# History of the Profession of Pharmacy in India In Relation To Pharmacy Education

- Pharmacy education in India at the certificate level, was started in 18/42 in Goa by the Portuguese. Formal training of the compounds was started in 1881 in Bengal and as a university level program in 1937 at the Banaras Hindu University (Varanasi). In Baghdad the first pharmacies or drug store, were established in 754.
- The revolution in the development of science and technology in post-world war-2 starter the change in pharmacy profession.
- Pharmacy being a health care profession, the independent government of India enacted 'The Pharmacy Act' to control the pharmacy profession as well as education, in 1948.
- Father of Pharmacy: 'William Procter Jr.' (American Pharmacist)
- Father of Indian Pharmacy: 'Mahadev Lal Schroff'
- Traditionally pharmacy has been known as an art and science of making drug/medicine. The word Pharmacy is derived from the Greek word 'PHARMAKON' meaning drug.
- In the ancient period, the physician themselves practiced pharmacy and it is believed that Hippocrates, the great Greek physician, regard as father of Medicine, used to make his own prescription or at least, supervise their preparation.
- Apothecary is a historical name of a medicine professional who, formulates and dispense medicine to physicians and patients, now this role served by the pharmacist. The earliest pharmacies were known as Apothecary shops.
- Pharmacist play a role in, compounding most of the medicine needs of the

people. Here the medicinal professional prepared and dispensed medicines to physicians and mixtures, ointments, pills, tincture, syrups, elixirs, powder etc.in their pharmacy, based on the prescriptions given by physicians. They packed them suitably labeled them and dispensed them along with appropriate advise for consuming them.

- In old time, direct crude drugs are used in the diagnosis by the physicians and require herbs and drugs are provided by pharmacist. At that time drugs are identified by their morphological appearance and organoleptic characters.
- Like other, countries In India too, pharmacy was part of medicine in our Ayurvedic, and Siddha system of medical practice.
- Pharmacy is a versatile, dynamic, growing and increasingly diverse profession, one which creates an excitement because there are so many opportunities for services. it is an old age profession which has transformed into ahub for 'Global health Care' and evolved as multidisciplinary and multifaceted field in recent times.

**Pharmacy relation in Industry-**

- In industry pharmacist perform many works in many ways.
- Formulation development— Commercial drug production is a difficult tasks for any pharmaceutical companies. Due to involvement of pharmacy in pharmaceutical, it is easy way to developed commercial formulation and developing a complete understanding of the form and structure of the drug substance and drug products.
- Pharmacist also involved in the formulation testing and make a successful pharmaceutical formulation requires the combination of the Active Pharmaceutical Ingredients(API) with inactive excipients.
- Physicochemical analysis can aid excipient selection, enable the stability ofthe drug substance and drug product to be assessed, and also ensure the critical

material attributes (CMAs) relating to formulation performance are identified as part of the design space definition applied for downstream manufacturing controls.

- Manufacturing department— Proper equipment, proper procedure and suitable conditions are the necessary conditions for any manufacturing units.In pharmaceutical it is also decided by the pharmacist. Pharmacist developedand maintain Standard Operation Procedure (SOP) and provide effective training to products staffs.
    - Proper sanitation and hygiene conditions are also developed by the pharmacist and it is also decided the safety area and safety environment for the manufacturing units.
    - Assist and review production batch records have all the necessary information for final approval and release decision and also conductand support companies research and development projects
- Quality control and Quality assurance: The main function of quality control is to test and verify the products quality according to pharmacopoeialstandards.
    - In Quality Control sampling inspection and testing of raw material and packaging material, release and documentation are control by the high skilled person (Pharmacists). QC department also define the stability testing and evaluation of self-life product and also monitor the microbial activity of raw materials and finished products.
    - Quality Assurance (QA) department execute the systemic monitoring and evaluation of the various expects of a project service or facility to ensure that standards of quality of the drugs. It also responsible of maintenance ofa desired level of quality in as service or product, especially by means of aattention to ever stage of the process of delivery or production. It also assured the doses and formulations of drugs according to patients need andconvenience.

- Drug Information: Pharmacists are also known as drug experts because it gains a lot of knowledge during the academic session. In industry it informed the drugs composition and formulation and also defined the drug advantage (useful effect) and disadvantage (Harmful or adverse effect).chemically drugs are active or inactive it is decided by the pharmacists and also provided the drugs reaction with other drugs.
    - Drug are the chemical substances, which are design for treating the disease .It is also provide the complete information about suitable excepients ( coloring agent, flavouring agent etc).

- Regulatory affairs: In industry, regulatory affairs is a profession developedfrom the desire of governments to protect public health by controlling the
    - Regulatory department promote strategic and technical advice at the highest level in their industries, making an important contribution both commercially and scientifically development.
    - Keeping track of the ever-changing legislation in all the regions in which a company wishes to distribute its products and give advice onlegal and scientific restraints and requirements.
- Sales and marketing: For any industry growth and development sales and marketing is a very important factor. Pharmaceutical marketing is presentlythe most organized and comprehensive information system for updating physicians about the availability, safety, efficacy, hazards, and techniques of using medicines.
    - Marketing is a process that starts with identifying and understanding the needs and wants of the customer (demand) and then fulfilling those needs and wants (supply). An effective marketing plan offers a solutionto fulfill the needs and wants of society (individuals and organizations), while achieving the goals of the organization.

- In addition, marketing can create new needs or reformat existing needs. Both customers (demand) and organizations (supply) have objectives.
- In marketing, pharmacists are direct attached to the patients and physicians so it provided the complete information about the publicneed and requirements.

- Management: Marketing management is the analysis, planning, an implementationthe control over actions, aimed on an establishment, fastening and support of favorable exchanges with target buyers for the achievement of certain problems of the organization, such, as profit reception, sales volume growth, increase market share, etc.

## Pharmacy Practice and Various Professional Associations/ Pharmacy As A Career

- **Introduction:** Pharmacy are developed to organize educational programs and research activities for spreading and establishing awareness on the need and scope of quality standards for drugs and related articles/ materials. Pharmacists is the first person of health care system by playing various roles like academic pharmacists, industrial pharmacist, community pharmacists, clinical pharmacists, hospital pharmacists, veterinary pharmacist etc. All pharmacists working in different fields of the profession are directly or indirectly related to nation's health. Finally pharmacists are responsible for insuring that "Right drug to right patient at right time in right dose through right route in right way." So that pharmacists is an integral part of health care system.

- **General/ clinical practice:**

- Clinical pharmacists often apply their knowledge of medications in the

medication plan ofa particular patient and evaluate the appropriateness of the dose, side effects, efficacy and drug interactions.

- In many cases, the clinical pharmacist with work directly with patients to help them understand the medications they take and encourage them to take the medications asdirected.
- Pharmacists are monitoring patient progress with medications and making relevant recommendations to change and evaluating medication therapy and making appropriate recommendations to patients or health practitioners. Pharmacists are also called as primaryinformers in the medical department.
- According to new authority by government pharmacists are also open our own clinics and provide the primary treatment to the patient and also treat the emergency condition in the absence of doctors.

- **Academic practice:**

- In academic pharmacist focus on teaching, research and training of the upcoming pharmacist. On the basis of knowledge and skill pharmacists are appointed for different-different post in the academic institute.
- By arranging seminar, project, or system academics, pharmacist plays valuable role in health care system. Education motivates the professionals in the health care system.
- From their basic education training and pre-registration training, students acquire a broad understanding of the scientific principles and techniques of the pharmaceutical sciences and the ability to keep pace throughout their careers with developments in medicine andpharmacy.
- Pharmacist also gave the knowledge about preparation, distribution, action and uses of drug. Educational training programs helps to professionals for their current knowledge. Pharmacist gets a specialized knowledge regarding to drugs and therapeutic action throughthere practical training overall we can say

academic pharmacist preliminary part in pharmacy profession.

- **In Health program**

    - According to WHO “Health is complete physical, mental and social well-being and not merely absence of disease. According to Ayurveda swath’s health is defined as“well balance metabolism. In spite of short coming in the WHO difference the Concept of the health is wide and positive and provides an overall goal towards which nations.
    - Health is an integral part of the development and health is central to the concept of quality of life hence, health is world Wide social-goal. To achieve this goal every nation sets professional persons in healthcare System Pharmacist, Physician/doctors, Nurses, Compounder, Dispenser. Health related other service provide by pharmacists that is.

- ***Health missions***
- ***Health consultant***
- ***Doctor’s assistant.***

- **In Hospital Pharmacy:**

    - Hospital pharmacists are play the key role in monitoring the supply of all medicines used in the hospital and are in charge of purchasing, manufacturing, dispensing and quality testing their medication stock along with help from pharmacy assistants and pharmacy technicians.
    - Hospital pharmacists can offer information on potential side effects and check thatmedicines are compatible with existing medication.
    - They will often also monitor the effects of treatments to ensure that they are proving effective, safe and appropriate to the user, Like doctors,

pharmacist regularly attends wardrounds and more involved in selecting treatments for patients.

