume II.
- Fourth edition was published in 1996.
- Supplements to IP 85 were published in 1989 and in 1991.

7 Give the salient features of IP 66 (second edition).

☞1. Titles of monograph have been changed from Latin to English.
2. Doses are expressed in metric system.
3. Solubility is expressed in parts of solvents.
4. The methods of preparation of the drug have been given immediately after the monograph.
5. New analytical techniques have been introduced.
6. The test for sterility has been modified.

8 Give the salient features of IP 85 (third edition).

☞1. The new analytical techniques such as flamephometry, fluorometry are introduced.
2. Dissolution test has been introduced in case of certain tablets.
3. Disintegration tests for tablets have been modified.
4. Pyrogen test is also modified.
5. Some drugs have been renamed, e.g. acetylsalicylic acid: aspirin.
6. Certain drugs are omitted and some drugs are newly added.
7. Test for determination of viscosity has been modified.
8. Many new broad-spectrum antibiotics are included.
9. Microbial test limits are prescribed for certain types of oral liquids and pharmaceutical aids.
10. IUPAC system of nomenclature of organic compounds has been used.

9 Write a note on "National Formulary of India" (NF).

☞ National Formulary of India was published for the guidance of medical practitioners, medical students, pharmacists in hospitals and sales department.

- The first edition of National Formulary was published in 1960 by Government of India, Ministry of Health.

- The second edition of National Formulary was published in 1966, under chairmanship of Dr BB Yodh.
- The third edition of National Formulary was published in 1979 under the chairmanship of Dr Wig KL.
- In third edition of NF 342 new formulations were added and separate chapters on drug interactions, drug dependence, prescription writing were included.

10 Give the salient features of fourth edition of Indian pharmacopoeia (IP 1996).

☞ 1. It contains 1149 monographs and 123 appendices and is available in two volumes.
2. The new analytical technique like HPLC is included.
3. Some titles have been changed to include more commonly accepted names, e.g. hyoscine hydrobromide for scopolamine hydrobromide.
4. The computer generated structural formulae have been introduced.
5. The test for bacterial endotoxin (LAL test) as a more suitable substitute for the test for pyrogen has been included.
6. A number of general monographs, e.g. eyedrops, eye ointments, suppositories, pessaries, oral liquid, nasal preparations have been included.
7. Infra-red and Ultra-red absorption spectrophotometric tests for identification of drug substance have been introduced as alternative tests to the classical chemical tests.
8. Specific biological assays and tests provided for vaccines, hormones, blood products and enzymes have been transferred from an appendix to the individual monographs.

11 Give the salient features of fifth edition of Indian Pharmacopoeia (2007).

☞ 1. The I.P. 2007 is presented in three volumes,
- Volume I contains the general notes, preface, the structure of IPC, introduction and general chapters.
- Volume II deals with the general monographs on drug substances, dosage forms and pharmaceutical aids.

- Volume III contains monographs on drug substances, dosage forms, pharmaceutical aids, vaccines, immunosera for human use, herbs and herbal products, blood and blood related products, biotechnological products, and veterinary products.

2. General chemical tests for identification have been almost eliminated and more specific infra-red and ultraviolet spectrophotometric tests have been given.
3. The test for pyrogens involving the use of animals has been virtually eliminated. The test for bacterial endotoxins has been introduced.
4. The test for abnormal toxicity is now confined to certain vaccines.
5. The use of chromatographic methods has been extended in assays to large number of pharmaceutical products.
6. Labelling and storage are featured at the end of a monograph.
7. Limit of bacterial contamination has been introduced for controlling microbial quality of all medicinal products.
8. Analytical methods are in general in harmony with those adopted internationally for maintaining the quality of drugs.

12 Give the salient features of 6th edition of Indian Pharmacopoeia (2010).

☞ I.P. 2010 is presented in three volumes I, II, III

1. Volume I contains notices structure of IPC, acknowledgement, introduction and general chapters.
   - Volume II contains general notice, general monograph on dosage forms, monograph on drug substances, dosage forms and pharmaceutical aids (A to M)
   - Volume III contains monograph on dosage forms (N to Z) followed by monographs on vaccines and immunosera for human use, herbs and herbal products, blood and blood related products, biotechnology products and veterinary products.
2. The pharmacopoeia has 2000 monographs, 287 new monographs and more than 600 monographs has been updated.
3. A new chapter of liposomal product is introduced.
4. A chapter on microbial contamination is also updated.
5. A chapter on NMR is in Appendices.

6. The standards for new drugs and drugs used under National Health Programmers are added in this edition.
7. Most of the existing assays and related substances tests are upgraded by liquid chromatographic methods.
8. The test for pyrogens involving the use of animals have been virtually eliminated.
9. The number of monographs of excipients, anticancer drugs, herbal products and antiviral drugs have been increased.
10. The drugs as well as their formulations not in use are omitted from this edition.

13 Give the salient features of seventh edition of Indian pharmacopoeia (2014).

☞1. The Seventh Edition of I.P. 2014 is presented in four volumes.
2. I.P. 2014 incorporates 2548 monographs of drugs out of which 577 are new monographs.
3. Many chapters have been revised in Appendices.
4. The monograph on water for injection in bulk and purified water are also upgraded to hormonise with prevailing international requirements.
5. General chemical tests for identification of an article have almost eliminated and more specific infra-red and ultraviolet spectrophotometric and HPLC tests have been given emphasis.
6. The test for pyrogens involving the use of animals has been replaced with bacterial endotoxin test.
7. More essential oils, monographs, crude herbal drugs and their extracts have been incorporated.
8. 19 monographs on radio pharmaceutical preparations along with chapter on Pharmaceuticals have been added in volume III of this edition.
9. A separate volume of veterinary monograph as volume IV of this edition of Indian pharmacopoeia has been designed to those concerned with the quality control of veterinary medicines.
10. A general chapter on cell cultures for the production of veterinary vaccines.
11. Standards for new drugs and drugs used under National Health programmes are added and the drugs as well as their formulations not in use now-a-days are omitted from this edition.

14 In which year various editions of pharmacopoeia of India came out/published.

☞ 1. First edition in 1955
2. Second edition in 1966
3. Third edition in 1985
4. Fourth edition in 1996
5. Fifth edition in 2007
6. Sixth edition in 2010
7. Seventh edition in 2014
8. Eighth edition in 2018

15 Give the salient features of IP 2018 (8th Edition).

☞ Salient features of Indian pharmacopoeia 2018 (8th Edition).

1. The IP 2018 is presented in four volumes.
2. IP 2018 incorporates 66 new monographs including chemical (61), herbs and herbal products (03) and radio pharmaceutical preparations (02).
3. One general monograph on lotion is also included.
4. Special emphasis has been given to the dosage forms of API whose dosage forms were not in the previous edition.
5. General chemical tests for identification of an article have been almost eliminated and more specific infra-red, ultraviolet spectrophotometric, HPLC and HPTLC tests have been given emphasis.
6. Special emphasis was given to include/upgrade dissolution test in existing monographs.
7. Most of the existing assays and related substances tests have been upgraded to liquid chromatography method.

16 Write in brief about "British Pharmacopoeia" (BP).

☞ **British Pharmacopoeia (BP):**

- The British Pharmacopoeia is the National Pharmacopoeia of the United Kingdom.
- It was published annually.
- It consists of all quality standards regarding British Medicinal substances, used by any individual or any industry involving

pharmaceutical research, manufacturing and quality control, assurance and analysis.

- The British Pharmacopoeia is an important legislative component in the control of medicines.
- The First British Pharmacopoeia was published in 1864.
- The 2nd edition of BP in 1867.
- The 3rd edition of BP in 1885.
- The 4th edition of BP in 1898.
- The 5th edition of BP in 1911.
- The 6th edition of BP in 1932.
- The 7th edition of BP in 1946 (Not published).
- The 8th edition of BP in 1953.
- The 9th edition of BP in 1958.
- The 10th edition of BP in 1963.
- The 11th edition of BP in 1968.
- The 12th edition of BP in 1973.
- The 13th edition of BP in 1980.
- The 14th edition of BP in 1988.
- The 15th edition of BP in 1993.
- The next editions of BP were 2007, 2009, 2010, 2012, 2013, 2014, 2016, 2017, 2018, 2019.
- The Latest/Recent edition of BP is published in 2020 which is classified in seven volumes:

Volume I and II	– Medicinal substances
Volume III	– Formulated preparations
Volume IV	– Blood related products, immunological products, surgical materials, herbal drugs, etc.
Volume V	– Supplementary chapters, index, appendices, infrared spectra
Volume VI	– British Pharmacopoeia 2020 (veterinary)

- The new BP 2021 edition is legally made effective from 1st January, 2021.

17 Write a note on "United States Pharmacopoeia (USP)".

☞ **The United States Pharmacopoeia (USP):**

- The USP is a pharmacopoeia of United States, which is published by US pharmacopoeial convention every year.
- The first USP was published in 1820 since then 44 editions were published till 2021.
- The first edition of USP was published in both Latin and English.
- In 1975, National Formulary is purchased by USP and now it is called USP-NF.
- USP standards are recognized and used in more than 130 countries throughout the world.
- USP creates the documentary and reference standards to ensure the quality of medications, food ingredients and other health care goods.
- USP creates and disseminates information about many aspects of drug use to physician, pharmacists and other healthcare professionals.
- USP also works to enhance health and promote effective public health care delivery in other parts of the world including Europe, the middle East, Africa, India, China, and Brazil.
- The USP-NF had been amended and released every year since 2002.
- The most recent edition, USP 39-NF34 was released on 1 May 2016.

18 Write in short about "Extra pharmacopoeia".

☞ **Extra pharmacopoeia:**

- The extra pharmacopoeia, originally produced by William Martindale in 1883.
- It was published under the title, "Martindale: The extra pharmacopoeia."
- Martindale contains information on drugs in clinical use world wide, as well as selected investigational and veterinary drugs,

herbal and complementary medicines, excipients, vitamins, vaccines, medicinal gases, disinfectants and pesticides.

- There have been 39 editions of "Martindale: The complete drug reference".
- The 39th edition was published in June 2017.
- Martindale aims to cover drugs and related substances reported to be of clinical interest anywhere in the world.
- It provides a useful source of information for patients arriving from abroad to identify their existing medication.
- The extra pharmacopoeia, i.e. "Martindale: The complete drug reference is a reference book published by pharmaceutical press listing some 6,000 drugs and medicines used throughout the world including details of over 180,000 proprietary preparations".

CHAPTER 3

Packaging Materials

1 Define container. Name the materials used for container.

☞ **Container**

It is the device that holds the drug and may or may not contact with drug.

- Materials used: Glass, plastic, metals, paper, board, etc.

2 Define closure. Name the materials used for closure.

☞ **Closure**

It is the device by means of which container can be closed and opened.

- Materials used: Glass, plastic, rubber, metal, cork.

3 Define 'package' and 'packaging'.

☞ **Package**

A package consists of:

1. A container which holds the product.
2. Closure which seals the container.
3. The carton (outer cover) which gives protection.
4. The box in which multiples of product are packed.

Packaging

It is the science and technology which deals with study of materials and methods used to pack the product and also provide the knowledge of the machinery used for packing the product.

4 What are the ideal qualities of a container?

☞
- It should hold the product without loss.
- It should protect the drug from air, moisture, light, dust, etc.
- It should be neutral.
- It should not wear and tear during normal handling.
- It should pour the drug properly.
- It should not be affected by temperature and pressure.
- It should not break during handling and transportation.
- It should be non-toxic.
- It should be attractive in size and shape.

5 What are various types of containers?

☞ According to protection provided by the container, they are classified as:

1. **Well closed container:** It protects the products from the loss during transportation, handling, storage, etc.
2. **Tightly closed container:** It protects the drug from contamination due to solids or liquids and also prevents loss due to evaporation.
3. **Airtight container/hermetically sealed container:** It prevents the entry of air inside the container during handling, distribution, storage, etc. For example, required for injectables.
4. **Light resistant container:** It protects the product from harmful effects of light. Usually amber-coloured glass is used. It is useful for photosensitive drugs.
5. **Tamper evident/tamperproof container:** It is fitted with device of mechanism that proves; where container has been opened.
6. **Single dose container:** It contains only single dose of the drug. It is usually used for injectables, e.g. ampoules.
7. **Multidose container:** It contains more than one dose of a drug, e.g. vials.
8. **Aerosol container:** It is used to hold aerosol products.

6 Give merits and demerits of glass. Why is glass used as a packaging material?

☞ **Glass**

Merits

1. It is transparent.
2. It is available in various shapes and sizes.
3. Not affected by temperature and pressure during sterilization.
4. It is neutral.
5. It is economical.
6. Light sensitive drugs can be stored in amber-coloured glass.
7. It is impermeable.
8. It has good protection power.
9. It does not deteriorate with age.

Demerits

1. Easily breakable.
2. Some glasses release alkali.
3. Bulk package should be labelled as: "Glass: Handle with care."
4. Chances of flake formation.

7 Discuss plastic as a material for packaging.

☞ **Plastic**

Merits

1. They are light in weight and can be handled easily.
2. Available in various shapes and sizes.
3. They are unbreakable.
4. They can be transported easily.
5. Resistant to inorganic chemicals.
6. Bad conductor of heat.
7. Good protection power.
8. They have sufficient mechanical strength.

Demerits

1. They may absorb the product.
2. Leaching problem.

3. Discolouration of the product.
4. Some plastics are permeable to gases, moisture, etc.
5. They are relatively expensive.

8 What is closure? Give its importance. Explain types of closure.

☞ Closure

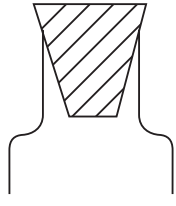
It is the device by means of which container can be closed and opened.

Advantages/Importance

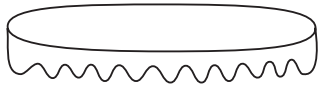
1. To protect the drug from air, dust, moisture, etc.
2. To prevent loss of preparation during handling.

Types of Closures

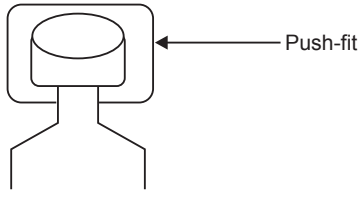
1. **Plug type:** It is fitted into the neck of the container, e.g. cork, rubber, glass stopper.



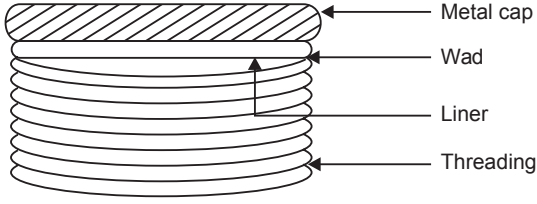
2. **Crown cap:** It is used for packing of beverage bottles, e.g. metals.



3. **Push-fit type:** It is simple slide fit over the neck of the container, e.g. plastic caps.



4. **Screw-cap:** It is very commonly used.



9 What are the ideal requirements of rubber closure?

☞ An ideal rubber closure must possess following properties:

1. It should be soft.
2. It should be quite elastic.
3. It should not absorb medicament.
4. It should withstand temperature and pressure of autoclave.
5. It should be compatible with product.
6. It should comply with pharmacopoeial standards.
7. It should be impermeable to moisture and air.
8. It should not release any substance in the product.

10 What are the various tests used for rubber closure? (Official tests/evaluation tests/pharmacopoeial tests)

☞ **1. Test for penetrability:** Rubber should have sufficient softners to penetrate the needle through it. Thus, hardness of the rubber closure is tested.

2. Extractive test: The rubber should not extract out the materials present in it beyond the prescribed limit.

3. Fragmentation test: Fragmentation of rubber due to penetration of hypodermic needle should be within the range.

4. Permeability test: It is performed to test permeability of the rubber to the water vapours.

5. Compatibility test: It is performed to ensure that there is no interaction between the rubber closure and the contents of product.

11 What is tamperproof/evident (resistant) container?

☞ **Tamperproof Container**

It is one having an indicator barrier to entry, which, if broken or missing, can provide visible evidence to the buyer that the product has been tampered or opened.

Tamper evident packagings are classified as:

1. Strip packaging
2. Blister packaging
3. Film wrappers
4. Bottle seal
5. Breakable caps
6. Sealed tubes
7. Sealed cartons
8. Bubble packs
9. Foil paper or plastic pouches
10. Aerosol.

12 Write a note on flexible packages.

☞
- These are used for packing of all types of products like solids, semisolids and also liquids.
- The concept of unit dose packaging in making flexible packages is more popular.
- The materials used for flexible packages are paper, plastic film, aluminium foil or combination of these two.
- Paper is widely used for drug and cosmetic packaging due to its light weight, enough strength, economy and convenience.
- Coated and laminated papers are more advantageous.
- Heat seal aluminium foil is most suitable for packaging of pharmaceutical products.
- Flexible packages are useful for unit containers.
- Strip-packed tablets and capsules are very popular.
- Cellophane is a material of choice for flexible packaging.

13 Give the composition of glass. Explain various types of glass used for making containers.

☞
- **Composition of glass:**
- Glass is composed of Sand Soda, ash, lime stone and cullet.
- Cullet is broken glass that is mixed with the batch and acts as a fusion agent for the entire mixture.
- Silicon, aluminium, boron, sodium, potassium, calcium, magnesium, zinc and barium are generally used for making glass.

- **Types of Glass:**

1. Lime soda glass:

- It is composed of SiO_2 (75%), Na_2O (15%), CaO (10%) along with traces of K_2O, MgO and Al_2O_3.
- Lime soda glass is used for preparing containers which are used for storage of solid medicaments
- Lime soda glass is not suitable as a container for storage of parenteral products because:

(i) It liberates alkali in aqueous solution.

(ii) After repeated use its surface looses some of its brilliance.

(iii) It is not resistant to sudden changes in temperature.

(iv) Flakes separate more easily as compared to other types of glass.

2. Borosilicate glass:

- It is composed of SiO_2 (80%), B_2O_3 (12%), Al_2O_3 (6%) and mixture of Na_2O, CaO and other oxides (2%).
- It is chemically more inert than lime soda glass.

3. Silicon-treated glass:

Glass is treated with silicon so that it can be used for preparing containers to store alkali sensitive products.

4. Sulphured glass:

The soda lime glass is exposed to moist SO_2 at about 500ºC to get sulphured glass. It does not liberate alkali.

5. Neutral glass:

- It is composed of SiO_2 (72–75%), B_2O_3 (7–10%), Al_2O_3 (4–6%), Na_2O (6–8%), BaO (2–4%) and K_2O (0.5–2%).
- It is used for the preparation of multi-dose vials, transfusion bottles and ampoules.

6. Amber colour glass:

- It is used for storage of photosensitive pharmaceutical products because it has capacity to filter out UV radiations.
- It is obtained by adding C, S or Fe and MgO_2.

14 Explain the types of glass used for storage of parenteral preparations?

☞ Types of glass used for storage of parenteral preparations:

(a) **Type I glass:**
- It is also called borosilicate glass or neutral glass.
- It offers a highly hydrolytic resistance due to its chemical composition.

(b) **Type II glass:**
- It is a soda-lime-silicate glass with highly hydrolytic resistance as a result of an appropriate surface treatment with ammonium sulphate or sulphur dioxide.
- The containers made from this glass are suitable for most acidic and neutral aqueous preparations.

(c) **Type III glass:**
- It is a soda-lime-silicate glass with only moderate hydrolytic resistance.
- The containers made from this glass are generally suitable for non-aqueous preparations for parenteral use.

15 Enlist various polymers used in plastic. Classify plastics.

☞ **Polymers used in plastic are:**

(a) Polyethylene (polythene)
(b) Polyvinyl chloride (PVC)
(c) Polymethyl methacrylate (PMMA)
(d) Polystyrene
(e) Polytetrafluoroethylene (PTFE)
(f) Polypropylene
(g) Polyamide (nylon)
(h) Polycarbonate

- **Classification of plastics:**

1. Thermoplastic type:
   This type of plastic gets softened to a viscous fluid on heating and hardens again on cooling, e.g. nylon, polystyrene and polymethyl methacrylate.

2. Thermosetting type:
   This type of plastic may become flexible but does not become fluid on heating, e.g. phenol formaldehyde resins and urea formaldehyde resin.

16 Enlist various metals used for construction of container. Give merits and demerits of metal containers.

☞ Metals used for container:

(a) Aluminium
(b) Tin plated steel
(c) Stainless steel
(d) Tin
(e) Lead.

- **Merits/Advantages of metal containers:**
  1. They are sturdy.
  2. They are impermeable to light, moisture and gases.
  3. They are light in weight as compared to glass containers.
  4. They can be made rigid unbreakable containers.
  5. Labels can be printed directly onto their surface.
- **Demerits/Disadvantages of metal containers:**
  1. They are expensive.
  2. They may shed metal particles into the pharmaceutical product.
  3. They are not generally used for extemporaneous dispensing.
  4. They react with certain chemicals or drugs.

17 What are various types of packaging?

1. Blister package
2. Strip package (used for tablets and capsules)
3. Bubble package
4. Sachet package
5. Oral liquid dispensers.

18 Define packaging. Give advantages of packaging. What are various selection criteria for packaging materials.

☞ Packaging:

Packaging is the science and technology which deals with study of materials and methods used to pack the product and also provide the knowledge of the machinery used for packing the product.

☞ Advantages of packaging:

- It helps to maintain stability of the product.
- Detail labeling on the package helps the consumers to understand the methods of administration, etc.
- It provides hygiene.
- It decreases product cost by packaging in small quantities.
- It protects the products from effect of environmental factors.
- It helps for easy storage the product.
- It helps to reach the product to the consumer in an economic way.

☞ Selection criteria for pharmaceutical packaging materials:

The selection of packaging material depends on the requirement such as protection from environmental factors and degree of protection required.

• Criteria for selection:

1. Physical properties of the product.
2. Facilities available for packaging.
3. Formulation components.
4. Stability of the formulation
5. Economy.
6. Convenience.
7. Government regulations.
8. Buyers specifications.
9. Sociocultural criterion.
10. Retailing characteristics.
11. Environmental criteria.
12. Disposability.

CHAPTER 4

Pharmaceutical Aids

1 What are pharmaceutical Aids?/Define and classify pharmaceutical aids with suitable examples.

☞ **Pharmaceutical Aids:**

The substances which are of little or no therapeutic value but essentially used in manufacture of or compounding of various pharmaceutical dosage forms are known as pharmaceutical aids.

- Pharmaceutical aids are also known as adjuvants, adjuncts, excipients, necessities, additives.
- **Classification of pharmaceutical aids:** Pharmaceutical aids are classified on the basis of their functions as follows:

1. **To produce a particular dosage forms:**
   (a) Diluents or fillers of solid dosage forms
   For example, lactose, mannitol, dibasic calcium phosphate.
   (b) Vehicles or solvents for liquid dosage forms
   For example, water, syrups, chloroform, glycerol, propylene glycol, vegetable oils, mineral oils.
   (c) Semisolid bases for ointments, creams, jellies, etc.
   For example, petrolatum, beeswax, wool fat, lanolin, macrogols.
   (d) Propellants for sprays and aerosols:
   For example, compressed gases like CO_2, N_2, liquefied gases like ethane, methane for aerosols, e.g. trichlorofluoromethane, dichlorofluoroethane, difluoroethane.
2. **To attain and maintain physical stability of formulation:**
   (a) Solubilising agents, co-solvents for solutions
   For example, polyethylene, glycols/cyclodextrins.
   (b) Suspending agents, e.g. acacia, tragacanth.
   (c) Emulsifying agents, e.g. acacia, beeswax.

(d) Thickening agents, e.g. starch, agar.
(e) Binders for solid dosage forms, e.g. acacia, sodium alginate, starch paste.
(f) Disintegrating agents, e.g. starch, microcrystalline cellulose.

3. **To attain and maintain chemical stability of formulation.**
   (a) Antioxidants, e.g. tocopherols, propyl gallate BHA, BHT, sodium bisulphate.
   (b) Buffers, e.g. sodium citrate, sodium acetate.
4. **Preservatives to control microbial contamination,** e.g. methyl paraben, propyl paraben, benzalkonium chloride, phenyl mercuric nitrate.
5. **To ease manufacturing of products:**
   (a) Lubricants, e.g. talc, magnesium stearate.
   (b) Glidants, e.g. talc, corn starch
   (c) Anti-adherents, e.g. corn starch, colloidal silica.
   (d) Anti-foaming agents for liquids and semisolids, e.g. cetostearyl alcohol, castor oil, silicon derivatives.
6. **Organoleptic additives:**
   (a) Colouring agents, e.g. titanium dioxide, ferric salts, amaranth, caramel, yellow oxide, cochineal.
   (b) Flavouring agents, e.g. aromatic waters, flavoured syrups, volatile oils, lemon grass oil, peppermint oil, mentha oil.
   (c) Sweetening agents, e.g. sucrose, syrups, sorbitol, sodium saccharin, dextrose.
7. **Miscellaneous:**
   (a) Adsorbents, e.g. bentonite, magnesium silicate, kaolin
   (b) Humectants, e.g. glycerin, sorbitol.
   (c) Tonicity adjusters, e.g. sodium chloride.
   (d) Granulating agents, e.g. water, alcohol.

2 What are the ideal properties of pharmaceutical aids (additives)?

☞ **Ideal properties of pharmaceutical aids:**

1. It should be physiologically inert.
2. It should be effective in low concentration.
3. It must not interfere with the bioavailability of the drug.
4. It must be non-toxic, non-irritant and non-sensitizing.

5. It does not impart any undesired taste, odour or colour to the product.
6. It should be physicochemically stable over a wide range of temperature, pH, etc.
7. It must be free from microorganisms.
8. It must be commercially available at a reasonable cost.
9. It must be accepted by regulatory authorities.

3 Define and classify organoleptic additives used in pharmaceutical formulation.

☞ **Organoleptic additives:**
The substances which promote appearance and palatability (colour, odour, taste) of pharmaceutical dosage forms are called as organoleptic additives.

Classification/Types of Organoleptic Additives

Colouring agents	**Flavouring agents**	**Sweetening agents**
e.g. Brilliant blue	e.g. Cherry	e.g. Sucrose
Tartazine	Rasberry	Fructose
Indigo	Strawberry	glucose
Caramel	Chocolate	Invert sugar
Cochineal	Lemon	Syrup
Titanium dioxide	Orange	Sorbitol
Ferric oxide	Cinnamon	Mannitol
Carotene	Clove	Xylitol
Chlorophyll	Peppermint	Saccaharin
		Cyclamates
		aspartame
		Acesulfame K

4 Write a note on "colouring agents" used in pharmaceutical formulations.

☞ **Colouring agents:**
- The substances which give distinct colour to the pharmaceutical formulation are called as colouring agents.
- The main categories of dosage forms that are coloured are tablets, capsules, oral liquids, topical creams and ointments.

- **Need/purpose/use of colouring agents:**
  1. To impart a distinctive appearance to a pharmaceutical dosage form.
  2. Unattractive medication can be made more acceptable to the patient by the use of colour.
  3. To identify the product.
  4. To provide useful opacity.
  5. The use of different colours for different strengths of the same drug can help to eliminate errors.
- **Classification of colouring agents:**
  The list of colouring agents permitted under Drugs and Cosmetics Act, 1940 are:
  1. **Natural colours:**
  (a) Vegetable colours: Chlorophyll (green), carotene (yellow), caramel (black, brown), riboflavin (yellow)
  (b) Animal colour: cochineal (red)
  (c) Mineral colours: Titanium dioxide (opaque), ferric oxide (red, yellow)
  2. **Artificial colour:** Caramel.
  3. **Coal tar colours (synthetic colours):**
  Black: Naphthol blue black
  Blue: Brilliant blue, indigo carmine
  Brown: Resorcin brown
  Green: Fast green, quinazoline green
  Orange: Orange G
  Red: Amaranth, erythrosine, eosine, Sudan III carmoisine, fast red E.
  Yellow: Tartrazine, sun set yellow, quinoline yellow.
  4. **Lakes:** Aluminium or calcium salts of any of the water-soluble colours listed above.

5 Write a note on "Flavouring Agents" used as additives in pharmaceutical dosage forms.

☞ **Flavouring agents:**

- The substances which give flavours to the pharmaceutical preparations are called as flavouring agents.
- Flavouring refers to a complex effect taste, odour and feeling factor.

- Examples: Lemon, orange, ginger, cinnamon, rasberry, liquorice, Anise.
  - Flavours are added to the formulation to make a medicine more acceptable to take, especially if the drug has an unpleasant taste.
  - The age of the patient should be taken into account when selecting a flavour, as children will tend to enjoy fruit or sweet flavours.
  - **Role of flavouring agents in pharmaceutical products:**
    1 It is usual to use flavour in association with colour and category of the product.
    For examples, vitamin preparations are deep red coloured with cherry, strawberry or raspberry flavour.
    2. Paediatrics prefer chocolate of fruity flavours and sweet taste. Adults prefer sour, citrus and intense flavours.
    3. Viscous flavoured preparations such as flavoured syrup (lemon syrup, orange syrup) or flavour blended with glycerine, sorbitol imparts better mouth feel effect.
    4. Volatile oils including cinnamon, clove, lemon, orange, peppermint produce aromatic vapours which activate olfactory cells.
    5. Chloroform, carbon dioxide are desensitising agents. They have mild anaesthetic effect on the sensory receptors.
    6. Stronger flavours such as liquorice extract overshadows the unpleasant taste of medicament.

6 Write a note on "Sweetening Agents" as pharmaceutical aids.

☞ **Sweetening Agents/Sweetners:**

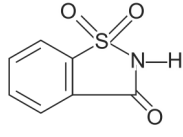
The substances which mask unpleasant taste of the pharmaceutical formulations are called as sweetening agents.

Types of sweetening agents:

Sweetening agents may be natural or synthetic:

1. **Sugars:** Sucrose, fructose, glucose, invest sugar, syrup.
2. **Polyhydric alcohols:** Sorbitol, mannitol, xylitol, glycerin.
3. **Artificial sweetners:** Saccharin, cyclamates, aspartame, acesulfame K.

- **Need/Purpose/Use of Sweetening Agents:**
  - To increase the palatability of the preparation.
  - To mask unpleasant taste of the formulation.
  - The main sweetening agents used in oral preparations are sucrose, liquid glucose, glycerol, sorbitol, etc.
  - They are used in chewable tablets, oral suspensions, oral solutions.
- **Saccharin Sodium:**
  - Functional category: Sweetening agent (artificial sweetner)
  - Formula: $C_7H_5NO_3S$



- **Applications of saccharin sodium in pharmaceutical formulations:**
  1. Saccharin sodium is an intense sweetner used in beverages, food products and pharmaceuticals such as tablets, powders, medicated confectionery, gels, suspensions, liquids and mouthwashes.
  2. It is also used in vitamin preparations.
  3. Saccharin sodium is considerably more soluble in water than saccharin, and is more frequently used in pharmaceutical formulations.
  4. Its sweetening power is approximately 300–600 times as that of sucrose.
  5. Saccharin sodium enhances flavour and mask some unpleasant taste characteristics.

Method of preparation of saccharin:

- Saccharin is produced by oxidation of o-toluene sulphonamide by potassium permanganate in a solution sodium hydroxide.
- Acidification of the solution precipitates saccharin, which is then dissolved in water at 50°C and neutralized by addition of sodium hydroxide.
- Rapid cooling of the solution initate crystallization of saccharin sodium from the liquors.

7 What are preservatives? Classify preservatives with suitable examples.

☞ **Preservatives:** Preservatives are the chemical substances used to stop the multiplication of microbes present and to minimize further contamination during storage of the products.

Preservatives are the chemical substances used to improve shelf-life of drugs by decreasing oxidation of active drug and excipients and reducing microbial production in the pharmaceutical preparations.

Classification of preservatives

Preservatives are classified as:

(A) On the basis of mechanism of action:

- **(a) Antioxidants,** e.g. BHA (butylated hydroxyanisole) BHT (Butylated hydroxytoluene) propyl gallate, vitamin E, vitamin C (ascorbic acid)
- **(b) Antimicrobial agents,** e.g. benzoic acid, methyl paraben sodium benzoate, chlorobutanol, phenylmercuric nitrate, chlorocresol, hexachlorophene)
- **(c) Chelating agents,** e.g. EDTA, citric acid

(B) On the basis of source:

- **(a) Natural,** e.g. salt, lemon
- **(b) Synthetic,** benzoates, sodium benzoate

8 Mention the ideal qualities of preservatives. Give the uses/need of preservations.

☞ **Ideal qualities of preservatives:**

1. It should be stable.
2. It should effective in aqueous phase.
3. It should be non-toxic and non-reactive.
4. It should be compatible with drug components.
5. It should be cost effective.
6. It should be highly soluble.
7. It should be odourless, tasteless.
8. It should remain, in undissociated state at the pH of preparation.

☞ **Need/Uses of preservatives:**

1. To protect the drug from microbial attack.
2. To enhance activity and efficacy of a drug.
3. To stabilize the product.
4. To increase shelf-life of the product.
5. Preservative are mainly included in liquid preparations for the fungistatic action.

☞ **Preservatives and their concentrations used in pharmaceutical dosage forms:**

(a) For liquid oral preparations: Benzoic acid (0.1 to 0.2%), sorbic acid (0.1 to 0.2%), methyl paraben (0.25%), propyl paraben (0.5 to 0.25%), sodium benzoate (0.1 to 0.2%), bronidol (0.001 to 0.05%), alcohol (15 to 20%), glycerin (45%)

(b) For dermatological preparations: Phenol (0.5%), cresol (0.3%), chlorocresol (0.1%).

(c) For ophthalmic preparations: Benzalkonium chloride (0.01%), thiomersal (0.01%), phenyl mercuric nitrate/acetate (0.002%), chlorhexidine acetate (0.01%).

(d) For nasal and otic preparations: Benzalkonium chloride (0.01%)

CHAPTER 5

Size Reduction

1 Define size reduction. Give importance/significance of size reduction in pharmacy.

☞ **Size Reduction**

Size reduction is the process of reducing drugs into smaller pieces, coarse particles or fine powder.

Importance/Significance of Size Reduction

1. It increases rate of dissolution of drug.
2. It increases rate of absorption of drug.
3. It helps in extraction process.
4. It increases stability of the preparation.
5. It increases solubility of the drug.
6. It gives proper consistency to the preparation.
7. It increases uniformity and elegance of the preparation.
8. It helps in drying of various drugs.
9. It provides uniform mixing of the particles.
10. It helps in size separation.

2 Discuss various factors affecting size reduction.

☞ **(a) Hardness:** It is easy to break soft material than hard material.

(b) Toughness: Fibrous drugs or having higher moisture contents are generally soft but tough. Thus, they produce difficulties in size reduction.

(c) Stickness: Drugs like gums, resins are sticky and may adhere to the grinding surfaces. Thus, stickness creates difficulties in size reduction.

(d) Moisture content: The presence of moisture in the material affects hardness, toughness and stickness. Thus, drugs

containing high moisture content are difficult to reduce their size.

(e) Material structure: Vegetative drugs produce fibrous particles while minerals produce flakes.

(f) Softening temperature: During size reduction heat is generated, so some drugs may melt during size reduction.

(g) Physiological effect: During size reduction dust is produced which is dangerous to workers.

(h) Ratio of feed size and product size: If feed size is large the coarse particles are obtained.

(i) Purity required: Due to wear and tear of the parts of machine, product may contaminate.

3 What are the principles/mechanism involved in size reduction methods?

☞ **(a) Cutting:** The material is cut into small pieces by a sharp blade, or knife, e.g. cutter mill.

(b) Compression: The material is crushed by application of pressure, e.g. roller mill.

(c) Impact: In this case material is hit by an object moving at high speed and material breaks into smaller pieces, e.g. hammer mill, disintegrator.

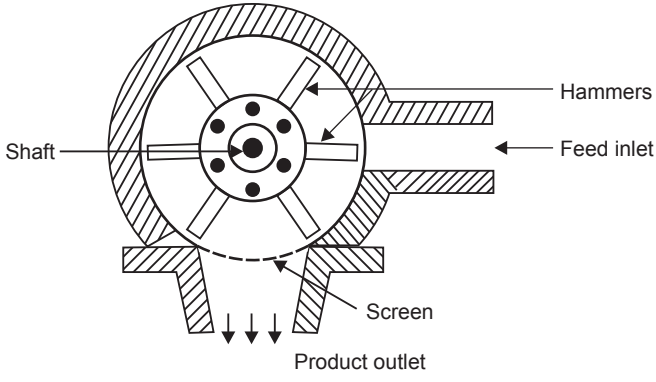
(d) Attrition: In this case mechanical pressure is applied on the material in two moving surfaces, resulting in shear forces which break the particles, e.g. roller mill.

(e) Combined impact and attrition: In this case both impact and attrition are involved to get better results, e.g. ball mill, fluid energy mill.

4 Write a note on hammer mill.

☞ It is based on the principle of impact.

- **Construction:** It consists of strong metal casing enclosing central shaft to which many hammers are fixed. At the lower side there is a screen through which powder passes. There is a feed inlet and product outlet.



- **Working:** During operation, central shaft rotates with high speed. The hammers bite the material entering from feed inlet and powdered material is collected through the outlet.
- **Advantage:** It is used for producing intermediate grade of powder.
- **Disadvantage:** Due to high speed heat is generated and therefore, it is not suitable for heat-sensitive materials.
- **Uses:** It is used for producing intermediate grades of powders.

• Applications/Uses of Hammer Mill:

1. It is used for producing intermediate grades of powders.
2. It can be used to cut brittle material by impact of blunt hammers.
3. It can be used to crush fibrous materials using cutting edges.
4. It is useful for powdering of roots, barks, leaves, crystals, etc.
5. It is used in granulation to cut the damp mass into granules.

5 Write a note on ball mill.

☞ • **Principle:** Combined impact and attrition.

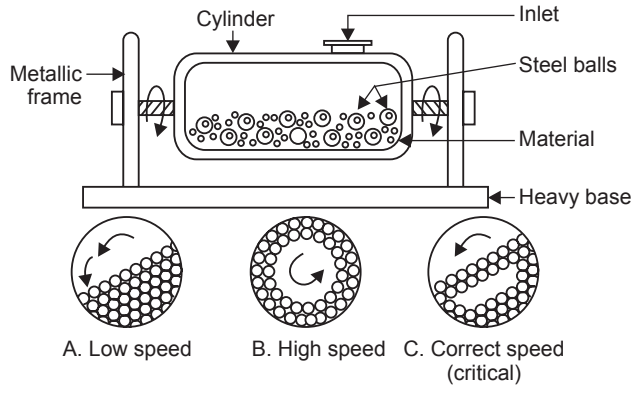


Figure 'A': At low speed, there is very negligible size reduction.
Figure 'B': At very high speed, balls will thrown out due to centrifugal force. Hence, no grinding will occur.
Figure 'C': At critical speed, the balls fall on the material and maximum size reduction will occur.