- Some pharmacists specialize as consultant in many areas as Hematology (blood), Nephrology (kidneys), Cardiology (heart), Urology (urinary), pediatrics (children),Diabetes and infections disease etc. it also participate in.
- Prescribing
- Dispensing
- Administration
- Documentation
- Monitoring

- **Pharmacovigilance:** Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine/vaccine related problem. The word ***"pharmacovigilance***" are**- pharmakon (means drug)** and **vigilar ( to keep watch).** Pharmacovigilance is concerned with identifying the hazards associated with pharmaceutical products and with minimizing the risk of any harm that may come to patients.

- **Research and development**:

  - Pharmacist contributes to research, and their expertise in formulation development is of particular relevance to the biological availability of active ingredients. Pharmacists perform the many experiments and develop the drug formulation and develop the convenient dosages form according to demands and need and maintain the resister of the drugs. It also decided the suitable excipients for APIs. It also help in the development of combination drugs.

- Pharmacists are also involved in the vaccine preparation.

- **Pharmaceutical marketing and Management:**

  - Pharmacist are participate in the marketing and distribution by provide the knowledgeabout the drugs to the physicians.
  - Advertisement, news, and multimedia are also the components of the pharmaceuticalmarketing.
  - Management, is the key features of any jobs and companies. In the pharmaceutical regular checkup of drug, temperature maintaining, moisture regulation, light availability etc. are include in management. In any job regular practice and time management is very important factors. The inclusion of pharmacist in all levels of management promotes an ethical approach within management policies.

- **Chemist shop and Medical store:**

  - Pharmacists are also authorize to open our own chemist shop and checking , dispensing ofprescription drugs and providing advice on drug selection and usage. It also called community pharmacist. Community pharmacist are directly closed with the public and provide the complete information about disease.
  - Community pharmacist is also taking on more of the clinical roles that have traditionally been undertaken by doctors, such as the management of asthma and diabetes as well as blood pressure testing.

- They also help people give up smoking, alter their diets to make them healthier and adviseon reproductive health matter.

- **In Industry:**

- Pharmacists are involved and responsible for wide area activities in industry. Pharmacists are involved in drug discovery process, drug safety studies, formulations of dosage forms, clinicaltrials, marketing and management.

- **Role of pharmacist in industry**
- **Formulation development.**
- **Manufacturing department.**
- **Quality control and Quality assurance.**
- **Sales and marketing.**
- **Management.**

**Pharmacopoeia**

- **Introduction of Pharmacopoeia:**
- Pharmacopoeia has been the authoritative organization working to ensure the consistency and quality ofmedicines.

- Pharmacopoeia is the formulation of drugs. It is the standard book for preparation of drugs.The book is published in a country under the authority of its own government.
- Pharmacopoeia is derived from Greek word **Pharmakon - Drugs Copoeia - Means to make**
- **Type of Pharmacopoeia / List of Pharmacopeia**
    - We cannot call it a specific type because every country has a own Pharmacopoeia.

- **Indian Pharmacopoeia**
- **British Pharmacopoeia**
- **United States Pharmacopoeia**

- **Indian Pharmacopoeia:**
- The Indian Pharmacopoeia is published by the Indian Pharmacopoeia commission (IPC) on behalf of the ministry of health and family welfare Government of India.
- Bengal Pharmacopoeia 1844 - But this book was not made public, just this name was kept.
- Legal and official book published by IPC-1945.
- Indian Pharmacopoeia Headquarter - Ghaziabad (Uttar Pradesh)
- Indian Pharmacopoeia commission (IPC) regulated by Ministry Of Health And Family Welfare.
- Indian Pharmacopoeia is written in English and official title of monographs given in Latin.
- The Indian Pharmacopoeia is being processed to fulfill the requirement in the Drug And Cosmetics Act 1940 and rules 1945.
- In 1946 the government of India published the Indian Pharmacopoeia list which served as the suppliment to British Pharmacopoeia.
- After publication of list the government of India constituted a parmanent Indian Pharmacopoeia committee in 1948.
- Indian Pharmacopoeia committee under chairmanship of Dr. B.N. Ghosh published First Edition of Indian Pharmacopoeia in 1955.
- (Dr. B.N. Ghosh professor of pharmacology. R.Gkar medical College Kolkata who died 1958. After Dr. B.N. Ghosh, Dr. B Mukerji Director Central Drug Research Institute Lucknow (CDRI) was appointed as chairman of the Indian Pharmacopoeia committee.)

- Second Edition of Indian Pharmacopoeia was published in 1966. Supplement to this edition waspublished in 1975.
- (On 30 June 1978 the Indian Pharmacopoeia committee was reconstituted by the government ofIndia Ministry Of Health and Family Welfare) under the Chairmanship Dr. Nityanand Directer of Central Drug Research Institute Lucknow (CDRI).
- Third Edition of Indian Pharmacopoeia was published in 1985.
- This Pharmacopoeia include two Addendum with two Volumes.
- Addendum (Volume-1) to Indian Pharmacopoeia published in 1989. They contain legal notice prephase acknowledgement, Introduction, General notice and monographs from A to P.
- They contain 46 new monographs added and 126 amended.
- Addendum (Volume-2) was published in 1991 contain monographs from Q to Z and they contain 62 new monographs added and 110 amended.

- Fourth edition of Indian Pharmacopoeia was published in 1996 under the chairmanship of Dr.Nityanand.
- In Fourth edition addendum from veterinary product in 2002, 2005 and supplement volume-1 A toP, Volume-2 Q to Z.
- The veterinary supplement to Indian Pharmacopoeia 1996 contain 208 monographs.

- Fifth Edition of Indian Pharmacopoeia was published in 2007 and addendum to this edition waspublished in 2008.
- Fifth Edition Indian Pharmacopoeia is presented in three (3) Volume.
- Volume-1st contains general notices and general chapters.
- Volume-2nd contains general monographs on Drugs substances Dosage forms and PharmaceuticalAids.
- Sixth edition of Indian Pharmacopoeia was published in 2010.
- The 6th edition of the Indian Pharmacopoeia 2010 is published by the Indian Pharmacopoeiacommission (IPC).
- The Indian Pharmacopoeia 2010 is presented in 3 volumes.
- Volume-1st contains the notices, Preface the structure of the IPC, Acknowledgements,Introduction and the general chapters.
- Volume-2nd contains the General notice, monographs on Dosage forms and monographs on Drug substances, dosage forms and Pharmaceutical Aids (A to M).
- Volume-3rd contains monographs on Drug substances, dosage forms and Pharmaceutical Aids (N to Z) followed by monographs on Vaccines and Immunosera for human use.
- Herbs and Herbal products. Blood and blood related products biotechnology product andveterinary products.
- The seventh edition of the Indian Pharmacopoeia was published in 2014 by the Indian Pharmacopoeia commission (IPC) on behalf of the Government of India Ministry of Health AndFamily Welfare.
- The Indian Pharmacopoeia 2014 is presented in four Volumes.

- The Indian Pharmacopoeia 2014 incorporates 2550 monograph of drugs out of which 577 are new monographs consisting of APIs, Excipients, Dosage forms and herbal products etc.
- The Eight edition of Indian Pharmacopoeia was published in 2018 by the IPC on behalf of the Ministry of Health and Family Welfare, Government of India.

- **Indian Pharmacopoeia 2018 salient features-**

    - **Incorporating with 4 volume.**
    - **220 New monographs**
    - **170 New chemical monographs**
    - **49 API**
    - **64 Formulation**
    - **53 Fixed dose formulations**
    - **02 Excipients**
    - **02 Antibiotics**
    - **15 New herbs and Herbal products monographs**
    - **03 New Radiopharmaceutical monographs.**
    - **14 New veterinary Non-biological monographs.**
    - **18 New Biological monographs**
    - **02 Vaccines and Immunosera for human use**
    - **06 Biotechnology derived therapeutic products.**
    - **10 Blood and Blood related products.**

    - **Silent features of Indian pharmacopoeia**

- I.P is published in continuing pursuit of the mission of I.P.C to improve the health of thepeople through ensuring the quality, safety and efficacy of medicines.
- I.P contains procedures for analysis and specifications for the determination of quality of pharmaceutical substances, excipients, and dosage form.
- General chapter on volumetric glassware, conductivity, dissolution test, disintegration test, dimensions of hard gelatin capsule shell etc. have been revised.
- I.P has been extended to include products of biotechnology indigenous herbs and herbals products, veterinary vaccines and additional antiretroviral drugs and formulations, inclusive of commonly used fixed dose combinations (FDC).
- I.P contains the 170 chemical monographs, 15 herbal monographs, 10 blood and blood related products monographs, 6 biotechnology monographs, 3 pharmaceuticals monographs, 2 vaccines and immune-sera monographs, 14 veterinary and non biological products monographs.
- I.P monograph for an official substances or preparation includes the articles definition, description, identification, packaging, storage, specifications, impurities, assay and specifictests, one or more analytical procedures for each test, acceptance criteria, other requirementetc.
- General chemical tests and TLC for identification of an article have been almost eliminated and more specific infrared, ultraviolet spectrophotometer and HPLC tests have given emphasis.
- The uses of chromatographic methods have been greatly extended to cope with the need for more specificity in assays and in particular, in

assessing the nature and extent of impurities in ingredients and products.

- For controlling the microbial quality of all the medicinal products- Maintenance, preservation, identification, disposal of microorganism have been revised and pyrogen tests have replaced by Bacterial Endotoxin Test(BET) in parenteral preparation.

| **Edition** | **Year** | **Addendum / Supplement** | **Chairmanship** | **Volume** |
|---|---|---|---|---|
| **1St** | **1955** | **1960** | **D. B.N. Ghose** | **One** |
| **2nd** | **1966** | **1975** | Dr. B. Mukherjee | One |
| **3rd** | 1985 | 1989/1991 | Dr. Nityanand | Two |
| **4th** | 1996 | 2000/2002/2005 | Dr. Nityanand | Two |
| **5th** | 2007 | 2008 | Dr. Nityanand | Three |
| **6th** | 2010 | 2012 | Shri K.Chandramouli | Three |
| **7th** | 2014 | 2015/2016 | Gulam Nabi Azad (HealthMinister) | Four |
| **8th** | 2018 | 2019/2021 | Dr. C.K. Mishra | Four |

- **United States Pharmacopoeia (USP)**
- The United States Pharmacopoeia has been authoritative organization working to ensure the constituencyand quality of medicine and vitamin.
- USB United States pharmacopeia standards are recognised by the FDA as the standard for testing vitamins and medicines against, ensuring quality products that contribute to public health and wellness.
- **United States Pharmacopeia-National Formulary**
- The United States Pharmacopeia-National Formulary (***USP-NF***) is a book of public pharmacopeial standards. It contains standards for medicines, dosage forms, drug substances, excipients, medical devices, and dietary supplements.

**British Pharmacopoeia (BP)**

- British Pharmacopoeia was published by the Health ministry of the United Kingdom. In is also known as National Pharmacopoeia of the United Kingdom.
- **British Pharmacopoeia**

- **Headquarters: London, United Kingdom**

- **<u>PHARMACEUTICAL PACKAGING.</u>**

- **Definition—** Pharmaceutical packaging is the phenomena or operation, as the part of any drug discovery and development program. Pharmaceutical products generally require a standard of packaging which is superior to that of most other products in order to support and comply with their main requirements, i.e. proven efficacy, safety, uniformity, reproducibility, integrity, purity with limited impurities, minimum side-effects coupled to minimum product liability risks, and a good shelf-life stability profile.
- For any packaging require a discipline and lots of knowledge about the drugs formulations and dosages form, and the general physical and chemical properties of drug substances. Packaging helps in the products stability, transportation, storage, and deterioration conditions.

- Pharmaceutical packaging of the economical means providing protection identification information, convenience and stability of the product.
    - **Factor affecting pharmaceutical packaging—**

- The type of dosage form
- The route or mode of administration or use
- The type of pack (Blister or strip)
- The mode of sale/marketing area
- The mode of dispensing via a combined device/pack.
    - **Types of packaging testing—**
    - Drop test.

- Collapsibility test.
- Vibration test.
- Shock test.
- Inclined impact test.
- Revolving drum test.

- **Ideal characteristic of packaging—**

  - Provide the high degree of protection against any contamination like environment as well as artificial issues.
  - Do not show any incompatibity (physical or chemical) with the product material.
  - Easy to handling, storage and transport according to the customer convenience.
  - Easy to sterilization method and easily participate in recycling process.
  - Show more longevity and high printing property.
  - Affordable economical value.

  - **Types of packaging—**

- **Primary packaging—** In primary packaging material are directly covered the products and come close to the products and hold it. It provides the initial safety barrier for product. This type of packaging is often intended for the end user or consumer so it is also called consumer unit packaging. Example:- Strips, Blister, bottle, spray cane.

- **Secondary packaging—** These types of packaging apply, outside of the

primary packaging and it facilitates the handling of smaller products by combining them into a single pack. Example:- Boxes.

- **Tertiary packaging—** It is used for bulk handling and shipping. It facilitates the handling, storage and transport of goods. It provides the final barrier to products from damage.
    - **Types of packaging materials—**
    - Glass material.
    - Plastic material.
    - Metals materials.
    - Rubber materials.
    - Paper board materials

## Glass packaging.

- **Definition—** Neutral glass is a borosilicate glass containing significant amounts of boric oxide, aluminium oxide, and alkali or alkaline earth oxides. It has a high hydrolytic resistance and a high thermal shock resistance.
    - Glass has been widely used as packaging materials and it is moulded in any shape, size, and thickness. Most of parenteral preparation are used the glass materials.
- On the basis of hydrolytic resistance it divides into three parts.
- **Type I glass containers** which are of neutral glass, with a high hydrolytic resistance, suitable for most preparations, not for parenteral use.

- **Type II glass containers** which are usually of soda-limesilica glass with high hydrolytic resistance are suitable for most acidic and neutral, aqueous preparations, not for parenteral use.
- **Type III glass containers** which are usually of sodalime- silica glass with only moderate hydrolytic resistance. They are generally suitable for non-aqueous preparations for parenteral use.
    - **Advantages of glass packaging—**
    - They are transparent or uncolored packaging to permit the visual inspection of the products contents.
    - They have a good protection for powder because powder very sensitive against the moisture and temperature.
    - Available in variety of shape and size according to our needs.
    - Colored glass (amber colored) is also used in the packaging for the more sensitive materials.
- **Disadvantage of glass packaging—**
    - High risk during the transport and handling because it is fragile in nature.
    - Glass is heavy in weight than other.

- High risk of product contamination due to broken glass piece and some time release alkali to aqueous preparation

- **<u>Plastic packaging.</u>**

- **Definition—** Plastic packaging for pharmaceutical products is made from plastics based on the following polymers: polyethylene (low or high density), polypropylene, and polyvinyl chloride, polystyrene and to

a lesser extent polyethylene terephthalate. The containers consist of one or more polymers together with certain additives if necessary. They should be manufactured from materials that do not include in their composition any substances that can be extracted by any contents in such quantities so as to alter the efficacy or stability of the product or to present a toxic hazard. Additives may consist of antioxidants, lubricants, plasticizers and impact modifiers but not antistatic agents and mould release agents.

- **Advantages of plastic packaging—**

- It is flexible in nature so it cannot easily breakable.
- Due to less weight than the glass it is easy to transport and handling.
- Verity of shape and size are available according to our convenience.
- The high versatility of plastic allows for ease of reuse and recycling. In fact, these days' companies are creating specialized plastic bag making

- machines that help you optimize on the recyclability of plastic.
- The durability offered by plastic packaging also allows manufacturers to print eye-catching, high-quality custom designs, and thereby increase product visibility in a retail setting.

- **Disadvantage of plastic packaging—**

- Plastics are highly sensitive for light so it is easily effects by heat
- It is easily reacts with the products materials and alters the products physical and chemical properties.

- It is not easily degrades by the nature, so it shows harmful impacts on the environment and health.
- Plastics show the poor longevity and poor printing.

- **Metal packaging.**

- **Definition—** Metal is one of the way for packaging of most hazards substances the metals commonly used for this purpose are aluminium foil, tin plated , steel, lead etc. Metals are used in most of the collapsible tubes packaging.
    - The common expression used to describe such a process is “canning”. Canned food has become an important part of the human diet in developed countries during the past century.
    - **Advantages of metal packaging—**
    - Metal covering is impermeable for the light, moisture and gases so it provide high degree of protection against the environment issue.
    - Due to hardness of metal it is not easily breakable, and easy in transports and handling.
    - They are light in weight compared to glass containers.
    - Attractive labels are easily printed on the surface of metals.
- **Disadvantage of metal packaging—**
    - They show high economical value.
    - Due to heavy weight it is easy in transport.

- Some metals are reacts to the products and cause poisoning conditions.
- Rusting is cause in some metals by absorbing the moisture.

- **Rubber packaging.**

- **Definition—** Rubber is used mainly for the construction of closure meant for vials, transfusion fluid bottles, dropping bottles and as washers in many other types of product. The main types of rubber used for pharmaceutical products include natural rubber, neoprene, nitrile, butyl chlorobutyl, bromobutyl and silicone.
- Silicone is the most expensive and although the most inert, is readily permeable to moisture, gases and absorbent to certain preservative.Advantages of rubber packaging—
  - Water absorption is very low, so it provides the better resistance against the moisture and humidity.
  - Due to stretchable nature, it is easy to handling and transport.
  - It is the cheaper materials than metal and glass. It shows good economical value.
  - Most of the rubber materials are used for the closing apparatus and provide the addition protection against any contamination.
  - Nitrile rubber is heat resistant and oil resistant due to presence of nitrile group.
- **Disadvantage of rubber packaging—**
  - Absorption of bactericide and leaching of extractives are

considerable.