- **Construction:**
  (i) It consists of hollow cylinder fixed on metallic frame.
  (ii) It contains steel heavy balls about 2–5 cm in diameter.
  (iii) Sometimes cylinders are lined with rubber.
  (iv) The cylinder revolves longitudinally.
  (v) The cylinder contains balls that occupy 30–50% of the mill volume.
- **Working:**
  (i) The drug is placed into the cylinder and lid is closed.
  (ii) The cylinder rotates longitudinally.
  (iii) The speed of rotation is very important.
  (iv) Low and high speed does not reduce the material.
  (v) At critical speed balls fall from the top due to centrifugal force thus, size reduction takes place.
- **Advantages:**
  (i) It can produce very fine powder.
  (ii) It can be used for continuous operation, if sieve is attached to mill.
  (iii) Toxic materials can be reduced, as it is closed to mill.
  (iv) It is useful in large scale.
  (v) It is capable of grinding wide variety of materials of different degree of hardness.

- **Disadvantages:**
  (i) It is very noisy machine.
  (ii) Wear and tear of balls may contaminate the product.
  (iii) Not suitable for sticky materials.
  (iv) Regular maintenance is required.
- **Applications/Uses of Ball Mill:**
  1. The ball mill is used in grinding brittle and amorphous materials into fine powders.
  2. These mills are used to grind powders for ophthalmic and parenteral products, milling of pigments and insecticides for industrial purpose.
  3. Rubber ball mills are used for blending of explosive materials.
  4. Small capacity ball mills are used for wet grinding, e.g. for suspension.
  5. The high capacity ball mills are used for milling of certain metals like cinnabar (HgS).

CHAPTER 6

Size Separation

1 Define size separation. What are various official standards for powders/grading of solids (Classify powders)?

☞ Size Separation

It is a technique used to separate the particles of specified size.

Official Standards for Powders* (*According to IP, 2010)

Grade of powder	Sieve through which all particles must pass	Sieve through which only 40% of particles pass
1. Coarse powder	10	44
2. Moderately coarse powder	22	60
3. Moderately fine powder	44	85
4. Fine powder	85	–
5. Very fine powder	120	–
6. Microfine powder	–	–
7. Superfine powder	–	–

Definitions

1. **Coarse powder:** It is the powder of which all the particles pass through sieve no. 10 and not more than 40% pass through sieve no. 44.
2. **Moderately coarse powder:** It is the powder of which all the particles pass through sieve no. 22 and not more than 40% pass through sieve no. 60.
3. **Moderately fine powder:** It is the powder of which all the particles pass through sieve no. 44 and not more than 40% pass through sieve no. 85.
4. **Fine powder:** It is the powder of which all the particles pass through sieve no. 85.

5. **Very fine powder:** It is the powder of which all the particles pass through sieve no. 120.
6. **Microfine powder:** It is the powder of which not less than 90% by weight of particles pass through sieve with nominal aperture size of 45μm.
7. **Superfine powder:** It is the powder of which not less than 90% by the number of particles are less than 10 micron size.

2 Define the terms 'sieve no.', sieve no. 10'.

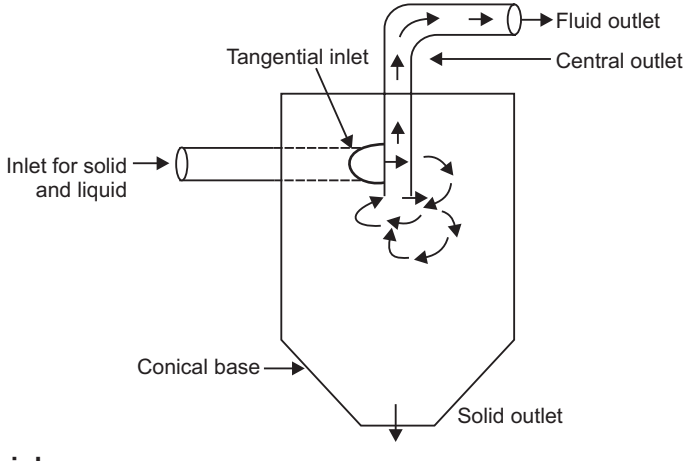
☞ **(a) Sieve no:** It means number of meshes in a length of 2.54 cm (1 inch) in each transverse direction parallel to the wire.

(b) Sieve no 10: It means 10 number of meshes in a length of 2.54 cm (1 inch) in each transverse direction parallel to the wire.

3 Name various methods used for size separation.

☞ 1. Sieving/screening
2. Cyclone separator
3. Air separator
4. Elutriation/sedimentation
5. Centrifugal classification.

4 Give the construction and working of cyclone separator.



Principle

In cyclone separator centrifugal force is used to separate solids from the fluid. Separation depends not only on the particle size but also on the density of particles.

Construction

In consists of cylindrical vessel with conical base.

- It has fluid outlet at the top and solid outlet at bottom.
- There is a tangential inlet through which suspension is passed.

Working

The suspension of solid in gas or liquid is introduced under very high velocity into the vessel so that rotatory movements take place within the vessel. Due to centrifugal force the particles having high density are thrown towards the wall and are collected through conical base. The fine particles are collected along with the fluid.

Uses: These are used to separate the suspension of solid in a gas (air).

5 What are various standards for sieves ?

☞ **Standards for sieves:**

1. **Number of sieve:** Sieve number indicates the number of meshes in a length of 2.54 cm in each transverse direction parallel to the wires.
2. **Nominal size of aperture:** It indicates the distance between the wires. The IP has given the nominal mesh aperture size for majority of sieves in mm or in μm.
3. **Nominal diameter of the wire:** Wire mesh sieves are made from the wire having the specified diameter in order to give a suitable aperture size and sufficient strength to avoid distortion of the sieve.
4. **Approximate percentage sieving area:** This standard expresses the area of the sieving as a percentage of the total area of the sieve. It depends on the size of the wire used for any particular sieve number. Generally the sieving area is kept within the range of 35 to 40 percent in order to give suitable strength to the sieve.
5. **Tolerance average aperture size:** Same variation in the aperture size is unavoidable and when this variation is expressed as a percentage; it is known as the 'aperture tolerance average'.

6 What is size separation? Give aims and objectives of size separation.

☞ Size separation:

The technique which is used to separate the particles of specified size from the mixture is called size separation.

Objectives of size separation:

1. To classify the materials into different sizes.
2. To carryout grading of powders or granules.
3. To control size and avoid variations in the materials.
4. To increase performance, efficacy and stability of dosage forms.
5. To judge uniformity in mixing materials.

7 Define sieve. Enlist various sieves commonly used in pharmaceutical processing. Give the applications/uses of sieves.

☞ Sieve (Sifter):

Sieve/sifter is a device used for separating wanted elements from unwanted material of a sample.

- Sieve is made up of using a woven sieve such as a mesh or net or metal.
- A sieve has very small holes.
- Sieves are common devices used for particle size analysis.

Types of sieves:

Pharmaceutical sieves are extensively used for size separation from 300 mm to around 38 μm.

1. Vibrating sieves.
2. Inclined or circular motion sieves.
3. Static sieves.
4. Horizontal low-head sieves.
5. Banana or multislope sieves.
6. Rotary scrubbers.

Applications/uses of sieves:

- Sieves are used for size separation of coarse materials down to 150 μm.
- Sieves are used to determine product quality.
- Sieves are used for particle size analysis.
- Sieves are used to ensure the quality of ingredients and finished products before use or dispatch.

CHAPTER 7

Mixing

1 What is mixing? Give the objectives of mixing.

☞ **Mixing**

Mixing is a unit operation in which two or more substances are combined together in such a way that each particle of material looks similar to particles of other material.

Objectives of Mixing

1. To form a uniform mixture.
2. To promote chemical reaction to get uniform product.
3. It helps in formation of suspension or paste.
4. It helps in mixing of water and oil, e.g. emulsion.

2 Give the types of mixing on mixtures and their stability.

☞ There are three types of mixtures:

1. **Positive mixtures:** When two or more miscible liquids are mixed together or solid is dissolved in water. Such types of mixtures are called positive mixtures.

   They are irreversible and stable in nature, e.g. solutions.
2. **Negative mixtures:** When two immiscible liquids are mixed with water, the mixture is called negative mixture. It is reversible mixture and requires high degree of mixing of materials, e.g. emulsion.
3. **Neutral mixtures:** It is neutral in behaviour. The substances do not have tendency to mix but once they are mixed they do not separate after mixing, e.g. ointment, paste, creams.

3 What are the mechanisms of mixing?

☞**(a) Convective mixing:** It means transfer of group of particles from one location to another and it is carried out by means of blades or paddles.

(b) Shear mixing: In this case mixing of powders takes place due to shear force.

(c) Diffusion mixing: It occurs due to the random motion of particles within the powdered bed which causes change in position of particles relative to each other. It is carried out by stirring.

4 Explain factors affecting powder mixing (solid mixing).

☞**(a) Particle size:** It is easy to mix the powders having approximately same particle size.

(b) Particle shape: For uniform mixing ideal particle shape should be spherical.

(c) Density of material: It is difficult to mix the powders having different densities.

(d) Particle attraction: Some particles exert attractive forces due to electrostatic charges on them.

(e) Proportion of materials: The materials to be mixed should be in the proportionate quantities and if they are not, they are mixed in the ascending order of their weight.

(f) Material density: It is difficult to mix two powders having different density.

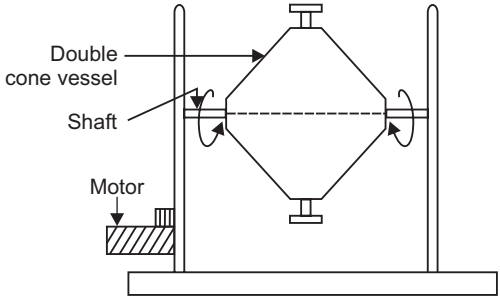
5 Name the equipment used for mixing of solids, semisolids and liquids.

☞

Type	Equipment used
1. Mixing of solids/ powders	Tumbler mixer, agitated powder mixer, double cone blender, air mixer
2. Mixing of semisolids	Triple roller mill, agitated mixer, sigma blade mixer
3. Mixing of liquids	Propeller mixer, turbine mixer, paddle mixer

6 Write a note on double cone blender (mixer).

☞ It is also known as twin shell blender.



Mechanism

Diffusion mixing.

Construction

It consists of two cone-shaped vessels fixed base to base and mounted in shaft. It is made up of stainless steel. The shaft is fixed and cone-shaped vessel revolves at optimum speed. The apparatus is connected to an electric driven motor.

Working

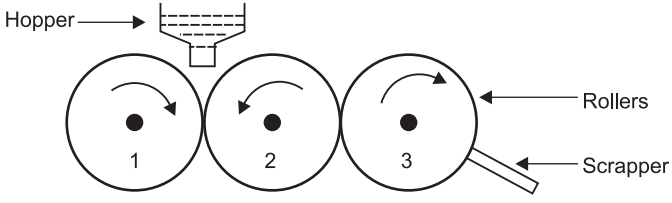
The solids to be mixed are taken in the conical shape vessel. Due to rotation, material moves to top and falls down at the bottom. Mixing takes place by tumbling of vessel and shearing action with blade. The speed of rotation is 30–100 rpm.

Applications

(a) Used for mixing of powders to be filled in capsules.
(b) Mixing and lubrication of granules.
(c) It is suitable for mixing of dry powder to wet mixing.
(d) It can be used for mixing food, chemical and cosmetic product intermediates.
(e) It is used in mixing of highly flowable, powdery and granular materials with superior mixing quality.

7 Write a note on "triple roller mill".

☞ It is used for mixing of semisolids.



Triple roller mill

Mechanism

Shear mixing.

Construction

1. It consists of three rollers which are arranged in such a way that they come very close to each other.
2. The rollers are rotated at different rates of speed.
3. Hopper is located above the 1st and 2nd roller.
4. Scrapper helps to remove the material from the roller.
5. The material coming between the rollers is crushed depending on the gap between them.

Working

1. As shown in figure, material is supplied in between roller 1 and 2 and it gets reduced.
2. The gap between 2 and 3 is usually less than 1 and 2 roller.
3. A scrapper is arranged to the 3rd roller which removes the fixed material.

Application/Uses

(a) It is used for grinding as well as for mixing of solid powders with the uniform quality and consistency is produced.
(b) It is used to disperse material within a semi-viscous material such as cream.
(c) It is used in homogenization.
(d) It is used for mixing pharmaceuticals, herbals, chemicals, etc.
(e) It is also used for mixing of coating compositions, adhesives and foods, etc.

8 Define homogenisation. Describe Silverson mixer homogeniser.

☞ Homogenisation

It refers to mixing of biphasic liquid systems in which product with uniform quality and consistency is produced.

- It is useful for preparation of fine suspension and emulsions.
- It is carried out in the apparatus known as homogeniser.

Silverson Mixer Homogeniser

☞ Principles

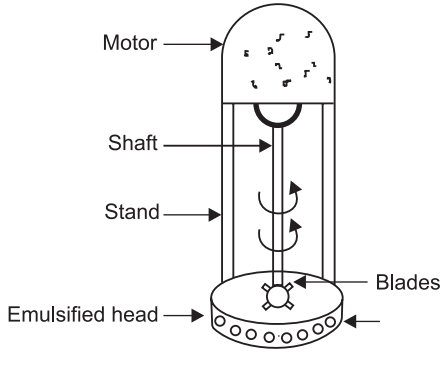
- The principle of Silverson mixer is based upon shearing force.
- It produces intense shearing forces and turbulence by use of high speed rotors.
- The circulation of material takes place through the head by the suction produced in the inlet at the bottom of the head.
- The circulation of the material ensures rapid breakdown of the dispersed liquid into smaller globules or fines.

Construction

1. It consists of emulsifier head, covered with stainless steel sieve.
2. Emulsifier head consists of blades attached to the shaft and rotates at high speed.
3. Electric motor is fitted at the top.

Working

1. Emulsifier head is placed in the vessel containing immiscible liquids.
2. When motor is started the liquid gets sucked through fine holes and the oil is reduced into fine globules due to the rotation of the blades.



3. The high speed rotation of the rotor blades exert a powerful suction of liquid and solid materials into the motor assembly helps in mixing.
4. The centrifugal force drives the material towards the periphery and milling action takes place.
5. Fresh material is continually drawn into the work head, maintaining the mixing and pumping cycle.
6. It operates at high speed up to 8000 rpm.

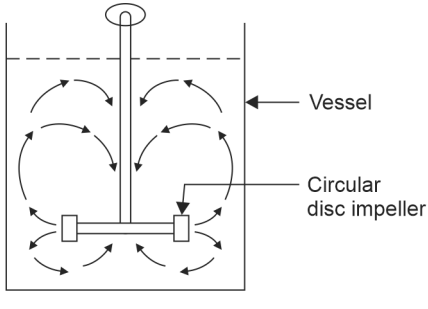
Applications/Uses of Silverson Mixer:

- It is used to mix, emulsify, homogenise, solubilize, suspend, disperse and disintegrate solids.
- It is used for homogenization of products such as creams, ointments, lotions, etc.
- It can be used to disintegrate the materials of animal, vegetable, mineral or synthetic origin in a single operation.
- It is also used in rapidly gelling, solubilizing and dispersing gums, alginates, carbopol, etc.

9 Write a note on "Turbine Mixer". Or Give the principle, construction, working and applications of turbine mixer.

☞ **Turbine Mixer:**

- It is used for mixing of liquids.
- Turbine mixer is another type of process agitator.



Turbine mixer

Principle:

Turbine mixer agitators can create a turbulent movement of the fluids due to the combination of centrifugal and rotational motion.

Construction:

- It consists of a circular disc to which a number of short blades/ impellers are attached.
- The blades may be straight, short or curved or disk type.
- The diameter of the turbine ranges form 30–50% of the diameter of the mixer vessel.
- Turbine rotates at a lower speed usually 50–200 rpm.

Working:

- A turbine mixer is filled through an opening at its top.
- The mixing blades revolves around the vertical axis.
- The variable speed drills with turbine mixer Whip air into the mixture of materials.
- The air in mixture yield bubbles contributing mixing.
- Top entry high shear causes uniform emulsification and homogenization.

Applications/Uses:

- It is used in chemical reactions and extraction operations, e.g. liquid and gas reactions.
- Used in preparing emulsions, suspensions and syrups.
- Used to mix high viscosity liquids, semisolids and paste.

CHAPTER
8

Filtration

1 Define filtration and clarification.

☞ **Filtration**

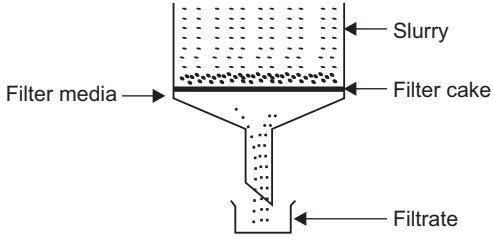
It is the process in which insoluble solids are removed from the liquid, by passing through a porous medium in which solids are retained and liquid is allowed to pass.

Clarification

It is the process of removal of relatively small amounts of suspended solids (not more than 0.15%) present in the liquid without using filter.

2 Define the terms:

☞



(a) Slurry: It is the suspension of solids to be filtered.

(b) Filter medium: It is the porous medium which retains the solids and allow the liquid to pass.

(c) Filter cake: The deposited layer of solids on the filter medium is called filter cake.

(d) Filtrate: It is the clear liquid passing through the filter.

(e) Collation/straining: When object of filtration is to remove large visible particles by using a coarse filtering medium like muslin cloth, glass wool, cotton wool, etc. Such process is known as straining/collation.

3 Distinguish between filtration and clarification.

☞

Filtration	Clarification
(i) Filter medium is required	Filter medium is not required
(ii) Useful for removal of large amount of solids	Useful for removal of small amount of solids
(iii) Any percentage of solids can be removed	Only less than 0.15% of solids can be removed
(iv) Bacterial filtration can be possible	Cannot be used for bacterial filtration
(v) Useful for filtration of injection, eyedrops	Useful for filtration of syrups, honey
(vi) Equipment used: Filter press, candle filter, filter leaf	Equipment used: Metafilter, stream line filter

4 Describe theory of filtration/Darcy's law of filtration.

☞ The theory of filtration gives the idea about rate of filtration and is explained by Darcy.

Scientist Darcy studied the factors affecting rate of filtration and equation derived is known as Darcy's law.

Darcy's law

$$V = \frac{KA\Delta P}{\eta l}$$

where, V = Rate of filtration
A = Area of filter bed
K = Permeability co-efficient
ΔP = Pressure difference above liquid and below filter medium
η = Viscosity of liquid (slurry)
l = Thickness of filter cake.

Thus,

(i) Increase in pressure above the liquid causes increase in rate of filtration.
(ii) An increase in area increases rate of filtration.
(iii) Increase in viscosity decreases rate of filtration.
(iv) Increase is thickness of cake decreases rate of filtration.
(v) Increase in area of filter bed increases rate of filtration.

5 Explain various factors affecting rate of filtration.

☞ **(a) Surface area of filter bed:** The increase in surface area of the filter bed increases the rate of filtration.

(b) Viscosity of slurry: The rate of filtration is inversely proportional to viscosity of liquid. Thus, increase in viscosity decreases filtration.

(c) Thickness of cake: If thickness of filter cake is more then rate of filtration is decreased.

(d) Temperature: Increase in temperature decreases viscosity of a liquid, thus, increases rate of filtration.

(e) Pressure difference: If pressure above the liquid is more than the pressure below liquid then rate of filtration is more.

(f) Particle size: Rate of filtration is directly proportional to the size of particles to be filtered. Smaller particles will block the filter media and form a cake, thus, decrease rate of filtration.

(g) Pore size of filter media: The rate of filtration is directly proportional to the pore size of the filter media.

6 Define filter media. Give the ideal properties of filter media.

☞ **Filter Media**

It is the porous medium which retains the solids and allows the liquid to pass.

A good filter medium should possess following properties:

1. It should not absorb the liquid to be filtered.
2. It should have smooth surface.
3. It should be chemically inert.
4. It should have good mechanical strength.
5. It should be resistant to corrosive action of liquid.
6. It should allow free flow of liquid.
7. It should be economical.
8. It should be reusable.

7 Explain various filter medias used in pharmacy.

☞ **(a) Filter paper:** It is a commonly used filter medium. The filter papers are also of coarse, medium and fine pore size.

(b) Cotton wool: It is used for filtering of moderately coarse particles.

(c) Glass wool: It consists of fine fibres of glass which resist corrosive liquids. Hence, used for filtration of strong acids and alkalies.

(d) Asbestos: It is also useful for filtration of acids and alkalies.

(e) Fine muslin cloth: It is used for separation of coarse particles.

(f) Filter cloth: It may be both synthetic or cotton and is used for large scale filtration.

(g) Membrane filter: It is made up of cellulose derivatives and used for filtration of injections, eyedrops, etc.

(h) Sintered glass filter: It is made up of borosilicate glass and is used for sterile filtration.

8 Write a note on "filter aids".

☞ **Filter Aids**

The substances which reduce the resistance to filtration and increase rate of filtration are called filter aid, e.g. talc, bentonite, kaolin, activated charcoal, diatomite, kieselguhr.

Ideal Qualities of Filter Aids

1. It should remain suspended in the liquid.
2. It should be free from impurities.
3. It should be chemically inert and insoluble.
4. It should form porous cake.
5. It should have low specific gravity.

9 Name various pieces of equipment used for filtration.

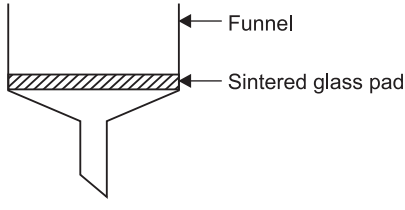
☞ (i) Filter press.
(ii) Filter leaf.
(iii) Filter candles.
(iv) Metafilters.
(v) Membrane filters.
(vi) Sintered glass filters.

10 Name the filtering devices used for sterile filtration (bacteria-proof filtration).

☞ (i) Membrane filter.
(ii) Sintered glass filter.
(iii) Seitz filter.
(iv) Edge filter.
(v) Candle filter.

11 Write a note on sintered glass filter.

☞ **Sintered Glass Filter**



☞ **Principle:**

1. The liquid to be filtered is poured into the sintered glass funnel and drawn through the perforations by vacuum suction.
2. These flasks are attached to vacuum pump to carry out filtration under reduced pressure to allow for the suction and collection of the filtrate.

☞ **Construction:**

- It is made from borosilicate glass.
- The glass is powdered and sifted to produce uniform particles.
- These are heated and moulded or fused together to form a disc.
- These discs are then fitted into a suitable funnel.
- They are available in different pore sizes.
- They are graded as:

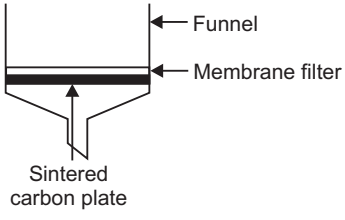
Grade 1	Pore size	90–150 μ
Grade 2	Pore size	40–90 μ
Grade 3	Pore size	15–40 μ
Grade 4	Pore size	5–15 μ
Grade 5	Pore size	up to 2 μ

Applications

1. It is useful for filtration of liquids like parenterals, corrosive liquids, oxidising agents.
2. Sintered glass filters with finest porosity are used for bacterial filtration.
3. It is useful for sterilization of thermolabile material.
4. It is useful for filtration of broth cultures of bacteria.

12 Write a note on "membrane filter".

☞ Membrane Filter:



- A membrane is a thin layer of semi-permeable material that separates substances when a driving force is applied across the membrane.
- It is used for ultrafiltration.
- It works on the principle of physical separation.

Principle:

- It works on the principle that the membrane acts as a very specific filter that allows water to flow through, while it catches the suspended solids and other substances.
- Membrane filter uses the sieving mechanism of the microfiltration membrane driven by pressure to trap particles, bacteria, some viruses, etc.

Construction:

- This filter is made up of cellulose acetate, nylon or PVC as a thin and flat membrane.
- Pore size is 500 millions per square centimeter of the filter paper.
- It is available in pore size of 8 µ to 0.22 µ. Hence called ultrafilter.
- For sterile filtration 0.22 to 0.45 µ pore size is used.

- The membrane filter may get clogged, therefore, prefiltration is required.

Applications/Uses:

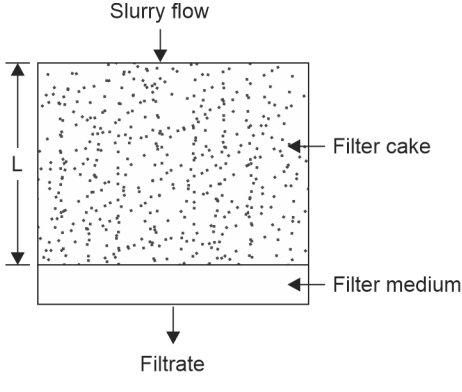
1. It is used for filtration and sterilisation of pharmaceutical products like eyedrops, injections, solutions hormones and vitamins.
2. It is useful in isolation of microorganisms.
3. It is used in the industrial production of enzymes.
4. It is used in the removal of ammonium ions from potable water.
5. It can also be used in the manufacture of dairy ingredients such as milk.

13 Explain "Liquid Filtration Theory". Or Explain "Kozeny-Carman equation" and "Poiseuille's Law" of filtration?

☞ Liquid Filtration Theory:

(a) Kozeny-Carman equation:

- This equation is used in the field of fluid dynamics to calculate the pressure drop of a fluid flowing through a packed bed of solids.
- In the filtration, as particles forming the cake are small and the flow through bed is slow.



Filtration process

Kozeny-Carman equation is as follows:

$$U = \frac{1}{A}\frac{dV}{dt} = \frac{\Delta p}{r\mu(l + L)}$$

Where,

U – Flow rate
A – Filter area
V – Volume of filtrate delivery
t – Filtration time
l – Thickness of cake
L – Thickness of cake equivalent to medium resistance

This equation relates with permeability of tube packed with particles to interparticle porosity, bed morphology and particle size and shape.

(b) Poiseuille's law of filtration:

- This law considers membrane properties, kinetic viscosity and density of a solution flowing across the membrane.
- The membrane filtration coefficient is inversely proportional to the concentration of the solution.
- The direction of flow is from greater to lower pressure
- Poiseuille's law considers that filtration is similar to the streamline flow of liquid under pressure through capillaries.

$$\frac{1}{dv}\frac{A}{dt} = \frac{\Delta P}{\mu(R_m + R_c)}$$

$$\text{Cake resistance } (R_m) = \frac{\sigma W}{A}$$

$$\text{Specific cake resistance } (\sigma) = \sigma^1 \Delta p^s$$

The filter resistance is much less than the cake resistance, i.e. $R_c << R_m$.

Therefore, on rearranging the equation is,

$$\frac{1}{dv}\frac{A}{dt} = \frac{\Delta P}{\mu(\sigma^1 DP^s \times WA)}$$

Where,

V – Filtrate volume
A – Filter area
t – Time

Δp – Pressure driving force
μ – Broth viscosity
W – Mass of filter
R – Resistance
σ – Specific cake resistance
S – Compressibility factor

- Poiseuille's law describes the relationship between pressure, fluidic resistance and flow rate.

14 What is filtration? Give the objectives of filtration.

☞ Filtration:

Filtration is the process in which insoluble solids are removed from the liquid, by passing through a porous medium in which solids are retained and liquid is allowed to pass.

Objectives of filtration:

- To separate the solids from liquid or gas medium.
- To produce high-quality solvents and solids.
- To purify air and pharmaceutical useful gases by removing particulate matter.
- To sterilize thermolabile parenteral products.
- To eliminate the contaminant particles so as to recover dispersing fluid.

CHAPTER 9

Drying

1 Define drying. Give the pharmaceutical significance/ applications/importance of drying.

☞ **Drying**

Drying means final removal of liquid from the solids with the help of heat.

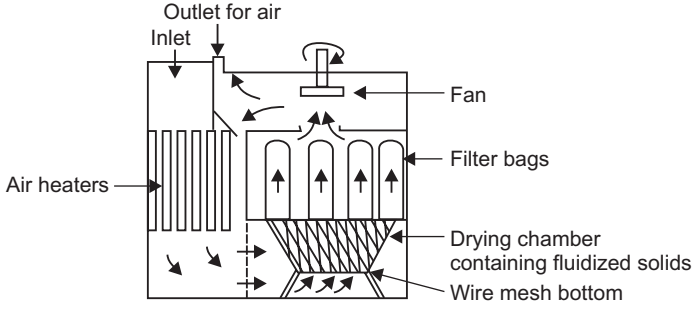
Importance of Drying in Pharmacy

1. In pharmaceuticals industry it is used in drying of granules, powders, etc.
2. Drying reduces weight of the substance, thus, reduces the cost of transportation and storage.
3. Drying helps in preservation of drug.
4. Drying helps in the size reduction of drugs.
5. Drying improves flow property of drugs.
6. Drying is useful in manufacturing of different biological products.
7. Drying is useful in production of lactose, aluminium hydroxide, etc.

2 Name various pieces of equipment used in drying.

☞ (i) Tray dryer
(ii) Tunnel dryer
(iii) Spray dryer
(iv) Fludised bed dryer
(v) Rotary dryer
(vii) Freeze dryer
(vi) Vacuum dryer
(viii) IR dryer.

3 Write a note on "fluidized bed dryer" (FBD)



☞ **Principle:**

- It works on the principle of fluidization of the feed materials.
- In this process, hot air is introduced at high pressure through a perforated bed of moist solid particulate.
- If air is allowed to flow through a bed of solid material in the upward direction with the velocity greater than the setting rate of the particles, the solid particles are blown-up and remain suspended in the air stream.

Construction and Working

1. The dryer consists of conical vessel with perforated bottom into which material is placed.
2. Filter bags are fitted to the conical vessel above which fan is fixed.
3. There is an inlet for air and outlet for air.
4. The fluidizing air stream is created by means of fan which is placed at the upper part of dryer.
5. Filtered and heated air then pass through powder bed.
6. The filter bags are provided to trap the fines produced during drying.

Advantages of FBD

1. High rate of drying.
2. Suitable for heat-sensitive materials.
3. Economical process.

4. Efficient and uniform drying.
5. It is mostly used for drying of granules.
6. Uniform temperature of drying can be maintained.
7. Product obtained is free flowing.

Disadvantages of FBD

1. High air velocity causes friction of particles.
2. High friction between particles generates electrostatic charges.
3. Due to turbulance fines are produced.

Applications/Uses of FBD:

1. It is used for drying and mixing of powders.
2. It is used in granulation and coating of powders, granules, tablets, etc.
3. It is used as fluidized bed reactors for solid separation and heat transfer.
4. The modified FBDs are used in precision granulation, spray drying granulation.

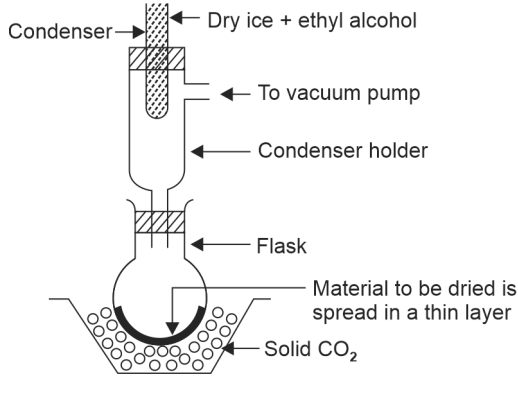
4 What is freeze drying? Explain lyophilization.

☞ It is also known as sublimation drying.

Lyophilization (freeze drying)

It is the process of freeze drying in which the moisture present in the material is frozen and then removed by sublimation of ice, i.e. ice is converted into vapours.

Freeze Dryer



☞ **Principle:**

- The principle of freeze drying is sublimation, where water passes directly from solid states (ice) to the vapour state without passing through the liquid state.
- Sublimation of water take place at pressures and temperature below triple point of water.
- The material to be dried is first frozen and subjected under a high vacuum to heat, so that frozen liquid sublimes, leaving only non-volatile solids, dried components of the original liquid.

Construction

Freeze dryer consists of four main parts:

1. A chamber for vacuum drying.
2. A vacuum source.
3. A heat source.
4. A vapour removal system.

Working

The material to be dried is frozen in a thin layer with the special type of freezing bottle. Spreading of material provides a large surface area for drying. The flask is connected to vacuum pump through the condenser. The temperature of condenser is maintained 20°C below the temperature of material to be dried. By creating vacuum in the flask the temperature and pressure conditions are set below the triple point value of water. Under such conditions if heat is supplied to the material it acts as a latent heat and sublimes the ice into vapour state. The vapours of water get condensed on the surface of condenser. The product obtained after freeze drying is light, porous and lyophilic in nature.

Advantages

1. Drying takes place at low temperature thus, decomposition of product is minimized.
2. The product is more porous and light and readily soluble.
3. Oxidation of product can be minimized.
4. It is useful for drying of thermolabile materials.

Disadvantages

1. It is very slow process.
2. The process is very costly.
3. The product obtained is very hygroscopic, therefore, requires special packaging conditions.

Pharmaceutical Applications

1. It is used for drying of biological products like plasma, serum, vaccines, enzymes, etc.
2. It is used for preservation of human tissue for research.
3. It is also used in food industry.
4. It is used to increase the shelf-life of the thermolabile products such as vaccines.
5. It is used to enhance stability of products during storage, shipping and transportation.
6. Freeze drying is used to reduce weight of the products.
7. It is used in chemical synthesis to make products more stable and easier to dissolve in water.
8. It is used to preserve blood products in freeze-dried form.
9. Freeze-drying can effectively be used in bio-separation in purification procedure.
10. Freeze drying can be used to concentrate low molecular weight substances that are too small to be removed by a membrane filtration.

CHAPTER 10

Extraction

1 Define the terms.

☞• **Extraction:** It is the process of removal of active constituents from crude drug by using a suitable solvent in which it is soluble.

- **Menstruum:** The solvent used for extraction is called menstruum, e.g. alcohol, water, chloroform, ether, light petroleum.
- **Marc:** The residue left after extraction is called marc.
- **Expression:** It means extraction carried out by mechanical means.
- **Galenicals:** The various preparations which are prepared by using extraction methods are called galenicals, e.g. infusions, decoction, tinctures, liquid extracts semisolid extracts.

2 Name various processes used for extraction.

☞1. **Infusion:** It consists of pouring water over the drug and then allowed it to keep in contact with water for a period of usually 15 minutes, with occasionally stirring and finally filtering of liquids. The marc is not pressed. The boiling water is commonly used as a solvent, since it has a greater solvent action.

2. **Decoction:** It is the process in which drug is boiled with water for a stated period of usually 10 minutes. After boiling liquid is strained and water is passed through the content of the strainer to make the required volume.

3. **Maceration:** Maceration is the process of extraction in which the drug and whole quantity of menstruum is placed in closed vessel and allowed to stand for 7 days with occasionally shaking. Thereafter liquid is strained, marc is pressed. The strained liquid and expressed liquid are combined and volume is not adjusted.

4. **Digestion:** It is the modified process of maceration in which drug and menstruum are heated throughout the extraction period to increase penetration power of the menstruum.

   The apparatus used for digestion is called digestor and temperature to be maintained is usually between 40° and 60ºC.

5. **Percolation:** Percolation is the process in which a comminuted drug is extracted by the passage of suitable solvent through the column of a drug, packed in a percolator.

3 Write a note on solvents (menstruum) used for extraction.

☞ Menstruum is a solvent used for the process of extraction.

- An ideal menstruum should possess following properties
  1. It should penetrate plant and animal tissues and cells.
  2. It should dissolve active ingredient from crude a drug.
  3. It should be non-toxic, non-inflammable.
  4. It should not cause degradation of dissolved substances.
  5. It should be cheap and easily available.

Examples of Menstruum

A. Water

Water is a solvent for protein, colouring matter, gums, glycosides, sugars, alkaloidal salts, enzymes, etc.

Advantages

(i) It is cheap.
(ii) It has wide solvent action.
(iii) It is non-toxic.
(iv) It is non-inflammable.

Disadvantages

(i) It is not selective solvent.
(ii) It is sensitive to bacterial and mould growth.
(iii) It promotes hydrolysis of many substances.
(iv) Large amount of heat is required to concentrate the product.

B. Alcohol

Alcohol is a solvent for alkaloids, glycosides, volatile oils and resins. Alcohol also dissolves many colouring matters, tannins, etc.

Advantages

(i) It is a selective solvent.
(ii) It is non-toxic.
(iii) It acts as a preservative.
(iv) It is neutral.
(v) It dissolves selective constituent of drug.
(vi) A small amount of heat is required to concentrate the product.

Disadvantages

(i) It is volatile.
(ii) It is inflammable.
(iii) It is costly.

4 Why is powdered drug used for extraction? Or Why comminution of drug prior to extraction is required?

☞ Because:

(i) In case of organised drug, the cell constituents are present in the fluid known as cell sap, in the form of solution or in colloidal state.
(ii) When the drug is dried, the constituents are precipitated or deposited in the cell structure. The dried cell sap becomes resistant to the action of menstruum.
(iii) The comminution of drug ruptures the cell sap and exposes the cell constituents to the action of menstruum.
(iv) Comminuted drug provides large surface area for penetration of the menstruum and effective extraction takes place.

5 Differentiate between the process for tinctures made from organised and unorganised drugs (maceration).

☞

Tinctures made from organised drug	Tinctures made from unorganised drug
1. The drug is placed with whole quantity of menstruum in a closed vessel	The drug is placed with only 4/5th volume of menstruum
2. Maceration period is 7 days	Maceration period is 2 to 7 days
3. The marc is pressed	The marc is not pressed

Contd.

Tinctures made from organised drug	Tinctures made from unorganised drug
4. The final volume is not adjusted	The final volume is adjusted
5. Examples:	Examples:
(i) Tincture of lemon	(i) Tincture of benzoin
(ii) Tincture of orange	(ii) Tincture of toluene

6 Distinguish between 'infusion' and 'decoction'.

☞

Infusion	Decoction
1. Cold or boiling water is used as menstruum	Drug is boiled in water
2. Drug having soft tissue is used	Drug of a hard tissue is used
3. Drug constituents may be volatile	Drug constituents should be nonvolatile
4. Final volume is not adjusted	Final volume is adjusted

7 Define extraction. Give the classification of extraction.

☞ **Extraction:**

Extraction is the process of removal of active constituent from crude drug by using a suitable solvent in which it is soluble.