- It does not perform well when exposed to the chemicals substances.
- It is very expensive.

- Some time rubber materials also reacts the products material and alters the products physical and chemical properties.

# • PHARMACEUTICAL AIDS.

- **Oragnoleptic character**—Oragnoleptic character mainly based on the sensory organs. Oragnoleptic character involves color, odor, taste, flavor etc.

- **Pharmaceutical aids: -** The substances which are essentially used in manufacturing or compounding of various pharmaceutical dosages form is called as pharmaceutical aids. It helps in masking the unpleasant odor, taste, and flavour of any dosages form and made to more elegant during the dosages administration.

- Drugs are the preparation which contains the active pharmaceutical ingredients and excipients (coloring, flavouring, sweetening agents, preservatives etc). Excipients are also known as the pharmaceutical aids.

- **Pharmaceutical aid or excipients** shown no or little pharmaceutical effect but it play an important role to modifying the drugs dosages form (tablets, capsule, syrups, emulsion, solution etc). Example of pharmaceutical aids contains— coloring agents, sweetening agents, emulsifying agent, suspending agents, flavouring agents, diluents, lubricants etc.

- **Importance/Application of pharmaceutical aids—**

- It helps in masking the unpleasant odor, taste, and color etc.
- It insures safe, efficiency, reproducible, and convenient manner of drug delivery.
- Pharmaceutical aids increase the shelf life of the drugs.

- It protects the chemical changes and microbial action of main API, they include antibacterial agents and antioxidants.
- Due to involvement of the pharmaceutical aids we design the different form of shape, size of the dosages form.
- It is overcomes the patients inconvenience and helps in manufacturing, to design attractive dosages form.
- **Ideal characteristics of the pharmaceutical aids—**

- It does not change chemical nature of the drugs.
- It is does not cause any toxic effects.
- Masking the unpleasant color, odor, and taste.
- During administration it does not cause any allergic reactions.
- Overcomes the patient inconvenience.
- It prevents the microbial activity or contamination in the pharmaceutical products.
- It improves the shelf life of the products.
- It works on low concentration.
- Cheap and easily available

- **Coloring agent**

- **Colorants or coloring agents** are mainly used to improve the distinctive appearance of pharmaceutical dosages form, which are helps in the identification during manufacturing and increase the patient acceptance towards the pharmaceutical dosages form.

- In pediatric and geriatrics coloring agents play a major role and attract the consumer by providing the aesthetic appearance to dosages form.

- **Classification of coloring agents—**

- On the basis their origin it is divided into two parts—
    - **Synthetic—**Tartrazine, Azorubine, brilliant blue, erythrosine.
    - **Natural—**Animal—carmine, tyrian purple. Plants—Annatto, caramel, lycopene Mineral—malachite, cinnabar, aragonite.
- On the basis of their solubility it is divided into two categories—
- **Colorant dyes (soluble in the medium)** —Indigo carmine, brilliant blue, caramel.
- **Pigments (insoluble in the medium)** — Cadmium pigment, chromium pigment, cobalt pigment.
- **Uses/Applications of coloring agents—**

- Coloring agent provide the suitable color to formulation and helps in the identification.
- Increase the consumer acceptance.

## ▪ Flavouring agents

- **Flavourants or flavouring agents** are mainly used for masking the unpleasant or unacceptable odor from formulation and provide more pleasant taste or flavour.
- There are four basic taste sensations are salty, sweet, bitter, and sour. Flavour added to drug solutions can make a medicine more acceptable to take especially if the drug has an unpleasant taste. In the pediatrics dosages form flavour play a key role for administration of the drugs.

- Flavouring agents are more sensitive against the heat (thermolabile nature) so it cannot be added prior to an operation involving heat, they

are often mixed with the granules as an alcohol solution. In market many coating tablet are present for masking the flavour.

- **Classification of flavouring agents—**

- **It is classify into two categories—**
- **Natural flavouring agents**—Citrus fruit (lemon, orange), spice (cinnamon, peppermint, ginger, onion), fruits (apple, banana).
- **Synthetic flavouring agents**—Benzaldehyde, cinnamic aldehyde,coumarin,ethyl methyl ketone.

- **Uses/Applications of flavouring agents—**

- Masking the unpleasant taste or flavour and provide suitable flavour.
- Increase the consumer acceptance.

## Sweetening agents

- **Sweetening agents or sweeteners** are mainly used for masking the undesirable or bitter taste of any drug formulation and increase the patient acceptance towards pharmaceutical dosages form. In pediatric dosages form it is widely used because children prefer more the sweetening drugs.

- In Homeopathic medication, small sugar pills are used during the drug delivery. Recently it is widely used in the Ayurvedic medicine also.

- Sugar is the most widely used sweetening agent, due to its viscosity nature it also used as preservative for liquid preparation.

- **Classification of sweetening agents—**

- **It is divided into two categories**—

- **Natural sweetening agent**—Glucose, fructose, sucrose, dextrose, sorbitol.
- **Artificial coloring agent**—sucralose, aspartame, saccharin.
- **Uses/Applications of sweetening agents—**
- Sweetening agent masking the undesirable or bitter taste.
- Increase the consumer acceptance.

## ▪ Presevative

- **Preservative** are the chemical agent which prevents the product contamination or product decomposition by the action of any contaminant (environmental or biological). Preservative commonly add in the pharmaceutical and various food products for enhancing their stability and shelf life. Phenolic compounds like sodium benzoate are highly used as preservative during the manufacturing.
- **Classification of preservative—**
- **On the basis of mechanism of action it is divided into three categories**—
    - **Antimicrobial agents—**that agent which prevents the contamination (gram positive and gram negative) and degradation by microbes is called as antimicrobial agents. These agents are active in low concentration.Example- phenolic compounds, parabens, propylene glycol,BHT,BHA.

        - On the basis of their activity it is further divided into two parts.

- **Microbiostatic—**that inhibits the growth and multiplication of the microbes.
- **Microbiocidal—**that agent direct kills the microbes.
    - **Antioxidants agents**—those agents which prevents the products oxidation or degradation in the presence of molecular oxygen. Generally API is more reactive towards the oxygen, so antioxidants are mix with the product and overcome the product reactivity.
        - Example— ascorbic acid, citric acid, tocoferols, BHA, BHT.
    - **Chelating agents**—those agents which form the cyclic compounds or complexes with the pharmaceutical ingredients and prevent the degradation of pharmaceutical formulation
        - Example—EDTA, polyphosphates.
- On the basis of sources it is divided into two parts—
- **Natural preservatives**—vinegar, honey, castor oil, salt, sugar.
- **Synthetic preservatives**—sodium benzoate, BHA,BHT.

- **Uses/Application of preservatives—**

- Preservative enhance the stability and shelf life of the products, so it maintain the product activity for long time.
- It prevents the product by any microbial contamination increase their resistance power against the microbial growth.
- Many environmental factors effect the products property, for overcoming this activity preservative are also used.

- It also mixes with the food preparation for prevention their oxidation.

## Chapter -4

- **Size Reduction:-**
- It is the process of reducing drugs size in smaller particles, or fine powder. The term size reduction is applied to ways in which particles of solids are cut or broken into smaller pieces. Size reduction is necessary if the starting material is too coarse, and final product needs to be a fine powder.
- **Importance of size reduction.**

- To improve the stability of certain pharmaceutical dosage forms such as suspension the rate of sedimentation decrease to a large extent by reducing the particle size of the drug.
- To help in the process of separation of the solid from liquids by filtration by the rate of filtration depend upon the particle size.
- To increase the rate of absorption of a drugs the smaller particle size the greater is the rate of absorption.
- To increase the rate of solution is case of chemical substance become reduction of the particle size increases the surface area for the action of solvent.
- Due to size reduction, we are design the different type of drug dosages form (tablets, capsules, suspension and emulsion etc).

### Factor affecting size reduction

- **Hardness:-** The hardness of the material affect the process of production it is easier brakes soft material to a small size then hard

material. Due to the hardness of any material it affects the drug solubility and modification of any drug dosages form.

- **Toughness:-**The crude drugs of fibrous nature, it is not easily break down in smaller particle and shows the tough nature. In the toughness, materials
- fibrous are attached to each other in the layering form and affect the solubility of materials.
- **Material structure:-** Material structure is one of the major problem during the size reduction because special size and shape materials are easily break down by special machine or by special method.
- **Moisture content: -** The presence of moisture in the material influences a number of its properties such as hardness stickiness which in its turn effect the particle size reduction.
- The material having 5% moisture in case of drying grinding and 50% moisture in wet grinding does not create the problem.
- **Stickiness:-** Stickiness cause a lot of difficulty in size reduction this is due to the fact the material adhere to the grinding surface or sieve surface of the mill. Due to stickiness of material it affects the material weighing accuracy.
- **Softening temperature:-** Waxy substance (Stearic Acid, or drugs containing oil or fat) because softened during the size reduction process if a heat generated then the material not easily breakdown and sticks on the mill. If more the temperature generate in the machine, it affects the material stability and change their activity.
- **Purity required:-** Various mill are used for size reduction often cause the grinding surface to wear off and thus impurities come in the power

if a high degree purity is required such mill must be avoided.

- **Physiological effect:-** Some drugs are very patent during their particle size reduction in a mill dust is produced which may have an effect on their operator in such cases the enclosed mill may be used avoid dust.
- **Bulk density:-** The output of the size reduction of material in a machine depends upon the bulk density of the substance.
- **Ratio of feed size to product size:-**To get a fine powder in a mill. It is required to fairly small feed size should be used hence it is necessary to carry out the size reduction process is several stage using different equipment.
- ***Example:-*** Preliminary crushing following by coarse powder and then fine grinding.
- **Methods of Size Reduction.**
    - Cutting
    - Compression
    - Impact
    - Attrition
    - Combined impact and attrition
- **Cutting:-** The material is cut on a small scale by means of a sharp blade knife, root cutter or other any sharp instruments on a large scale a cutter mill is used cutting of the drug is usually done to hasten the drying ofdrugs.

- **Compression:-**In this method the material is crushed by the application of pressure on a small scale using mortar and pestle where as on a large

scale roller mill is used.

- **Example: Roller mill,**

- **Impact:-**
- Impact occurs when the material more or Less stationery and is hit by an object moving at high speed or when the moving particles strikes a stationary surface either case the material break into small pieces there is no apparatus which can be used on a small scale to effect side reduction by impact but on a large scale hammer mill and disintegrator are used.
- Example: Hammer Mill, Ball Mill

## ▪ Hammer Mill

- **Principal:-** It work on the principle of impact.

- **Construction:-**
- It consists of metal causing inclosing a control shaft to which four or more swinging hammer are attached the lower part of the mill, consists of a screen through which material can pass in a suitable receiver when the discrete of size reduction is reached.

- **Working:-**

- The material is put into the hopper.
- Which is connected with the drum the material is powered to the desire size due to fast rotation of hammer and is called under the screen this mill has the advantage of continuous operation because the chance of jamming is less as the hammer are not fixed the material can product

coursed to moderately fine powder.

- Due to the high speed of operation heat is generated which may affect themselves drugs are material more ever high speed of operation.

- **Advantage:-**

- It is used for production of intermediate grade of powder.
- It can be operated continuously.
- It is effecting in function and can grind different type of material.
- **Disadvantage:-**

- Due to high speed heat is generated.
- It is not suitable for heat sensitive material.
- **Attrition**:- the action or process of gradually reducing the strength or effectiveness of someone or something through sustained attack or pressure. The attrition mill is a device for mechanically reducing solid particle size by intense agitation of slurry of material being milled and coarse milling media.
- **Combined impact and attrition—**it is based on the impact and attrition principle. Example— Ball mill,
- It work on the principle impact and attrition.

- **Construction:-**

- It consists of a hollow cylinder which is mounted on a metallic frame.
- In such a way that it can be rotated on it clockwise (Longitudinal axis) the cylinder contains balls that occupancy 30 to 50% of the mill.
- Volume the weight of cabal consists the ball size depends on the size of the feed and the diameter of mill the cylinder and balls are made up of metal and are usually Lined with chrome in pharmaceutical industry some time the cylinder of the ball mill is lined with rubber or porcelain.

- **Working:-**

- The drug to be round to put into the cylinder of the mill and is rotates the speed of rotation is very important at a low the mass of ball will slide or rollover each other and only a negligible amount of size reduction at a high speed the ball mill will be thrown out to the walls by centrifugal force and grinding but at about to 2/3rd of the speed the centrifugal force just occur with the results that the balls are carried or most to be the top of the mill and then fallen by this way the mix size reduction is effect by attrition after a suitable time the material is taken out and pass through a sieve to get powder of the required size.

- **Advantages:-**

- It can product very fine powder.
- It can be used for continues operation.
- If sieve are classified classifier to attach to the balls.
- The suitable for both weight and drug grinding process.

- **Disadvantage:-**

- The ball mill is a very noise.
- Wear occurs from the ball as well as from the cassing which may result contamination.

# Size Separation

- Definition: - Size Separation is a unit process that involved the separation of a mixture of various size particles into two or more portion by means of screening surface or by shifting. it is also known as sieving, sifting, and screening.
- Size separation technique is based on different physical properties of the separating mixture or substance like size, shape and density.
- Initially crude drugs (Nuxvomica, Rauwolfia, Ephedra, Ashoka etc.) are present in large size but involvement of size reduction and size separation we are obtain the desired size granules and particles and improve the pharmaceutical and pharmacological activity.
- **Applications/objectives of size separation:-**
- Size separation technique determines the particle size for the production of tablets capsules, suspension and emulsion etc.
- Due to separation, we obtain the desired granules or particles and ensure their flowability and uniformity.
- Undesirable substances are removed by the size separation technique.
- By obtaining the desired size particles we improve the mixing properties of the powders.

- To improve the solubility and stability of particles during production.
- Size separation technique optimize feed rate, agitation, screening during production.
- Quality control of raw materials.

- **<u>Official standards for powders accoding to Indian pharmacopoeia.</u>**

- The Indian Pharmacopoeia has defined the standard of powder for Pharmaceutical purpose. The Indian Pharmacopoeia specified five grade of powder.

- **Coarse powder: -** A powder of which all the particles pass through a No.10 sieve with nominal mesh aperture of 1.7mm and not more than 40.0 percent through a No.44 sieve with nominal mesh aperture of 355µm, this is usually referred to as a 10/44 powder or coarse powder.

- **Moderately coarse powder**: - A powder of which all the particle pass through a No.22 sieve with the nominal mesh aperture of 710µm and not more than 40.0 percent through a No.60 sieve with nominal mesh aperture of 250µm, this is usually referred as a 22/60 powder or moderately coarse powder.

- **Moderately fine powder:-** A powder of which all the particle pass through a No.44 sieve with the nominal mesh aperture of 355µm and not more than 40.0 percent through a No.85 sieve with nominal mesh aperture of 180µm, this is usually referred as a 44/85 powder or moderately coarse powder.

- **Fine powder: -** A powder of which all the particles pass through a No.85

sieve with nominal mesh aperture of 180µm, it is called as fine powder.

- **Very fine powder: -** A powder of which all the particles pass through a No.120 sieve with nominal mesh aperture of 125µm, it is called as fine powder.

- **SIEVE/SHIFTING.**

- Sieve for Pharmaceutical testing are constructed from wire cloth with square meshes woven from wire of brass, bronze, stainless steel or any other suitable material. The wire should be of uniform circular cross-section and should not be coated or plated these should not be any reaction between the material of the sieve and the substance which is being shifted from it.
    - Generally iron wire is used as screen material because it is cheap but their disadvantage and corrosive nature and chances of contamination by iron. This disadvantage can be overcome by coating iron with galvanizing agents which increase the strength and also make it corrosive resistant.
    - For separation of fine powder bolting cloth sieve are used. They are woven from twisted multi strand fibers made of silk, nylon and cotton. Nylon cloth is generally designated for their micrometer opening and also their availability in different grades.
- **Sieve Analysis: -** the International Standards Organization (ISO) fix lowest a sieve diameter 45µm. powder are generally defined as particles having a maximum diameter of 1000µm, so this is the upper limit. In practice, sieve analysis can be performed in a range of 5 to 125,000µm.

sieve analysis used to monitor material quality based on particle size.

- **Standard for Sieve**

- Standards for sieves used to testing must specify the following:

- Holes in the screen are called mesh. Mesh number indicate number of holes included in a length of 1 inch. Aperture of screen is the clear space between wires of screen opening and screen number denotes number of meshes in a linear length of 25.4mm.

- 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.
- Nominal size of aperture: - Nominal size of aperture indicates gap between two adjacent wires. It represents the length of the side of the square aperture. The I.P. has given the nominal mesh aperture size for majority of sieves in mm or in cm.
- 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.
- Approximate percentage sieving area: - This standard expresses the area of the meshes 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.
- Tolerance average aperture size: - Some variation in the aperture size is unavoidable and when this variation is expressed as a percentage, it is known as the 'aperture tolerance average'.