Classification of Extraction:

1. Liquid-Liquid Extraction (solvent extraction):

- In this extraction, the components of the liquid mixture are separated by contacting them with a suitable insoluble solvent which dissolves one or more components.
- Separation of the components from liquid mixture depends upon the unequal distribution of the components between two immiscible liquids.
- In this extraction the feed solution is phase 1 and the solvent used for extraction is phase 2.
- Both the feed and solvent forms a homogeneous mixture which is separated by contacting them with one another to separate out one of the two liquids.

- This type of extraction is most widely used to separate active and aromatic compounds from plants.

2. Solid Phase Extraction:

- Solid phase extraction is used for isolation, enrichment and purification of components from aqueous solutions depending upon their physical and chemical properties.
- It involves contacting of aqueous samples with a solid phase or sorbent, where the component under consideration is adsorbed on the surface of the solid phase prior to elution.
- This type of extraction is widely used in analytical laboratories.

3. Solid-liquid Extraction (Leaching):

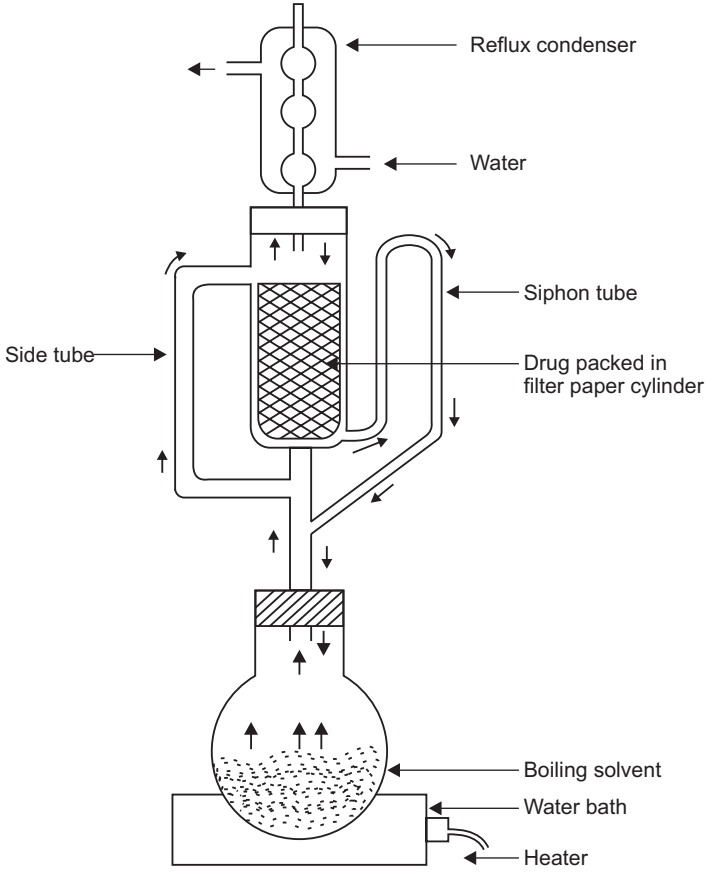
- Solid-liquid extraction means the removal of constituents from a mixture of solids by bringing the solid material into contact with a liquid solvent that dissolves these particular constituents.
- Leaching may either be used for production of concentrated solution of an active principle, or in order to free an insoluble constituent from a soluble material with which it is contaminated.

8 Write a note on "soxhlation" or "Soxhlet's extraction" or "continuous hot percolation/extraction process".

☞ Soxhlation

When the active constituents of the crude drug are soluble in the menstruum or difficult to extract from the cells then the drug is treated with hot menstruum for considerable period of time. The apparatus is known as Soxhlet's extractor and process is known as soxhlation.

Soxhlet's Apparatus



Apparatus

It consists of three main parts:

(i) The flask containing boiling solvent.

(ii) Soxhlet's extractor in which drug is packed.

It has a side tube through which vapours of the solvent carried into the extractor. It has siphon tube which siphons over the extract from the Soxhlet's extractor to the flask.

(iii) A condenser in which the vapours of the solvent are condensed and again converted into solvent.

Working

(i) The drug to be extracted is packed in a paper cylinder made from filter paper and it is placed in the body of Soxhlet's extractor.

(ii) The solvent is placed in the flask and then apparatus is fitted as shown in the figure.

(iii) When solvent is boiled on heating the flask, it gets converted into vapours. These vapours enter into the condenser through the side tube and get condensed into hot liquid which falls on the column of the drug.

(iv) When the extractor gets filled with solvent, the level of siphon tube also raises up to its top. The solvent containing active constituents of the drug in the siphon tube siphon over and run into the flask. The process of filling and emptying of extractor is continued until the drug is completely exhausted.

Advantages

1. Faster method.
2. Complete extraction of drug takes place.
3. Concentrated extract can be obtained.
4. Minimum requirement of menstruum.
5. Fireproof assembly.

Limitations/disadvantages

1. Method is not suitable for drugs which are sensitive to high temperature, e.g. enzymes, glycosides.
2. Only pure solvents can be used.
3. Gummy substances cannot be extracted by this method.

9 What is extraction? Give the application/Uses of extraction.

☞ Extraction:

It is the process of removal of an active constituent from crude drug by using a suitable solvent in which it is soluble.

Application/Uses of Extraction:

1. It is used for extraction of natural compounds.
2. It is useful for selective removal of components.
3. It is used in the separation of antibiotics and protein recovery.
4. It is used in perfumery and food industries.
5. It is used in DNA purification.
6. It is used to obtain active constituents from parts of plant by eliminating the inert material.
7. It is used to isolate enzymes and hormones from animal sources.
8. It is used in extraction of fixed oils from seeds.

CHAPTER 11

Tablets

1 Define tablet. Give advantages and disadvantages of tablet.

☞ **Tablet**

Tablets are solid, flat or biconvex disc-shaped, prepared by compressing a drug or mixture of drug with or without diluents.

Advantages/Merits

1. Tablets are easy for administration.
2. Tablets are easy to dispense.
3. Tablets are stable dosage forms.
4. Tablets give accuracy of dosage.
5. Masking of taste is possible by tablet coating.
6. Rapid disintegration, dissolution and onset of action.
7. They are light in weight.
8. Packaging and transportation of tablets is cheapest.
9. Tablets are economical dosage forms.
10. They can be formulated as a sustained dosage form.

Disadvantages/Demerits

1. Tablets are difficult to be swallowed by children and ill patients.
2. Some drugs are difficult to compress into tablet due to their low density.
3. Bitter and nauseous drugs require coating or encapsulation.
4. The drugs with poor wetting and slow dissolution property are difficult to convert into tablets.

2 Classify tablets.

☞ **Classification/Types of tablets**

A. Tablets Ingested Orally

1. Compressed tablets.
2. Multiple compressed tablets.
3. Multilayered tablets.
4. Sustained action tablets.
5. Enteric-coated tablets.
6. Sugar-coated tablets.
7. Film-coated tablets.
8. Chewable tablets.

B. Tablets Used in Oral Cavity

1. Buccal tablets.
2. Sublingual tablets.
3. Lozenge tablets.
4. Dental cones.

C. Tablets Used by other Routes

1. Implants.
2. Vaginal tablets.

D. Tablets Used to Prepare Solution

1. Solution tablets.
2. Effervescent tablets.
3. Dispensing tablets.
4. Hypodermic tablets.
5. Tablet triturates.

3 Write a note on additives/excipients/adjuvants used in tablets.

☞1. **Diluents:** When quantity of medicament in each tablet is very small then to make a tablet diluent is necessary, e.g. lactose, sucrose, dextrose, starch.

2. **Granulating agents:** These are used to convert fine powder into granules. Granulating agent provides proper moisture to convert fines into granules, e.g. water, alcohol, starch paste.

3. **Binding agents/binders:** These are used in granulation to provide proper strength to the granules, e.g. gum acacia, gum tragacanth, gelatin, starch paste, sucrose.
4. **Disintegrating agents:** These agents cause breakdown of tablet into small pieces. When medicament is insoluble in water, a disintegrating agent is required, e.g. starch, cellulose, alginates.
5. **Lubricants/glidants:** These are added to improve flow property of granules and to prevent sticking of materials to die and punches, e.g. talc, magnesium stearate, boric acid, calcium stearate.
6. **Adsorbents/adsorbing agents:** These are used to adsorb volatile oils, liquid extracts and tinctures, e.g. magnesium carbonate, kaolin, starch.
7. **Colouring agents:** These provide attractive colour to the tablet, e.g. amaranth, indigocarmine.
8. **Flavouring agents:** These provide pleasant flavour to the tablet, e.g. mentha oil, peppermint oil.
9. **Sweetening agents:** These mask the bitter taste of the tablet, e.g. sucrose, lactose.

4 What are various steps involved during manufacturing of compressed tablets?

☞ 1. Preparation of granules for compression:
   (a) Weighing the ingredients.
   (b) Mixing the powdered ingredients and excipients.
   (c) Converting the mixed ingredients into granules.
2. Compression of granules into tablets.
3. Coating of tablets.
4. Evaluation of tablets.

5 What are different methods of preparation of granules?

☞ Granulation Methods

(a) Moist/wet granulation.
(b) Dry granulation.
(c) Slugging/preliminary compression method.

(a) Moist/Wet Granulation

1. All powdered medicaments are mixed together.
2. By adding granulating agent powdered ingredients are converted into coherent mass.
3. This coherent mass is then passed through sieve no. 8 or 10.
4. The wet granules are dried in the oven below 60ºC.
5. The dried granules are again passed through sieve no. 20 to obtain uniform-sized granules.
6. Then lubricants and remaining part of the disintegrating agents are added to the granules and thus, granules are ready for compression.

(b) Dry Granulation

This method is used when certain medicaments are available in crystalline form or in the form of granules. Such medicaments are passed through sieve no. 20 or any other specified sieve and then mixed with any additional excipient. The resulting mixture is ready for compression, e.g. aspirin, sodium bromide, potassium chlorate.

(c) Slugging/Granules Prepared by Preliminary Compression

This method is used if drug is unstable in presence of moisture.

1. In this process the dry powder is compressed into large tablets or "slugs".
2. These slugs are broken into small pieces which are passed through specified sieve to collect the granules of suitable size.
3. A lubricating agent and a disintegrating agent are mixed with these granules and granules are ready for compression.

6 Why are granules preferred for compression than powders?

☞ Granules are preferred for compression than powders because:

1. Granules have uniform distribution of active ingredients.
2. Granules have spherical shape.
3. Granules give sufficient strength to tablets.
4. Granules of different sizes produce good die filling.
5. Granules are packed down easily and produce hard tablet.
6. Granules are heavier thus, do not blow out of die cavity.

7 Explain various defects/problems in manufacturing (processing) of tablets.

(a) Capping

☞ It means partial or complete removal of top or bottom portion of the tablet.

Causes/Reasons

1. Excessive fines in the granules which entrap air in the tablet.
2. Defective punches and dies.
3. High speed of the tablet machine.
4. The granules are too dry.
5. The punches are not set properly.
6. High degree of compression.

Remedy

1. Reduce the percentage of fines in granules.
2. Defective punches should be replaced.
3. Regulate the speed of the tablet machine.
4. Maintain desired moisture in the granules.
5. Set the punches and dies properly.
6. Regulate the pressure and reduce degree of compression.

(b) Picking and Sticking

"Picking" means the upper punch removes/picks up the material from the upper surface of the tablet.

"Sticking" means the material sticks to the walls of die cavity and punches.

Causes/Reasons

1. Use of scratched dies and punches.
2. Presence of moisture in the granules.
3. Use of small quantity of lubricant.
4. Excess of powder in the granules.
5. Defects in formulation.

Remedy

1. Use new set of die and punches.
2. Reduce moisture in the granules (dry the granules).
3. Increase quantity of lubricant.

4. Reduce percentage of powder in the granules.
5. Formulation should be checked.

(c) Mottling (Colour) Variation

"Mottling" means unequal distribution of colour on the surface of a coloured tablet.

Reasons/Causes

1. Migration of dye in the granules during the process of drying.
2. Use of different coloured medicaments and additives.
3. Non-uniform drying of granules.

Remedy

1. Drying of granules at a low temperature.
2. Using the dye which masks the colour of all ingredients.

(d) Weight Variation

It means the tablets do not have uniform weight.

Causes/Reasons

1. Granules are not uniform in size.
2. Excess of powder in the granules.
3. No proper mixing of lubricant.
4. No uniform flow of granules from hopper to die.
5. Due to change in capacity of die during compression.
6. Variation in speed and vibration of machine.

Remedy

1. Make granules of uniform size.
2. Reduce % of powder in the granules.
3. Uniform mixing of lubricant.
4. Maintain uniform flow of granules.
5. Reduce vibrations of machine and control variation in speed.

(e) Hardness Variation

- It means tablets do not have uniform hardness.
- The causes of hardness variation are similar to weight variation.
- By adjusting distance between punches and volume of material entering the die, hardness variation can be controlled.

(f) Double Impression

- This defect occurs when the lower punch has a monogram.
- This defect occurs because of improper movement of lower punch.
- This defect can be removed by controlling undesirable movement of the lower punch.

(g) Lamination

It refers to breakdown of tablet into two or more layers.

(h) Chipping

Chipping refers to coming off of a small portion of tablet.

8 Explain why tablets are coated? Name types of coating.

☞ The tablets are coated for the following reasons:

1. To mask the unpleasant taste of tablet.
2. To control the site of dissolution.
3. To protect the drug from atmospheric effects like air, moisture, etc.
4. To make the tablet attractive.
5. To provide sustained release action of drug.
6. To produce pharmaceutically superior products.
7. To prevent interaction of incompatible ingredients.
8. To convert liquid into free-flowing solids.

Types of Tablet Coating

1. Film coating, e.g. polyethylene glycol, hydroxy propyl methyl cellulose.
2. Sugar coating, e.g. plane/coloured syrup.
3. Enteric coating, e.g. shellac, cellulose acetate phthalate.
4. Compression coating
5. Controlled release coating.

9 Write a note on "sugar coating of tablets".

☞ Sugar coating is an art and requires skilled workers.
It is done by pan coating method.

Stages Involved during Sugar Coating

1. **Sieving:** The fine powder and broken pieces of tablet are removed by sieving.
2. **Sealing:** It involves layering of tablet by waterproof materials like shellac, cellulose acetate phthalate. The material is dissolved in water/solvent and spread over the rotating tablets on the pan, which causes evaporation of volatile solvent and thin coat of waterproof material remain, i.e. sealing.
3. **Subcoating:** In this stage several coats of sugar and other materials such as gelatin, acacia, etc. are given to round off tablet and helps to build up the tablet size. During subcoating dusting powder is sprinkled to prevent sticking of tablets.
4. **Syrup coating:** This is done to give sugar coat and colour to the tablet. Colouring materials and opacifying agents are also added to the syrup.
5. **Finishing:** At the end of the process 3–4 coats of syrup are applied in rapid succession. Cold air is circulated to dry each coat. Finishing provides smooth and hard surface to tablet.
6. **Polishing:** Polishing pan is made of canvas cloth. Tablets are placed in rotating polishing pan. Before polishing, layer of bees wax is applied.

10 Explain "film coating of tablets".

☞ Film coating means coating by means of film forming agents such as hydroxy ethyl methyl cellulose, polyethylene glyco-400, carbowax, PVC, CMC, ethyl cellulose, etc.

Method of Film Coating of Tablets

1. The tablets are placed in the coating pan.
2. The speed of the pan is so adjusted that the tablets tumble in pan.
3. Hot air is blown in.
4. The film coating solution is added.
5. After each addition, dusting powder is sprinkled, if necessary.
6. In the end, the coated tablets are dried off.

Advantages of Film Coating

1. It is less time-consuming technique.
2. Not much labour is required.

3. No significant increase in tablet weight or size.
4. No effect on disintegration of tablet.
5. The product cost is low because of cheaper coating material.
6. Film coating protects the drug from air, moisture, light, etc.
7. Coating is resistant to cracking and chipping.
8. No waterproofing is required before actual film coating.
9. The tablets become elegant.

11 What is enteric coating? Why is it necessary? Explain its method.

☞ "Enteric coating" means coat is applied to the tablet so that tablet shall disintegrate in the intestine and not in the stomach.

The Tablets are Enteric Coated Because

1. Some medicaments produce severe irritation in the stomach.
2. The action of medicament is required in the intestine.
3. Some medicaments get destroyed by acidic medium of the stomach.
4. Drug absorption is better in the intestine.
5. Delayed action is needed.
6. When sustained action of drug is required.

Materials Used for Enteric Coating

1. Shellac.
2. Cellulose acetate phthalate.
3. Synthetic resins.
4. Salol.

Properties of an Ideal Enteric Coating Material

1. Resistant to gastric fluid.
2. Non-toxic in the required quantity.
3. Economical.
4. Ease of application.
5. Compatible with drug on which coating is done.
6. Formation of continuous film.
7. Film should not change on aging.
8. Should readily dissolve in intestinal fluids.

Method of Entering Coating

1. On large scale enteric coating is done in rotating pan.
2. The tablets to be coated are taken into the pan.
3. The pan is rotated with a sufficient speed.
4. First waterproofing of the tablet is done by solutions of shellac.
5. Then enteric coating solution is sprayed over the tablets rotated in the coating pan.
6. The hot air is blown into the pan to evaporate the organic solvent.
7. The process is repeated a number of times till the required number of coatings are done.

12 Give the difference between 'pan coating and press coating'.

☞

Pan coating	Press coating
1. The solution of coating material is used	1. Coat is used
2. Tablets must be hard to withstand tumbling with the coating pan	2. Tablets need not to be hard
3. It is a batch process	3. It is continuous process
4. It is skilled process	4. It is mechanical process
5. Embossing of tablet is not possible	5. Embossing of tablet is possible

13 Name and explain common defects in film coating.

☞ 1. **Blistering:** A film surface shows number of uneven spots called blisters.

2. **Wrinkling:** It means formation of wrinkles on surface of film by improper drying.
3. **Orange peel:** It means formation of film surface like orange peel due to rapid drying.
4. **Sweating:** It means presence of an oily film or liquid droplet on the surface of the coat.
5. **Flaking:** It means removal of coating material like a flake.
6. **Blooming:** If the product is processed under high humidity conditions, there is a formation of dull film known as blooming.

7. **Cratering:** It is a defect of film coating whereby volcanic-like craters appears on the tablet surface which in turn results in the exposure on the tablet surface.
8. **Pitting:** It is the defect where by pits (deformation) occur in the surface of a tablet core without any visible signs of disruption of the film coating.
9. **Cracking/Splitting:** It is a defect in which the film either cracks across the crown of the tablet or splits around the edges of the tablet.
10. **Scuffing:** It involves the generation of gray-to-black marks on the surface of white film-coated tablets.
11. **Spotting:** It means formation of spotted area on the surface of tablet film because of migration of dyes, plasticizers, etc.
12. **Bridging:** It means there is a lack of adhesion of the film to the tablet surface showing bridge-like appearance.
13. **Twinning:** It means two or more tablets stick together.

14 Write a note on microencapsulation.

☞ Microencapsulation

It is the technique in which a thin coating is applied on the particles of solids, liquids, resulting in formation of microcapsules ranging from 5 μm to 5 mm.

Microencapsulation is used to:

1. Mask the taste of bitter drugs.
2. Formation of sustained release dosage form.
3. Separation of incompatible materials.
4. Protection of drugs against moisture, oxygen, etc.
5. Conversion of liquid to solids, etc.

The materials used for microencapsulation are gelatin, PVC, ethyl cellulose, shell, etc.

- **Techniques of microencapsulation:**

1. Pan coating
2. Fluidised bed drying
3. Coacervation
4. Electrostatic deposition
5. Vacuum deposition
6. Polymerisation
7. Multiorifice centrifuge process

15 Name various official and unofficial tests for evaluation of tablet quality control tests/pharmacopoeial tests (standardisation tests).

☞ **Evaluation of Tablets**

A. Official Tests

1. Shape of tablets
2. Appearance
3. Content of active ingredient in tablets
4. Uniformity of weight (weight variation)
5. Uniformity of contents
6. Disintegration test
7. Dissolution test

B. Unofficial Tests

1. Hardness test
2. Friability test

16 Write a note on 'weight variation' of tablets.

☞ Every individual tablet in a batch should be uniform in weight but a small variation in the weight of individual tablets occurs. Therefore, little variation is allowed in the weight of a tablet by pharmacopoeia.

Average weight of tablet	% Deviation
1. 80 mg or less	10
2. More than 80 mg and less than 250 mg	7.5
3. 250 mg or more	5

Weigh 20 tablets selected at random and determine their average weight. Not more than 2 tablets may deviate from the average weight.

17 Write a note on "disintegration test" for tablets.

☞
- Disintegration: Disintegration of a tablet means to break the tablet into smaller particles after swallowing.
- Disintegration time: Time required to disintegrate the tablet is called disintegration time.
- This test is performed to determine whether the coated or uncoated tablets disintegrate within the prescribed time, when placed in the liquid medium under prescribed experimental conditions.

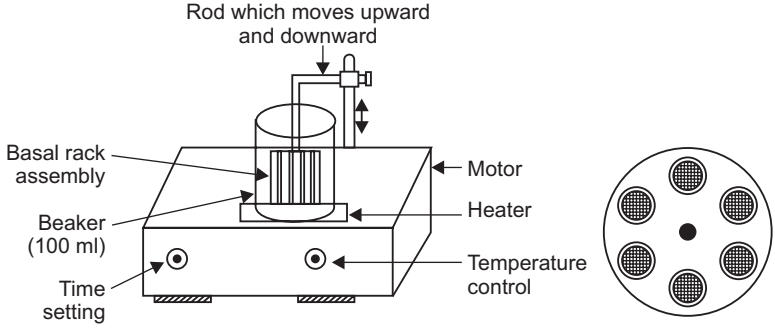
- Rate of disintegration depends upon the nature of drug and hardness of the tablet.
- In general, pharmacopoeia prescribed a limit of 15 minutes for most of the tablets.

The Official Disintegration Test as per IP, 1985

- **Disintegration Test Apparatus**

It consists of:

1. A rigid basket-rack assembly supporting 6 cylindrical glass tubes 77.5 mm long, 21 mm in diameter and 2 mm in thickness.
2. Lower size of the tube is covered with a stainless steel mesh of 2 mm apertures.



Disintegration test apparatus

3. Metal rod is fixed to the centre of the basket and attached to a mechanical device which moves up and down through a distance of 50 to 60 mm at frequency of **28 to 32 cycles/min.**
4. The assembly is suspended in the liquid medium in a 1000 ml beaker.
5. Below the beaker there is a heating device which maintains temperature of liquid 37ºC during test (37ºC $\pm$ 2ºC).
6. There is a separate arrangement of knobs for time setting and temperature control.

Method for Uncoated Tablets

1. Six tablets are placed in each of the 6 tubes of the basket and disc is added to each tube.
2. The beaker should be filled with water and temperature should be 37ºC.

3. The machine is started.
4. The tablets pass the test if all 6 tablets have disintegrated in not more than 15 minutes. If one or two tablets fail to disintegrate, the test is repeated on 12 additional tablets. The tablet passes the test if not less than 16 of toal 18 tablets disintegrate.

Disintegration Time as per IP

1. Not more than 15 minutes for uncoated tablets.
2. One hour for coated tablets.
3. Three hours for enteric coated tablets.

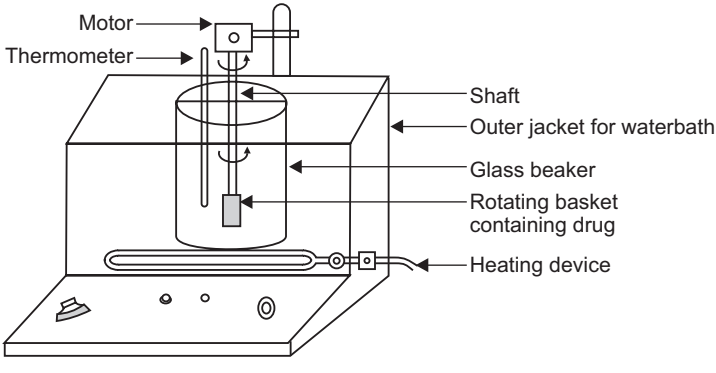
18 Explain "dissolution test" for tablets as per IP, 1985.

☞ Dissolution test is done for measuring the amount of time required for a given % of the drug in a tablet to go into solution under specified conditions *in vitro*.

Dissolution Test Apparatus

It consists of following parts:

1. A cylindrical covered beaker made up of glass having 1000 ml capacity.
2. The stirring shaft is placed in the beaker which is fitted with motor at upper end. To the lower end of the shaft a basket is fixed.



Dissolution test apparatus

3. A cylindrical stainless steel basket is made up of woven wire cloths having an aperture size 425 μm.

4. An electric motor which is capable of rotating the basket in the vessel have a speed of 25 to 150 rpm.
5. The beaker is fixed in the waterbath which is maintained at 37ºC ± 0.5ºC.

Method

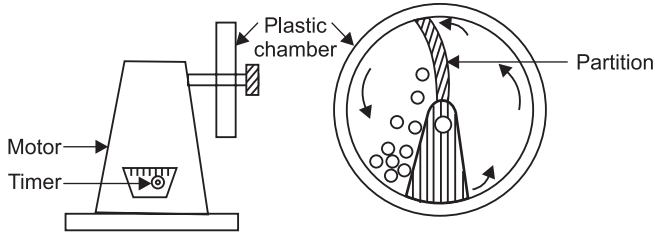
1. Place 1000 ml of water which should be free from dissolved air and warm it up to 37ºC.
2. Place specified number of tablets in the dry basket. Set the apparatus.
3. Start the motor and adjust rotation speed of 100 rpm and wait for 45 minutes.
4. After 45 minutes, withdraw the stated volume of solution from the vessel.
5. By analysing each sample dissolution rate is determined.

19 Define friability. Explain "friability test" for tablets.

☞ **Friability**

Friability means tablets may show powdering, capping, chipping, breaking into smaller pieces during normal handling, packing or transportation and produce loss in weight.

- Friability test is performed to determine ability of a tablet to withstand wear and tear during packing, handling and transportation.
- The apparatus used to perform friability test is known as **friabilator.**



Friabilator

Apparatus

1. It consists of plastic chamber, which is divided into two parts by partition.

2. Plastic chamber is attached with a motor which revolves 25 rpm.
3. Timer is arranged at the bottom.

Method

1. Twenty tablets are weighed and placed in the plastic chamber and lid is closed.
2. The chamber is rotated for 4 minutes or 100 revolutions.
3. During each revolution the tablet falls from a distance of 6 inch.
4. After 4 minutes, the tablets are removed from the chamber and weighed.
5. The **loss in weight indicates friability.**
6. The tablets are considered to be of good quality if the loss in weight is less than 0.8%.

20 What do you mean by Modified Tablets? Give its advantages and examples.

☞ **Modified Tablets/Modified Release Tablets:**

Modified tablet are designed to release their medication in controlled manner, at pre-determined rate, duration and location in the body to achieve and maintain optimum blood levels of drug.

Advantages of Modified Tables:

1. Less frequency of administration.
2. Reduction in drug release variation.
3. Improved bioavailability.
4. Prolonged drug action.
5. Providing specific effects.
6. Achieves optimum blood levels of drug.

Examples of Modified Tables:

(a) Sustained released tablets.
(b) Extended-released tablets.
(c) Fast dissolving tablets.
(d) Double layered tablets.

21 Define sustained Release Tablets ? Give its advantages and disadvantages or write a note on "Sustained Release Tablets".

☞ **Sustained Released Tablets:**

These are the tablets that achieve slow release of drug over an extended period of time.

Advantages:

1. It reduces drug concentration fluctuation in the body.
2. It reduces drug dose.
3. It improves patient compliance.
4. It provides safety of drug.

Disadvantages:

1. Chances of dose dumping.
2. Difficulty in dose retrieval.
3. High cost of production.
4. Needs patient education and counseling.
5. Difficult to adjust the dose of drug.

Examples:

- Paracetamol sustained release tablets.
- Indapamide sustained release tablets.

22 Define extended release tablets ? Give its advantages and disadvantages. Or write a note on "extended release tablets".

☞ **Extended Release Tablets**

- These are the dosage forms that allow at least a two-fold reduction in dosing frequency as compared to an immediate-released tablet.
- Extended release tablets slowly release drug into the body over a period of time, usually 12 hours or 24 hours and are taken once or twice a day.

Advantages:

- Less frequency of dosing.
- Fewer side effects.
- Less fluctuation in blood levels.
- Complete absorption.
- Improves patient compliance and convenience.
- Increases stability.
- Improves bioavailability of drug.
- Provides specific drug effects.

Disadvantages:

- Slow onset of action.
- High cost of the dosage form.
- Side effect may be for longer period of time.
- The drug release rates may be affected by presence of food in GIT.

Examples:

1. Ranolazine extended release tablet.
2. Venlafaxine extended release tablet.

23 What do you mean by fast Dissolving Tablets ? Give its advantages and disadvantages or write a note on "Fast Dissolving Tablets".

☞ **Fast Dissolving Tablets (FDT):**

- These are solid dosage forms designed to dissolve in saliva very faster, with a few second, usually less than 60 sec.
- FDTS disintegrate rapidly in saliva without the need to take water and are commonly used for the pediatric and geriatric patients having difficulties in swallowing.
- In this case first pass metabolism is reduced as compared to conventional tablets.

Advantages:

1. No need of water to swallow the tablet.
2. Ease of administration.

3. Useful for pediatric, geriatric and mentally disabled patients.
4. Acute dosing can be given.
5. Fast dissolution and absorption of drug.
6. Rapid onset of action.
7. Increased bioavailability.
8. Reduces first pass metabolism.
9. Improves safety and high drug loading.

Disadvantages:

1. Low mechanical strength.
2. Highly porous dosage form.
3. More friable and brittle, thus difficult to handle.
4. Difficult to formulate the drugs having bad taste or odour in FDT.
5. Same FDT are hygroscopic, so requires some specialized package.
6. Dryness of mouth may hamper dissolution and absorption rate of drug.

Examples:

1. Piroxicam fast dissolving tablet.
2. Ondensetron fast dissolving tablet.

24 Write a note on "Double Layered Tablets".

Or

What are Double Layered Tablets? Give its advantages and disadvantages ?

☞ **Double Layered Tablets (DLT)/Bilayer Tablets:**

- These are the controlled release formulation that have a combination of two or more drugs in a single tablet.
- Double layer tablet technology separates two incompatible drugs in which one layer is immediate released as a loading dose and the second layer is controlled release as a maintenance dose.
- Two incompatible drugs can also be formulated into a bilayer tablet by adding an inert intermediate layer.

Advantages:

1. Greater dose precision and less content variability.
2. They are lighter and compact.
3. Easier and cheaper to package and strip.
4. Easy to swallow.
5. It can mask objectionable odour and bitter taste and are suitable for large production.
6. Chemical and microbial stability.

Disadvantages:

1. Manufacture is more expensive.
2. Requires more time for formulation and development, analysis and validation.
3. Sometimes layer separation may occur.
4. Cross-contamination between the layers may occur.

Examples:

- Diclofenac potassium and paracetamol double layer tablet.
- Glimepiride and metformin hydrochloride bilayer tablet.

CHAPTER 12

Capsules

1 Define capsule. Give merits and demerits of capsule.

☞ Capsule

Capsules are a solid dosage form in which the drug substance is enclosed in a water soluble shell.

Advantages

1. It is attractive in appearance.
2. It can mask the odour, taste and colour of the medicament.
3. It is tasteless.
4. It is simple to use and handling.
5. It is smooth, slipped thus, easily swallowed.
6. It is economical.
7. It is available in wide range of colours and sizes.
8. Microencapsulation provides the sustained released dosage form.
9. Requires minimum additives.
10. It is physiologically inert.

Disadvantages

1. The hygroscopic drugs cannot be filled in capsules.
2. Not suitable for extremely soluble materials as they cause GIT irritation.
3. Not suitable for highly soluble compounds.
4. Aqueous or hydroalcoholic liquids cannot be enclosed in the capsules.
5. Proteolytic enzymes may interact with gelatin, thus, not suitable.

2 Distinguish between 'hard gelatin and soft gelatin capsules'.

☞

Hard gelatin capsules	Soft gelatin capsules
1. It is composed of gelatin, water and less % of plasticizer	1. It is composed of gelatin, water and 100% plasticizer
2. It has two parts—body and cap	2. It has unit body
3. It is cylindrical and hemispherical	3. It is available in different shapes like oval or spherical
4. Available in 8 standard sizes 000 to 5 (smallest)	4. No standard size but available in different sizes
5. Only suitable for solids	5. Suitable for both solids and liquids
6. Capsules are sealed after they are filled	6. Filling and sealing are done in a combined operation on machine
7. Hand filling and sealing is possible	7. Machine is required
8. Shell is perfectly dry.	8. Shell is not dry.
9. These capsules can be adulterated.	9. These capsules cannot be adulterated.
10. For example, amoxycillin capsule.	10. For example, Pudina Hara capsule.

3 Give different forms of hard gelatin capsule according to the size and capacity in milligram.

☞

Capsule number	Approximate capacity in mg
000	950 (largest)
00	650
0	450
1	300
2	250
3	200
4	150
5	100 (smallest)

4 What are additives/excipients used in filling of hard gelatin capsule?

☞ 1. **Diluent:** The diluent is needed when the quantity of medicament is too small, e.g. lactose, mannitol, starch.
2. **Absorbents:** These are used to absorb moisture and protect the hygroscopic substances, e.g. kaolin, magnesium oxide.
3. **Glidants:** They increase the regular flow of powder during filling, e.g. talc, magnesium stearate, calcium stearate.
4. **Antidusting agents:** During filling of capsule, a lot of dust comes out from the machine which may be harmful to workers. To avoid this some antidusting agents are added, e.g. inert edible oils.

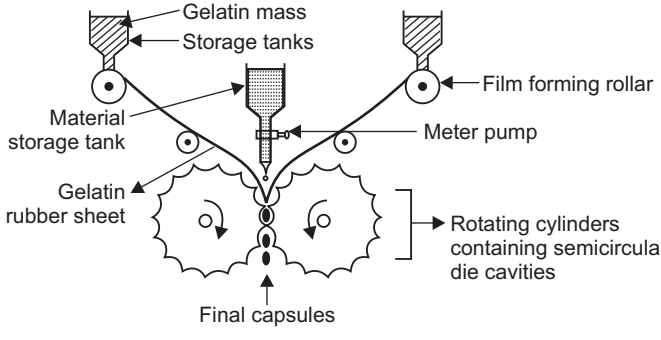
5 What are the special applications of capsule?

☞ 1. **Enteric coated capsules:** These capsules disintegrate in the intestine and not in the stomach. The shell is coated with enteric coated materials like shellac.
2. **Sustained release capsules:** These capsules produce prolonged action and reduce repeated administration of the drug. In this case coated and uncoated granules/pellets of drug are filled in a definite proportion. Uncoated granules are quickly absorbed and produce quick action while coated granules dissolve slowly thus, produce prolonged drug action.
3. **Rectal capsules:** These are used for rectal administration and are substitute for rectal suppositories. These capsules contain semisolid/liquid medicament.
4. **Capsules containing ophthalmic ointment:** Nowadays ophthalmic ointments are packed in soft gelatin capsules. They contain single dose and thus, they can maintain sterility of the ointment. At the time of application, the tip of capsule is punctured with sterile needle and its contents are instilled into the eye cavity and then capsule is discarded.

6 Explain the processing/filling/manufacturing of soft gelatin capsules.

☞ • Soft gelatin capsules are generally filled mechanically.
• The manufacturing of capsule shell and the filling of the medicament take place simultaneously.

- Rotary die machine is used for this purpose.
  1. The machine consists of two hoppers in which liquid gelatin mixture is placed.
  2. The middle hopper contains liquid medicament.
  3. There are two rotating dies which rotate in opposite direction.
  4. When fluid gelatin mixture enters the machine from the hopper, it produces two continuous ribbons.



Processing of soft gelatin capsule

5. These ribbons come over the rotating dies and thus, half shell of the capsule is formed.
6. In between the two cylinders the material is supplied through the pump.
7. The material exert the pressure on the gelatin sheet and press the sheet into the die cavity.
8. Due to pressure and heat two halves of the capsule are sealed.
9. The capsules formed are washed thoroughly and dried.
10. Finishing of capsule:
    – In this stage undesired matter adhered to the capsule is removed by rubbing the capsules on the piece of cloth containing inert oil.
    – Finishing provides clean and attractive appearance and lustre to the capsules.

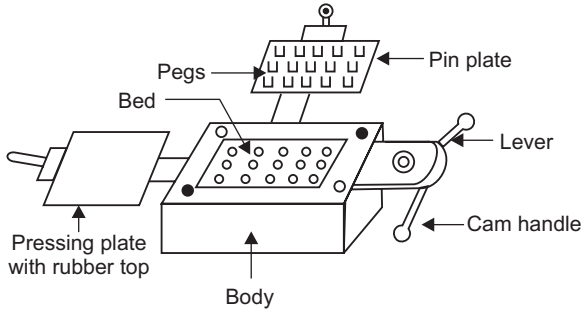
7 Discuss processing of hard gelatin capsule. Or Discuss the operations of hand-operated hard gelatin capsule filling machine.

☞ Processing of hard gelatin capsule is divided into following steps:

1. Separation of cap from the body.

2. Filling the body.
3. Rejoining the cap and body, cleaning and polishing.
4. Packing/sealing.

Hand-operated capsule filling machines are available:



Operation

1. The empty gelatin capsules are filled in the loading tray and it is placed over the bed.
2. The cam-handle is operated to separate the caps from their bodies.
3. The powder tray is placed in a proper position and filled with an accurate quantity of powder with scrapper. The excess powder is removed.
4. The pin plate is lowered and the filled powder is pressed.
5. Then remove the pin plate and again remaining powder is filled into the bodies of capsule.
6. The powdered tray is removed after its complete filling.
7. The cap holding tray is again placed in position.
8. The plate with the rubber top is lowered and the lever is operated to lock the caps and bodies.
9. Loading tray is then removed and filled capsules are collected.
10. Cleaning of capsule is necessary to remove adhered fine dust of the material with soft cloth.
11. A cloth containing slight amount of mineral oil or a wax is used to give shining to the capsules.
12. Finally capsules are packed by using machines.

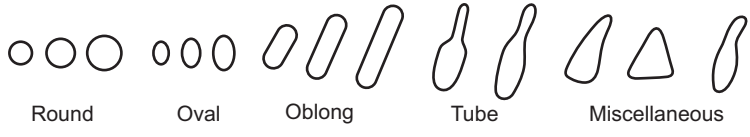
8 Give the composition of soft gelatin capsules. Give their types.