- **The working of mechanical sieving devices is based on any of the following methods.**
    - Agitation.
    - Brushing.
    - Centrifugal.
- **Agitation methods-** Sieves may be agitated in a number of different ways, such as:
- **Oscillation:** This sieve is mounted in a frame that oscillates back and forth. It is a simple method but the material may roll on the surface of the sieve.
- **Vibration:** The sieve is vibrated at high speed by means of an electric device. The rapid vibration is imparted to the particles on the sieve which helps to pass the powdered material through it.
- **Gyration:** In this method, a system is made so that sieve is on rubber mounting and connected to an eccentric flywheel. This gives a rotary movement of small amplitude to sieve which turn gives spinning motion to the particles that helps to pass them through a sieve.
- Agitation methods are not continuous methods but can be made so by inclination of the sieve and the provision of separate outlets for undersize and oversize particles**.**
- **Brushing methods-** In this case, a brush is used to move the particles on the surface of the sieve and to keep the meshes clear. The brush is

rotated in the middle in the case of a circular sieve but spiral brush is rotated on the longitudinal axis in case of a horizontal cylindrical sieve.

- **Centrifugal methods-** In this method, a high speed rotor is fixed inside the vertical cylindrical sieve, so that on rotation of rotor the particles are thrown outwards by centrifugal force. The current of air which is produced due to high speed of rotor helps in sieving the powder.

- **SIEVING METHOD**

- In this method, the fine powder is separated from the coarse powder by using sieves of desired number. The degree of fineness of a powder is known with the help of sieve through which the powdered material is passed. Sieves are numbered in order to distinguish from each other.

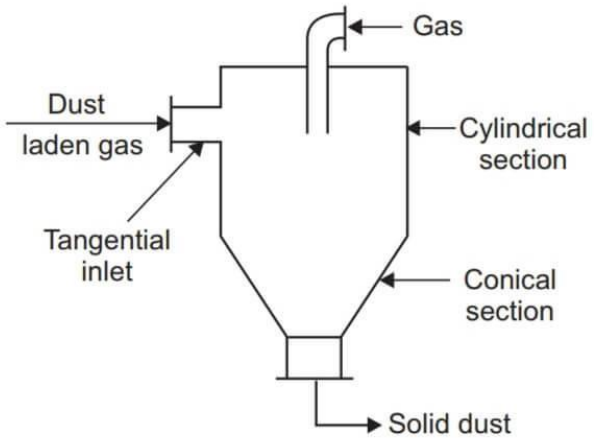
- **Working & construction: -** Size separation of powder is done by passing the powdered material through a set of sieves. Sieves are arranged in descending order
- i.e. sieve of larger size is at the top and the smallest one at the bottom. The bottom sieve is attached to the receiving pan. The material is placed in the uppermost sieve. The sieves are shaken with the help of mechanical sieve shaker or electromagnetic devices. It helps the particles to pass through the sieves.

- **CYCLONE SEPARATOR**

- **Principle: -** In cyclone separator, the centrifugal force is used to separate solids from fluids. The separation depends not only on the

particle size but also on density of particles. Hence depending on the fluid velocity, the cyclone separator can be used to separate all types of particles or to remove only coarse particles and allow fine particles to be carried through with the fluid.

- **Construction: -** It consists of a tapering cylindrical vessel which consisting of a top vertical section and lower conical/tapering section terminating in an apex opening - a short vertical cylinder which is closed by a flat plate on top and by a conical bottom. It is provided with a tangential feed inlet nozzle in the cylindrical section near the top and an outlet for the gas, centrally on the top. The outlet is provided with a downward extending pipe that extends inward into the cylindrical
- section to prevent the gas short-circuiting directly from the inlet to the outlet and for cutting the vortex.




- **<u>Cyclone separator.</u>**

- **Working: -** The suspension of a solid in gas (usually air) is introduced tangentially at a very high velocity, so that rotary movement takes place within the vessel. The fluid is removed from a central outlet at the top. The rotatory flows within the cyclone separator generate the centrifugal force on the particle. The solids are thrown out to the walls; thereafter it falls to the conical base and discharged out through solids outlet.
- **Uses: -** Cyclone separators are used to separate the suspension of a solid in a gas (air). It can be used with liquid suspensions of solids

# Mixing

- **Mixing** is defined as a process that tends to result in a randomization of dissimilar particles within a system. Mixing refers to the random distribution into are through one another of two or more separate phases. Some of the mixing operations in the dispensing practice are spatulation, trituration, tumbling, geometric dilution etc.
- **Agitation—**Agitation refers to the induced motion of a material in a specified way, usually in a circulatory pattern inside a container.
- The term mix means to put together in one mass or assemblage with more or less through diffusion of the constituent elements among one another.
- The term blending means to mix smoothly and inseparably together.

During blending minimum energy is imported to the bed

- **Factor influencing mixing process—**

- Nature of surface.
- Density of the particles.
- Particle size and shape.
- Particle charge.
- Proportion of materials.

- **Mechanism of mixing in Solids—**

- **Convective mixing**—It is achieved by the inversion of the powder bed using blades or paddles or screw element. A large mass of material moves from one part to another. Convective mixing is referred to as macro mixing.
- **Shear mixing—**In this type, the forces of attraction are broken down so that each particle moves on its own between regions of different composition and parallel to their surface.
- **Diffusive mixing—**It involves the random motion of particles within the powder bed, there by particles change their position relative to one another. Diffusive mixing is referred to as micro mixing.

- **In Solid-solid mixing operation four steps are involve—**

- Expansion of the bed of solids.
- Application of three dimensional shear forces to the powders.

- Mix long enough to permit true randomization of particles.
- Maintain randomization (no segregation after mixing).

- **Equipment used for solid Mixing—** V cone blender, Double cone blender, Ribbon blender, sigma blade mixer etc.
- **Mixing Of liquids.**

- **Liquid-liquid mixing** is considered as a simple operation compared to that of solid-liquid mixing. It involves the formulation of a homogeneous system.
- According to theories of solutions, liquid mixtures are classified as follows—

- **Miscible liquids**—Miscible in all proportion. Example- Ethyl alcohol and water.
- **Partially miscible liquids—**Miscible in one another at one particular proportion. Example- P-cresol and water.
- **Immiscible liquids—**these are not miscible. Example- vegetable oils and water.

- **Equipment used for liquid mixing—** Propellers, turbines, Airjet mixer.

- **Mixing of Immiscible liquids.**
- Mixing of immiscible liquids is carried in pharmacy mainly in the manufacturing of emulsions. The equipment used for preparation of an emulsion is known as emulsifier. Generally a fine emulsion can be obtained and therefore, equipment is also known as homogenizer.

- Sometimes, the above equipment directly gives fine emulsion. Otherwise, coarse emulsion is subjected to homogenization in the second stage to get fine emulsion by using one of the following- Silverson emulsifier, colloid mill, rapisonic homogenizer.

- **Mixing of semisolids.**

- Semisolid dosages forms include ointments, pastes, creams, jellies etc. while mixing such dosages forms, the material must be brought to the agitator or the agitator must move the material throughout the mixer.

- The mixing action includes combination of low speed shear, smearing, wiping, folding, stretching and compressing. Mixing equipment are also used for preparing tooth paste, pill mass and wet mass for granulation.

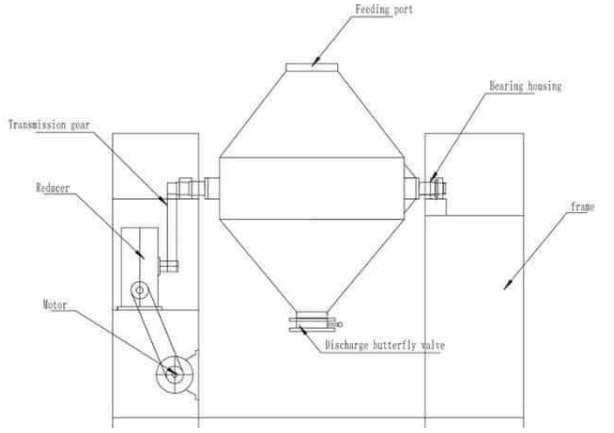
- Some semisolids exhibit dilatants property that is viscosity increase with increase in shear rates. Therefore, mixing must be done at lower speeds. The speed must be changed accordingly to thixotropic, plastic and Pseudo plastic materials.

- Equipment used for mixing of semisolid— Sigma mixer and planetary mixer (Solid-solid mixer), triple roller mill, colloidal mill.

    - **Double cone blender.**

- **Principle—**It is an efficient design for mixing of powder of different densities. It is usually charged and discharged through the same port. These are used mostly for small amounts of powders.

- The rate of rotation should be optimum depending on the size and shape of the tumbler, nature of materials to be mixed. Commonly the range is 30 to 100 R.P.M.
- **Construction—**




- The conical shape at both the end enable uniform mixing and easy discharge.
- The cone is statically balanced which protects the gear box and motor from any excessive load.
- Powder is loaded into the cone through a wide opening and discharged through a butterfly or a slide valve.
- Depending upon the characteristic of the products, paddle type baffles can be provided.
- **Working—**The material is loaded approximately 50% to 60% of its total volume. As the blender rotates, the material undergoes tumbling motion. This motion dividing and recombination continuously yields ordered mixing by mechanical means. Blender speed is the key for mixing

efficiency. At high speed, more dusting or segregation of fines is possible, while at low speeds, not enough shears may be applied.