☞ Soft gelatin capsules are also known as "soluble elastic"/"soft elastic capsule".

Composition

- Soft gelatin capsules consist of **gelatin, water** and high percentage of **plasticizer**, i.e. sorbitol or glycerin plasticizers give elastic properties to capsules.
- Preservative—methyl or propyl paraben.
- Opacifying agent—titanium dioxide.
- Flavouring agent.

Types/Shapes of Soft Gelatin Capsules



9 Write the packing and storage conditions of capsules.

☞ 1. Capsules are closed in the glass/plastic containers.
2. Capsules are also packed in the form of blister or strip packing.

Storage

The capsules should be stored at a temperature not exceeding 30ºC and in dry place.

- Storage at high humidity causes increase in moisture content and capsules stick together and at high temperature, capsule may get cracked.

10 Explain various quality control tests for capsules.

☞ Quality Control Tests for Capsule:

1. **Size and Shape:**
   This test ensures the testing capsules of uniforming of size and shape and compared with standard.

2. **Unique identification marking:**
   Capsule surfaces may bear symbols or other unique identification markings for better identification.
3. **Moisture permeation:**
   This test is used to calculate the amount of moisture permeated within the package of capsule.
4. **Weight variation/Uniformity or mass:**
   Weight variation is calculated and compared with the limits given as per IP ranges.
5. **Content of the active ingredient in the capsule:**
   The contents of the active ingredient in the capsule are analysed by suitable analytical method of equivalent accuracy and precision.
6. **Disintegration test:**
   To test for disintegration time, one capsule is placed in each tube of disintegration test apparatus. Capsules comply with the test, if disintegrates and all particles pass through the 10-mesh screen within the specified time.
   Disintegration time: For hard gelatin capsule — 30 min.
   For soft gelatin capsule — 60 min.
7. **Dissolution test:**
   The USP or BP dissolution test apparatus (basket type) is used to determine amount of drug released. A single capsule is placed in the apparatus and the apparatus is operated at the specified rate. The sample of the solution is assayed as per the method given in the individual monograph.

CHAPTER 13

Liquid Oral Preparations

A Syrups and Elixirs

B Solutions

C Suspensions and Dry Powder for Reconstitution

D Emulsion

A

Syrups and Elixirs

1 Give merits and demerits of liquid dosage forms/liquid oral preparations

☞ **Merits**

1. Onset of action is quick as compared to tablets and capsules.
2. Certain medicaments can only be given in liquid form, e.g. castor oil.
3. Certain drugs are to be given in suspended form to produce maximum surface area.
4. A few drugs if taken in dry form may cause pain and irritation.
5. Psychological satisfaction to a patient of something is in the bottle.

Demerits

1. Dose has to be measured.
2. Stability and preservation possess a problem.
3. Storage should be proper.
4. Possibility of breaking the containers during transport.
5. Costly dosage form than the solid dosage form.

2 What are syrups? Give types and method of preparation of syrup/write a note on syrups.

☞ **Syrups**

Syrups are sweet, viscous, concentrated aqueous solutions of sucrose or other sugars.

Types of Syrups

(a) **Medicated syrups:** These contain a medicinal agent.
(b) **Non-medicated/flavoured syrups:** These syrups do not contain medicinal agent but contain flavouring agent.

Methods of Preparation of Syrup

i. Hot process.
ii. Cold process (percolation).
iii. Agitation without heat.
iv. Addition of medicating or flavouring liquid to syrup.

Explanation of Syrups

- Syrups are used for administering the drugs with a disagreeable or bitter taste.
- Syrups are mostly used in pediatric patients (children).
- Syrups are used in the formulations like antibiotics, anticough, vitamins, antihistaminics.
- Syrups are good demulscents and soothing agents, hence, used in cough syrups.
- Sucrose is commonly used in syrups but may be replaced by dextrose.
- Non-glycogenic substances like methyl cellulose can be used for preparation of syrups suitable for diabetic patients.
- Dilute solutions of sucrose shows growth of micro-organism, whereas saturated solution may lead to crystallisation of sucrose. Hence, 65% or more of sucrose solution, i.e. syrups are useful to prevent above problems.
- Syrup IP is a 66.7% w/w solution of sucrose in purified water.
- Syrup containing lesser concentration of sucrose requires preservatives.

Storage

Syrups should be stored in well dried, completely filled and carefully stoppered bottles in a cool and dark place.

Examples of Syrups

i. Citric acid syrup.
ii. Orange syrup.
iii. Lemon syrup.
iv. Codeine phosphate syrup.
v. Piperazine citrate syrup USP.

Advantages of Syrup:

- Syrup has an ability to mask the bad taste of drug.
- Syrup produces soothing effect on irritated tissues of throat.
- Syrup does not contain alcohol as preservative.
- Syrup resists microbial growth.
- Syrups are widely acceptable due to the wide variety of flavours used.

Disadvantages of Syrup:

- Regular use of syrups may have risk of dental caries.
- Crystallization of sugars takes place if container is left open.
- Syrups are not suitable for diabetic patients.

Quality Control Tests for Syrup:

(a) **Visual Inspection:** Syrups are carefully examine for purity and for good appearance.

(b) **Cap Locking:** It is performed to check that the cap could not be easily opened.

(c) **Light Transmittance:** A light transmittance meter is used to check syrup colour. A syrup sample is checked for colour by passing light through the sample.

(d) **Sucrose Concentration:** High concentration of sucrose may crystallize the syrup while low concentration may favour the microbial growth. So syrups must be checked for percentage of sucrose in it.

(e) **Physical Stability:** The syrups must be checked for its physical stability, e.g. its appearance.

(f) **pH:** The pH of syrup can be determined can by using pH meter.

3 Write a note on elixirs.

☞ **Elixirs**

Elixirs are clear, sweetened, aromatic, hydroalcoholic liquids intended for oral use.

Types of Elixirs

a. **Medicated elixirs:** These contain medicinal agents like chlorpheniramine.
b. **Non-medicated/flavoured elixirs:** These do not contain a medicament and may be used as flavouring agents, e.g. aromatic water.

Methods of Preparation

Simple dissolution with agitation or by addition of two or more liquid components.

Explanation of Elixirs

- Elixirs are less sweet and less viscous than syrups.
- Elixirs may contain less or no sucrose.
- Elixirs are more stable than syrups.
- Elixirs contain alcohol and vary from 4 to 40%.
- They may also contain flavouring and colouring agents.
- Elixirs do not contain preservative as their alcohol content is sufficient as a self-preservative.

Storage

Stored in well dried completely filled and carefully stoppered bottles in cool dark place.

Examples of Elixirs

i. Aromatic elixir USP
ii. Piperazine citrate elixir
iii. Benzaldehyde elixir NF.

Advantages of Elixirs:

- More stable because of self preservative property.
- Easy to prepare.
- Used as a vehicle for dilution of medicated elixirs.
- Used to mask the taste of bitter drugs.
- Because of low viscosity, elixirs flow more freely.
- Easy to administer.

Disadvantages of Elixirs:

- As elixirs contain volatile components, they should be stored in airtight containers to prevent losses.
- Elixirs should be kept away from heat source.
- Elixirs are less effective than syrups in masking taste of medicated substances.

Quality Control Tests for Elixirs:

(a) Sucrose concentration.

(b) Alcohol content.

(c) Refractive index.

(d) Visual inspection.

(e) Clarity.

(f) Pourability and viscosity.

4 Difference between syrups and elixirs.

Syrups	*Elixirs*
1. These are concentrated solutions	1. These are clear, pleasantly flavoured, sweetened, hydroalcoholic solutions.
2. Concentration of sugar is high.	2. Concentration of sugar is low or sometimes absent.
3. Alcohol is present in very small concentration or may even absent.	3. Alcohol is always present in concentration of 4 to 40%.
4. These are prepared by hot, cold or agitation method.	4. These are prepared by agitation method only.
5. Examples • Orange syrup • Lemon syrup	5. Examples • Aromatic elixir • Piperazine citrate elixir

B

Solutions

1 Define Solutions. Classify solutions giving examples Give advantages, disadvantages and quality control tests of solutions. Or Write note on "solutions".

☞ **Solutions:**

A solution is a homogeneous liquid dosage form prepared by dissolving active ingredients in an aqueous or non-aqueous solvents.

☞ **Classification/Types of solutions:**

(A) As per composition and uses:

(i) **Syrups:** Aqueous solution containing sugar.
(ii) **Elixir:** Sweeten hydro-alcoholic solution.
(iii) **Spirit:** Solution of aromatic material in alcohol.
(iv) **Aromatic water:** Solution of aromatic material in water.
(v) **Tincture:** Solution prepared by extracting constituents from crude drugs.
(vi) **Injection:** These are sterile and pyrogen free solutions intended for parenteral administration.

(B) As per vehicle:

(i) **Aqueous solutions:** Solutions that contain water as a solvent, e.g. sugar in water.
(ii) **Non-aqueous solutions:** Solutions that contain solvents other than water, e.g. ethanol, ethyl ether.

(C) Others:

(i) **Concentrated and dilute solutions:** The solutions with greater proportion of solute is called concentrated solution,

where as solution with less proportion of solute is called dilute solutions.

For examples: Dilute ammonia solution, concentrated almond extract.

(ii) **Saturated solution:** A solution in which no more solute can be dissolved at give temperature is called unsaturated solution. For examples: Simple syrup IP.

(iii) **Unsaturated solution:** A solution in which more solute can be dissolved at given temperature is called unsaturated solution. For examples: Aqueous iodine solution.

Advantages of Solution:

- Solutions are easy to swallow hence suitable for children and old aged patients.
- Dose adjustments are possible as per need.
- Absorption is rapid and become more quickly effective.
- Uniform dose can be taken from the container.
- The drug is uniformly distributed throughout the solution.

Disadvantages of Solution:

- Low stability because of aqueous nature.
- Solutions are bulky and inconvenient to transport and store.
- Measuring device is required during administration.
- Solutions are susceptible to microbial growth and thus may required preservatives.

Storage:

Solutions for oral use are usually packaged in a plain or amber coloured bottle and are stored in cool and dry place away from the light.

Quality Control Tests of Solution:

1. **General tests:** Visual appearance, colour, taste, odour, labelling, etc.
2. **Identification tests:** Performing physiochemical tests for identification.
3. **Assay:** Solution preparations are assayed by titrimetry, colourimetry methods to estimate percentage of drug content.

4. **Pourability:** Solution preparations are tested to determine pourability by measuring the flow time and flow rate.
5. **Viscosity:** It is measured by using viscometers.
6. **Clarity:** It is determined using clarity test apparatus.
7. **Crystallization and precipitation:** Supersaturation is performed to test crystallization and precipitation process.
8. **Gas evolution:** Gas chromatography is used to determine evolution of gas from the solution preparation.
9. **Relative density:** Pycnometer or density bottle is used to determine density of solution.
10. **pH:** pH of solution preparations can be determined using pH paper or pH meter.
11. **Surface tension:** Surface tension of a solution is a physical property determined using various instruments such as stalagmometer.
12. **Microbial limit test:** Microbial contamination is determined by the total viable aerobic count.
13. **Stability:** Solution preparations can be tested for short-term and long-term durations against different temperature, light and humidity conditions.

C

Suspension and Dry Powder for Reconstitution

1 Define suspension. Give the desirable/good/ideal/ properties of suspension.

☞ **Suspension**

It is a biphasic dosage form comprising a dispersion of solid fine particles in a suitable solvent in which these are insoluble.

Desirable/Ideal Properties of Suspension

- It should have a uniform particle size.
- The viscosity of suspension should be such that it should be easily pourable.
- It should be physically and chemically stable during its shelf life.
- It should be redispersible upon shaking to ensure correct quantity of medicament in each dose.
- The sediment should be bulky in nature which gives elegant appearance.
- It should not form a cake (cement) upon settling of particles.
- The sediment produced on standing shall be easily redispersible upon shaking.
- It should have good flavour and colour and should be palatable.
- It should not cause GIT irritation.

2 Write a note on formulation of suspension/additives/ excipients/adjuvants used in suspension.

Additives for the suspension are selected according to weather flocculated or non-flocculated suspension is to be prepared.

a. Flocculating Agents

These are the agents which produce flocculation. For example, electrolytes, polymers, surfactants, tweens, spans, carbowaxes, sodium lauryl sulphate, etc.

b. Suspending Agents/Thickening Agents

- The additives which increase the viscosity of continuous phase are known as suspending agents.
- They reduce the rate of sedimentation of particles.
- Suspending agents may also affect pourability, spreadibility, flow property of the final product.
  For example, methyl cellulose, gelatin, acacia, tragacanth, strarch, sodium alginate, clay (bentonite, aluminium, magnesium trisilicate).

c. Wetting Agents

- These reduce the interfacial tension between the solid particles and dispersion medium (solvent) and make wetting of solids.
- These are necessary when poorly wettable solids are present.
- These agents also produce flocculation.
  For example, sulphur, hydrocortisone, soap, benzalkonium chloride.

d. Dispersants

- These are necessary in a deflocculated type of suspension.
- Dispersants prevent aggregation of particles and thus, make individual particle in a dispersed state, e.g. darvans, daxads, marasperas.

e. Preservatives

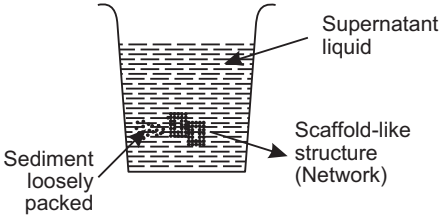
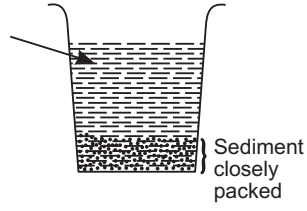
Preservative is necessary to prevent microbial growth in suspension, e.g. esters of p-hydroxy benzoic acid, benzoic acid, sodium benzoate, methyl paraben, propyl paraben.

f. Organoleptic Additives

Orally used suspensions require organoleptic additives like:

a. **Colouring agent:** For attractiveness and elegance, e.g. caramel.
b. **Flavouring agent:** For good smell and pleasantness, e.g. peppermint.
c. **Sweetening agent:** For palatability, e.g. syrups.

3 Give the types of suspension (difference).

Flocculated suspension	*Deflocculated/Non-flocculated suspension*
	
1. In this case particles form a network which looks like scaffold-like structure.	1. In this case each particle presents as a separate entity.
2. Particles settle rapidly forming bulky but loosely packed sediment.	2. Particles settle slowly forming closely packed sediment.
3. Sediment is easily redispersible upon shaking.	3. Sediment is difficult for redispersion.
4. It is not elegant to look.	4. It is elegant to look.
5. It has poor drainage property because floccules adhere to the sides of the container.	5. It has good drainage property.
6. Chances of cake formation are less.	6. Chances of cake formation are more.
7. Structured vehicle is necessary to suspend the floccules.	7. Structured vehicle is not necessary.
8. The floccules stick to the sides of the bottle.	8. The particles do not stick to the sides of the bottle.

4 What are suspensions? Classify suspensions giving examples. Give merits, demerits and quality control tests for suspensions?

☞ Suspension:

Suspension is a biphasic dosage form comprising a dispersion of solid fine particles in a suitable solvent in which these are insoluble.

☞ **Classification/Types of suspensions:**

(A) On the basis of therapeutic use:

(i) Analgesic suspension, e.g. paracetamol oral suspension.
(ii) Anthelmintic suspension, e.g. albendazole and suspension.
(iii) Antacid suspension, e.g. magnesium hydroxide oral suspension.
(iv) Antibacterial suspension, e.g. ciprofloxacin oral suspension.
(v) Anticonvulsant suspension, e.g. phenytoin oral suspension.
(vi) Antifungal suspension, e.g. posaconazole oral suspension.
(vii) Dry antibiotic powder for oral suspension, e.g. azithromycin oral suspension.

(B) On the basis of route of administration:

(i) For oral administration, e.g. milk of magnesia IP.
(ii) For external use, e.g. calamine lotion BP.
(iii) For parenteral administration, e.g. insulin zinc suspension IP.
(iv) Ophthalmic suspensions, e.g. ciprofloxacin otic suspension.

(C) On the basis of nature and behaviour of solids:

(i) Flocculated suspension.
(ii) Deflocculated/non-flacculated suspension.

Merits of Suspension:

1. Suspensions gives better chemical stability to water insoluble drugs.
2. Suspension shows sustained drug action.
3. Suspension can be used to mask the bitter taste of drugs.
4. Suspensions are more palatable and are easy to swallow.
5. In suspension form, drugs may show higher bioavailability

Demerits of Suspension:

1. Physical stability and sedimentation problems.
2. Some drugs may undergo degradation where water acts as a catalyst.
3. Uniform and accurate dosing cannot be possible.
4. Vigorous shaking of container is required before taking the preparation.

Quality Control Tests of Solution:

1. Visual inspection.
2. pH.
3. Assay.
4. Uniformity of content.
5. Uniformity of mass.
6. Uniformity of volume.
7. Uniformity of weight.
8. Dose and uniformity of dose.
9. Uniformity of mass of delivered doses.

5 What do you mean by "Dry Powders for Reconstitution"? Give its classification.

☞ **Dry Powders for Reconstitution:**

- These are the preparations consisting of loose, dry powder mixtures of varying degree of fine particle size that require the addition of water for reconstitution at the time of dispensing or administration, mostly used for pediatric use.
- Dry powders for reconstitution are marketed as oral reconstitutable medications in Unit-dose sachet or multidose bottles.
- Dry powders for injection are also available.

☞ **Classification of Dry Powders for Reconstitution:**

(A) Dry powder for oral suspension:

- These are powder mixtures that require the addition of water (reconstitution) at the time of dispensing and are mostly for pediatric use.
- These are called dry syrups or reconstitutable oral suspensions.
- Sometimes these are reconstituted by adding a specified quantity of freshly boiled and cooled water before use, e.g. antibiotics in suspension for pediatric use.

(i) **Unit single dose powders for oral suspension:**
A unit dose sachet of powder is administered by sprinkling on the top of a semisolid food, such as jelly or ice cream, or

by suspending in a suitable vehicle, such as water or juice, immediately before administration.

(ii) **Multi-dose powders for oral suspension:**
These powders are dispensed in a suitable-sized bottle for reconstitution with water immediately before dispensing.

(B) Dry Powders for Injection:

- In this case the drugs are instable in an aqueous environment.
- Therefore, the drugs in dry powder form is supplied in a glass vials with rubber plugs.
- The dry powdered drugs are mixed or reconstituted with a diluent (usually 5% dextrose solution, normal saline solution, water for injection). For example, penicillin-G procaine injectable suspension.

6 Give the advantages, disadvantages and quality control tests of "Dry Powders for Reconstitution".

☞ **Dry Powders for Reconstitution:**

Advantages:

- Use of sachets makes accurate single dosing possible.
- These preparations have improved appearance and flow characteristics.
- Packaging in sachets makes the formulation easy to carry.
- Well accepted by pediatric population due to colour, flavour and sweetner.
- Stable on storage.

Disadvantages:

- Dosing accuracy problems.
- Stability of the reconstituted preparation largely depends on storage temperature.
- Caking may occur upon longer storage times.
- There may be loss of the drug during mixing.

Quality Control Tests of Dry Powders for Reconstitution:

1. Flow properties
2. Rheology
3. pH
4. Sedimentation
5. Drug content
6. *In vitro* drug release
7. Particle size
8. Zeta potential
9. Stability.

7 What are different methods used for evaluation of suspension?

☞ A stable suspension can be redisperse homogenously with moderate shaking and can be easily poured throughout its shelf-life.

Evaluation methods of stability of suspension:

1. Sedimentation method.
2. Micromeritic method.
3. Rheological method.
4. Electrokinetic method.

D

Emulsion

1 Define emulsion. Explain types of emulsion.

☞ **Emulsion**

Emulsion is a biphasic dosage form in which two immiscible liquids are mixed, one of which is distributed throughout the other in a minute globule and the system is stabilized by addition of third substance known as emulsifying agent.

Types of Emulsion

a. **Oil in water (O/W):** In this type, the oil is dispersed phase (internal) and water is dispersion medium (external phase).
b. **Water in oil (W/O):** In this type, the water is dispersed phase (internal) and oil is dispersion medium (external phase).
c. **W/O/W Or O/W/O emulsion.**

2 Why are orally used emulsions always formulated as o/w?

Because

i. Water is external phase which can mask disagreeable taste of medicinal oils such as liquid paraffin, castor oil, etc.
ii. The aqueous phase can be pleasantly flavoured and make the preparation palatable for taste.
iii. To improve absorption of oils, fine globular size is required.

3 What are various tests for identification of emulsion type?

or

How will you identify emulsion type?

Tests for identification of emulsion are:

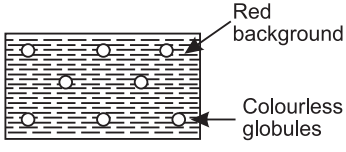
i. Dilution test
ii. Staining test
iii. Electric conductivity test
iv. Fluorescence test.

1. Dilution Test

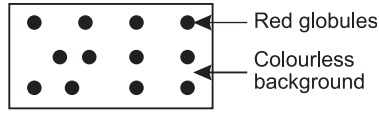
The principle behind this test is that unlimited addition of external phase into emulsion does not break the emulsion but addition of internal phase will break the emulsion.

Examples

i. o/w emulsion remains stable upon unlimited dilution with water but unlimited addition of oil will break the emulsion.
ii. w/o emulsion remains stable upon unlimited dilution with oil, but unlimited addition of water will break the emulsion.



w/o type emulsion



o/w type emulsion

2. Staining Test

This test can be performed by using either

i. Oil-soluble dye, i.e. scarlet red
ii. Water-soluble dye, i.e. saffranin.
During the preparation of emulsion triturate scarlet red dye with emulsion. Take a drop of such emulsion on a glass slide and observe under microscope.

Since scarlet red is soluble in oil, therefore, if:

i. Red dispersed globules are seen on colourless background then it is O/W type of emulsion.
ii. Colourless dispersed globules are seen on red background, then it is W/O type of emulsion.
Opposite result will be observed when water-soluble dye saffranin is used.

3. Electric Conductivity Test

The principle behind test is that water conducts the electricity while oil does not.

Thus, O/W type emulsion will conduct the electricity, because water is the continuous phase.

W/O type of emulsion will not conduct the electricity because oil is the continuous phase.

4. Fluorescence Test

- Many oils when exposed to UV light, give fluorescence.
- If a drop of such emulsion is observed under microscope using UV light and if entire field gives fluorescence then it is W/O type emulsion.
- If emulsion shows spoty fluorescence then it is O/W type emulsion.

4 Define and classify emulgents (emulsifying agents) with examples.

☞ **Emulgents**

The agents which stabilize the emulsion are called emulsifying agents.

Classification

I. ***Naturally Occurring***

(a) **Plant source:** Acacia, tragacanth.
(b) **Animal source:** Beewax, gelatin.
(c) **Mineral source:** Bentonite, magnesium oxide.

II. ***Semisynthetic***

For example, methyl cellulose, ethyl cellulose.

III. ***Synthetic***

(a) **Anionic:** Soap of divalent metals, sodium lauryl sulphate.
(b) **Cationic:** Cetrimide, benzalkonium chloride.
(c) **Non-ionic:** Tweens.
(d) **Ampholytics:** Dodecyl alamine.

5 What are desirable (ideal) properties of emulsifying agents?

An emulgent should possess following properties:

i. It should be surface active.

ii. It should reduce surface tension below 10 dyne/cm.
iii. It should be adsorbed quickly around the dispersed phase globules by forming a complete and coherent film.
iv. It should increase the viscosity of emulsion.
v. It should be effective in a reasonably low concentration.
vi. It should be non-toxic.
vii. The odour and taste should be compatible with the preparation.
viii. It should be chemically compatible with the other ingredients of the preparation.

6 Why is primary emulsion necessary to prepare? Give the proportions of oil, water and gum required for preparation of primary emulsion.

☞ Primary Emulsion is Necessary

Because if all the quantities of oil and water are mixed together, the volume of liquid is very large and thus, shearing force required to cut one of the phases in a suitable size is difficult.

On the other hand, if small quantities of oil and water are mixed, the less shearing force is required to cut the globules and the satisfactory emulsion can be prepared.

• For primary emulsion the proportions of oil, water and gum are:

Type of oil	*Example*	*Oil*	*Water*	*Gum*
Fixed oil	Almond oil, arachis oil, castor oil, cod liver oil	4	2	1
Mineral oil	Liquid paraffin	3	2	1
Volume oil	Turpentine oil, cinnamon oil, peppermint oil	2	2	1
Oleoresin	Male fern extract	1	2	1

7 Describe methods of preparation of emulsion.

A. Wet Gum Method

In this method mucilage of acacia is made.

i. *Primary Emulsion*

- Triturate acacia with twice the quantity of water as that of acacia in the mortar to form a mucilage.
- Measure out required quantity of oil and add dropwise into the mortar with trituration in one direction until primary emulsion is formed.
- The crackling (chit-chat) sound indicates the formation of primary emulsion.

ii. *Dilution of Emulsion*

Emulsion is diluted up to prescribed volume by adding slowly the external phase with trituration.

B. Dry Gum Method

In this method dry acacia is used. This method requires certain precautions such as:

i. Always use dry measure to measure oil.
ii. Pestle and mortar must be absolutely dry.
iii. Quantities of oil, water and gum should be weighed accurately.
iv. There must be vigorous trituration after addition of water.
v. Trituration should always be in single direction.

(a) *Primary Emulsion*

- Take oil in dry mortar by measuring it by measuring cylinder.
- Water is measured separately and kept in a beaker.
- Acacia is weighed and added to the mortar, already containing oil.
- Mix gently with pestle to just disperse the gum in oil uniformly.
- Add the measured water at once and triturate immediately in a single direction with full speed.
- A thick white cream-like product is formed.
- The crackling (chit-chat) sound indicates the formation of primary emulsion.

(b) *Dilution of Emulsion*

Dilute the primary emulsion by adding more vehicle to make prescribed volume.

8 Give the difference between wet gum and dry gum method.

Wet gum method	*Dry gum method*
1. Mucilage of acacia is used.	1. Dry acacia is used.
2. Oil is added dropwise.	2. Whole quantity of oil is added at a time.
3. Primary emulsion is viscous, creamy in nature.	3. It is thick and oily in nature.
4. It is relatively slow process.	4. It is quick process.
5. All apparatus are not required to be dried.	5. All apparatus should be dried like mortar, pestle, etc.

9 Write a note on instability in emulsion.

or

What are various problems in emulsion?

Instabilities in the emulsion are:

1. Creaming in emulsion.
2. Cracking of emulsion.
3. Phase inversion/phase reversal.

1. Creaming in Emulsion

- Creaming is nothing but the formation of relatively concentrated layer of emulsion from the original.
- Creamed emulsions can be reformed by shaking because cream is relatively concentrated layer of emulsion.
- This layer can be broken into small globules by shaking.
- The creaming will take place at the top or the bottom, depending upon density of dispersed phase.

Example

Most of the oils have density less than one and therefore, in o/w type, emulsion oil globule will rise at the top and creaming will take place at the top.

Whereas in a W/O type, water is the dispersed phase, having specific gravity more than oil, water globule will sink at the bottom pro-ducing creaming at the bottom.

- Creaming in emulsion can be minimised by using “Stokes law”. Stokes law is expressed as,

$$V \propto \frac{r^2 (d_1 - d_2)}{\eta}$$

Where,

V : Rate of creaming.
r : Radius of dispersed globule.
d_1: Density of continuous phase.
d_2: Density of dispersed phase.
η : Viscosity of dispersion medium.

Thus, 'Stokes law' states that:

i. Rate of creaming is directly proportional to the radius of dispersed globule.
ii. Rate of creaming is directly proportional to the difference between the density of aqueous and oily phases.
iii. Rate of creaming is inversely proportional to the viscosity of dispersion medium.

The rate of creaming can be minimised/avoided by:

i. Reducing the size of globules.
ii. Increasing the viscosity of continuous phase to retard or prevent movement of globules.
iii. By storage in cool place (increase in temperature causes creaming).

2. Cracking of Emulsion

- Cracking of emulsion means separation of dispersed phase as a seperate layer which is not redispersible upon shaking.
- Cracking of emulsion may be caused by changes in the nature of interficial film of an emulsifying agent.
- Cracking of emulsion can be done by:
    1. **Addition of opposite type of emulsifying agent:** For example, soap of monovalent metal is added in a divalent soap emulsion.
    2. **Precipitation of emulsifying agent:** Addition of acid or electrolytes in the emulsion causes precipitation of fatty acids and produces cracking of emulsion.
    3. **Addition of common solvent:** Addition of liquid in which both dispersed phase and continuous phase are soluble, forms one-phase system and destroys the emulsion.

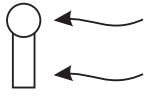
4. **Microbial attack:** Careless storage of emulsion not containing preservative is susceptible for microbial growth and destroys the emulsifying agent causing cracking.
5. **By incorporation of excess of dispersed phase (dilution by internal phase):** Addition of excess of internal phase will break the emulsion, i.e. cracking.
6. **By increasing temperature:** Increase in temperature causes decrease in viscosity leading to creaming of emulsion and is liable for cracking.

3. Phase Inversion/Phase Reversal

- The phenomenon of conversion of o/w type into w/o type of emulsion is called phase inversion, i.e. conversion of dispersed phase into continuous phase and continuous phase into dispersed phase.
- The addition of any substance that alters the solubility of emulsifying agent may cause phase inversion.
- For example, bees wax produce w/o emulsion and addition of soap causes inversion, i.e. produces o/w emulsion.

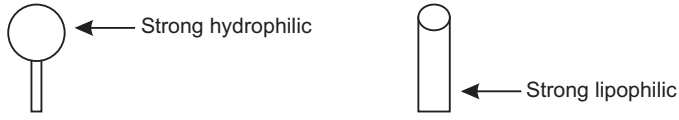
10 Write a note on HLB. Give its importance.

- HLB means hydrophilic lipophilic balance.
- Griffin in 1949 devised a useful method for calculating balance mixture of emulsifying agent to provide a particular type of emulsion, which is called HLB method.
- Surfectant molecule (emulsifying agent) shows two parts.



- For satisfactory and stable emulsion, a surfectant should get absorbed at the interphase between aqueous phase and oily phase.
- If surfectant molecule has strong hydrophillic part, it will orient more towards aqueous phase and if it has strong lipophilic part, it will orient more towards the oily phase. In both cases surfectant will not produce satisfactory emulsion (stable).

- For calculating the balance mixture, emulsifying agent has given a number on HLB scale.



(Unstable emulsions)

- The scale varies from 1 to 40.
- Higher number indicates hydrophilic properties and thus, the emulgents with high number produce o/w type emulsion.
- The emulsifying agents with low number indicate lipophilic properties and thus, emulgents with low number produce w/o type of emulsion.
- Generally emulsions having HLB numbers.
  - Below 9 produce w/o emulsion.
  - 9 to 11 are intermediate.
  - Above 11 produce o/w type emulsion.

Other properties of emulgent with respect to HLB number are as follows:

HLB No.	*Applications*
1–3	Anti-foaming agent
3–6	w/o EA
7–9	Wetting agent
8–18	o/w EA
13–15	Detergents
15–18	Solubilising agents

Importance of HLB

i. It plays an important role in formulation and stability of emulsion.
ii. It has a value in non-ionic type of emulgent.
iii. It is useful for selecting emulsifying agents.
iv. It is useful to avoid the problems like creaming and cracking.

11 What are emulsions ? Give advantages and disadvantages of emulsion. Enlist various quality control tests of emulsion.

☞ **Emulsion:**

Emulsion is a biphasic dosage form in which two immiscible liquids are mixed, one of which is distributed throughout the other in a minute globules and the system is stabilized by addition of third substance known as emulsifying agent.

Advantages of Emulsion:

1. Emulsions are non-toxic and non-irritant in nature.
2. They can be used to mask the taste and improve physical stability of the preparation.
3. Small-sized droplets provide greater surface area for increased drug absorption.
4. Emulsions helps to solubilize lipophillic drugs with less amount of energy.
5. Emulsions can be used as substitute for liposomes and vesicles.

Disadvantages of Emulsion:

1. Storage conditions may affect stability of emulsion.
2. Emulsions are bulky, hence difficult to transport and possibility of breaking the containers.
3. Emulsions are thermodynamically unstable and thus are difficult to manufacture.
4. Microbial contamination may produce cracking or emulsion.
5. Emulsions need to be shaken well before use for uniform and accurate dosing.
6. Emulsion needs a special manufacturing process, instruments and a trained person.

Quality Control Tests of Emulsion:

1. Appearance
2. Identification tests
3. Specific gravity
4. pH
5. Viscosity
6. Particle size
7. Phase separation
8. Zeta potential
9. Microbial test
10. Assay.
11. Stability testing.

CHAPTER 14

Topical Preparations

A Ointments

B Creams

C Pastes

D Topical Gels

E Liniments

F Lotions

G Suppositories and Pessaries

H Nasal Preparations

I Ear Preparations (Otic/Aural Preparations)

A

Ointments

1 Define ointment and ointment base. Give the ideal qualities of ointment base.

Ointments are defined as homogenous, semisolid preparations intended for external application to the skin or mucous membrane that provides emollient, protective, therapeutic or prophylactic functions.

Ointment base:

Ointment base is a vehicle or carrier for the medicament which helps for spreading, absorption and penetration of the medicament.

Qualities/properties of an ideal ointment base:-

- It should be not interfere with wound healing.
- It should have low sensitization index.
- It should be pharmaceutically elegant.
- It should release the medicament efficiently at the site of application.
- It should have low index of irritation.
- It should be non-dehydrating, nongreasy and neutral in reaction.
- It should possess good keeping qualities.
- It should be compatible with common medicaments.
- It should be easily washable with water.
- It should have minimum number of ingredients.
- It should be easy to compound and remain stable on storage.
- It should be cheap.

2 Give the classification of ointment bases.

☞ **Classification of ointment base:**

a. **Oleagenous bases:** These are entirely lipophilic (oily).
   For example: Yellow soft paraffin (YSP), coconut oil, beewax.

b. **Absorption bases:** These are entirely hydrophilic, i.e can absorb water.
   For example: Wool fat, wool alcohol, lanolin

c. Water miscible bases: Easily removed after application,
e.g Emulsifying ointment IP.
Cetrimide emulsifying ointment BP

d. Water soluble bases (washable):
For example, Macrogol 200, 300, 400 : Viscous liquid.
Macrogol 1500 : Greasy semisolids
Macrogol 1540, 3000, 4000, 6000 : Waxy solids

3 What are the factors which should be considered while selection of an ointment base?

☞ Factors for selection of ointment base

Dermatological factors
- Absorption and penetration
- Effect on skin function
- Miscibility with skin secretion and sebum
- Compatibility with skin secretion
- Freedom from irritant effect
- Emollient properties
- Ease of application and removal

Pharmaceutical factors
- Stability
- Solvent property
- Emulsifying property
- Consistency

4 Define ointments. Classify ointments giving suitable examples.

☞ **Ointments:**

Ointments are defined as homogeneous, semisolid preparations intended for external application to the skin or mucous membrane that provides emollient, protective, therapeutic or prophylactic functions.

Classification of Ointment

A. As per penetration into skin:

1. Epidermic ointments:

These ointments are intended to produce their action on the surface of the skin and produce local effect. They are not absorbed into the skin layers. They act as protective antiseptic and parasiticides.

2. Endodermic ointments:

These ointments are intended to release the medicaments that penetrate into the skin they are partially absorbed into the skin layers and act as emollient, stimulants and local irritations.

3. Diadermic ointments:

These ointments are intended to release the medicaments that pass through the skin and produce systemic effects.

B. As per therapeutic use:

1. Antibiotic ointment, e.g. neomycin ointment.
2. Antifungal ointment, e.g. salicylic acid ointment.
3. Anti-inflammatory ointments, e.g. hydrocortisone acetate
4. Anti-pruritic ointments, e.g. benzocaine ointment
5. Astringent ointment, e.g. zinc oxide ointment
6. Antieczematous ointment, e.g. sulphur ointment
7. Keratolytic ointments, e.g. resercinol ointment
8. Counter irritant ointments, e.g. methyl salicylate ointment
9. Antidandruff ointments, e.g. cetrimide ointment
10. Parasiticide ointment, e.g. hexachloride ointment

5 Give advantages, disadvantages and quality control tests for ointments.

☞ **Advantages of Ointments:**

- Ointments are useful alternatives to avoid first past metabolism of drug.
- Ointments are suitable for prolonged site specific application of drug on affected area.
- Handling of ointments is easier than bulky liquid dosage forms.
- Ointments are chemically more stable than liquid dosage forms.
- Ointments are suitable for application to unconscious patients.

Disadvantages of Ointments:

- Due to staining properties, ointments are cosmetically less aesthetic.
- Application with fingertip may contaminate the formulation or cause irritation.

- Compared to solid dosage forms, ointments are bulky in nature.
- Using ointments it is difficult to achieve dose accuracy.
- Ointments are physically less stability than solid dosage form.

Quality control test for ointments:

1. Weight variation
2. Sterility
3. Metal particles (for ophthalmic ointment)
4. *In vitro* drug release
5. Non-irritancy
6. Rate of penetration

6 What are the methods of preparation of ointment?

☞ **Method of preparation of ointment:**

1. Ointment prepared by fusion method
2. Ointment prepared by trituration.
3. Ointment prepared by chemical reaction

1. Ointment prepared by fusion method

a. For non-medicated ointment:

- It contains all fatty substances without medicament.
- All ingredients are taken together and melted over water bath and then cooled.
- If ointment base contains several ingredients of different melting point then the ingredient of highest melting point is added first and then others in descending order of melting point.
- After melting the ingredients should be stirred until the ointment is cooled

b. For medicated ointment

- The solid medicaments are passed through sieve number 180 and added in small amount into the melted base when it shows first sign of thickening.
- Each addition is thoroughly dispersed by stirring which is continued until the preparation is thickened enough to prevent sedimentation.

2. Trituration method

This method is applicable when the medicament is solid insoluble.

- *Stage 1*: Finely powder the solid and pass through sieve number 250.
- *Stage 2*: Weigh the base and add a small portion of it in the mortar containing powdered solid triturate thoroughly until smooth product is formed.
- *Stage 3*: Add reminder of the base and triturate until the homogeneous product is obtained.

Levigation method: Trituration of base with the powdered medicament may also be carried out by using tile and spatula. This process is called levigation method.

3. Ointment prepared by chemical reaction method:-

Example: Iodine in ointment

(a) Ointment containing free iodine

- This type of ointment gives staining to clothes because of free iodine.
- Iodine is very readily soluble in the concentrated aqueous solution of potassium iodide due to formation of polyiodide.
- This solution can be easily incorporated in the absorption type of ointment base.

Example : Rx

Iodine
Potassium iodide
Wool fat
Glycerin
YSP

(b) Ointment containing combined iodine

- Vegetable and fixed oils absorb iodine which combines with double bonds of the unsaturated constituents and thus iodine does not remain in free state.

  Such type of ointment is applied to the skin, does not give the stain of iodine, therefore, it is called non-staining iodine ointment.

$$R - CH = CH - (CH_2)_7\,COOH + I_2 \xrightarrow[\text{In a closed vessel}]{\text{Heated at } 50^\circ C} R - \underset{\displaystyle I}{\underset{|}{CH}} = \underset{\displaystyle I}{\underset{|}{CH}} - (CH_2)_7\,COOH$$

(Di-iododerivative)

Example: Rx

Iodine
Arachis oil
YSP

7 Difference between ointments and pastes

Ointments	Pastes
1. Ointments contain low concentration of solids.	1. Pastes contain high concentration of solids.
2. They are soft and greasy consistency.	2. They are stiffer, less greasy and in consistency.
3. They are less absorptive.	3. They are more absorptive.
4. They flow more easily with increase in force of application.	4. They resist to flow with increase in force of application.
5. They do not adhere to skin well as compared to paste.	5. They adhere well to the skin.

8 What do you mean by bleeding in ointment?

When fluid component such as mineral oil is separated from the top of ointment, it is called bleeding in ointment. It is observed visually.

B

Creams

1 Define and classify creams giving examples. Give the ideal characteristics of cream.

☞ Creams

Creams are homogeneous, viscous emulsions of semisolid consistency intended for application to skin or mucous membrane.

Classification/Types of creams:

1. **Oily creams (W/O type):** These are hydrophobic W/O emulsion that absorb only small amount of water. They contain W/O emulsifying agents such as wool fat, sorbitan esters.
2. **Aqueous creams (O/W type):** These are hydrophilic O/W emulsion that contain water miscible bases, e.g. moisturising cream
3. **Cosmetic creams:** These are both W/O type of creams used as cosmetic preparations, e.g. vanishing cream, foundation cream, cold cream
4. **Medicated cream:** These may be W/O or O/W types of creams containing medicaments, e.g. cetrimide cream, hydrocortisone cream.

Ideal characteristics of creams:

- It should be non-irritating and non-sensitizing and non-toxic.
- It should be compatible with skin pH and with the incorporated drug.
- It should have low viscosity and easy spreadability.
- It should liquify at body temperature.

- It should be non-greasy and easily removable.
- It should release medicament readily at the site of application.
- It should be pharmaceutically elegant and posses good quality.
- It should not retard wound healing.

2 Give advantages and disadvantages of cream. Mention quality control tests for creams.

☞ **Advantages of Creams:**

1. Creams provide prolong contact at their site of application.
2. Creams help to dry, injured area more quickly.
3. Creams are usually non-irritating when applied to the skin.
4. Creams are used to deliver drugs that exhibit a low aqeous solubility.
5. Creams are water washable, less greasy and easy to wipe away.
6. Creams are simple to apply as they spread more easily.

Disadvantages of Creams:

1. Creams are thermodynamically unstable.
2. They are less hydrophobic, so risk of contamination is high.
3. Some creams can cause irritation on exposure to sunlight.
4. Application of exact quantity of creams is difficult.

Quality Control Tests for Creams:

1. Physical appearance
2. Particle size and viscosity
3. Type of emulsion
4. Homogenicity
5. Spreadability
6. Removal from skin
7. After feel (emolliency, slipperiness)
8. Irritancy test

3 Give the difference between 'Cold cream' & 'Vanishing cream'

Cold cream	Vanishing cream
1. It is usually W/O type of emulsion.	1. It is O/W type of emulsion.
2. It contains absorption type base such as wool fat, beeswax.	2. It contains O/W type of emulsion bases, e.g. emulsifying ointment.
3. It contains small portion of water.	3. It contains higher proportion of water.
4. Texture is greasy, semisolid.	4. Texture is white, shiny, semisolid, which is cosmetically acceptable.
5. It is used as emollient and skin protective	5. It is used as skin protective and as a foundation cream for other cosmetics.
6. After application it gives oily stain.	6. After application it vanishes or disappears.
7. It is somewhat difficult to wash after use.	7. It is easily washable.

C

Pastes

1 Write a note on pastes.

☞ **Pastes:**

Pastes are semisolid preparations for external application containing a large amount of finely powdered solids (50%).

Explanation:

- Pastes contain a large amount of solids, hence they are very stiffy in nature.
- Their base is usually non-greasy and washable.
- Pastes when applied to the skin, adhere well, forming a thick coat that protects and soothes inflamed and rough surfaces and minimize the damage done by scratching in itching conditions.
- "Pastes usually contain glycerin":
  - Because glycerin is non-volatile hygroscopic solvent and thus it acts as antidrying agent (humectant) for the paste.
  - Glycerine has emollient and preservative properties.
  - "Pastes are unsuitable in scalp condition"
  - Because they are very difficult to remove from the hairs (scalp)

Classification of Paste:

1. Paste with hydrocarbon base, e.g. comp. zinc paste BPC.
2. Paste with water miscible base, e.g. magnesium sulphate paste BPC.
3. Paste with water soluble base.
4. Paste with gelatin base, e.g. Unna's paste
5. Paste with starch base

6. Paste with tragacanth base
7. Paste with cellulose derivative base
8. Paste with pectin base
9. Paste with solid colloid base.

Storage:

They should be stored in airtight container so as to prevent evaporation of moisture present in the paste.

Container:

Wide mouthed glass or plastic containers and collapsible tubes.

Label:

For external use only.
Replace the cap after use.

2 Give advantages, disadvantages and quality control tests for paste.

☞ **Advantages of pastes:**

- Pastes easily spread on the skin.
- Pastes persist at the site of application, enabling longer duration of drug release.
- Pastes protect an inflamed site
- Pastes may act to absorb moisture and chemicals within the exudates.
- The chemical stability of hydrolytic drugs is enhanced.

Disadvantages of Pastes:

- Pastes may be greasy and difficult to remove.
- Pharmaceutical pastes may stain clothes
- Viscosity of pastes creates a problem of spreading over the affected site.
- If drug has limited solubility in the base, it may show poor drug release from paste.
- Pastes have limited applications to the hair due to difficulty in its removal

Quality Control Tests for Pastes:

1. Physical appearance
2. Homogenicity
3. Impurities
4. Water content
5. Preservative content
6. pH
7. Irritancy test
8. Antioxidant contents

D

Topical Gels

1 Define gels and topical gels. Give the classification of gels.

☞ **Gels:** Gels are semisolid systems in which there is an interaction between colloidal particles within a liquid vehicle.

Topical gels: Topical gels are defined as homogenous, clear, semisolid preparation consisting of a liquid phase within a three-dimensional polymeric matrix with physical or sometimes chemical cross-linkage by means of suitable gelling agents meant for topical application.

Classification of Topical Gels:

1. Hydrophilic gel, e.g. active gel
2. Non-aqueous gel, e.g. hyaluronic acid gel.
3. Organogel, e.g. nifedipine and lidocaine gel.
4. Xerogel, e.g. silica xerogel
5. Ampiphilic gel, e.g.: L-ascorbic acid, 22% topical serum gel.
6. Supramolecular gel e.g. diclofenac gel.
7. Hydrogel, e.g. oxalgin gel.

2 Give advantages and disadvantages and quality control test for topical gels.

☞ **Advantages of Topical Gels:**

1. Gels provide optimal cutaneous and percutaneous drug.
2. Gels are used to avoid gastrointestinal drug absorption difficulties.

3. Gels are used to avoid the first pass metabolism effect.
4. Gels are non-invasive application and have better patient compliance.
5. Gels can be applied over skin for slow and prolonged drug absorption.

Disadvantages of Topical Gels:

- Gels may be allergic.
- Enzymes in epidermis may degrade drugs in gel.
- Gels may show poor permeation and bioavailability of large size drugs.
- Continuous application of gel may cause adverse effects.
- Gels for application to body cavities must be sterile.

Quality Control Tests for Gels:

1. Alcohol content
2. Rheology
3. Bioadhesion
4. Stability testing
5. *Ex vivo* penetrability

Containers and Storage Conditions of Gels:

- Gels are packaged either in large mouth jars or in metal or plastic collapsible tubes, light containers, or well-closed containers.
- Gels are stored in well-closed containers to protect against contamination and in cool place
- Gels are not to be refrigerated.
- Gels should be protected from heat as product separation takes place.

E

Liniments

1 What are liniments? Describe in brief liniments.

☞ **Liniments:** Liniments are medicated fluid, semifluid preparations intended for application to the skin with friction or rubbing.

Explanation:

- Liniments may be alcoholic, oily solutions or emulsions.
- Liniments with alcoholic vehicle are used for counterirritant and rubefacient action.
- Oily liniments are used when massage is required.
- Liniments usually contain counterirritants like terpentine oil, methylsalicylate.
- Alcohol produces rubefacient action and facilitates the absorption of medicament.
- For oily liniments solvent used may be almond oil, turpentine oil, arachis oil, etc.
- "Liniments are never applied to broken skin" because they contain counterirritants which produce severe irritation to the broken skin.

Label

- For external use only.
- Do not apply on broken skin.
- Apply with friction.
- Shake well before use.

Storage

Store in well-closed container and in a cool place because most of the liniments contain volatile ingredients.

Container

Narrow mouth, screw cap, coloured flutted bottles.

2 Define and classify liniments giving suitable examples.

☞ **Liniments:** Liniments are medicated fluid, semifluid preparations intended for application to the skin with fiction or rubbing.

Classification / types of liniments

A. As per nature of dispersion medium:

1. **Oleaginous liniments:** These liniments contain fatty oils or lanolin as a dispersion medium.
2. **Alcohol liniments:** These contain alcohol and liqueurs with various medicinal substances.
3. **Soap-alcohol liniment:** These liniments contain alcoholic solutions of soap as a dispersion medium.

B. As per type of disperse system:

1. **Homogenous liniments:** In this case drugs are distributed homogenously in the dispersion medium.
2. **Heterogenous liniment:** In this case drugs are in suspension or emulsion form, dispersed in the medium.

C. As per therapeutic use:

1. Analgesic liniment, e.g. camphor liniment.
2. Counterirritant liniment, e.g. methylsalicylate liniment.
3. Emollient liniment, e.g. bast liniment.
4. Rubefacient liniment, e.g. mustard liniment
5. Astringent liniment, e.g. Kloss liniment
6. Antipruritic liniment, e.g. Sanhuang liniment
7. Anti-inflammatory liniment, e.g. Dhanwantharam liniment
8. Fungicidal liniment, e.g. Himalaya Rumalaya liniment

3 Give advantages, disadvantages and quality control tests for liniments.

☞ **Advantages of liniments:**

- Liniments are usually non-staining.
- Liniments are less viscous compared to creams, ointments and gels.
- Liniments are well absorbed by the skin to achieve high bio-availability.
- Liniments improve muscle flexibility and provide nerve nourishing properties.

Disadvantages

- Liniments are meant for external application only.
- While applying liniments, care needs to be taken to avoid exposure to eyes.
- Liniments needs to be compulsorily stored in coloured fluttered bottles.
- Liniments are not suitable for application to broken skin.
- Friction/ rubbing are required during application of liniment for better penetration of drug.

Quality control test for liniments

1. Dilution test

- It is performed by mixing 1 ml liniment with 1 ml water.
- The miscibility of liniment with water is observed.
- The result of this test determines the type of liniments and the possibility of phase separation.

2. Stability

- Accurately 50 ml liniment is taken in a measuring cylinder and kept aside for 24 hours
- After this time the volume of external phase separated is noted.
- The phase volume is calculated to establish stability.
- The phase volume ratio is calculated:

$$\text{Phase volume ratio} = \frac{\text{Volume of internal phase}}{\text{Volume of liniment}}$$

3. Other tests:

Viscosity, pH , irritancy, removal from skin.

F

Lotions

1 Write note on lotions.

☞ **Lotions:**

Lotions are fluid preparations intended for application to the skin without friction.

Explanation

- Lotions may be simple solutions, emulsions or suspensions.
- Lotions are used for soothing, cooling and softening effects on the skin.
- Lotions may contain ingredients such as copper sulphate, zinc sulphate, salicylic acid.
- Lotions are used for protective, astringent and antiseptic action.
- Lotions when applied to the skin spread easily on the surface of skin and upon drying leave a thin coat, on the skin which may produce skin protective, astringent action.
- Alcohol is sometimes included in lotions, which produces cooling and soothing effect on the skin.

Label

- For external use only.
- Shake well before use.

Storage

Lotions are stored in a well closed, narrow mouthed, amber coloured, fluted plastic bottles and stored in a cool place away from the light.

Examples

- Calamine lotion IP
- White lotion BPC.
- Salicylic acid lotion BPC.

2 Define and classify lotions giving examples.

☞ **Lotions:**

Lotions are fluid, semisolid preparations intended for application to the skin.

Classifications/Types of Lotions

1. Astringent lotions, e.g. Ayur astringent lotion
2. Face lotion, e.g. Oriflame face lotion
3. Hair lotion, e.g. Biodens hair lotion
4. Body lotion, e.g. Oley body lotion
5. Humectant lotion, e.g. Oilatum lotion
6. Emollient lotion, e.g. Parasoft lotion
7. Ceramide lotion, e.g. Ceramedx lotion
8. Occlusive lotion/moisturizing lotion, e.g. Atogla lotion
9. Sunscreen lotion, e.g. Flocare SPF 30 plus sunscreen lotion

3 Give advantages, disadvantages and quality control tests for lotion.

☞ **Advantages of lotions:**

- Lotions are not greasy and suitable for normal or dry skin.
- Lotions have high water contents so viscosity is very low.
- Lotions may spread thinly to cover a large area of skin.
- Lotions possess long-term stability.
- Drugs from lotions are well-absorbed from the skin, and have high bioavailability.
- Lotions are ideal for daytime application and during summer season.

Disadvantages:

- Lotions may block the skin pores and increase acne.
- Lotions may accelerate skin aging and also can irritate skin.
- Precaution should be taken to avoid the exposure of lotion to eyes.
- Lotions may show systemic effects such as hyperglycemia and glycosuria.

Quality control tests for lotions:

1. **Spectrophotometric evaluation:** This test determines UV light absorption ability of components incorporated in sunscreen lotion formulation.
2. **Erythemal dosage:** This test determines the erythermally effective radiations, transmitted by suntan preparations.
3. **Other tests:** pH, viscosity, assay, irritancy, removal from the skin, etc.

4 Differentiate between liniments and lotions.

Liniments	Lotions
1. Liniments are fluid preparations intended for application to the skin with friction.	1. Lotions are fluid preparations intended for application to the skin without friction.
2. Liniments may be alcoholic or hydroalcoholic or oily solutions or emulsions.	2. Lotions may be simple solutions, emulsions or suspensions.
3. Not applied to broken skin.	3. Can be applied to broken skin.
4. They contain volatile substances like alcohol, camphor, turpentine, oil, etc.	4. They contain simple salts like sinc sulphate, copper sulphate, etc.
5. Official examples: • Turpentine liniment IP • Camphor liniment IP, BP • Soap liniment IP.	5. Official examples: • Calamine lotion IP • White lotion BPC • Salicylic acid lotion BPC

5 Why liniments are required to be applied with friction but lotions without friction?

☞ **Because:**

- Most of liniments are used for their counterirritant and rubefacient action and for therapeutic activity. For such action penetration of drug through the skin is necessary and degree of penetration depends upon the friction or rubbing on the skin.
- Whereas lotions are applied for their skin protective, soothing astringent properties, which do not require penetration of medicament through the skin. Hence friction is not required for lotions.

G

Suppositories and Pessaries

1 Define suppositories, pessaries, bougies.

☞ **Suppositories:** Suppositories are solid or semisolid bodies, suitably shaped, containing medicament for insertion into body cavities like rectum, vagina and urethra. They disintegrate or melt at body temperature.

Pessaries: Suppositories intended for the vagina called pessaries.
Bougies: Suppositories intended for the nose and urethra are called bougies.

2 Give advantages and disadvantages of suppositories.

☞ **Advantages:**

- They are used to treat local infections like haemorrhoids in rectum (piles) and infections of vagina.
- When oral administration of drug is not possible in case of infants, unconscious patients or patients suffering from vomiting, nausea, the suppositories are useful.
- The drug is absorbed from mucous membrane, therefore, used for systemic absorption.
- They have been used to obtain prolonged action of drugs.
- They provide faster onset of action than oral route.
- They save the destruction of drug in GIT.
- They are unit dosage forms, therefore, there is no dose variation.

Disadvantages

- They should be stored at freeze conditions, otherwise their shape may be disturbed.
- There is leaking problem, hence feels uncomfortable.

- Absorption of drug through rectum is irregular.
- Patient does not like this route for drug administration.
- Administration requires a skill.

3 Classify suppositories on the basis of their route of administration.

(a) Rectal suppositories

- They are used for rectum.
- General weight is 1–2 gm.
- They are either cone or torpedo-shaped.

(b) Vaginal suppositories (pessaries)

- They are used for vagina.
- General weight is 4–8 gm.
- They are either cone or wedge shaped.

(c) Urethral bougies

- They are used for urethra.
- They are long thin and cylindrical.
- Usually 1gm in weight and about 8 cm in length.

(d) Nasal bougies (boginaria)

- They are used for nasal cavity.
- They are about 9–10 cm long and 1 gm in weight.
- They are made with glycerogelatin base.

(e) Ear cones

- They used for introduction into ear.
- They are long and cylindrical.
- They usually contain lubricants and anti-inflammatory drugs.

4 Define suppository base. Give ideal qualities of suppository base.

The vehicle or carrier used in preparation of suppository is known as suppository base.

Ideal qualities of suppository base

- It should melt at body temperature.
- It should release medicament readily.
- It should be compatible with added medicaments.
- Its shape should not be changed during handling.

- It should be non-toxic and non-irritant to the mucous membrane.
- It should be stable on storage.
- It should be stable if heated above its melting point.
- It should be easily mouldable or compressible.
- It should not adhere to the mould.

5 What are types of suppository base?

(a) **Fatty bases**, e.g. theobroma oil (cocoa butter)
(b) **Water soluble/miscible**, e.g. glycerogelatin base, soap glycerine base, macrogols, polyethylene glycols.
(c) **Emulsifying bases,** e.g. Witepsol, Massuppol, Massa estarium

6 What are various methods of preparation of suppositories?

(a) Cold hand shaping/rolling method
(b) Cold compression
(c) Fusion heating method/hot process

7 Describe general method of preparation of suppository.

☞ **Fusion method:**

1. Cleaning and washing of mould

The mould is cleaned by immersing in hot water and is dried well.

2. Lubrication of mould

Lubrication of mould is necessary because some bases may adhere/stick to the mould and it is difficult to remove them from the mould. Otherwise suppository may be damaged.

Lubricants used:

Soft soap	10 gm
Glycerol	10 ml
Alcohol (90%)	50 ml

- After lubrication, mould is kept inverted on ice to drain excess of lubricant and cool.

3. Calibration of mould

- Calibration of mould is carried out by preparing suppositories with suppository base and then weighed the same, it is the capacity of the mould.
- Calibration of mould is necessary to calculate actual capacity of a mould.

4. Melting the base and addition of ingredients

- Required amount of base is weighed and placed in a dish and warmed over water bath with stirring until it melts. Over heating is avoided.
- Weighed quantity of finely powdered drug is mixed with melted base with constant stirring to form a smooth cream.

5. Filling of mould

- After mixing, the fluid is filled in the moulds slightly above the cavities of the mould.

6. Solidification and removal

- The moulds were kept in the freeze for cooling and after solidification suppositories are removed and packed.

8 Write note on packaging and storage of suppositories.

☞ Packaging of suppositories

- Suppositories are usually packed in partitioned boxes which hold the suppositories in upright position.
- Glycerogelatin-based suppositories are packaged in tightly closed screw capped glass containers.
- Some suppositories are wrapped individually in aluminium foil or PVC polythene strip packaging.
- Nowadays new method is, suppository is directly moulded into its primary packaging.

Storage

Suppositories should be stored in freeze conditions.

9 Explain various quality control tests for suppositories.

☞ **Quality control tests for suppositories:**

1. **Water content:** It is determined by Karl Fischer titrator using special titration set-ups and reagents.
2. **Microbial screening:** It is done to check the presence of microorganisms in the suppository.
3. **Weight variation:** Twenty suppositories are individually weighed and the average weight is calculated.
4. **Hardness (mechanical strength):** This test is performed to check the mechanical strength of the suppository so that it cannot be damaged during transportation. This test is performed using Erweka hardness tester.
5. **Disintegration test:** It is performed on six suppositories using tablet disintegration test apparatus. The suppositories are immersed in 160 ml distilled water, maintained at 370°C. The time of complete disintegration of water soluble bases and complete melting point of oily bases is determined.
6. **Melting point:** The ascending melting point method is used to determine the melting point of suppository.
7. **Content uniformity:** It is calculated by measuring absorbance of the dissolved samples with UV visible spectrophotometer.
8. **Assay:** The quantity of drug present in a unit weight of suppositories is determined using titrimetric, spectroscopic methods.
9. ***In vitro* drug release:** It is estimated using USP rotating basket dissolution test apparatus in 900 ml Sorensen's phosphate buffer (pH 7.4), similar to tablets.

10 Define displacement value. Why is it necessary to calculate displacement value?

☞ **Displacement Value:**

The quantity of medicament which displaces one part of any base is defined as displacement value of medicament.
The volume of suppository from a particular mould is uniform but its weight will vary according to the density of medicament as compared with base which the mould are calibrated. Therefore, displacement value of medicament must be calculated.

11 Why is cold storage necessary for suppositories?

☞ **Because:**

1. Above room temperature suppositories melt and loose their shape and size.
2. Suppositories may be converted into liquid state, hence they require a cold storage.

12 Write a note on pessaries.

☞ **Pessaries:**

- Pessaries are suppositories intended to use in vagina.
- Pessaries release the medicament into the vagina.
- Pessaries are larger than rectal suppositories.
- Pessaries vary in weight from 4 to 8 gm.
- The pessaries may be conical, wedge-shaped or rod-shaped.
- The pessaries are also available as tablets and capsules and are known as vaginal tablets and capsules respectively.
- Moulded suppositories are packed similar to glycerol gelatine suppositories.
- The pessaries should be stored in a cool place.
- The pessary is an effective tool in the management of number of gynaecologic problems.
- Pessaries melt at body temperature.
- Pessaries contain excipients such as diluents, adsorbents, surface active agents, lubricants, antimicrobial preservatives and colouring matter.

Method of application/use

- Pessaries can be inserted using fingers into vagina but for special-shaped pessaries applicators are provided to facilitate insertion into vagina.
- Sometimes pessaries are moisten with water before insertion into vagina as per the labelling instructions.

Storage:

Pessaries are stored in a cool place.

H

Nasal Preparations

1 What are nasal preparations? Enlist various nasal preparations. Give advantages and disadvantages of nasal preparations or Write a note on nasal preparations.

☞ **Nasal Preparations:**

Nasal preparations are solutions or suspensions administered by drops or fine mist or spray to treat the nasal symptoms of allergic rhinitis and common cold.

1. Nasal powders
2. Nasal gels
3. Nasal spray
4. Nasal drops

Advantages of Nasal Preparations:

1. First pass metabolism of drug is avoided.
2. They show rapid drug absorption and quick onset of action.
3. The bioavailability of smaller drug molecules is good.
4. Nasal preparations are suitable for drugs that are orally unabsorbed.
5. These are alternative to parenterals to deliver protein and peptide drugs.
6. Administration of drug easy.

Disadvantages of Nasal Preparations:

1. Nasal preparations are primarily suitable only for potent drugs.
2. Continuous and frequent administration of drug may cause harmful long-term effects.

3. Variations in absorption of drugs.
4. Inconvenient to some patients due to nasal irritation.
5. Smaller surface area is available for absorption of drugs.

2 Write a note on nasal powders.

☞ Nasal Powders:

Nasal powders are dosage forms simply formulated by active pharmaceutical ingredient with filler.

Classification of Nasal Powders Devices:

1. **Insufflations:** These are the devices used to administered insufflations. e.g. insulin insufflations.
2. **Dry powder inhaler (DPI):**
   Dry powder inhalers are devices through which a powder formulation of a drug is delivered for local or systemic effect via the pulmonary route. These are commonly used to treat respiratory diseases like asthma, bronchitis, etc.
3. **Pressurized metered-dose inhaler (PMDI):**
   A PMDI is a device that delivers a specific amount of medication to the lungs, in the form of a short burst of aerosolized medicine that is inhaled by the patient.

It is the most commonly used delivery system for treating asthma, COPD, etc. For example, salbutamol pressurized inhalations BP

Advantages of Nasal Powders:

- Nasal dry powders are alternatives to solution and suspension dosage forms.
- Dry powders show prolonged contact time, thus produce enhance bioavailability.
- These are the best alternative to parenteral injections.
- Faster onset of action due to rapid transmucosal diffusion
- They are stable formulations.
- These are simple, easy and safe to reconstitute and are cost-effective.

Disadvantages of Nasal Powders:

- May cause nasal irritation.
- Metered dose delivery may not possible.
- The delivery of drug is not clear from the nasal cavity because of physical barrier.
- There may be rapid removal of the therapeutic agent from the site of absorption.
- In cold and allergic conditions bioavailability of the drug gets altered.

Storage of Nasal Powders:

Nasal powders are stored at controlled room temperature and the relative humidity between 40 and 50% in a sealed packaging.

Quality Control Tests for Nasal Powders:

1. Angle of repose
2. Carr's Compressibility Index
3. Emitted dose
4. General sizing
5. *Ex vivo* advantages of nasal perfusion
6. *In vivo* characterization

3 Write a note on "Nasal Drops".

☞ **Nasal Drops:**

Nasal drops are topical aqueous solutions of drugs that are instilled into the nose with the help of dropper usually containing medicament.

Explanation:

- Nasal drops are usually aqueous solutions:
  - Because oily drops inhibit the movement of cilia in the nasal mucosa.
  - If oily drops are used for longer period, they may reach the lungs and cause lipoidal pneumonia.
  - Hence aqueous solutions are used in nasal drops.

- Nasal drops must be isotonic with nasal fluid.
- Nasal drops should be buffered to maintain stability and pH is adjusted to nasal fluid (pH 5.5 to 7.5)
- Preservative is required in nasal drops.

Use:

Nasal drops are used in the treatment of:

i. Nasal congestion
ii. Rhinitis of the common cold.
iii. Allergic rhinitis (inflammation of nasal mucosa)
iv. Hay fever (seasonal form of allergic rhinitis)
v. Sinusitis.

Container:

Coloured fluted glass bottle with dropper in the cap or separate dropper may be provided or plastic squeeze type container.

Storage:

Nasal drops are packed in coloured, fluted glass bottle and supplied with dropper. They are stored in well-closed glass container in a cool place.

Label:

- For external use only.
- Store in cool place.
- Not to be taken.

Examples:

Ephedrine hydrochloride nasal drops, betamethasone nasal drops.

4 Define nasal drops. Give the classification of nasal drops.

☞ **Nasal drops:**

Nasal drops are topical aqueous solutions of drugs that are instilled into the nose with the help of dropper usually containing medicament.

Classification of Nasal Drops:

1. Nasal Decongestants:

These are used for temporary relief from congestion in the nose caused by condition like common cold, sinusitis, hay fever, allergies. For example, Otrivin nasal drops.

2. Antibacterial Nasal Drops:

These are aqueous preparations of antibacterial drug intended for instillation into nostrils with the help of a dropper.

3. Nasal Antihistaminic:

These nasal drops relieve symptoms such as sneezing, a runny nose. For example, Phenylephrine nasal drops.

4. Nasal lubricants, Moisturizers and Irrigations:

These used to treat irrigated and dry nasal passages caused by hay fever, cold, etc. For example: Sodium chloride nasal drops.

5. Nasal Steroids:

These contain corticosteroids such as beclomethasone and are effective for reducing inflammation caused by allergies. They relieve nasal and sinus congestion mucus production and nasal swelling. For example: Triamicinolone nasal drops.

5 Give advantages, disadvantages of nasal drops and quality control tests for nasal drops.

☞ **Advantages of nasal drops:**

- Nasal drops require lower dose, thus less possibility of side effects.
- Nasal drops cover large surface area to have a rapid absorption, quick onset of action and good bioavailability.
- First pass metabolism of drug is avoided.
- Nasal drops are simple to use by self administration.

Disadvantages of nasal drops:

- No accurate doses are administered.
- Not suitable for children.

- They may cause regular nose bleeding, sinus dryness upon prolonged use.
- It can cause irritation, tachyphylaxis, rebound congestion and headache.

Quality Control Tests for Nasal Drops

1. Mean delivered dose
2. Delivered dose uniformity
3. Content uniformity
4. Sterility
5. Microbial test
6. Preservatives and stabilizing excipients assay
7. Appearance, colour, clarity
8. pH, viscosity, isotonicity

6 Write a note on "Nasal spray".

☞ **Nasal spray:** Nasal spray is the liquid solution or suspension formulations designed to spray directly into the nose in order to treat nasal allergy symptoms.

Explanation:

- Nasal sprays are sprayed by means of an automiser or nebulizer.
- The choice of pump and actuator assembly depends upon particle size and morphology of the drug in suspension and the viscosity of the formulation.
- Nasal spray devices are used to deliver drug both locally and systemically and are readily available as unit dose and metered multi-dose forms.

Storage:

Nasal spray bottles are always stored in upright position as directed and away from sunlight. Some nasal sprays are stored at room temperature while some require use of refrigerator (4–8°C) but not to freezed.

Label:

- Store in cool place.
- Store the bottles in upright positions.
- Discard the darken solution.

Uses of nasal spray:

- These are used intranasally to relieve nasal congestion and inflammation.
- These may contain antihistaminics, sympathomimetic or antibiotic medicaments.
- They can be used to control chronic rhinitis and allergic rhinitis.
- They can be used for the relief of nasal congestion due to common cold and flu.

Examples of nasal spray:

- Phenylephrine nasal spray
- Naphazoline nasal spray

7 Define and classify nasal sprays.

☞ **Nasal Sprays:**

Nasal sprays are the liquid solution or suspensions formulations designed to spray directly into the nose in order to treat nasal allergic symptoms.

Classification/Types of Nasal Sprays

1. **Nasal steroid sprays:** These are usually one of the first line therapies for treatment of allergies. These sprays give relief from nasal congestion, sneezing, watery eyes and runny nose.
2. **Nasal antihistaminic sprays:** These are used to treat runny nose aspect of allergies.
3. **Combination of nasal steroid or antihistaminic sprays:** These contain both nasal steroid and antihistaminic drug.
4. **Nasal anticholinergic sprays:** These sprays work by blocking acetylcholine which decreases secretions from the glands in the nasal passage. These are used for treatment of runny nose in patients with both allergic and non-allergic rhinitis, e.g. ipratropium bromide nasal spray.

5. **Nasal chromolyn sodium spray:** This nasal spray helps to treat nasal congestion, sneezing and runny nose in patients with allergies, e.g. chromolyn nasal spray.
6. **Nasal decongestant sprays:** These sprays provide temporary relief from nasal congestion by constricting blood vessels in the nose which reduces nasal swelling and congestion, e.g. phenylephrine nasal sprays.
7. **Nasal saline spray:** These sprays contain saline solution. These sprays are good to keep the nose moist, e.g. nasal saline spray.
8. **Nasal irrigations:** These are used to rinse out the nasal mucus. These are used before using a nasal spray.

8 Give advantages, disadvantages and quality control tests for nasal sprays.

☞ **Advantages of Nasal Sprays:**

- Easy delivery and favourable tolerability
- Rapid drug absorption
- Quick onset of action
- Avoid first-pass metabolism of drug.
- Bioavailability is improved.

Disadvantages of Nasal Spray:

- Small area is available for absorption of drugs.
- Bitter taste and time available for drug absorption is limited.
- Not suitable for diseased nose that may impair drug absorption.
- Nasal sprays may cause nasal irritation, flushing and headache.

Quality Control Tests for Nasal Spray:

1. Impurities and degradation of product.
2. Preservative and stabilizing excipients assay.
3. Particulate matter
4. Microbial limits
5. Net content and weight loss.
6. Appearance, clarity, pH, viscosity.
7. Particle, pump delivery.
8. Spray content uniformity, spray pattern.
9. Droplet size distribution.
10. Number of doses.

9 Write in brief about "Nasal Gels".

☞ **Nasal Gels:**

Definition: Nasal gels are defined as highly viscous, thickened solutions or suspensions that provide soothing, moisturizing relief to dry, stuffy, irritated nasal passages and used to relieve nasal congestion.

Explanation:

- Nasal gels are less viscous and free flowing to allow for repeated administration of drug to nasal cavity, as droplet mist or as spray.
- Nasal gel is very useful in dry climates of low humidity (during winter) for individuals with nasal allergies or sinusitis.

Uses:

- Nasal gel is used to treat dry irritated nose passages.
- Nasal gel is used to thin fluid in the nose passages.
- Nasoclear gel is used to treat nasal congestion (blocked nose).

Storage:

Nasal gels are stored in cool and dry place usually in refrigerator. It should not be freezed. Nasal gels are protected from heat and light as they may get dried up upon exposure.

10 Define and classify nasal gels.

☞ **Nasal Gels:**

Nasal gels are defined as highly viscous, thickened solutions or suspensions that provide soothing, moisturizing relief to dry, stuffy, irritated nasal passages and used to relieve nasal congestion.

Classification of Nasal Gels:

1. **Inorganic nasal gels:** These are usually two phase systems, e.g. Bentonite magma.
2. **Organic nasal gels:** These are usually single phase systems, e.g. carbapol gel, tragacanth gel

3. **Nasal hydro gel:** For examples, methyl cellusose, sodium carboxymethyl cellulose
4. **Nasal Organogels:** These are hydrocarbon type animal, vegetable, fat soap base greases, hydrophilic organogels.

11 Give advantages and disadvantages and quality control tests for nasal gels.

☞ **Advantages:**

- Nasal gels reduce post-nasal drip due to high viscosity.
- They reduce taste impact due to reduced swallowing.
- They are less irritant because of soothing excipients.
- Nasal gels target to mucosa for better absorption.
- They provide rapid onset of action.
- Nasal gels have increased contact time and showed improved patient compliance.
- They protect the drug from enzymatic degradation.

Disadvantages:

- Delivery volume in the nasal cavity is restricted to 25–200 µl
- Drug delivery through the nasal gel is adversely affected by pathological conditions.
- Some drugs in nasal gel can cause irritation of nasal mucosa.
- Nasal gels have small absorption surface as compared with GIT.

Quality control tests for nasal gels.

1. Bioadhesion measurement
2. Mucoadhesion measurement
3. Formulation tolerance
4. Isotonicity
5. Gelation temperature
6. Gel strength
7. Other tests: Clarity, viscosity, pH, drug content, *in vitro* drug release, etc.

1

Ear Preparations (Otic/Aural Preparations)

1 Write a note on ear preparations.

☞ Ear preparations/Otic preparations

Ear preparations are the products applied to or in the ear to treat conditions of the external and middle ear as well as to remove the excessive cerumen (wax) from the ear.

Explanation

Ear preparations include:

1. Ear drops
2. Ear foam
3. Ear gels
4. Ear creams
5. Ear ointments
6. Ear powders
7. Ear irrigation solutions

- Ear preparations are used to treat the conditions of external and inner ear.
- Bacterial growth in the external auditory canal is treated with solvents containing glycerine, vegetable oils, mineral oils, and PEG 300.
- Antibiotics are also used in combination with other solvents.
- The viscosity of ear preparation provides sufficient contact time of dosage forms to release the drug at site of infection effectively.
- The active agents in ear preparations for local use include antibiotics antifungal agents, anti-inflammatory agents, antiseptic, cleansing solutions and wax softners.

- Generally topical ear preparations prepared in the form of acidic solutions or suspension with a pH 3–4 for inhibition of bacterial growth.

Advantages of ear preparations

1. It exerts direct contact on the organ site and is thus suitable for local effects.
2. It can achieve higher local drug concentration at the site of action.
3. It shows rapid dispersion and has good patient compliance.
4. It has an ability to combine different drugs into single formulations.

Disadvantages of ear preparations

1. It shows potential ototoxicity of some drug at high concentration.
2. The patient with ear infection has to wait in a position for 3–4 minutes to facilitate drops to reach at the sites.
3. Accurate dose measurement is not possible.

Storage

Ear preparations are stored at either at room temperature or refrigerated temperature and are not be frozen.

Label

The important directions on the label must include

- For the use of ear only.
- Not to be taken
- External use only.
- Store in a cool place
- Not to be diluted with water.
- Discard after appropriate use.
- Keep out of reach of the children.

Quality control tests for ear preparations:

1. Appearance
2. Odour
3. Assay

4. Volume/weight
5. pH
6. Viscosity
7. Density

2 What are otic/ear preparations? Explain different types of ear preparations. Or Write a note on types of ear preparations.

☞ Ear preparations:

Ear preparations are the products applied to or in the ear to treat conditions of the external and middle ear as well as to remove the excessive cerumen (wax) from the ear.

Types of ear/otic preparations:

1. Ear drops:

- Ear drops are solutions, emulsions or suspensions of one or more active ingredient which exerts a local effect in the ear.
- Ear drops are placed in the ear canal drop wise for the removal of excessive cerumen or for the treatment of outer ear and ear canal infections, inflammation or pain.
- Ear drops are used to soften dry and hardened ear wax.
- There are four main types of ear drops used to treat ear canal infections:
  - Antibiotic ear drops: To treat an underlying bacterial infection.
  - Corticosteroid ear drops: To treat an underlying fungal infection
  - Acid ear drops: To kill bacteria
  - Examples: Ciprodex ear drops, otic drops

2. Ear foams: Ear foams are commonly used to increase drug contact time in the ear canal.

3. Ear irrigation solutions:

- These are used for irrigating the ear to remove ear wax.
- These may consist of surfactant, weak sodium bicarbonate, boric acid (0.5–1%) or aluminium acetate solutions.
- These solutions may be warmed to 37°C before instillation into the ear.

- These may also be used to remove pus discharge of infection and foreign bodies from the ear canal.
- Examples: Normal saline solution, hydrogen peroxide 2%, plain warm water, boric acid 2–4%, sodium bicarbonate solution 1%.