- **Uses/Applications—**It is an efficient and versatile machine for mixing of dry powders and granules homogeneously.
- **Advantage—**

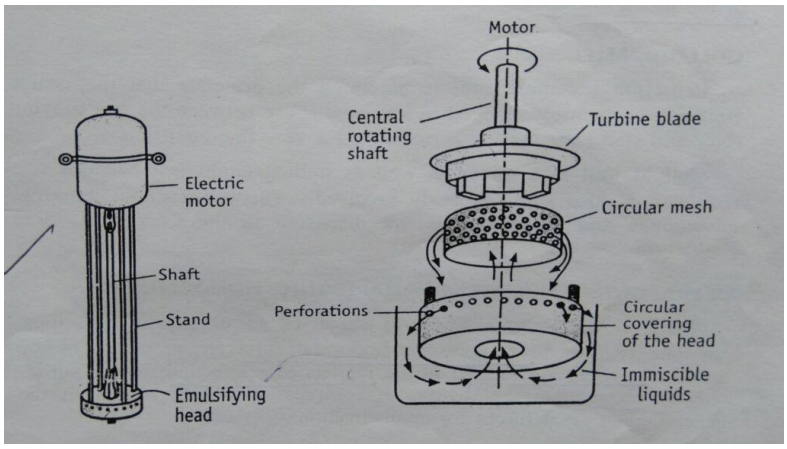
- It is suitable for fragile granules because of minimum attrition.
- Easy to clean, load and unload.
- They handle large capacities.
- This equipment requires minimum maintenance.

Disadvantage—

- Need high head space for installation.
- It is not suitable for fine particulate system or ingredients of large differences in the particle size distribution because not enough shears is applied.

    - **Turbine Mixer.**

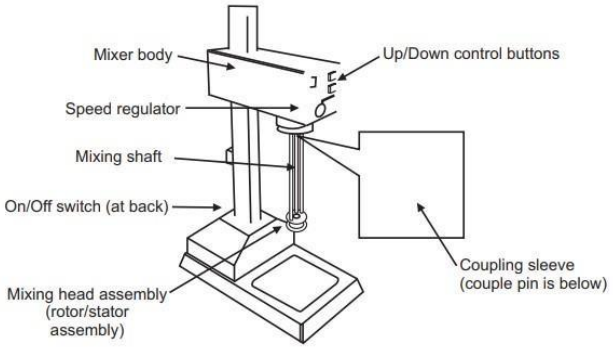
- **Principle—**A turbine mixer is a mechanical device that is used in mixing different types of liquids. The turbine mixer works mainly on the principle of shearing action.
- **Construction—**




- A turbine consists of a circular disc to which a number of short blades are attached. The diameter of the turbine ranges from 30% to 50% of the diameter of the vessel.
- It rotates at a lower speed than propeller (50-200 R.P.M).
- The blades may be straight, curved, pitched or vertical.
- **Working—**A flat bladed turbine produces radial and tangential flow, but as speed increase radial flow dominates. A pitched blade turbine produces axial flow.
- Near the impeller, the zone of rapid currents high turbulence and intense shear is observed. The shear produced by turbines can be further enhanced using a diffuser ring.
- A diffuser ring is a stationary perforated or slotted ring, which surrounds the turbine. It increase shear forces, the liquid passes through the perforations reducing rotational swirling and vortexing.
- **Uses/Applications—**Turbines are effective for high viscous solutions

with a very wide range of viscosities up to 700 Pascal/seconds (syrups, liquid paraffin, glycerin etc). They can handle slurries with 60% solids. Turbines are suitable are suitable for liquids of large volume and high viscosity, if the tank is baffled.

- **Advantage—**Turbine gives greater shearing forces than propellers, through the pumping rate is less. Therefore, turbines are suitable for emulsification.
- **Disadvantage—**Turbine has less pumping rate.
    - **Silverson Mixer.**
- **Principle—**Silverson mixer produces intense shearing forces and turbulence by the use of high speed rotors. This turbulence causes the liquids to pass through fine interstices formed by closely placed perforated metal sheets. Circulation of material take place through the head by the suction produced in the inlet at the bottom of the head. Circulation of the material ensures rapid breakdown of the dispersed liquid into smaller globules.
- **Construction—**



- It consists of long supporting columns connected to a motor which give support to the head. The central portions contain a shaft, one end of which is connected to the motor and the other end is connected to the head.
- The head carries turbine blades. The blades are surrounded by a mesh, which is further enclosed by a cover having openings.
- **Working—**

- The emulsifier head is placed in the vessels containing immiscible liquids in such a way that it should get completely dipped in the liquid.
- When the motor is started, the central rotating shaft rotates the head. This in turn rotates turbine blades at a very high speed.
- This creates a pressure difference; as a result liquids are sucked into the head from the center of the base and subjected to intense mixing action.
- The intake and expulsion of the mixture set up a pattern of circulation to ensure rapid breakdown of the bigger globules into smaller globules.

- **Uses/Applications—**Silverson mixer is used for the preparation of emulsions and creams of fine particle size.

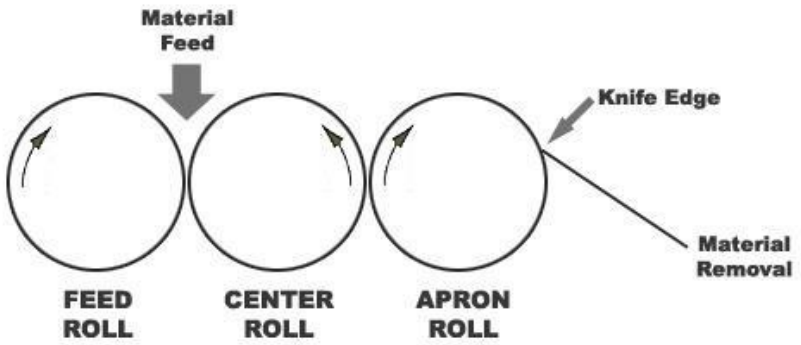
- **Advantage—**Silverson mixer is available for thousand liter of mixing.

- **Disadvantage—**Occasional there is a chance of clogging of pores of the mesh.

- **Triple Roller Mill.**

- **Principle—** The differential speed and narrow space between the rollers develop high shear over the materials. This shear causes crushing of aggregates particles and also distributes the drug uniformly throughout the semisolid base.

- **Construction—**




- It consists of three parallel rollers of equal diameters. These are made up of hard abrasion resistant material, normally stainless steel.
- The pressure and gap between the rollers are independently adjustable. A hopper is arranged between the first two rollers. A scrapper is attached to the last roller.
- **Working—**

- The rollers are rotted at different speeds. In practice, the first roller (receiving roller) rotates at a slower speed compared to the second roller. Similarly second roller speed is less than that of third roller (discharged roller).

- The feed is passed through the gap between the first and second roller. The aggregates and particles are crushed and then abraded by the rubbing action of the roller, which is developed due to different speed of rotation.
- A film of appreciable thickness of the feed is produce. The material passes from slow rotating to fast rotating roller.
- Between second and third roller, the gap is small and produces a thinner film of feed. The speed of the third roller is increased to compensate the reduction of cross-sectional area. In the thinning film, more crushing and more abrasion are developed.
- Finally the scrapper removes the material completely from the last roller which can be collected immediately into the receiver or transported through a suitable conveyor.
- **Uses/Applications—**It is uses for production of fine or thinner film, on by large particle feed.
- **Advantage—** Triple roller mill is suitable for continuous process extremely uniform dispersion obtained.
- **Disadvantage—**Roller may cause the abrasion and speed maintain is key tasks.

    - **Pharmaceutics | Chapter-4.**

- **<u>Unit- 4 — Filtration.</u>**
- **Filtration—** It is defined as a process of separation of solid from fluids

by passing mixture through a porous medium that retain the solid but allows the fluids to pass through. The mixture or suspension to be filtered is known as slurry. The porous medium used to retain the solids is known a filter medium. The accumulated solid on the filters are referred to as filter cake, while the color liquid passing through the filter is filtrate.