4. Ear ointments or gels:

- These are semisolid preparations that are applied to the exterior of the ear.
- Their preparations may be antibacterial, antifungal, or corticosteroid ear ointments.
- Examples: Otic ointments, Tech-care gel

5. Ear insufflations/Powders:

- Ear insufflation is an innovative therapy where small puffs of powder are applied to the eardrum to relieve the patient from migraines, headaches, sinus issues.
- Insufflations are preparations made of finely divided powders that are administered to the ear canal.
- Fine powder used as insufflations may contain antibacterial and antifungal drugs that create a repository for the drug.
- A small rubber or plastic bulb insufflators can be used to blow or insufflate the powder into the ear.
- For example, CSF otic insufflations
- Uses: To treat chronic otitis media and otitis externa

3 Write note on ear drops/ Otic drops.

☞ Ear drops

Ear preparations are the products applied to or in the ear to treat conditions of the external and middle ear as well as to remove the excessive cerumen (wax) from the ear.

Explanation

- Ear drops are also called otic or aural preparations.
- Ear drop solutions of drugs in water, dilute alcohol, glycerine used for instillation into ear.
- Glycerine is included in ear drops because secretions in ear are mainly fatty. The glycerine has softening effect on the wax. The glycerine is highly viscous, hence it assists adherence to the infected surfaces and produces prolonged drug action.

Use

The medicaments prescribed in ear drops used for the following ear conditions:

(a) For treatment mild infections: Chloramphenicol, neomycin.
(b) For softening/removing wax: Hydrogen peroxide, sodium bicarbonate.
(c) Cleansing after ear infections: Spirit, hydrogen peroxide.
(d) Drying and wetting surfaces: Astringents such as aluminium acetate.
(e) Antiseptic: Phenol
(f) Local anaesthetics:Bezocaine, xylocaine.
(g) Anti-inflammatory agents: Hydrocortisone, dexamethasone.
(h) Analgesics: Antipyrin

Container

- They are packed in small volume containers (5–10 ml).
- Ear drops are dispensed in coloured flutted glass bottles with a dropper and plastic screw cap closure.

Label

The important directions on the label must include:

- For the use of ear only
- Not to be taken.
- For external use only.
- Store in a cool place.
- Not to be diluted with water.
- Discard after appropriate use.
- Keep out of reach of children

CHAPTER 15

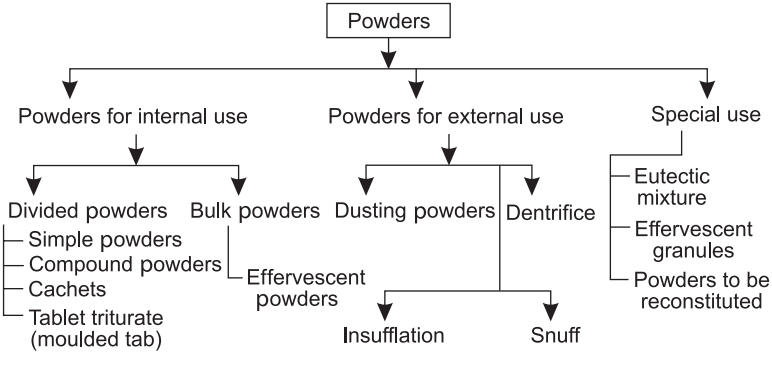
Powders and Granules

1 Define and classify powders.

☞ Powders

"Powders are solid dosage forms which contain mixture of powdered substances intended for both internal and external use."

Classification



2 What is double wrapping of powders? Why is it necessary?

☞ Double Wrapping of Powders

The wrapping of powders in two paper (packing) coverings is called double wrapping.

In this case inner paper is waxy and outer paper is an ordinary paper. The wax paper is cut slightly smaller than the ordinary paper.

Double wrapping is essential for volatile or hygroscopic drugs like menthol, thymol, citric acid, pepsin, camphor, etc.

3 What are advantages and disadvantages of powder as a dosage form?

☞ Advantages of Powder

1. Powders are convenient to prescribe, compound and administer.
2. Powders are more stable than liquids.
3. Powders can be easily swallowed and large quantities can be administered with foods or drinks.
4. Powders provide accuracy of dose.
5. There are less chances of chemical reactions in the ingredient because of absence of moisture.
6. Powders are available in a very fine state, hence, provide rapid dissolution and absorption.
7. Incompatibility is less in case of powders than liquids.
8. They are more easy to carry than liquids.
9. They are taken easily in bulk quantities with food or some drinks.
10. These are economical dosage forms since they do not require large number of machineries or special technique.

☞ Disadvantages

1. Certain drugs are sensitive to atmospheric conditions like air moisture and light, are not suitable for dispensing in the form of powder.
2. Drugs which are bitter, nauseous, corrosive and unpalatable are not suitable for dispensing in powder form.
3. Manufacturing of powders requires operations like milling, sieving, mixing, drying, etc. Hence, it is time-consuming.
4. Powders are not suitable when they contain volatile, deliquescent, hygroscopic or oxygen sensitive substance.

4 Write a note on "dusting powders".

These are fine powders for local application and to be applied externally.

- They are free flowing, very fine powders for external use containing antiseptic, astringent, antiperspirants, absorbants, protectives, etc.
- Dusting powders commonly contain zinc oxide, starch, boric acid, kaolin, talc, etc.

Types of Dusting Powders

a. Medicated dusting powders
b. Surgical dusting powders.
c. Cosmetic dusting powders.

a. *Medicated Dusting Powders*

- These are applied externally to superficial skin condition and sterility is rarely essential.
- They must be free from spores of dangerous pathogens like tetanus, gas gangrene and anthrax.
- They are sterilized by dry heat at 100°C for 1 hr.
- They generally contain starch, kaolin, talc, zinc.
- They contain medicaments having antiseptic, astringent, absorbent properties.

Label

- For external use only.
- Do not apply on open wound or broken skin.

b. *Surgical Dusting Powders*

- These are used:
  - In body cavities
  - On major wounds
  - On burns
  - On umbilical cords of infants.
- They must be sterile.
- They usually contain antibacterial agents like chlorhexidine and hexachlorophene.

c. *Cosmetic Dusting Powders*

These contain various oils, special dyes, fragrances and essential oils. These powders are prepared by mixing different powers such as kaolin, talc and starch.

Advantages of dusting powders:

- These are used during excess perspiration.
- These are used as lubricants, protective, absorbents.
- These powders have good chemical stability.
- Easy to carry and apply over wounds.
- Rapid onset of action.
- Economical.
- Suitable for children and elderly patients.

Disadvantages of dusting powders:

- Not intended for systemic action.
- Not applied to broken skin.
- Dusting powders containing hygroscopic ingredients may undergo hydrolysis.
- Not suitable for drugs unstable in normal storage condition.
- These powders are susceptible to physical instability.

5 Write a note on "effervescent granules".

"Effervescent granules are specially prepared solid dosage form of a medicament, meant for internal use."

- They usually contain a soluble medicinal agent mixed with tartaric acid, citric acid and sodium bicarbonate.
- Before administration they are suspended, dissolved in water or mixed with soft drinks.
- On mixing with water the CO_2 is released as a result of acid–base reaction producing effervescence and mixture is taken while effervesing.
- The carbonated H_2O produced from the release of CO_2 serves to mask the saline and bitter taste of drugs.
- The CO_2 is said to stimulate the flow of gastric juice and accelerate absorption of medicament.

Mechanism

1. *Sodium Bicarbonate*

It reacts with citric and tartaric acids when granules are added in water and evolves CO_2 which gives effervescence.

2. *Citric Acid*

It gives palatable acidic taste and also neutralizes the excess of sodium bicarbonate.

It provides moisture needed for granulation.

3. ***Tartaric Acid***

It gives acidic palatable taste.

Direction for use:

Before administration they are dissolved in water and mixture is taken while effervescing.

Advantages of Effervescent Granules:

- Rapid onset of action.
- Rapid disintegration and dissolution.
- Liberated CO_2 acts as a local anaesthetic to mask the undesirable drug taste.
- It exerts psychological effect which makes the patient feel comfortable to it.
- It provides alkaline solution up to neutralization of acidic drugs.

Disadvantages of Effervescent Granules:

- They are unstable upon absorption of moisture from atmosphere.
- In case of effervescent granules, estimation of accurate dose is different.
- Due to sodium overload, these granules are not suitable for hypertensive patient.
- Effervescent granules may have drug–drug interactions.

6 Give the packing, labelling and storage conditions of powders.

☞ Packing of Powders

1. Simple and compound powders containing stable drug are packed in single dose paper packet or if the drug is moisture sensitive they are packed in double wrap paper (line with wax paper) packets.
2. Granuler powders or effervescent powders are supplied in wide-mouthed, airtight, glass or plastic containers.
3. Nowadays single dose or minute dose aluminium foil sachets are also used for this purpose.
4. Dusting powders are packed in sifter, top packages or aerosol container.

☞ Labelling of Powders

1. Name of the preparation.
2. Strength of the therapeutic agents.
3. Directions for use:
   a. Frequency of dose for powders internally taken.
   b. How to apply on the affected part for externally applied powders.
   c. For external use only in case of dusting powder.
   d. Not to be applied to open wounds in case of dusting powders.
   e. Batch no., Mfg. no., expiry date, name of dispensary and company.

☞ Stability and Storage

Storage condition depending upon the stability requirement of drugs.

a. Store in a cool place.
b. Protect from light.

7 What are "insufflations"? Give advantages, disadvantages and uses of insufflations. Or "Write a note on insufflations".

☞ Insufflations

Insufflations are medicated dusting powders which are blown into the body cavities such as ear, nose, throat and vagina, with the help of an apparatus known as "Insufflator".

- Insufflator sprays the powder into a stream of finely divided particles all over the site of application.
- Insufflations should be in finely divided powders so that a stream of fine particles of medicament gets applied to the site of application.
- Nowadays insufflations are available in the form of pressure aerosols.
- Aerosol insufflations are used for administration of potent drugs.

- Insufflations are used to produce a local effect as in the treatment of ear, nose and throat infections with antibiotics or to produce a systemic effect from a drug that is destroyed in the gut.

Advantages of Insufflations:

- Rapid, safe and convenient method.
- Suitable for administration of potent drugs.
- Avoid degradation of drug in GIT.
- Avoid first–pass metabolism of drug and enhance bioavailability.
- Reduce systemic side effects.
- Ease of administration.

Disadvantages of Insufflations:

- Rapid elimination of drug from nasal cavity due to nasal secretions.
- Nasal congestion may interfere during drug delivery.
- Frequent use may cause irritation of nasal mucosa.
- Drug loss may occur.
- The drugs need to be finely divided powder form.

Uses of Insufflations:

1. Insufflations are used to treat the infections of nose, ear, throat, vagina, etc.
2. Nasal insufflation may produce a local or a systemic effect.
3. Anti-asthmatic medication, hormone replacement given in the form of insufflations.

8 What are snuffs?

- Snuffs are finely divided solid dosage forms.
- Snuffs are very fine medicated powders which are inhaled into nostrils for its antiseptic, bronchodilator and nasal decongestant action.
- Snuffs are dispensed in a flat metal boxes with hinged lid.

CHAPTER 16

Sterile Formulations

A Injectables/Parenteral/Sterile Dosage Forms

B Ophthalmic Products [Eye Drops, Eye Ointments]

A

Injectables/Parenteral/Sterile Dosage Forms

1 Define parenterals injectables. Give essential qualities of parenterals.

Parenteral preparations are injectable or sterile solution or suspensions of drugs in aqueous or oily vehicles meant for introduction to the body by means of an injection under more layers of skin or mucous membranes.

Par: Means 'other than'.

Enteron: Means intestinal tract.

Essential Qualities of Parenterals/Injectables

The parenterals product must possess the following properties:

1. The parenterals must be free from the living microbes as well as microbial products.
2. They should be free from pyrogens.
3. They should be free from foreign particles such as dust, fibres, etc.
4. They should be free from chemical contaminants.
5. They should be isotonic with body fluids.
6. They should be compatible with some body fluids.
7. Multidose injection must contain preservative.
8. Container or closure must not affect the product.
9. The ingredients which are used must be of the highest quality.

2 What are the advantages and disadvantages of parenteral dosage forms/injectables?

Advantages

1. They produce rapid action.
2. They are useful in emergency cases.

3. They are useful in unconscious and uncooperative patients.
4. Smaller doses of drugs are required.
5. Useful in patients suffering from vomiting and diarrhoea.
6. 100% bioavailability can be given by IV route.
7. Drugs which are destroyed in GIT, can be given parenterally.
8. Larger quantity of drugs can be administered by IV route.
9. Adverse effects can be reversed or controlled easily.

Disadvantages

1. Skilled person is required for administration.
2. Possibility of pains and edema at the site of injection.
3. Sterilization of syringe and needle is required.
4. Self-medication is difficult.
5. Frequent administration possesses difficulties to the patients.
6. The treatment is costly.

3 Give various types of parenteral products (classification).

1. Solutions ready for injection.
2. Suspensions ready for injection.
3. Emulsions suitable for parenteral administration.
4. Dry soluble products which are dissolved in suitable solvent immediately before its administration.
5. Dry insoluble products which are combined with suitable vehicle just before its administration.

4 Explain various additives used in parenterals/injections. (Write a note on adjuvants used in parenterals)

1. Vehicles.
2. Solubilizing agents.
3. Stabilizers.
4. Buffers.
5. Antibacterial contributors.
6. Isotonicity contributors.
7. Wetting agents, suspending agents, emulsifying agents.

1. Vehicles

- Vehicles used in parenterals may be:
  i. Aqueous vehicles
  ii. Non-aqueous vehicles
  iii. Water-miscible vehicles.
- Aqueous vehicles, e.g.
  – Water for injection IP
  – Purifier water
  – Distilled water
  – Dextrose injection
  – Saline solution.
- Non-aqueous vehicle (oily), e.g. Arachis oil, cottonseed oil, almond oil, seasame oil.
- Water-miscible vehicle, e.g. ethyl alcohol, glycerin.

2. Solubilizing Agents

These are necessary to increase the solubility of poorly water soluble drugs, for example, polysorbates

3. Stabilizers/Antioxidants

To prevent oxidation of product, antioxidants are added. For example, tocopherols, BHT, BHA, thiourea, ascorbic acid.

4. Buffers

Buffers are used to maintain pH of preparation. For example, phosphate buffers and acetate buffers, citric acid, sodium citrate acetic acid, sodium acetate.

5. Antibacterial Agents

Bacteriostatic or fungistatic agents must be present in multidose containers to prevent growth of bacteria, etc. For example, benzalkonium chloride (0.01%), chlorocresol (0.2%), methyl paraben, propyl paraben, benzyl, alcohol, chlorobutanol.

6. Isotonicity Contributor

To maintain isotonicity, borax or sodium chloride, dextrose, boric acid are added.

7. Wetting Agents

They help to increase the wettability of poorly wettable substances. For example, sorbitol.

8. Suspending Agents

They help to suspend the particles in preparation. For example, acacia, methyl cellulose, gelatin, carboxy methyl cellulose.

9. Emulsifying Agents

They help to stabilize the emulsion. For example, lecithin.

10. Chelating Agents

These form a complex which gets dissolved in the solvent, e.g. EDTA.

5 What are intravenous fluids (IV fluids)/infusion fluids/ large volume parenterals (LVPs)? Write their uses.

or

Write a note on intravenous fluids.

Large volume injections intended to be administered by intravenous route are called IV fluids or intravenous infusions.

- These are administered in volumes of 250 ml to 1000 ml per day by slow IV drip.
- IV fluids should possess some ideal qualities.
  - They must be isotonic with blood.
  - They must be free from foreign particles and microbes.
  - They must be free from pyrogens.
  - They must be compatible of all ingredients.
  - They must be stable.
  - They must contain bacteriostatic agent or preservative.
- LVPs are packed in large single dose glass or plastic containers.

Examples

1. Dextrose injection.
2. Dextrose and sodium chloride injection.
3. Fructose injection (10%).
4. Mannitol injection (5 to 20%).
5. Sodium chloride injection or saline solutions (0.9% NaCl).

Uses of IV Fluids

1. Electrolyte replenisher: To maintain electrolyte balance in conditions like burns, diarrhoea, etc.
2. As a fluid replacement: In dehydration condition.
3. To provide nutrition: If nutrition is not possible by oral route, then nutrition is given by IV fluids.

4. Total parenteral nutrition (TPN): IV fluids are used to provide TPN in conditions like unconsciousness, coma.
5. Drug carrier: IV fluids may be used as carrier for the drugs.

6 Write a note on "Small volume parenterals" (SVPs).

☞ **Small Volume Parenterals:**

- The volume of small volume parenterals is less than 100 ml.
- SVPs are also called injections.
- These are also sometimes manufactured as multidose container.
- These can be given by IV as well as by other route.
- Preservative is needed in SVPs.
- These are also used for treating diseases and also for prophylaxis purpose.
- SVPs include local anaesthetics, vaccines and other traditional injectable products.
- SVPs are packed in ampoules, vials, prefilled syringes, etc.
- For example, adrenaline injection IP, BP, ascorbic acid injection IP.

7 Differentiate between "SVPs" and "LVPs".

Small volume parenterals (SVPs)	Large volume parenterals (LVPs)
1. SVPs have volume less than 100 ml.	1. LVPs have a volume 100 ml or more.
2. These are called injections.	2. These are called infusions.
3. These may be single or multidose preparation.	3. These are single dose preparations.
4. These are given by IV, IM, SC routes.	4. These are given by IV route.
5. Preservatives are used.	5. Preservatives are not needed.
6. Buffers are used.	6. Buffers are not used.
7. Isotonicity is not essential.	7. Isotonicity is essential.

8. These are used for therapeutic and diagnostic purposes	8. These are used for nutrition, detoxification, rehydration and during surgery.
9. Pyrogenicity is not essential	9. Pyrogenicity is must.
10. For example: Adrenaline injection IP.	10. For example: Normal saline solution.

8 Discuss various evaluation tests/quality control tests of parenteral or sterile dosage forms.

☞ Evaluation of Parenterals

1. Leaker test
2. Clarity test
3. Sterility test
4. Pyrogen test

1. *Leaker Test*

- Leaker test is carried out to detect capillary pores, cracks or incomplete seals in the ampoules.
- The ampoules are completely immersed in a dye solution (1% methylene blue) in a vacuum chamber.
- Vacuum is applied and is released after 10 minutes.
- If the seal is imperfect or a crack, then coloured solution enters into ampoules.
- This shows sample fails to pass leaker test.

2. *Clarity Test*

- Clarity test is used to detect presence of particulate matter in parenteral products.
- This test is useful only for solution.
- In this test visual inspection of product (ampoule) against a black and white background in bright light is done.
- Transparent particles are visible against black background and coloured particles against white background.
- If visible particles are found in the sample, then sample is found to be contaminated.

3. *Sterility Test*

Principle

- Sterility test is a technique for checking the complete freedom from living microbes and their spores in a dosage form.
- Sterility test is based on the principle that if any contaminating bacteria or fungi present are placed in a nutrient medium under favourable conditions, it shows growth of microbes.

The growth of micro-organisms can be detected easily because clear medium turns turbid.

Official methods of sterility testing

a. Direct inoculation method (Petri dish/plate).

b. Membrane filtration method.

a. Direct inoculation method

- A sterile Petri dish is taken and a sterile nutrient agar medium is added in it.
- The sample which is to be tested, is mixed with nutrient medium.
- Then it is kept in incubator for 7 days under specified conditions.
- After 7 days, if turbidity appears, then it is said that product is not sterile.

b. Membrane filtration method

- In this method sample is filtered through a sterile membrane filter having a porosity of 0.45 μm.
- After filtration membrane is washed with a sterile diluting fluid to remove traces of bacteriostatic agent.
- Then the membrane is aseptically removed and placed into a nutrient agar medium and incubated at 22°C for 7 days.
- The product passes the sterility test if no turbidity appears at the end of the incubation period.

4. *Pyrogen Test*

- Pyrogens are the metabolic products of living or dead microbes.
- Pyrogens cause rise in body temperature upon injection.
- The parenterals must be free from pyrogens.
- There are two methods of pyrogen testing.

Biological test (using rabbits)

- Rabbits are used for this test as they are highly sensitive to pyrogens.
- Three healthy rabbits are selected and suitable amount of sample is injected into the ear vein of the three rabbits.
- The rectal temperatures of all three rabbits are recorded.
- Any animal showing a rise in temperature of 0.6°C or more or if sum of the responses exceeds 1.4°C, then it indicates the presence of pyrogens in the parenteral preparation and vice versa.

Disadvantages or limitations of pyrogen test using rabbit method

1. Healthy animals are required.
2. Animals show variations in their responses.
3. Influence of other factors may occur.
4. Some drugs cannot be tested satisfactorily because drug shows pharmacological action.
5. Time-consuming method.
6. Rectal thermometers with digital control is required.
7. Constant recording of temperature is necessary.
8. Sensitivity of test is less.

LAL test/BET test (*bacterial endotoxin test*)

- It is based upon the gelling of the reagent called limulus amebocyte lysate (LAL) in the presence of bacterial endotoxins.
- Amebocytes or the circulating blood cells of the horseshoe crab contain a protein that clots in presence of pyrogens.
- If lyophilised (freeze dried) powder of LAL is added in the solution containing pyrogens, it causes gel formation within 30 minutes.
- Thus, in the test sample limulus amebocyte lysate powder is added, if gelling appears, then it shows presence of pyrogens.

Advantages of LAL test

1. Test is very simple.
2. It gives quick result.
3. Use of animals like rabbits is avoided.
4. Greater sensitivity than the rabbit test.
5. Very cheap method as it does not require complicated equipment.

9 Write in brief about "containers and closures used for parenteral products/injectables."

☞ The containers and closures used for parenteral products are either made from glass or plastic material.

As per pharmacopoeia requirement of containers and closures for parenteral are–

i. It should not release foreign substances to the product.
ii. It should be transparent to allow visual inspection of the contents in it.
iii. It should not have any adverse effect on the product.
iv. It should prevent diffusion in or across the walls.

☞ Types of glasses used for the preparation of containers used for storage of parenteral preparations:

1. Type I glass:

- It is also called borosilicate glass or neutral glass.
- It offers a high hydrolytic resistance due to its chemical composition.
- It can withstand autoclaving and weathering.

2. Type II glass:

- It is a soda-lime-silicate glass with high hydrolytic resistance as a result of treatment with moist sulphur dioxide at high temperature.
- The containers made from this glass are suitable for most acidic and neutral aqueous preparations.

3. Type III glass:

- It is a soda-lime-silicate glass with only moderate hydrolytic resistance.
- The containers made from type III glass are generally suitable for non-aqueous preparations and powders for reconstitution immediately prior to administration.
- Containers of type II and type III glass should be used once only.
- Containers for human blood and blood components must not be reused.

B

Ophthalmic Products [Eye Drops, Eye Ointments]

1 Define ophthalmic products. Give their types.

These are the products which are to be instilled into the eye in the space between the eyelid and eyeballs.

Types of Ophthalmic Products

1. Eye drops
2. Eye lotions or eyewashes
3. Eye ointments
4. Contact lens solution
5. Ophthalmic insert
6. Eye suspensions
7. Eye drop microemulsions.

2 Define eye drops. Give the ideal qualities of eye drops.

"Eye drops are sterile aqueous or oily solution or suspensions for instillation into eye."

Ideal Qualities of Eye Drops

1. They should be sterile.
2. They should be free from foreign particles.
3. They should be isotonic with lacrimal secretions.
4. They should be free from irritant effect.
5. They should contain suitable preservative, e.g chlorocresol.
6. They should contain buffering agent for adjustment of pH.
7. They should have adequate viscosity for longer contact of drug with corneal tissue, e.g methyl cellulose.
8. They should be chemically stable.

9. They usually contain substances having antiseptic, anaesthetic, mydriatic, miotic properties.
10. Vehicles used in ophthalmic preparations must have good wetting ability to penetrate cornea and other tissues.

3 What are eye drops? Classify eye drops. Give advantages and limitations of eye drops.

☞ Eye Drops:

Eye drops are sterile, aqueous or oily solutions or suspensions for instillation into eye.

Classification/ Types of Eye Drops:

(a) Eye drop solutions: These are saline containing drops used as an ocular route to administer. They are sterile, aqueous solutions used for cleansing and rinsing eyeballs. They have a pH near to neutral, i.e 6.8.
For example: Ciprofloxacin eye drop.

(b) Eye drop microemulsion:
- These drops are generally dispersions of oily droplets in an aqueous phase.
- Eye drop in emulsion form offers to improve both solubility and bioavailability of drugs.
- Lipid–soluble drugs has problems in formulating them as aqueous solutions in such cases microemulsions were prepared.
  For example: Chloramphenicol eye drop.

(c) Eye drop suspensions:
- When the drug is not sufficiently soluble, in such cases formulated as suspension.
- Eye drop suspensions are formulated to improve stability, bioavailability or efficacy of the water insoluble and unstable drugs.
- Eye drop suspensions having steroidal drugs are useful for the treatment of ocular inflammatory disease.
- "Do not freeze" warning is given on the label because they may agglomerate on freezing.

- Usually 95% or more of the particles should have a diameter of 10 μm or less.
  For example: Prednisolone acetate ophthalmic suspension eye drop.

Advantages of Eye Drops:

- They are convenient to use.
- They do not interfere with vision of patient.
- Suspension eye drops have good patient compliance.
- Suspension eye drops have longer contact time.
- Emulsion eye drops have prolonged release of drug from vehicle.

Limitations/Disadvantages of Eye Drops:

- Solution eye drops are rapidly eliminated from the eyes.
- Frequency of administration of solution eye drops is more.
- Emulsion eye drops may cause blurred vision.
- Improper use of eye drops may lead to ocular complications.

4 Give the general methods of preparations of eye drops. What are the additives used in eye drops.

☞ **Methods of Preparation of Eye Drops:**

- Dissolution of drug in suitable sterile solvent.
- Transfer of solution into a sterile container aseptically.
- Sterilization of final container.

Adjuvants/Additives used in Eye Drops:

(a) Vehicles: It contains aqueous vehicles such as sterile water for injection IP or oily vehicles such as sterile oils.

(b) Wetting agents: They are used for proper penetration of eye drops into the cornea of eye, e.g. polysorbate-20, polysorbate-80

(c) Preservative: It contains preservatives to prevent microbial growth e.g benzalkonium chloride (0.01%), Phenyl mercuric nitrate /acetate (0.002%), chlorhexidine acetate (0.01%)

(d) Buffering agent: To maintain suitable pH stability, e.g boric acid solution (pH about 5), phosphate buffer (pH 5.9–8), sodium citrate, sodium acid phosphate

(e) Thickening agent: To maintain acceptable viscosity. It will also help to prolong the contact time of drug in the eye.
For example: Mehtyl cellulose, carboxymethyl cellulose, polyvinyl alcohol, polyethylene glycol.

(f) Antioxidants: To prevent oxidation of product, e.g sodium bisulphate, sodium thiosulphate (0.1 to 0.2%).

(g) Tonicity contributor: To maintain isotonicity, e.g sodium chloride solution.

5 Enlist various quality control tests of eye drops.

☞ Quality Control Tests of Eye Drops

1. Uniformity of volume
2. Assay
3. Concentration of preservative
4. Preservative efficacy testing
5. Appearance and clarity
6. pH
7. Isotonicity
8. Drop size
9. Viscosity
10. Water loss
11. Particle size
12. Drug release

6 Explain requirement of container and labeling conditions for eye drops.

☞ Container of Eye Drops

- Eye drops are packed in small volume container, i.e 5 to 10 ml to avoid bacterial contamination.
- Eye drop container is colourless or amber-coloured, small volume, narrow-mouthed glass bottle with the dropper in the pack.
- The containers of eyedrops should have the following properties:
  - It should comply with test for alkalinity of glass.
  - It should protect light sensitive drugs.
  - It should have satisfactory sealing properties.
  - They should provide dropper ready for use and protected against package and contamination.

Plastic bottle:

It is gas sterilized polyethylene squeeze bottle closed by a plug type bottle tip which is supplied inverted in a polypropylene outer screw cap.

Label for Eye Drops

1. For external use only.
2. Use the solution within one month after opening the container.
3. If irritation persists, discontinue the use and consult the physician.
4. Do not touch the tip of a dropper since it may contaminate the solution.
5. Not for injection.
6. Name and concentration of preservative used in eye drop.

7 Define eye ointments. Give the formula, method of preparation, advantages, limitations, packaging and labeling and storage conditions of eye ointments, Or Write a note on "eye ointment".

☞ Eye Ointment (Ophthalmic ointment)

Eye ointments are sterile, homogenous, semisolid preparation intended for application to conjunctiva to treat various eye disorders.

- Ophthalmic ointment must be free from irritant effect.
- They should be sterile.
- IP gives a suitable formula for eye ointment base.

Liquid paraffin	10%
Wool fat	10%
YSP	80%

Method of Preparation

- It is prepared aseptically.
- First all the ingredients are melted together and then filter to remove foreign particles and sterilized by heating at 150°C for 1 hr and cooled.
- Incorporate the medicament with eye ointment base.

Storage: Eye ointment should be stored in a cool place.

Container/Packaging of Ophthalmic Ointments

- Packaging should maintain sterility of the product.
- Ophthalmic ointments are filled in the collapsible tube having special nozzle.
- Nowadays ophthalmic ointments are packed in soft gelatin capsule for single use and thus maintain sterility.

Label

- For external use only.
- If irritation persists discontinue the use and consult the physician.
- Use of preparation within one month after its opening.
- Do not touch the tip of nozzle.
- Replace the cap immediately after use.

8 Mention different quality control tests for eye ointment.

☞ **Quality Control Tests of Eye Ointment:**

1. Assay
2. Concentration of preservative
3. Preservative efficacy test
4. Sterility testing
5. Metal particles in eye ointment
6. Eye irritancy test. (Draize eye test)

9 What is eye suspension? Give the essential/ideal characteristics of eye suspension.

☞ **Eye suspensions:**

- These are sterile preparations meant for application to the eye.
- These are prepared only in those cases, when the drug is insoluble in the desired vehicle or unstable in liquid form.
- These are also used to produce the sustained action of the preparation.

Essential/ideal characteristics of eye suspensions:

1. They should be sterile.
2. They should be isotonic.
3. They should be desired viscosity.

4. The particle size of the eye suspension should be fine.
5. They should be non-irritant to the eye.
6. They should be shaken thoroughly before use in order to distribute the drug particles uniformly.
7. They should be packed in a suitable container so that it can easily instilled into the eye.

10 What are eye lotions or eye washes?

Eye lotions are sterile, dilute or concentrated aqueous solution of medicament used for washing of the eye or wetting of the eye.

Explanation

- Eye lotions are usually applied to eye by means of eye bath.
- They are dispensed in concentrated form and should be diluted with warm water before use.
- Eye lotions are simple solutions and iso-osmotic with tears.
- Eye lotions are sterilized by autoclaving or bacteria proof filters.
- They should be prepared freshly and should not be stored for more than 2 to 3 days as they may be contaminated with micro-organisms on prolonged storage.

Requirements of Eye Lotions

- They must be isotonic with lacrimal fluids.
- They should be sterile.
- They should contain buffers, preservatives, etc.
- They usually contain antiseptic substances such as boric acid, borax.

Label

- For external use only.
- Dilute with warm water before use.
- Discard any unused part of eye lotion after 24 hr.

11 Why eye drops must be sterile?

Because, eye is very delicate organ. If eye drops are not sterile the pathogenic organism may enter the eye and cause damage to eye. In some cases, it may cause blindness. Thus they contain preservatives like benzalkonium chloride. They are sterilized in final container to maintain proper sterility of the product.

12 Why eye drops should be isotonic with lacrimal secretions?

i. If eye drops are not isotonic with lacrimal secretions, it will produce irritation to the eye.
ii. In case of hypertonic solution, it will draw water from eye tissues towards the site of solution applied.
iii. In case of hypotonic solution water will pass through the tissues of the eye from the site of application.

13 Why YSP is used instead of WSP in eye ointment?

Because WSP is prepared from YSP by bleaching with oxidising agent and acids. If the product is not thoroughly washed, traces of these may remain in WSP. This causes irritation and toxicity to the delicate tissues of eye. Hence YSP is used instead of WSP.

CHAPTER 17

Immunological Products (Sera, Vaccines, Toxoids)

1 Define the terms.

- **Immunity:** Immunity is the power of the body to resist effect of invasion of pathogenic micro-organism in the body.
- **Immunology:** The branch of science which deals with study of immunity is called immunology.
- **Immunological products:** These are the preparations having immunogenic properties which are used for the prevention of disease or treatment of disease and for diagnostic purposes.
- **Susceptibility:** It means an ability of the body to resist infection caused by pathogenic micro-organism.
- **Virulence:** It means an ability of the organism to produce infection.
- **Antigens:** Antigens are the substances which when introduced in the body stimulate the production of antibodies.
- **Antibodies:** These substances formed in response to the stimulation of antigens in the body.
- **Vaccines:** Vaccines are the preparations containing antigens which stimulate the body to produce antibodies, e.g. BCG vaccine, cholera vaccine.
- **Toxins:** The pathogenic bacteria during their growth in a liquid media release a toxic substance known as "toxin".
- **Toxoids:** When toxic properties of the toxin are destroyed by heat treatment or chemical treatment without loss of antigenic properties, such preparations are called toxoids, e.g. diphtheria toxoid, tetanus toxoid.
- **Antitoxin:** It means an antibody produced in response to and capable of neutralizing a specific biological toxin, e.g. diphtheria antitoxin, tetanus antitoxin.

- **Antisera:** These are the preparations from native sera containing specific immunoglobulins that have prophylactic or therapeutic action when injected into the person's body, e.g. rabies antiserum.
- **Pathogens:** These are organisms capable of causing infection.
- **Carrier:** Carrier is an individual which carries and transmits pathogens but does not display himself the clinical symptoms of the disease.

2 Explain various factors responsible for immunity?

☞ **Factors responsible for producing immunity in human beings:**

1. Phagocytosis.
2. Antibody formation.

1. Phagocytosis:

Phagocytosis means the ingestion of bacteria by certain cells of the body, which make them harmless.

Phagocytosis is caused by two types of body cells:

(a) Cells of reticuloendothelial system:

- This system is present in the liver and spleen
- These cells ingest the bacteria and make them harmless.
- From the blood circulation such harmless micro-organisms enter lungs and disintegrate there.

(b) WBCs (white blood corpuscles):

- WBCs help in the destruction of bacteria.
- When pathogenic bacteria enter the body, most of the leucocytes are carried to the infected area.
- They remain at the site of infection, ingest the bacteria and make them harmless.
- Leucocytes with their enclosed harmless micro-organisms help in the formation of pus.

2. Antibody formation:

- Antibodies may be defined as substances formed in the body in response to the presence of foreign proteins and certain other material in the tissues.
- The production of antibodies in the body is stimulated by the invasion of pathogenic micro-organisms.

- The nature of antibodies depends upon the manner in which pathogenic micro-organisms produce their harmful effects.
- For this purpose, pathogenic micro-organisms may be divided into the following two groups:

(a) Bacteria producing exotoxins:

- During their growth, some pathogenic bacteria form poisonous substances which diffuse through the bacterial cell wall into the medium in which they are growing, hence called exotoxins.
- These exotoxins are carried to all parts, thus producing harmful effects.
- In response to these exotoxins, the human body produces antibodies to neutralize its effect.
- The antibodies which are capable of neutralising the exotoxin are called antitoxins.

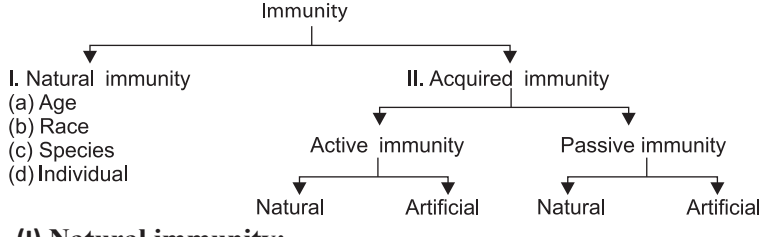
(b) Bacterial producing endotoxins:

- The toxins produced by some pathogenic microorganism do not diffuse through the bacterial cell wall, but it remains in the cell of the bacteria and, therefore, called endotoxins.
- Endotoxins are liberated only when the bacteria are disintegrated.
- In such cases the antibodies produced should be very effective against such bacteria.
- According to the mode of action endotoxins are:
  - **(i) Opsonins:** Antibodies which make the bacteria more susceptible to phagocytosis are called opsonins.
  - **(ii) Agglutinins:** Antibodies which cause agglutination of the bacteria are called agglutinins.
  - **(iii) Precipitin:** Antibodies which precipitate the endotoxins are called precipitin.
  - **(iv) Bacteriolysin:** Antibodies which prepare bacteria for lysis.

3 Distinguish/difference between "exotoxins and endotoxins".

Exotoxins	Endotoxins
1. They diffuse freely through bacterial cell wall into the medium	1. They are retained within the bacteria and freed only when cells die.
2. They are the products of metabolism of active bacteria	2. They are the structural elements of bacteria.
3. They mainly produced by Gram-positive bacteria	3. They are more found in Gram-negative bacteria
4. They are high molecular weight proteins.	4. They are complexes of phospholipids and polysaccharides
5. They are thermo-labile. They lose activity when heated to 60°C.	5. They are thermostable
6. They are extremely toxic to body.	6. They are less toxic to the human body
7. These toxins are carried to all parts of the body.	7. Endotoxins are liberated only when the bacteria are disintegrated.
8. For example: Diphtheria antitoxins	8. Diphtheria toxoid

4 Define and Explain types of immunity/classify immunity.



(I) Natural immunity:

This immunity is possessed by an individual naturally due to following factors:

1. **Age:** Majority of children in the age group between 2 and 5 years are susceptible to diphtheria disease, whereas adults are immune to it.

2. **Race**: The Negroes have a high resistance to yellow fever and white races are very susceptible to it.
3. **Species:** Men are susceptible to typhoid fever, whereas mice are immune to it. Fowls are immune to plague, whereas men are susceptible to it.
4. **Individuals:** Some persons have more resistance against cold and skin diseases than others.

(II) Acquired immunity:

Acquired immunity is acquired by an individual during his lifetime by producing antibodies in the body.

(a) Active immunity:

In this case body takes an active part in the formation of antibodies to develop resistance against disease.

i. Naturally acquired active immunity:

- The immunity is acquired as a result of infection by the causative organisms.
- The pathogenic micro-organisms may be virulent or attenuated.
- The infection stimulates the body to produce antibodies, which remain in the body to immune the person.
- This immunity may last for a lifetime, e.g. smallpox, polio, etc

ii. Artificially acquired active immunity:

- When antigenic substances such as vaccines are introduced into the body, it stimulates the body to produce antibodies and thus, immunity is produced in the body.
- The artificial active immunity is produced by injecting attenuated living micro-organisms, dead bacteria and bacterial derivatives. This process is also called immunisation.

(b) Passive immunity:

- In this case body does not play an active role in having immunity against a disease.
- Ready-made antibodies are introduced into the body to produce antibodies.

i. Naturally acquired passive immunity:

- Children aged less than a month are generally immune to certain infectious diseases. This is because they have received the antibodies from the mother.

- These antibodies then gradually disappear and the children become susceptible to infectious disease until they acquire active immunity either by natural or by artificial method.

ii. Artificial acquired passive immunity:

- This immunity is produced by injecting ready-made antibodies containing preparation (antiserum, sera) into the body.
- The passive immunity lasts for a short time only.

5 Distinguish/Difference between "active immunity and passive immunity".

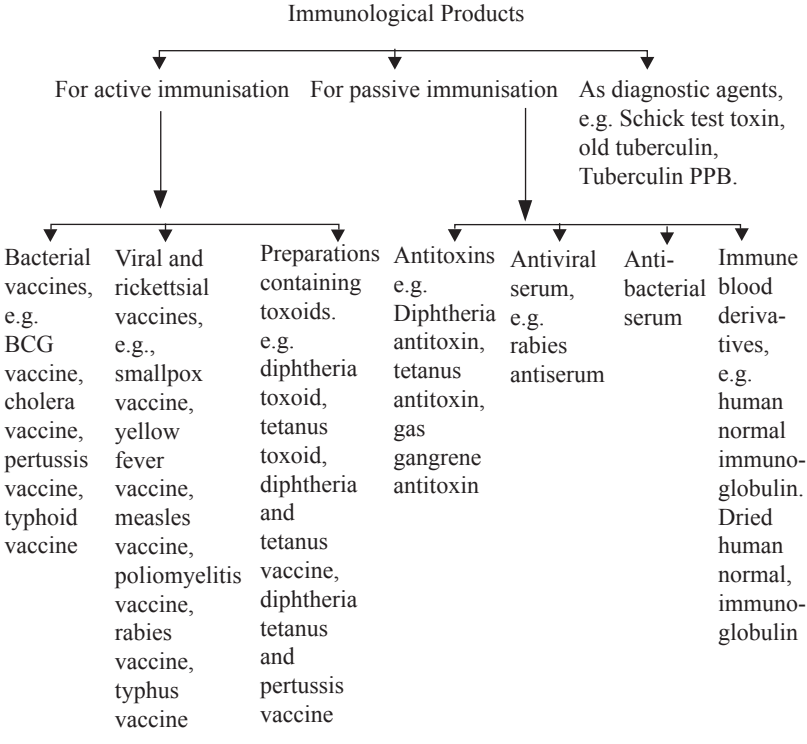
Active immunity	Passive immunity
1. Antigens are injected in the human body, as a result antibodies are formed	1. Ready-made antibodies are injected in the human body
2. It develops slowly.	2. It develops quickly
3. It remains for a longer time	3. It remains for a short period
4. The treatment is preventive	4. The treatment is therapeutic
5. Immunological memory is present	5. Immunological memory is absent
6. Not useful in immunodeficient hosts	6. Useful to immunodeficient hosts
7. No inheritance	7. May be acquired from mother
8. Preparations, e.g. vaccines, toxoids	8. Preparations, e.g. sera, antiserum.

6 Define and classify immunological products.

☞ **Immunological products:**

These are the preparations having immunogenic properties which are used for the prevention of disease or treatment of disease and for diagnostic purpose.

Classification of Immunological Products



7 What is BCG vaccine? How BCG vaccine is prepared by freeze drying method?

☞BCG vaccine (freeze dried):

It is a freeze dried preparation containing live culture of the Bacillus of Calmette and Guérin strain of *Mycobacterium tuberculosis*.

- **Method of preparation of BCG vaccine:**
  - The bacilli are grown on a suitable culture media until 1 mg when plated out on suitable solid culture media, shows less than 20 million colonies.
  - The growth period should not be more than 14 days in any case.
  - After suitable growth, they are separated by filtration in the form of a cake.

- The cake is homogenised in a grinding flask, and suspended in a suitable sterile liquid medium designed to preserve the antigenicity and the viability of the vaccine.
- The suspension is transferred into the final sterile containers and freeze dried.
- The containers are sealed so as to prevent contamination or deterioration of the vaccine.
- The vaccine contains no antimicrobial agent.

- **Storage:** BCG vaccines are stored in light resistant glass containers at a temperature between 2° and 8°C. The reconstituted vaccine should be used immediately after its preparation.
- **Uses:** BCG vaccine is used as an immunizing agent which provides protection against tuberculosis.
- **Dose:** Prophylactic 0.1 ml as a single dose by intracutaneous injection.

8 Give the method of preparation of "smallpox vaccine".

☞ **Smallpox Vaccine (freeze dried):**

Smallpox vaccine contains living attenuated vaccinia virus
Smallpox vaccine is prepared by two methods: (a) By using eggs and (b) by using animals.

(a) By using eggs:

Hen egg is used
(which is incubated after 12 days)
↓
Small cut on the shell
(exposed chorioallantoic membrane)
↓
In this membrane, viruses are innoculated
(by seed of known potency)
↓
Cut was sealed by flap or paraffin wax
↓
Again incubate for 72 hours
↓
Using aseptic condition, shell is removed and chorioallantoic membrane is separated.

↓

Contents are added in normal saline solution at 0°C

↓

Add 50% glycerin

↓

Material is ground to produce homogenized suspension.

↓

Transfer to suitable sterile container and freeze dried.

(b) Smallpox vaccine preparation by using animals:

The smallpox vaccine is prepared by using calves or sheep.

1. **Selection of animal free from disease:**
   - Healthy calves or sheep are used for the production of vaccine.
   - The animals are kept for 10–14 days in an isolated area under observation to prevent them from communicable diseases.
2. **Preparation of animal for scarification:**
   - The abdomen and flanks (the sides of the body between ribs and ilium) are thoroughly scrubbed, washed and disinfected.
   - The animals taken to a special room where abdomen and flanks are shaved, scrubbed and then thoroughly disinfected.
3. **Inoculation:**
   - Light incisions are made in the cleared skin without drawing blood with the help of scarifier.
   - The scarified area is then rubbed with some of seed vaccine of known potency.
4. **Incubation:**
   - During next 7–9 days pustules or vesicles form along the line of scarification.
   - During the incubation period, every precaution is taken to keep the animal as clean and aseptic as possible.
   - Animals showing sign of disease is rejected.
5. **Collection of viruses:**
   - The animal is taken to the operation table and killed.
   - A postmortem on the animal is made to check the absence of disease not detected otherwise.

- The abdomen and flanks are then washed with sterile water.
- The material in the pustules is withdrawn with the help of a sharp-edged spoon under aseptic condition.

6. **Purification:**
   - The contents of pustules are mixed with equal volume of glycerin, cooled and then finely ground to form homogeneous mixtures.
   - It is then stored for a long time at –10°C to remove impurities.

- **Storage of smallpox vaccine:**
  The smallpox vaccines are stored at a temperature between 2° and 8°C. The reconstituted vaccine may be expected to retain its potency for 7 days when kept at temperature between 2° and 8°C.
- **Uses of smallpox vaccine:**
  The smallpox vaccine is used for a small number of laboratory workers who are likely to have contact with vaccinia virus and for travellers to those countries which require vaccination as a condition for entry.
- **Dose of smallpox vaccine:**
  For prophylaxis of smallpox, about 0.02 ml is applied to the skin and innoculated by scarification or pressure.

9 What are antitoxins? Give the method of preparation of diphtheria antitoxin.

☞ **Antitoxins:** Antitoxins are the antibodies which are capable of neutralizing the specific toxin (causative agent of the disease).

Diphtheria Antitoxin:

Method of preparation:

1. **Preparation of toxin for active immunisation of horse:**
   - A pure culture of *Corynebacterium diphtheriae* is grown in a suitable culture media at 37°C for 4–7 days.
   - After incubation, 0.5% phenol is added and the culture media is filtered through bacteria proof filters.
   - The filtrate is a crude toxin and is converted into toxoid.

2. **Selection of horse:**
   - The horse selected must be free from disease.
   - The horses are kept in an isolated place for 7 days and then carefully examined.
   - They are immunised against tetanus by injecting tetanus toxoid.
3. **Active immunisation of the horse:**
   - To the selected horses diphtheria toxoid is given for active immunization.
   - The toxoid is given by IM route in the gradually increasing doses.
   - The first dose is 5 ml and further injections are given at the intervals of 2–3 days by doubling the dose.
   - In this way the volume of last dose is about 600 ml.
4. **Separation of serum from the horse:**
   - After a period of about 10 days from the final dose. The blood is collected under aseptic conditions to see the adequate antitoxin has been obtained.
   - Eight liters of blood is collected three times during a period of 8 days.
   - Further injections of diphtheria toxoids are given as per the past schedule to stimulate the production of antibodies and blood is collected as per previous stop.
   - After the collection, the blood is allowed to clot to separate the serum.
   - The serum contains antitoxin along with proteins such as beta-globulins, gamma-globulins and albumins.
5. **Concentration and refinement:**
   The serum is concentrated by fractional precipitation of the proteins and finally the preparation is freeze dried without any preservative.
   - **Storage of diphtheria antitoxin:**

   It is stored in containers protected from light at a temperature between 2° and 8°C. It should not be allowed to freeze.
   - **Dose of diphtheria antitoxin:**

   It is administered by SC or IM injection in the following dose schedule:

   (i) Prophylactic: 500 to 2000 international units.

   (ii) Therapeutic: Not less than 10,000 international units.

10 Give the method of preparation, storage, uses and dose of the following.

(a) Cholera vaccine
(b) Pertussis vaccine
(c) Typhoid vaccine
(d) Yellow fever vaccine
(e) Measles vaccine live
(f) Poliomyelitis vaccine (oral)
(g) Rabies vaccine
(h) Typhus vaccine
(i) Tetanus toxoid
(j) Diphtheria and tetanus vaccine (absorbed)
(k) Diphtheria, tetanus and pertussis vaccine (absorbed)
(l) Tetanus antitoxin
(m) Gas gangrene antitoxin
(n) Rabies antiserum.
(o) Human normal immunoglobulin

(a) Cholera Vaccine:

Cholera vaccine is a colourless, whitish or slightly coloured opalescent liquid.

It is a sterile suspension of killed cholera vibrios (*Vibrio cholerae*) of a strain selected for high antigenic property and purity.

Preparation: It is prepared from equal portions of suspensions of *cholera vibrious* of *Vibrio cholerae* Inaba and Ogawa strains selected for high antigenic efficiency. Either a single strain or several strains of each type may be used.

Each strain of cholera vibrios is grown separately on a solid medium for 24 to 48 hours. Bacteria are then washed with normal saline solution. The suspension of bacteria thus obtained is killed either by heating at 56°C for one hour or adding alcohol or other bactericide, such as, phenol or formaldehyde. All precautions must be taken to ensure that the antigenic property of the preparation is not destroyed. The preparation is then standardised so that 1 ml of vaccine contains not less than 12,000 million bacteria. After adding a suitable preservative, it is transferred into final containers and then sealed.

The vaccine must comply with the tests for sterility and also the test for undue toxicity of vaccine.

Storage: Store at a temperature between 2° and 8°C.

Uses: It is used for immunisation against cholera. But it has a limited use as it has only about 50% effectiveness for a period of 3 to 6 months. The vaccine does not prevent transmission of the disease.

Dose: Prophylactic initial dose 0.5 ml; second dose, 1 ml after an interval of 4 to 6 weeks.

(b) Pertussis Vaccine (Whooping Cough Vaccine):

It is available as more or less turbid, whitish liquid nearly odourless or having faint odour due to antimicrobial agent.

Pertussis vaccine is a sterile bacterial suspension of killed pertussis bacilli (*Bordetella pertussis*) of a strain or strains selected for high antigenic efficiency.

Preparation: It is prepared by culturing *Bordetella pertussis* in a suitable culture media. It is separated, washed and suspended in normal saline solution. The bacteria are killed either by heating or by adding some chemicals. The suspension is standardised. The vaccine may show abnormal toxicity in animal tests and this is removed by cold storage for up to three months.

Storage: Store at a temperature between 2° and 8°C.

Uses: For active immunisation of children against whooping cough especially when diphtheria and tetanus toxoids and pertussis vaccine (DPT) cause untoward reaction or is contra-indicated.

Dose: It is administered by subcutaneous injection in three doses of 0.5 ml, 1.0 ml and 1.5 ml at least 4 weeks apart.

(c) Typhoid vaccine:

Typhoid vaccine is white or creamy white turbid liquid free from clumps.

It is a sterile suspension prepared from one or more strains of *Salmonella typhi* that are smooth and have the full components of OH and VI antigens.

Preparation: *Salmonella typhi* organisms are grown on a suitable culture media. The bacteria are killed by heat or by a bactericide such as phenol, formaldehyde or by a chemical such as acetone. It is then standardised, so that 1.0 ml of the typhoid vaccine contains not less than 1000 million bacteria (*S. typhi*).

The vaccine must comply with tests for sterility and the test for undue toxicity for vaccine.

Storage: Store at a temperature between 2° and 8°C. The vaccine must not be frozen.

Uses: It is used for immunisation against infections caused by typhoid bacilli.

Dose: Prophylactic, initial dose 0.5 ml followed by second dose of 1.0 ml by subcutaneous injection after an interval of 4 to 6 weeks.

(d) Yellow Fever Vaccine:

It is white, slightly yellow or light brown scale or powder. The vaccine is prepared before use by reconstitution of the dried vaccine with normal saline solution.

Yellow fever vaccine is an aqueous suspension of chick embryo tissue infected with the strains of yellow fever virus which is virulent for mice, but although a virulent for man, still retains its immunising efficiency.

Preparation: The virus is injected into the embryo of fertile eggs which have been incubated for 7–8 days. After incubation for further 3 to 4 days, the embryos are removed pooled in batches, ground and then extracted with purified water. The suspension is then centrifuged. The supernatant liquid is separated to which a suitable preservative may be added. It is then distributed into sterile glass ampoules and freeze dried. The air is removed from the ampoules or replaced by oxygen free nitrogen before these are sealed.

Storage: Yellow fever vaccine is stored in the dark at a temperature of approximately 0°C. The vaccine loses its potency within a few days if it is stored at a high temperature.

Uses: It stimulates production of antibodies against yellow fever. Immunity develops within 7 days after vaccination and lasts for several years. Use of vaccine is recommended in the age group of 6 months or older, travelling or living in areas where yellow fever infection exists.

Dose: Prophylactic, by subcutaneous injection not less than 1000 LD50 doses.

(e) Measles Vaccine Live:

The vaccine is white or nearly white friable mass.

Measle vaccine live is a bacterially sterile aqueous suspension of a suitable live attenuated strain of measles virus grown on cultures of chick embryo cells.

Preparation: The strain of attenuated measles virus used in the manufacture of live vaccine is tested on the monkeys for freedom from neurovirulence. The strain is grown with aseptic precautions in cultures of chick embryo cells. The chick embryos are derived from healthy and pathogens free flocks. Only cultures of primary cells are used in the manufacture of the vaccine. The growth of virus is done within 14 days of inoculation. The virus suspension is tested for identity, sterility and for being free from adventitious viral agents.

The cultures which pass these tests are pooled and clarified to remove intact tissue cells. A suitable stabiliser is added and it is distributed into sterile containers freeze dried and sealed. The vaccine must comply with the test for sterility and also the test for undue toxicity.

Storage: The vaccine is stored in single dose in light resistant containers at a temperature between 2°C and 8°C.

The reconstituted vaccine should be used immediately after preparation.

Uses: It produces active immunity against measles in approximately 99% of recipients of a single dose. The immunity lasts for many years after vaccination.

Dose: Paediatric, by subcutaneous injection 0.5 ml of reconstituted vaccine.

(f) Poliomyelitis Vaccine (Oral):

It is clear liquid which may have a reddish colour if phenol red has been used in its preparation.

Poliomyelitis vaccine (oral) is an aqueous suspension of one or a combination of 2 or 3 types of live attenuated strains of poliomyelitis virus tested for neuro virulence on monkeys. It is a polyvalent vaccine.

Preparation: It is prepared by using three strains of poliomyelitis virus type I, II and III. The virus of each type is grown separately in cultures of suitable tissue with aseptic precautions. The tissue should be free from extraneous micro-organisms and adventitious agents. Suitable antibiotic other than penicillin and streptomycin may be used in small concentration. The medium is maintained at a temperature not exceeding 35°C during the growth of the virus.

The growth of the virus is done within four days of inoculation and the virus suspension is tested for identity, sterility and freedom from adventitious viral agents. The final vaccine is prepared by combining the appropriate dilutions of three virus types and by the addition of approved bactericide.

The vaccine must comply with the tests for sterility and the test for undue toxicity for vaccine.

Storage: The vaccine is stored in single dose or multidose containers in the frozen state at –28°C or below. When it gets melted it should be kept at a temperature of 0° to 40°C and used within three months. If stored at a temperature between 18°C and 20°C, it should be used within a few hours.

Uses: It is used to produce active immunisation against poliomyelitis.

Dose: The dose of each type of monovalent vaccine 6 to 8 weeks apart and a fourth reinforcing dose of the trivalent vaccine, 8 to 12 months later.

(g) Rabies Vaccine

The vaccine is white, flocculent suspension in a clear liquid or white to brownish or white turbid liquid.

Rabies vaccine is a sterile suspension in saline or other appropriate solution, isotonic with blood of a suitable killed rabies virus in uncontaminated brain tissues from animals previously injected intracerebrally with rabies virus.

Preparation: It is prepared by injecting sheep, rabbit, sucking rats mice or other animals intracerebrally with rabies virus. The animals which show typical paralysis are killed. The brains are harvested under aseptic condition, tested for absence of bacteria and then finally suspended in sodium chloride injection or any other suitable liquid. The suspension is inactivated by using phenol or beta propiolactone or any other means until the virus will no longer infect mice. It is diluted to produce a vaccine of required strength. The vaccine is preserved by adding 0.01% w/v thiomersal. The pH is adjusted between 7.0 and 7.2. It is then transferred into sterilised containers and sealed. The vaccine must comply with the tests for sterility and the test for undue toxicity of vaccines.

Storage: The vaccine should be stored in containers protected from light and at a temperature between 2°C and 8°C. It should not be used until the absence of live virus has been established.

Uses: It is used as prophylactic against rabies, either for post-exposure immunisation of person bitten by rabid animals or pre-exposure immunisation of high risk individuals.

Dose: By subcutaneous injection 1 to 5 ml daily for 7 to 14 days according to the site and severity of the bite and the risk of exposure to infection.

(h) Typhus Vaccine:

Typhus vaccine is a sterile suspension of the killed rickettsia organisms of a strain or strains of epidemic typhus rickettsia (*Rickettsia prowazeki*) selected for antigenic efficiency.

Preparation: It is prepared by injecting virulent rickettsia into the yolk sacs of fertile eggs which have been incubated for 7 days, within a period of 9–13 days after injection, the yolk sacs are collected under aseptic conditions. It is subjected to suitable treatment to liberate the maximum number of rickettsia. The material is suspended in normal saline solution. Formaldehyde solution is added, so that its concentration is between 0.2 and 0.5%. The suspension containing 10 to 15% w/w of yolk sac tissue is purified with solvent ether. The aqueous middle layer is collected and distributed into sterile containers under aseptic precautions. The vaccine must comply with tests for sterility and the test for undue toxicity for vaccines and sera. The vaccine can also be prepared from the lungs of small rodents in which rickettsial pneumonias have been caused by inhalation of large doses of virulent rickettsia or by giving intraperitioneal injections of rickettsia.

Storage: Store at a temperature between 2°C and 8°C.

Uses: Typhus vaccine is used as a prophylactic agent to protect against epidemic typhus. It is not effective against endemic typhus.

Dose: Prophylactic by subcutaneous injection, 0.25 to 1.0 ml.

(i) Tetanus Toxoid:

This is prepared from the exotoxin of *Clostridium tetani*, the specific toxicity of which has been completely removed by the action of chemical substances in such a way that it retains its antigenic properties.

Tetanus toxoid is available in the following forms–

1. Formal toxoid (FT): It is prepared by treating the sterile culture filtrate of *Clostridium tetani* with formaldehyde solution.

2. Alum precipitated tetanus toxoid: It is prepared by adding alum to tetanus toxoid in simple solution in the proportion which is necessary to produce a suitable precipitate. The precipitates are separated, washed and suspended in normal saline solution.

(j) Diphtheria and Tetanus Vaccine (adsorbed):

It is white turbid liquid, and is a sterile suspension of purified diphtheria vaccine and purified tetanus vaccine adsorbed on a mineral carrier, such as aluminium hydroxide or aluminium phosphate.

Preparation: The vaccine is prepared by mixing purified diphtheria toxoid containing not less than 1500 flocculation equivalents (1500 LF) and purified tetanus toxoid containing not less than 1000 flocculation equivalents (1000 LF) per mg of protein nitrogen with a suspension of aluminium hydroxide or aluminium phosphate in a normal saline solution. The vaccine contains a preservative other than any of the phenol or cresol groups. The vaccine must comply with tests for sterility and the test for undue toxicity for vaccines and sera.

Storage: The vaccine is stored in single dose or multidose containers at a temperature between 2°C and 8°C. The vaccine should not be frozen.

Uses: The vaccine is used to provide simultaneous active immunisation against both diphtheria and tetanus. The product should not be used after the age of 6 years since the diphtheria toxoid present in vaccine may cause undesirable reactions.

Dose: The vaccine is administered in 3 doses by deep intramuscular injection. The first dose of 0.5 ml followed by a second dose of 0.5 ml after 4 to 6 weeks and a third dose of 0.5 ml 6 to 8 months later.

A dose of 0.5 ml of vaccine contains not less than 15 LF of diphtheria toxoid and not more than 5 LF of tetanus toxoid.

(k) Diphtheria, Tetanus and Pertussis Vaccine (adsorbed):

It is a white sterile suspension prepared by adsorbing form—aldehyde treated diphtheria toxoid and tetanus toxoid on a mineral carrier, such as, aluminium hydroxide or aluminium phosphate and adding a suspension of killed *Bordetella pertussis*.

Preparation: The diphtheria toxoid containing not less than 1500 flocculation equivalents (1500 LF) and tetanus toxoid containing not less than 1000 flocculation equivalents (1000 LF) per mg of protein nitrogen are added to a suspension of hydrated aluminium phosphate on aluminium hydroxide in a normal saline solution. It is then mixed with a quantity of suspension of killed *Bordetella pertussis* so that the final product contains not more than 20×10^9 bacilli in each dose. A suitable preservative other than of phenol or cresol group is added. The vaccine must comply with tests for sterility.

Storage: It is stored in a single dose or multiple dose containers at a temperature between 2°C and 8°C. The vaccine should not be frozen.

Uses: The vaccine is used for simultaneous immunisation against diphtheria, tetanus and pertussis in infants and small children. The preparation is not generally used after the 6th years of age.

Dose: The vaccine is administered in 3 doses by intramuscular injection. The first dose of 0.5 ml followed by a second dose of 0.5 ml after 4 to 6 weeks and a third dose of 0.5 ml 6 to 8 months later.

(l) Tetanus Antitoxin:

It is almost colourless or a very faintly yellow liquid.

Preparation: It is prepared in the same way as diphtheria antitoxin. The toxin is obtained from *Clostridium tetani* which is used for active immunisation of the horse.

Tetanus antitoxin has a potency not less than 1000 international units per ml when intended for prophylactic use and not less than 3000 international units per ml when intended for therapeutic use.

Storage: Same as diphtheria antitoxin.

Dose: It is administered by Sc or Im injection in the following dose schedule.

(i) *Prophylactic*: Not less than 1500 international units.

(ii) Therapeutic: Not less than 50,000 international units.

(m) Gas Gangrene Antitoxin:

It is almost colourless or a very faintly yellow liquid, free from turbidity. It is a preparation containing the specific antitoxic globulins obtained by purification from native serum and

having the specific power of neutralising the toxin formed by *Clostridium oedematiens* or *Clostridium perfringens*.

It has a potency of not less than 3750 international units per ml.

Storage: Same as that of diphtheria antitoxin.

Dose: It is administered by intravenous or intramuscular injection.

(i) *Prophylactic*: 10,000 international units.

(ii) *Therapeutic*: Not less than 30,000 international units.

(n) Rabies Antiserum:

It is almost colourless or faintly yellow, slightly opalescent liquid free from suspended particles.

Preparation: The suspension of dead rabies viruses is injected into healthy horses. After a specified time period, the blood is collected and by a suitable method, the gamma globulin is separated which contains antiviral antibodies (same as diphtheria antitoxin).

It contains the specific neutralising power equivalent to not less than 80 international units per ml.

Storage: It is stored in single dose or multidose containers at a temperature between 2°C and 8°C. It is protected from light. It is not allowed to freeze.

Uses: It is used along with vaccine for preventing rabies when a person is bitten in an area, such as, the head or neck by a rabid dog or any other rabid animal.

Dose: By *Im* or *Sc* injection, 40 international units per kg of body weight.

(o) Human Normal Immunoglobulin:

It is a transparent or slightly opalescent liquid, colourless or brownish in colour which on storage may show a slight granular deposits.

It is a sterile solution containing antibodies derived from human blood. It contains gamma-G globulins together with smaller amounts of other plasma proteins obtained from blood, blood plasma or blood serum of healthy donors.

Preparation: It is prepared from the pooled material of a minimum quantity of 25 litres which is collected from about 1500 donors. The globulins are separated and are dissolved in a vehicle having a suitable preservative or a stabilising agent.

It is sterilised by filtration through bacteria proof filter and distributed to the final containers which are then sealed.

Storage: The preparation is stored in colourless, glass containers protected from light at a temperature between 2°C and 10°C.

Uses: The preparation is used for the prevention of measles in small children, infective hepatitis and rubella in a pregnant woman.

Dose: By intramuscular injection, a volume equivalent to the following amounts of protein is administered:

(i) For the prevention of measles: 250 mg for infants under one year of age, 750 mg for children aged three years and for attenuation of measles 250 mg.

(ii) For the prevention of rubella in pregnant women 750 mg.

(iii) For the prevention of infective hepatitis, 250 mg up to 10 years of age and 750 mg over 10 years.

11 Explain "Schick test".

☞ SCHICK TEST:

The Schick test is performed to test degree of immunity of an individual against diphtheria. For this test Schick test toxin is required.

(a) Schick Test Toxin:

It is a clear, colourless liquid or very pale straw coloured liquid, which is used in the Schick test to determine susceptibility to diphtheria.

Preparation: It is a sterile filtrate, prepared from a culture of *Corynebacterium diphtheriae* grown on a sterile liquid medium. The filtrate contains diphtheria exotoxin. It is then diluted so that the test dose is contained in 0.1 ml or 0.2 ml with a diluent isotonic with blood and containing suitable bactericides and stabilisers. It is then distributed into sterile containers which are sealed in order to exclude the micro-organism.

Storage: It is stored at a temperature between 2°C and 10°C.

Dose: 0.1 ml by intradermal injection.

(b) Schick Control or Schick Test Control:

It is a transparent liquid. Schick control is in fact a Schick test toxin of it is destroyed by heating at a temperature between

70°C and 85°C for 5 minutes. The Schick control must be prepared from the same batch of Schick test toxin as that with which it is to be used.

Storage: It is stored at a temperature between 2°C and 10°C.

Dose: 0.1 ml by intradermal injection.

Method of Schick Test:

- Schick test toxin is injected intradermally into the left forearm and at the same time an equal volume of Schick control is given into the right forearm.
- The arms are examined after 48 hours.
- The possible observations of the test are as follows:

S. No.	Left arm (Schick test toxin)	Right arm (Schick control)	Explanation	Result
1.	Large flushed area	No reaction	Toxin is not neutralised	Not immune
2.	No reaction	No reaction	Toxin is neutralised	Immune
3.	Large flushed area	Smaller flushed area	Not neutralised sensitivity to broth constituents	Not immune
4.	Small flushed area	Small flushed area	Neutralised, sensitivity to broth constituents	Immune and a pseudo-reactor

- From the above observation, it is concluded that a true positive persists longer than a pseudo-reaction and, therefore, the results at Sr. No. 3 and 4 in the above observation table are re-examined after a week when the false results would have faded.

12 Write a note on "tuberculin tests".

☞ Tuberculin Tests:

Tuberculin tests are performed to detect the immunity or susceptibility to tuberculosis.

1. **Mantoux test:** A dose of 5 tuberculin units of old tuberculin or an equivalent dose of PPD is injected intradermally. After 48 to 72 hours the reaction of the test is observed at the site of the injection. A positive reaction consists of a raised indurated area. Induration measureing 10 mm or more is interpreted as positive for past or present infection with *Mycobacterium tuberculosis.* Induration of 5 to 9 mm is regarded as a doubtful significance. The induration of less than 5 mm is interpreted as a negative. The presence of erythema without induration is not significant.
2. **Tine test:** In this test, a stainless steel disc with four tines (teeth) 2 mm long is attached to a plastic handle. The tines are dipped into the solution of old tuberculin containing acacia and lactose as stabilisers. These are then dried and sterilised using ethylene oxide gas.
   The uncovered disc is placed over the volar surface of the upper 1/3rd of the patient's forearm, over a muscle belly and a sufficient pressure is exerted on the plastic handle so that the four puncture site of the tines and a circular depression of the skin from the plastic base are visible. The criteria for evaluating the reactions are same as used in the Mantoux test.

13 State various quality control tests for "Immunological products."

☞ Quality Control Tests for Immunological Products:

1. **Increase in virulence tests:** All live vaccines should be tested for virulence. The most commonly used measurement of virulence is the lethal dose required to kill 50% of infected hosts, referred to as the LD_{50}. The LD_{50} measurement allows comparisons across microbes, and the use of host death provides a non-equivocal endpoint

2. **Assessing risk to the environment:** The ability of each live vaccine to shed, to spread to contact target and non-target people, and to persist in the environment must be evaluated to provide information for assessing the risk of the vaccine to the environment, taking into account human health.
3. **Interference tests:** For products with two or more antigenic components, tests are conducted to confirm that there is no interference between individual components, that is, one component causing a decrease in the protective immunological response to another component.
4. **Consistency of production:** Prior to marketing approval of any new product, each establishment should produce in its facilities three consecutive production batches of completed product to evaluate the consistency of production.
5. **Stability tests:** Stability studies (based on an acceptable potency test) are performed to establish the validity of the expiry date of the product.
6. **Batch purity test:** Purity is determined by testing for a variety of contaminant. Tests to detect contaminant are performed on master seeds, primary cells, MCSs (master cell stocks), ingredients of human origin, if not subjected to sterilisation, and each batch of final product prior to release.
   (a) **Batch safety test:** Batches are considered satisfactory if local and systemic reactions to vaccination with the batch to be released are in line with those described in the registration dossier and product literature.
   (b) **Batch potency test:** Batch potency tests are required for each batch prior to release. These are designed to correlate with the host animal vaccination-challenge efficacy studies.

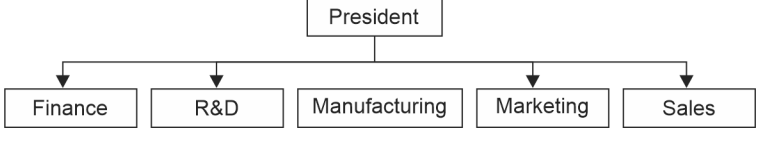
CHAPTER 18

Pharmaceutical Industry and Basic Concepts

1 Give the basic structure of pharmaceutical manufacturing plant.

☞ **Structure of pharmaceutical manufacturing plant:**

- The basic requirement of any manufacturing plant is personnel and their functions
- In pharmaceutical company there is a hierarchy of job positions, designations and roles.
- All the jobs and departments together are responsible for the success and profit of the organization.
- The organization structure of a "typical pharmaceutical plant" is categorized as:
  (i) Functional structure
  (ii) Product-oriented structure
  (iii) Matrix structure
- The basic functional structure of pharmaceutical manufacturing plant is as follows:



Organizational structure of pharmaceutical manufacturing plant:

An organizational structure is a system that outlines the activities which are directed in order to achieve the goals of an organization. These activities can include rules, roles and responsibilities. The organization structure also determines how information flow between levels within the company.

The hierarchical structure followed within a pharmaceutical industry is mainly categorised into three positions:

(a) Seniormost level positions:

These positions are administrators, owners, board of directors and important employees who are responsible for overall management and operation of the organization.

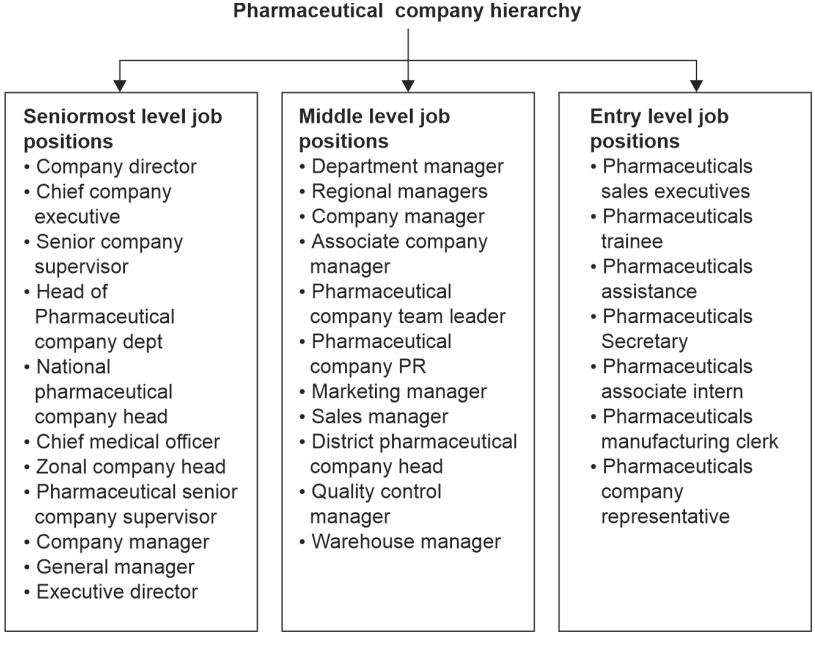
The seniormost position people decide and sets the goals of the organization and responsible for handling financial issues which is an important part of any industry.

(b) Middle level job positions:

These include executives and employees who work under senior level people execute the plans and projects planned and assigned by the senior level employees. They supervise and guide the lower level employees and make sure that the company runs smoothly. The middle level executives hold the most important positions which decide the profit and success results of the company.

(c) Entry level job positions:

These include the peoples who are vital part of the industry and are responsible for day-to-day work but does not hold important roles.

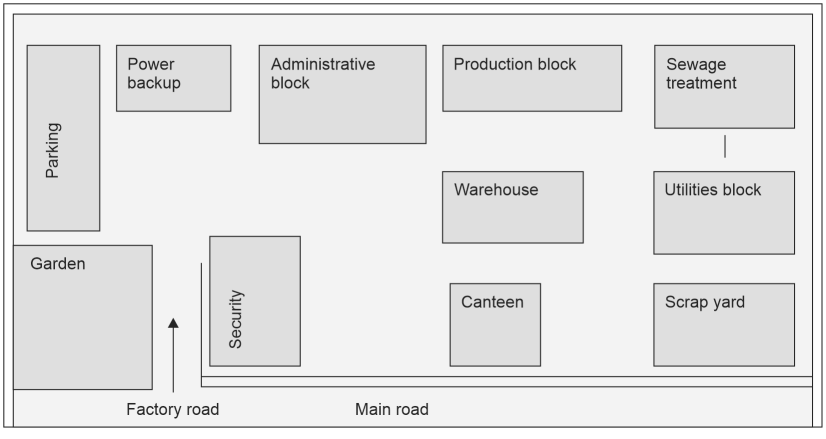


2 Give layout of pharmaceutical plant/ industry. Mention the feature/characteristics of good pharmaceutical plant.

☞ **Pharmaceutical plant layout:**

It is defined as the method of allocating machines and equipment, various production processes and other facilities to perform efficient operations and produce output of high quality and minimum cost.

Pharmaceutical plant layout:



Features/characteristics of a good pharmaceutical plant:

A good pharmaceutical plant layout should possess the following characteristics:

1. There should be adequate floor space for machines installation and utilization.
2. Machines should be properly arranged to facilitate minimum material handling necessary for low cost processing.
3. The layout should facilitate smooth and continuous flow of production process from one point to another to avoid delays.
4. It must incorporate adequate health, safety and security features, e.g. first aid box, fire extinguisher, emergency exit and access point, etc.
5. The layout should allow effective supervision, coordination and control of the production processes.

6. There should be room for adjustment and modifications whenever the need arises.
7. There should be sufficient space for workers to perform their functions.
8. The store facility for in-process material should be designed to minimize material handling.

3 Give the advantages of pharmaceutical company layout.

A good layout can provide a number of advantages to workers and management. The advantages of pharmaceutical plant layout include:

1. Easy administration and communication amongst the departments.
2. Optimum use of available floor space for production operations.
3. Improved quality of product due to reduced chances of cross contamination.
4. Low cost of material handling and minimized loss due to waste and spoilage.
5. Good working conditions resulting in improved efficiency.
6. Increased productivity with reduced risk of human error and occupational hazards.

4 Explain various sections/ departments in pharmaceutical plant/industry?

The pharmaceutical manufacturing plant/industry works smoothly with the interlinked communications of various sections or departments.

1. Security

Safety officers are appointed as per the factory act. Security services are required for access control, fire prevention, facilities protection, emergency and regular inflow and outflow of personnel from the factory. They are responsible for safety of people working in plant premises.

2. Garden

Gardening and tree plantation at proximity of the industry is important to maintain clean environment.

3. Vehicle parking

Parking is an essential component of the transportation system. There should be separate parking for two- and three-wheelers. The parking area depends upon size, scope and operations in the industry.

4. Power backup

Generating power during interruption of regular power supply, power backup systems are required.

5. Administrative block

Administrative block has cabins for heads of various departments, conference room, directors' room, account sections, library, pantry, etc.

6. Production block

It is the main department/block where the actual manufacturing / production of pharmaceuticals takes place.

These blocks should be designed as the requirement of GMP (schedule M)

7. Sewage treatment

To treat waste water and purify, every manufacturing plant must setup sewage water treatment plants.

8. Utility service departments

The utility system in pharmaceutical plant helps to check the quality and safety of their products and ensures that they comply with laws and statutes in FDA.

9. Canteen

It is usually located at the periphery of the industry.

Employees can have their food in the canteen.

Canteen area has to be maintained under total hygienic conditions.

10. Warehouse

The warehouse is responsible for storage of incoming goods as well as for finished goods.

Proper cleanliness, arrangement and temperature conditions must be maintained in warehouse.

11. Scrap yard

A large amount of scrap/waste material is generated in the industry includes plastic, aluminium, iron rejected components, etc. These scrap materials should be collected properly in this place and disposed of as per standard procedure.

5 Elaborate/describe various activities involved in pharmaceutical manufacturing industry/plant.

Activities involved in pharmaceutical manufacturing industry/plant are:

1. Research and development:

This is one of the critical activities in the drug development in the pharmaceutical plant.

This department is able to research and analyze the products

It involves the following steps:

- Drug discovery
- Clinical trials
- New drug approvals
- Post-marketing monitoring

2. Manufacturing:

This step involves the actual production of drugs on an industrial scale following clinical trials and regulatory approval.

3. Quality assurance (QA):

Quality assurance involves series of actions which collectively ensures product quality. In pharmaceutical marketing, quality assurance ensures that the products are designed and developed in accordance with the requirements of GMP and GLP.

4. Quality control (QC):

Quality control activity is concerned with supplying and testing as well as documentation and release of product procedures.

5. Warehousing:

Warehousing includes proper storage of products to prevent contamination. It preserves the integrity of drug products that affect the health and wellbeing of people.

6. Packaging:

Pharmaceutical packaging operations are of much importance as the packaging may protect the medicament till its utility. Finished products are packaged in different types of containers such as plastic or glass bottles, foil blister packs, pouches, sachets, tubes and sterile vials.

7. Product education and compliance:

The product compliance activity involves final licensing of the drug after clinical trials and subsequent labelling, education and information management related to that product.

8. Laboratory activities:

Laboratory operations in the pharmaceutical industry may cause biological, chemical and physical hazards, depending upon the specific agents, operations and equipment and work practices employed. Good laboratory practices (GLP) must be applied in the plants.

9. Cleaning and maintenance:

Workplace and equipment surfaces may be contaminated by hazardous material and drug substances during manufacturing and thus requires them to be cleaned. Cleaning activity is performed by wash-ing, wiping liquids and sweeping or vacuuming dust.

10. Pharmaceutical distribution:

It includes the supply of drugs to retail medical shops, hospital and healthcare facilities through supply chain management (SCM) to satisfy customer requirements as efficiently as possible.

11. Patient Assistance Programs (PAPs):

Patient assistance programs are initiatives funded by pharmaceutical manufacturers to distribute free or reduced rate medicines to people with low, moderate income or who are underinsured.

CHAPTER 19

Quality Control and Quality Assurance

1 Define quality control. Give the functions/activities of quality control/give the importance of quality control.

☞ **Quality Control (QC):**

Definition of QC by WHO:

Quality control is the part of GMP concerned with sampling, specifications and testing and with the organisation, documentation and release procedures which ensure that the necessary and relevant tests are actually carried out and that materials are not released for use, nor products released for sale or supply, until their quality has been satisfactory.

"Quality control is the day-to-day process of controlling quality of every incoming material till the finished product quality."

Functions of Quality Control:

- Analysis of raw materials.
- Analysis of packaging materials.
- Analysis of in-process products.
- Analysis of final dosage forms.
- Analysis of batch products (periodic analysis).
- Recording the results of analysis in a standard format.

Importance of Quality Control:

- To avoid toxic and unwanted effects of impurities.
- To avoid technical difficulties during manufacturing.
- To maintain safety and effectiveness of products.
- To maintain product with adequate physical and chemical stability.
- To ensure quality drugs for consumption to the patients.

- To maintain purity of product and thus protect public health.
- To help in maintenance of quality of product with better utilization of labours and machines.
- It helps in adjustment and setting of machineries.
- It helps in product development and in research with control over wastes and scraps.
- It helps in decreasing the cost of manufacturing so that cost of final product may be decreased.

Other activities of QC:

- To establish, validate and implement all the quality control procedures, maintain sufficient standards and reagents.
- To evaluate, maintain and store references and working standards for substances.
- To ensure the correct labelling of containers of materials and products.
- To ensure the stability of active pharmaceutical ingredient.
- To participate in the investigation of complaints related to quality of products.
- To participate in environmental monitoring.
- To access the finished products after evaluation.

2 What are major components of quality control?

Quality control head should have appropriate qualification and experience, who has one or several control laboratories to his/her disposal.

Major components of Quality Control (QC):

(a) Adequate facilities, trained personnel and approved procedures must be available for sampling, inspecting and testing of starting materials, packaging materials, intermediate bulk and finished products.

(b) The quality control labs should have minimum following facilities:

(i) Chemical testing laboratory supported with chemical, glassware and reagents, etc.

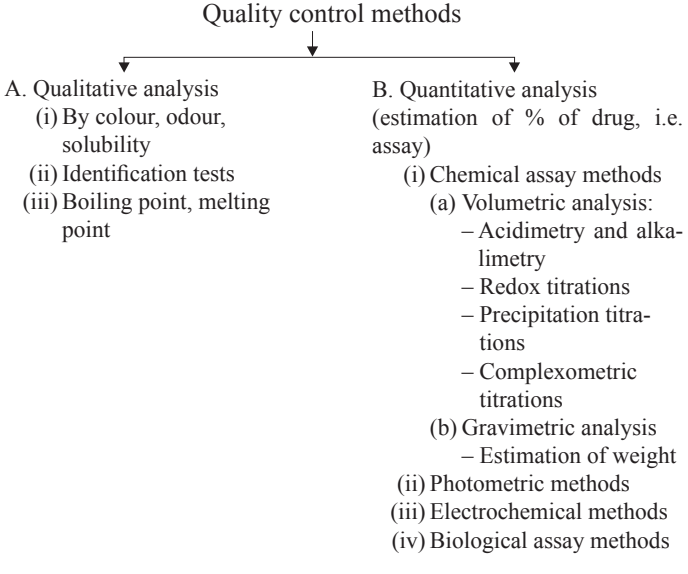
(ii) Instrumental laboratory with instruments like HPLC, GC, FTIR, etc.

(iii) Microbiology and toxicology lab with required culture media, microbial culture, incubators, etc.
(iv) Documentation room.
(v) Books like pharmacopoeias, analytical chemistry, microbiology, regulatory, etc.

(c) Personnel requirement: QC Lab should have trained personnel and should have qualifications like pharm/MPharm/BSc./MSc. PhD, etc.
(d) QC Lab should have SOPs related sampling and testing, instrumental analysis, etc.
(e) **Sampling of materials:**
QC should have SOPs for sampling of raw material/packaging material/intermediate products/finished products.
(f) Validation: All methods used by QC must be validated.
(g) Recording of the sampling, inspecting and testing procedures activities should be carried out.
(h) The finished product must contain ingredients complying with qualitative and quantitative composition of the product described in the marketing authorization.

3 What are different methods used for quality control in pharmacy?

☞ Quality control is to analyse a drug for quality and quantity. Following are various methods used for quality control.



4 Define quality assurance (QA). Mention the functions/ role of quality assurance.

☞ **Definition of Quality Assurance by WHO:**

"Quality assurance is a wide-ranging concept covering all matters that individually or collectively influence the quality of a product."
Quality assurance is the sum total of the organised arrangement made with object of ensuring the medicinal products are of quality required for their ultimate use.
Quality assurance is the department which includes the total quality control, government regulations, company standards and development of standard operating procedures of analysis.
The pharmaceutical product must meet the following five characteristics which are unanimously accepted regulatory authorities all over the world.
(i) Identity, (ii) strength, (iii) safety, (iv) purity and (v) efficacy.

Functions of Quality Assurance:

- Development of standard operating procedures and supply to every department of the company.
- It has a responsibility of "total quality of the products".
- It gives guidelines during adjustment and setting of the machineries.
- It helps to maintain quality of products with better utilisation of labours and machines.
- It helps in product development and research.

Components of Quality Assurance:

The components of the quality assurance in any pharmaceutical organisation:

(a) Pharmaceutical products are designed and developed in such a way that they should meet the requirement of GMP, GLP, GVP, GCP, etc.
(b) Production and control operations are clearly specified in written form and followed GMP.
(c) Managerial responsibilities should be clearly specified in job responsibilities
(d) Proper arrangement of manufacture, supply and used of the correct starting and packaging materials
(e) Correct in process controls, calibrations and validation are carried out.

(f) The finished product is correctly processed and checked, according to defined procedures.
(g) Satisfactory arrangements to ensure that quality is maintained throughout their shelf life
(h) Self inspection/quality audit must be followed.
(i) Production environment and service to production operations are monitored. Deviations are adequately recorded, investigated and responded
(j) The responsibility of top management/senior management is required for:
- Providing leadership
- Structure the organization
- Build quality system to meet the requirement
- Establish policies objectives and plans
- Review the system

Documents required for quality assurance department are:
- Company's quality policy
- Responsibility of QA department
- Job description of head of QA

5 What is GMP? Give the objectives and components of GMP.

☞ Good Manufacturing Practice (GMP)

As per WHO:

"GMP is a part of quality assurance which ensures that the products are consistently manufactured and controlled to the quality standards appropriate to their intended use".

- GMP is a set of principles and procedures which when followed by manufactures for therapeutic goods, helps to ensure that the products manufactured will have the required quality.
- Schedule 'M' of the Drugs and Cosmetics Act, 1940 explains the good manufacturing practices and requirements of premises, plants, equipment for pharmaceutical products.

Objectives of GMP:

- To produce products conforming to the predetermined specifications.
- To produce products of consistent quality.
- To minimise contamination
- To eliminate errors.

Components of GMP:

The total activity of GMP can be summarized as:

1. All manufacturing processes should be clearly defined.
2. Critical steps of manufacturing process and any significant changes made to the process validated.
3. All necessary facilities are provided as per schedule M, which includes qualified and trained personnel in sufficient numbers, premise, space, equipment, materials, procedures, instructions, etc.
4. Instruction and procedures are written in clear and unambiguous language, specifically applicable to the facilities provided, i.e SOPs in simple language.
5. Operators are trained to carry-out procedures correctly.
6. Appropriate maintenance of record during manufacture, batch wise.
7. The proper storage and distribution of the product minimise any risk of their quality.
8. A system is available to recall any batch of product from sale or supply, as and when required.
9. Complaints about marketed products are examined, the causes of quality defects investigated and appropriate measures taken in respect of the defective products and to prevent recurrence.
10. Documents required for GMP:
    (i) Responsibilities of GMP department
    (ii) Job description: Head of GMP

6 What is cGMP? Give its contents.

☞ **cGMP means current good manufacturing practice.**

Definition:

cGMP is defined as "it is a part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate for their intended use and the legal requirements".

- cGMP is concerned with both production and quality control matters.
- cGMP provides complete guidelines on designing material and product specifications, testing methods and reproducing methods for the same.

- cGMP regulations are established by FDA
- cGMP contains minimum requirements for the methods facilities, and controls used in manufacturing, processing and of a drug product packing.
- cGMP regulations make sure that a product is safe for use and that it has the ingredients and strength it claims to have.
- The approval process for new drug and generic drug marketing applications includes a review of the manufactures compliance with the cGMP.

cGMP for finished pharmaceutical includes following parts:

Subpart A	–	General provisions
Subpart B	–	Organisation and personnel
Subpart C	–	Building and facilities
Subpart D	–	Equipment
Subpart E	–	Control of components and drug product containers and closures.
Subpart F	–	Production and process controls.
Subpart G	–	Packaging and labelling control
Subpart H	–	Holding and distribution
Subpart I	–	Laboratory controls
Subpart J	–	Records and reports
Subpart K	–	Returned and salvaged drug products

7 What do you mean by validation/pharmaceutical validation? Give the need/purpose/advantages of validation.

☞ **Validation:**

"Validation is the documented act of proving that any procedure, process, equipment, material, activity or system actually leads to the expected results".

Need of validation:

1. Before introduction of a new method into routine use.
2. Whenever the condition change for which a method has been validated, e.g. instrument with different characteristics.
3. Whenever the method is changed and the change is outside the original scope of the method.

Object/purpose of validation:

To accept an individual sample as a member of a population under study.

- To admit samples to the measurement process.
- To minimize later questions on sample authenticity.
- To provide an opportunity for resampling when needed

Advantages of validation:

1. During the process the knowledge of process increases
2. Assures the repeatability of the process
3. Assures the fluency of production
4. Assures that the product is continuous according to the marketing authorisation.
5. Decreases the risk of the manufacturing problems
6. Decreases the expenses caused by failures in production.
7. Decreases the risk of failing in GMP.
8. Decreases the expenses of the everyday production even though the validation itself will create expenses.

Validation master plan (VMP)

A validation master plan is a document that summarises the firm's overall philosophy, intentions and approach to be used for establishing performance adequacy.

The validation master plan consists of:

- Approval page and table of contents
- Introduction and objectives
- Facility and process description
- Personnel, planning and scheduling
- Responsibilities of committee members
- Process control aspect.
- Equipment, apparatus, processes and system to be validated.
- Acceptance criteria
- Documentation, e.g. validation protocols and reports
- SOPs.
- Training requirements

Types of validation:

1. Process validation
2. Cleaning validation
3. Equipment validation
4. Validation of analytical methods

1. Process validation:

"The collection of data from the process design stage throughout production, which establishes scientific evidence that a process is capable of consistently delivering quality products is called process validation".

2. Cleaning validation:

"A process of attaining and document in sufficient evidence to give reasonable assurance, given the current state of science and technology, that the cleaning process under consideration does or will do, what it purposes to do" is known as clearing validation.

Objectives of clearing validation:

- To minimize cross contamination
- To determine efficiency of cleaning process
- To do troubleshooting in case problem identified in the cleaning process and give suggestions to improve the process

3. Equipment validation:

"Action of proving that any equipment works correctly and leads to the expected result is equipment qualification" is called equipment validation.

4. Validation of analytical methods:

"The process by which it is established by laboratory results that the performance characteristics of the method meet the requirements for the intended analytical application" is called the validation of analytical methods. It involves two components.

(a) Accuracy: The closeness of test results obtained by the method to the true value.

(b) Precision: The degree of agreement among individual test results when the method is applied repeatedly to multiple sampling of a homogenous sample.

8 What do you mean by calibration/pharmaceutical calibration? Give the scope/purpose of calibration. mention advantages of calibration.

☞ **Calibration:**

- Calibration of an instrument is the process of determining its accuracy.
- The calibration process involves obtaining a reading from the instrument and measuring its variation from the reading obtained from a standard instrument.
- Calibration of an instrument also involves adjusting its precision and accuracy so that its readings came in accordance with the established standard.

- Calibration is important for justifying the processes of qualification and validation.
- The instrument or equipment with the known accuracy is known as standards.
- Calibration achieves two main objectives:
  (i) It checks the accuracy of an instrument
  (ii) It determines the traceability of the measurement.

Scope/Purpose of calibration:

1. To make sure that the readings of equipment or instruments are consistent with other measurements and display the correct reading every single time.
2. To determine the accuracy, precision, reliability and deviation of the measurements produced by all the instruments.
3. To establish the reliability of the instrument being used and whether it can be trusted to deliver repeatable results each time.
4. Instruments have a tendency to produce inaccurate measurements over a period of time, following repeated use, thus, needs calibration.
5. To meet the requirements of cGMP and Government regulations, calibration of instrument is necessary.

Advantages of calibration:

1. It determines validity of measurements before the calibration.
2. It assures consistency and compatibility of the results/measurements.
3. It helps to test repeatability and reproducibility features of the instruments and processes.
4. It increases process and product efficiency through correct measurements.
5. It generates documentation of performance of instrument and processes to meet ISO 9000, ISO 1400 and QS-9000 standards.
6. Calibration of devices in the process industry helps to assure that the processes are well controlled and that the products meet standard specifications.

CHAPTER 20

Novel Drug Delivery Systems (NDDSs)

1 What do you mean by novel drug delivery system? Give its aim/objectives.

☞ **Novel Drug Delivery System (NDDS):**

- The term 'Novel' means something new.
- 'Novel Drug Delivery System' refers to dosage forms different from the conventional dosage forms such as tablet, capsule, injectable, etc.
- Any drug delivery system that tends to alter the release of the drug, rate or site of absorption of the drug or delivers the drug at its site of action is broadly categorized under 'Novel Drug Delivery System'.
- NDDS refers to the approaches, formulations, technologies and systems for transporting a pharmaceutical compound in the body as needed to safely achieve its desired therapeutic effect.

Aim/objectives of NDDS:

1. To provide a therapeutic amount of drug to the appropriate site in the body and then maintain desired drug concentration.
2. For drugs to reach the targeted site with a little or no side effects.
3. To minimize drug degradation and loss.
4. To increase bioavailability of the drug and the fraction of the drug absorbed in the required site.

2 What are the ideal characteristics of drug delivery system (DDS)?

☞ **Characteristics of an ideal DDS:**

1. It should increase the bioavailability.
2. It should provide controlled delivery of drug.
3. It should transport the drugs intact to the site of action.

4. It should be stable and delivery be maintained under various physiological variables.
5. It is easy to administer, safe and reliable.
6. It should be cost effective.

3 What are the advantages of Novel Drug Delivery System over the conventional dosage forms?

☞ **Advantages of NDDS over conventional dosage forms:**

(a) They give the controlled rate of delivery from the administered therapeutic dose.
(b) They maintain the optimum therapeutic drug concentration during prolonged duration of treatment.
(c) There is a maximum efficacy–dose relationship.
(d) The chances of adverse side effects are minimal.
(e) Frequencies of dose intake are minimized.
(f) These drug delivery systems are suitable for the hospitalized patients who are not to be disturbed during their sleeping time.

4 Give advantages and disadvantages of 'Novel Drug Delivery System (NDDS)'.

☞ **Novel Drug Delivery System (NDDS)**

- **Advantages:**
  1. Frequency of drug administration is reduced.
  2. Patient compliance is improved.
  3. Better control of plasma level of drug.
  4. Dose of drug is reduced.
  5. Reduced side effects.
  6. Enhanced bioavailability.
  7. Gradual rise of drug concentration in the blood.
  8. Achievement of a targeted drug release.
- **Disadvantages:**
  1. Dose dumping may occur.
  2. Dosage adjustment is difficult.
  3. Termination of therapy is difficult.
  4. In certain cases minor surgery is required, e.g. implants.
  5. Fluctuations in *in vitro* and *in vivo* results.

5 Define and classify 'Novel Drug Delivery System', giving examples.

☞ Novel Drug Delivery System (NDDS)

NDDS means the approaches, formulations, technologies and systems for transporting a drug in the body as needed to safely achieve its desired therapeutic effect.

Classification of NDDS:

NDDS can be classified in the following major categories:

1. Controlled drug delivery diffusion process:
- (a) Polymer membrane permeation controlled drug delivery systems.
- (b) Polymer matrix diffusion-controlled drug delivery systems.

2. Controlled drug delivery by modulation process:
- (a) Osmotically modulated drug delivery systems
- (b) Mechanically modulated drug delivery systems
- (c) Magnetically modulated drug delivery systems
- (d) Iontophoretically modulated drug delivery systems.
- (e) pH modulated delivery systems.

3. Prodrug concept

4. Special carrier system for targeting of drugs:
- (a) Liposomes
- (b) Monoclonal antibodies
- (c) Nanoparticles
- (d) Microspheres

5. Miscellaneous drug delivery systems:
- (a) Buccal strips
- (b) Bioadhesive microsphere delivery system
- (c) Erythrocytes (RBCs)
- (d) Niosomes/virosomes
- (e) Protein-based drug delivery system
- (f) Iontophoresis.

6 What are prodrugs? Give its applications/write a note on prodrugs.

☞ Prodrugs (proagents):

The compounds which undergo biotransformation before showing desired pharmacological action are called prodrugs or proagents. Prodrugs are generally the esters or amides of parent drug.

- **Aims and objectives of prodrug design:**
  1. To improve solubility.
  2. To improve stability.
  3. To improve bioavailability of drugs
  4. To mask unpleasant taste and odour of the parent drug.
  5. To reduce the toxicity of drug.
- **Properties of an ideal prodrug:**
  - It should rapidly transform chemically or enzymetically into active form when desired.
  - It should not have intrinsic pharmacologic activity.
  - The metabolic fragment apart from the active drug should be non-toxic.
- **Applications of prodrugs:**
  1. Chloramphenicol palmitate, the prodrug of chloramphenicol is used in the preparation of paediatric suspension because it has no bitter taste.
  2. Procaine-pericillin G and benzathin-penicillin G are prodrugs of penicillin-G, which shows resistance to hydrolysis as compared to parent drug.
  3. Testosterone cupionate, the prodrug of testosterone, is long acting in comparison to the parent drugs when injected in an oil base.
  4. Clindamycin 2-palmitate, the prodrug of clindamycin, has bitter taste of parent drug.
  5. Clindamycin 2-phosphate, the prodrug of clindamycin, causes a little pain and irritation at the site of injection when given by intramuscular route as compared to its parent drug.
- **Limitations of prodrugs:**
  1. Formation of an unexpected metabolite from the total prodrug that may be toxic.
  2. The inert carrier generated following cleavage may also transform into toxic metabolite.
  3. During its activation stage, the prodrug might consume a vital cell constituent such as glutathione leading to its depletion.

7 What are Liposomes? Give advantages and disadvantages and applications of lipsomes.

☞ **Liposomes:** Liposomes are minute spherical sac of phospholipid molecule enclosing a water droplet, especially as formed artificially to carry drugs or other substances into the tissues.

- Liposomes resemble cell membranes in structure and composition.
- Liposomes are several carriers in our body which transport biochemicals from the part of the body to an other, e.g. proteins, enzymes.
- Liposomes are phospholipids which can transport hydrophilic and hydrophobic drugs.
- Liposomes interact with the cell surface by two main mechanisms—adsorption and endocytosis.
- **Classification of Liposomes:**

1. Multilamellar vesicles (MLV) (0.5 to 5 μm):
- These are easy to prepare, generally heterogeneous in nature and may have several compartments.

2. Small unilamellar vesicles (SUV) (20 to 50 nm):
- They have a spherical shape and are homogeneous in nature.

3. Large unilamellar vesicles (LUV) (200 to 1000 nm):
- These are larger, having within them greater space for encapsulation of aqueous medium.

- **Properties/characteristics of liposomes:**
  - They are non-toxic, non-antigenic and permeable to water.
  - They are osmotically sensitive but in a selective manner.
  - They can adsorb to any type of cell in the body.
- **Advantages of liposomes:**

1. Liposomes can be administered by intravenously, topically and orally.
2. Liposomes can be metabolized *in vivo* since they are made of phospholipids.
3. Liposomes can protect encapsulated drug from degradation.
4. Liposomes facilitate site specific drug uptake and delivery.
5. Liposomes allow the sustained delivery of drug with low therapeutic index by altering their pharmacokinetic pattern.
6. Liposomes are non-toxic and non-antigenic because they are made of phospholipids.
7. Liposomes can increase the convenience of therapy by reducing frequency of drug administration.
8. Liposomes show compatibility with both lipophilic and hydrophilic drugs.
9. Liposomes can alter tissue distribution of drug in therapeutically favourable way.

10. Polar drugs can be enclosed in the aqueous compartment of liposames, e.g. methotrexate, fluorodeoxyuridine, etc.
11. Non-polar drugs can be enclosed in lipid compartment of liposome, e.g. actinomycin-D, vinblastine, etc.

- **Disadvantages of liposomes:**

1. Liposomes due to their liquid crystal structure hinder a true membrane transfer and cause physical instability.
2. Their drug loading capacity is weak.
3. Sometimes, allergic reactions are possible.
4. They are not stable for a long time on account of the use of phospholipids in their preparation.
5. Liposomes are rapidly eliminated from the system by reticulo-endothelial system of the body.

- **Applications of liposomes:**

1. Liposomes are used in diseases caused by intracellular parasites, e.g. malaria, tuberculosis and amoebiasis.
2. Liposomes entrapped insulin is active orally and can be replaced by intramuscular administration of insulin.
3. Liposomes can be used to transport functional DNA/RNA molecules into cells.
4. Liposomes can be used to transport radio-pharmaceuticals and immunological products.
5. Liposomal daunomycin has longer duration of action than free daunomycin which is used in treatment of neoplasia.
6. Liposomes entrapped actinomycin-D and nitrogen mustard are more effective than the parent drug.

8 Explain 'Nanoparticles' as a Novel Drug Delivery System. Or What are Nanoparticles? Give its advantages, disadvantages and applications.

☞ **Nanoparticles:**

- Nanoparticles are colloidal particulate drug delivery system in the sub-micron size range acting as carriers of drug molecules.
- The particle size of this system is in nanometer range, i.e. 200–500 nm. Therefore, it is called nanoparticles.
- Nanoparticles is broad class consist of both vesicular systems:
  (a) Nanocapsules: In this system the drug is confined to a cavity surrounded by unique polymeric membrane.
  (b) Nanospheres: In this system the drug is dispersed throughout the polymer matrix.

- The preferred mode of administration of nanoparticles is parenteral.
- Polymers used nanoparticles are gelatin, alginate, proplycaprolactone, epoxy polyester, polyurethane, polylactic acid.
- **Method of preparation of nanoparticles:**
  - The method of preparation of nanoparticle is similar to coacervation phase separation method used in microencapsulation.
  - An aqueous solution of natural macromolecules is prepared and drug is mixed in it.
  - In case the drug is hydrophobic, it is dissolved in a small quantity or organic solvents and mixed with the carrier taking precautions that the drug may not be precipitated.
  - The system is then desolvated in controlled manner by adding a solvent competing solute like sodium sulphate or alcohol.
  - This result in the formation of colloidal particles in nanometer range.
  - These nanoparticles may be hardened, isolated and dried for storage.
  - Nanoparticles can be dispersed in aqueous system.
- **Advantages of Nanoparticles:**
  1. Nanoparticles control both the site and rate of drug delivery.
  2. Adverse effects and toxic reactions are minimized.
  3. They enhance the therapeutic efficacy of the drug.
  4. Nanoparticles are non-toxic and biodegradable.
  5. Reproducibility is quite easily achieved.
  6. Nanoparticles also help to increase stability of drugs/proteins.
  7. Nanoparticles are safe and effective in site specific and targeted drug delivery.
  8. Size of nanoparticles allows them to be administered intravenously via injections.
- **Disadvantages of Nanoparticles:**
  1. High surface energy that may lead to high aggregation in biological system.
  2. Nanoparticles can be quickly removed by RES system of the body resulting in low biological half-life.
  3. Organic solvent remaining (residual) during the preparation of nanoparticles may cause toxicity.

4. Nanoparticles have a poor target and site specificity.
5. Nanoparticles have high immunogenicity.

- **Applications of Nanoparticles (pharmaceutical applications):**
  1. Nanoparticles can act as a carrier system for the parenteral delivery of cytostatic drugs like doxorubicin and methotrexate.
  2. Fluorescein isothiocyanate (FITC) nanoparticles have been used to incorporate cytotoxic agents into tumour cells in cancer chemotherapy.
  3. Nanoparticles along with biological maker like immunoglobulins can be used to target the drugs to very specific sites.
  4. In nuclear medicine 99m technetium nanoparticles are used to study the morphology, blood flow and functions of various organs of the body.
  5. Nanoparticles can give protective action to the drugs or proteins incorporated in them, e.g. nanoparticles can protect insulin from proteolytic action of enzymes present in the gut. Thus, nanoparticles may provide oral route for the delivery of proteins like insulin.
  6. Nanoparticles can also be used as a carrier for ophthalmic drugs. They exhibit longer half-life in eye than conventional eye drops.
  7. Nanoparticles can be used to deliver the drugs into the brain as they are capable of crossing the blood–brain barrier.

9 What are 'Microspheres'? Give its advantages and disadvantages.

☞ **Microspheres:**

- Microspheres are solid spherical particles made up of polymeric substances, in which the drug is dispersed throughout the microsphere matrix and its size ranges from 1 to 1000 μm.
- Microspheres are made of polymeric, waxy or other protective materials that is biodegradable synthetic polymers and modified natural products such as starches, gums, proteins, fats, waxes.
- The natural polymers include albumin and gelatin, synthetic polymer includes polylactic acid and polyglycolic acid.

- The drugs in solution or in crystalline form are dispersed in microspheres.
- **Advantages of Microspheres:**
  1. Microspheres provide a constant and prolonged therapeutic effect.
  2. They decrease the dose and toxicity of drug.
  3. They reduce the dosing frequency and thereby improve the patient compliance.
  4. Microspheres protect the GIT from irritant effect of the drug.
  5. Microspheres provide constant drug concentration in blood, thereby increasing patience compliance.
  6. Microspheres facilitate accurate delivery of small quantities of potent drugs.
  7. Microspheres injected in the form of suspension, do not require surgical implantation.
  8. In microspheres, the particle size reduction is helpful for enhancing the solubility of the poorly soluble drugs.
- **Disadvantages of Microspheres:**
  - The cost of materials and processing of the controlled release preparation is much higher.
  - Reproducibility is less.
  - Change in temperature, pH, solvent addition, evaporation, agitation may influence the stability of core particles to be encapsulated.
  - The environmental impact of the degradation products of the polymer matrix produced in response to heat, hydrolysis, oxidation, solor radiation or biological agents.
- **Applications/pharmaceutical applications of microspheres:**
  1. The number of drugs like antineoplastic, narcotic antagonists, steroids, and other macromolecules can be incorporated into microspheres.
  2. Microspheres have also been used for passive targeting of organs such as liver, spleen, lung and kidney.
  3. Microspheres are also used as antigen carrier.
  4. Microspheres have been developed for the taste masking of sulpha drugs, alkaloids, etc.
  5. Enteric coating of the drugs like aspirn and erythromycin, etc. is a major area of the microsphere-based drug delivery.

6. Microspheres are used for ophthalmic drug delivery, oral drug delivery, nasal drug delivery, buccal drug delivery, gastrointestinal drug delivery, transdermal drug delivery, colonic drug delivery, vaginal drug delivery, etc.

10 Write a note on "Films and strips" as a novel drug delivery systems.

☞ **Films and strips:**

- Films and strips are meant for topical application for slow release and drug over predetermined period of time.
- The films and strips which are becoming popular these days are:

1. Zero order release films.
2. Buccal strips.
3. Spray bandages.

1. Zero-order release films:

- Zero-order release, means a drug is released at a constant rate, and is the ultimate goal of all controlled release drug-delivery mechanisms.
- These films are called "Laminate" and are meant for topical applications.
- Nitroglycerine laminates are prepared by mixing propylene glycol with about 1% carbopol resin.
- The mixture is neutralised with sodium hydroxide solution and then 0.1% of nitroglycerin is added.
- It is then placed between polythene sheet 5 × 5 cm and its edges are sealed by heat. It is then placed on a pressure sensitive adhesive sheet of 5.5 × 5.5 cm so that it can be properly adhesive to the skin.
- Such laminates release the drug (nitroglycerine) slowly into circulation for about 12 hours.
- Similarly pilocarpine films are prepared from acrylates and metha crylates.

2. Buccal strips (Buccal film):

- Buccal strip is in the form of a small strip of pharmaceutical acceptable paper like material containing known amount of drug to be placed in the buccal cavity which dissolves on the tongue or buccal cavity.
- These strips consist of a thin absorbent base of fabrics, filter paper or cotton, etc.

- Carboxymethyl cellulose and microcrystalline cellulose have been used to prepare buccal strip.
- The buccal strips are prepared by immersing a long piece of fabric made from polyamide fibres into a molten mixture of carbowaxes and dissolved or dispersed drug (around 20%)
- The fabric is then cooled and cut into small pieces.
- The buccal strip is made in contact with buccal mucosa for about 15 minutes and then it is removed and disorded.

- **Advantages of Buccal Strips:**
  1. No need of water to swallow or chew.
  2. Buccal strips are available in various sizes and shapes.
  3. It hydrates and dissolves in the buccal cavity within a fraction of seconds.
  4. Fast disintegration or dissolution.
  5. It enhances stability of drug.
  6. Easy for handling and transportation.
  7. Excellent drug content uniformity.
  8. Smaller convenient size of dosage form.
  9. Rapid onset of action.
  10. To avoid first-pass metabolism.
- **Disadvantages of Buccal Strips:**
  1. Buccal strip is hygroscopic in nature so it must be kept in dry places.
  2. Packaging of films requires special equipment, and it is difficult to pack.
  3. High dose cannot be incorporated into the oral film.
  4. Eating and drinking may become restricted.
  5. Buccal films are moisture sensitive.

3. Spray Bandages:

- These bandages are prepared by spraying the solution of drug in polylactide (polymer of lactic acid anhydride).
- A 2% solution of purified lactide polymer is made in chloroform and the drug in the concentration of 0.01 to 90% is dissolved or dispersed in it.
- Such solution is then packed in an aerosol container having a suitable propellant, such as, CF_2Cl_2 (dichloro-difluoromethane).
- When this solution is sprayed, it will be a comfortable bandage which can be simply washed off with warm water.

11 Write a note on "erythrocytes" (RBCs) as a novel drug delivery system. / Write a note on resealed erythrocytes as a drug carrier.

☞ **Erythrocytes as a Novel Drug Delivery System:**

- Erythrocytes have also been tried in order to achieve controlled released of drugs.
- The lifespan of an erythrocyte is about 120 days.
- Erythrocytes can allow a drug to circulate in the body for a long time which helps in the slow release of drug in serum.
- When the drug is encapsulated in erythrocytes, the drug gets leaked out of its cell over to prolonged period of time.
- **Method of preparation/technique of incorporation of drug into red blood cells (erythrocytes):**
  - Resealed erythrocytes are prepared by putting them into a hypotonic medium, so that they can be swollen.
  - The aqueous solution of the drug is added to the medium so that the drug gets into erythrocytes through the open pores ranging from 200 to 500 Å.
  - When the isotonicity is adjusted the erythrocytes shrinks, thus encapsulating the drug within them.
  - The erythrocytes may be suspended in normal saline solution for preparing injections.
- **Advantages of Resealed Erythrocytes:**
  1. Erythrocytes are biodegradable and biocompatibility.
  2. They circulate throughout the circulatory system.
  3. They prevent undesired immune response.
  4. They can be utilized for organ targeting within RES.
  5. They have longer lifespan as compared to synthetic carriers.
  6. They decrease the side effects of drugs.
  7. They increase the drug dosing interval.
  8. Entrapped drugs are not susceptible to enzymatic degradation.
  9. Large quantity of material can be encapsulated within small volume of cells.
- **Disadvantages of Resealed Erythrocytes (Limitations):**
  1. They do not offer a wide choice of target areas.
  2. They do not support the drugs which are widely metabolized in the liver.

3. They are removed *in vivo* by RES so may cause toxicity.
4. Several molecules may alter the physiology of the erythrocytes.
5. They are liable to biological contamination due to the origin of the blood, the equipment and the environment.

- **Applications of Resealed Erythrocytes:**
  1. Resealed erythrocytes of urease have been used in kidney failure of degrade serum urea.
  2. Resealed erythrocytes of asparginase have shown good results in asparginase dependent leukaemia.
  3. Resealed erythrocytes of methotrexate and Adriamycin have been tried in cancer therapy. It has shown good results.
  4. Resealed enthrocytes of prednisolone have shown good result to prolong the antinflammatory action.
  5. Heparin encapsulated in enthrocytes has been proposed for prevention of thromboembolism.

12 Write a note on "Implants" as a novel drug delivery system.

☞ **Implants:**

- Implants are small sterile hypodermic tablets which are placed under the skin by a minor surgery in order to release drugs over prolonged periods of time.
- Implants are very small pellets composed of drug substance only without excipients.
- Nowadays magnetically controlled implants have been developed which can be opened or closed at will in order to release or stop the drug.
- The implants, which are in capsule form, consist of body and a cap. It can be opened by placing a magnet on the skin and moving it in the desired direction.
- These implants are placed in the upper thigh at a depth of 5 mm.
- These implants are useful in hormone therapy.
- Implants are available in many forms like biodegradable, non-biodegradable mini pumps.
- **Ideal properties of Implants:**
  1. They should be biostable and biocompatible.
  2. They should be easily removable.

3. They should be non-toxic and non-carcinogenic.
4. They should have minimum surface area and smooth texture.
5. It should have control over the rate of drug release.
6. It should have good mechanical strength.
7. It should be free of drug leakage and be easily sterilizable.

- **Advantages of implants:**
  1. It has controlled drug delivery for over a long time.
  2. It helps to improve patient compliance.
  3. It has targeted drug delivery.
  4. It decreases side effects of the drug.
  5. It improves stability of drugs.
  6. It improves availability of drugs.
- **Disadvantages of implants:**
  1. Minor sugery is needed for insertion of implants.
  2. It is uneasy to discontinue the therapy.
  3. It may produce same local reactions.
  4. The size of implants is usually small, so have limited loading capacity.
- **Applications of implants:**
  1. Implants are used to treat conditions such as heart failure, cardiac arrhythmia, ventricular tachycardia, valvular heart disease, angina pectoris, atherosclerosis.
  2. The implants are useful in hormone therapy.
  3. The implants are used in ocular drug delivery.
  4. The implants are used for long-term delivery of contraceptive agents.
  5. Polymeric implants have been useful in dental applications.
  6. Polymeric implants are being used for enhance immune response to antigens.

13 Write a note on "controlled drug delivery modules" (CDDM).

☞ **"Controlled Drug Delivery Modules" (CDDM):**

- These are devices which are formed by embedding the drug within a polymeric matrix so that it gets released slowly to the body over a long period of time.

- The polymeric matrices used to hold the drug reversibly are polyethylenes, silicone elastemers and cellulose esters.
- The drug polymer complex may be formulated into tablet, capsule or any other suitable formulation.
- These controlled drug delivery modules are punctured before administration with laser beam to make a small orifice of a few microns in diameter for the release of the drug.
- The drug is released from these modules by diffusion, osmosis or chemical reaction.
- **Advantages of CDDM:**
  1. It improves patient convenience.
  2. It increase the safety margin of high potency drug.
  3. It reduces cost of therapy.
  4. It increases patient compliance.
- **Disadvantages of CDDM:**
  1. It may decrease systemic availability.
  2. Poor *in vitro* and *in vivo* co-relation.
  3. Increased risk of toxicity.
  4. Retrieval of drug is difficult in case of toxicity.

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