- When solids are present in a very low concentration that is not exceeding 1.0% w/v the process of its separation from liquid is called clarification.
- **Application of Filtration.**
- **Production of sterile products—** Air is filtered through HEPA filters (high efficiency particulate air filters) or laminar air bench to obtain sterile air, which maintain good environment prior to and during manufacturing of sterile products.
    - A solution is passed through a bacteria proof filter in order to obtain sterile solution, particularly when heat sterilization is not suitable on account of the thermolabile nature of the contents. In case of sterile products particle as small as 0.2μm should be removed, which includes the bio- burden of fungi, bacteria etc.
- **Production of bulk drugs**—solids of intermediates and finished products are separated from the reaction mixture by filtration techniques by the method, impurities can be removed.
- **Production of liquid oral formulation**—Filtration is an essential steps in the production of liquid oral for obtaining clear solution.
- **Affluent and waste water treatment**—Waste solid must be separated

from the waste liquid prior to its disposal. Sometimes, the soluble components are precipitated and the separated by filtration.

- **Factor influencing filtration.**

- A simple straining process does not provide a complete description of how particles are removed from s suspension. The particles are exposed to a number of forces including gravity or electrical fields. Some of the factors influencing the filtration rate-

- **Properties of the liquids**—Density, viscosity, and corrosiveness.
- **Properties of the solids**—Particle shape, particle size, particle charge, particle density, rigidity or compressibility of the solid under pressure and tendency of particle to flocculate or adhere together.
- **Temperature of the suspension.**
- **Filter cake formation rate**.
- **Surface area of the filter medium**.
- **Gravity forces**.
- **Appling pressure**.
- **Viscosity of filtrate**.
- **Centrifugal forces**— Centrifugal force could replace the gravitational force and is used to increase the rate of filtration.

- **Theories of filtration**

- The flow of a liquid through a filter follows the basic rules that govern the flow of any liquid through the medium offering resistance. The rate of

flow may be expressed as--

- **Rate = driving force/resistance.**
    - The rate of filtration may be expressed as volume/time.
    - The driving force is the pressure differential between the upstream and downstream of the filter.
    - The resistance is not constant .it increase with an increase in the deposition of solids on the filter medium.
- **Poiseuille's Equation— Poiceuille** considered that considered that filtration is similar to the streamline flow of a liquid under pressure through Capillaries.
    - **$V = \pi \Delta P r^4 / 8 L \eta$.**
    - Where →V = rate of flow, that is volume of liquid flowing in unit time $m^3/s$.
        - ΔP = Pressure difference across the filter. Pascal. r = radius of the capillary in the filter bed. Meter
        - L = Thickness of the filter cake (capillary length). Meter η = Viscosity of the filtrate. Pascal/second.

- **Darcy Equation—**
    - **$V = KA\Delta P / \eta L$.**
    - K = permeability coefficient of cake $m^2$.
    - A = Surface area of the porous bed (filter medium) $m^2$.
    - The term k depends on the characteristics of the cake, such as

porosity, specific surface area and compressibility.

- **Kozeny-Carman Equation—**
  - **$V = A/\eta s2 \times \Delta P/KL \times \varepsilon^3/(1-\varepsilon)^2$**
  - Where → Ɛ = porosity of the cake (bed)
    - S = Specific surface area of the particles comprising the cake $m^2/m^3$. K = Kozeny constant (usually taken 5).
- **Membrane Filter.**
- **Principle**—Membrane filter consists of microsporous plastics films of specific pore sizes, therefore it is also known as screen, sieve or microsporous filter.
- Membrane present in these filters retains particles or microorganism (larger than the pore size) by surface capture. It act like sieve and the particulate matter is retained on the surface of membrane.
- **Construction**— Membrane filter consists of membrane of cellulose acetate, cellulose nitrate in mixed cellulose ester. The pores size of filter in micron or submicron range.
- A membrane filter is 150µm thick and contains about millions of microscopic pores. The diameter of these spores is uniform. Based on the requirement the size of these pores is adjusted, during the process of polymerization. The most widely accepted membrane filter possesses a pore size of 0.22µm and 0.45µm.
- **Working**—The membrane filter functions like a sieve and thus removes particle. The filter of 0.010 – 0.10 µ pore sizes remove even viruses from

water or air and filter of 0.30 – 0.65 μ pore sizes remove bacteria. Filter with largest pore sizes is used in aerosol radioactivity and particle sizing applications.

- For sterile filtration, the membrane is autoclaved in the holder and to prevent curling they are packed between thick filters. Some membrane filters which are pre-sterilized (by ethylene oxide or ionizing radiation) are also available.
- A rigid base of perforated metal, plastic, or coarse sintered glass is used to support the membrane filter during filtration process (as in the case of fibrous pad filters).
- **Uses/Applications—**

- It is used for sterilization and clarifying aqueous and organic solvents including buffers, microbiological and tissue culture solution.
- It is suitable for filtration of enzyme solution.
- It is used for diagnostic cytology and receptor binding studies.

- **Advantages—**

- It does not allow any cross contamination.
- Its filtration rate is rapidly.
- It can be easily disposed off.
- Since absorption is negligible, it does not import any fibers or alkali into the filtrate.

- **Disadvantages—**

- It may get clogged
- It ordinary, it is less resistant to solvents like chloroform.

    - **Sintered glass filter.**

- **Principle**—It is works on the principle of Reducing pressure. During the filtration high pressure exerts on the sintered glass disc and lower pressure exert on the base of funnel. Due to pressure difference filtration is performing.

- **Construction**—It consists of the glass funnel and sintered glass disc. These filters have as a filtering medium a flat or convex plate of Jenna glass powdered and shifted to produce granules of uniform size that are molded together. The variation in porosity depending on size of granules used in the plate. A vacuum attachment is necessary to facilitate the passage of liquid through the filter plate.

- **Working**—the sintered glass filters are available in different pore size. Hence the funnel with a sintered filter is numbered according to the pore size. The filtration is carried out under reduced pressure. These funnel are used for bacterial filtration.

- **Uses/Applications**— Sintered filters are also available in stainless steel which has a greater mechanical strength. However these are very much liable to attack by the solutions passing through them.

- **Advantage—**

- It is easy to clean and labor requirement is very low. Its shows low

absorption properties.

- **Disadvantage—**

- It is fragile in nature so its handling is very tough task. It is very expensive and time consuming.

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## Tablets

- Tablets are defined as solid flat or bi-convex discs, prepared by compressing a drug or a mixture of drugs with or without diluents.
- They are available in different size, shape and weight.

    - **Advantage of Tablets:**

- They are easily swallowed.
- They are easy to carry.
- Unpleasant taste can be masked by sugar coating.
- They provide prolong stability to medicament.
- They maintain the accuracy of dosage.

    - **Disadvantages of Tablets:**

- Some drugs cannot be compressed because of their low density and amorphous nature.
- Drugs with poor wetting , slow dissolution and large dose are difficult to convert into tablets.

- **Coated tablets:**

- Tablets can be either coated with a sugar or film coating.
- A coated tablets generally goes down easier and with less after taste.
- It can be used to improve product apperance organoleptic properties.

- **Uncoated Tablets:**

- Uncoated Tablets are rougher, may be more difficult to swallow and often leave a bad taste in the mouth swallowed.
- They are generally single layer tablets prepared by single compression of granules or multi-layer tablets consists of parallel layers prepared by compression of granules of different compositions.
- The formulated of uncoated Tablets to be chewed or to effect a slow release and local action of the active ingredient.

- **Various modified tablets:**

- **Sustained release tablets:**
  - These tables are used to get a sustained action of medicament.These tables when taken orally release drugs at a desired time and maintain the maximum effective concentration of drug in the blood throughout the period of treatment.
- **Extented release tablets:**
  - The drug is released slowly over time.
  - The advantage of taking pills less often and there maybe fewer side-effects as the levels of the drug in the body are more consistent in extended release formulations.

- **Fast dissolving:**
    - A tablet that dissolve or disintegrates quickly in the oral cavity upon the contact with saliva, resulting in solution or suspension of administered medicine.

- **Double layered tablet:**
- These tables consist of two medicaments compressed successively in the same Tablets.

- Capsules - Hard And Soft Gelatine Capsules

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- **Capsules:**
- They are solid dosage forms consisting of single dose of drug enclosed in a water soluble shell of a suitable form of gelatin.
    - **Advantage of Capsules:**

- The labour and production cost is less.
- The unpleasant taste and odour of medicaments can be masked by enclosing in Capsules.
- They are smooth and become slippery on moistening.
- They are easily swallowed.
- Enteric coating releases the medicament in the intestines.

- They are easy to handle and carry.
- They are attractive in appearance.
    - **Disadvantages of Capsules:**
- Hygroscopic drugs can not be filled in capsules, since they absorb water present in the capsules shell which ultimately breaks into pieces.
- Capsules can not be given orally to infants and children.
- The absorption rate of certain drugs like aspirin is reduced if given in capsules.
    - **Type of capsules:**
- Hard gelatin capsules
- Soft gelatine capsules

- **Hard gelatin capsules:**
    - They are used for administration of powders or solid medicaments.
    - It consists two cylindrical halves.
- ***Body***
- ***Cap***
    - The diameter of the body is slightly smaller than the diameter of the cap but larger in length and the cap is slightly longer in diameter and smaller in length.

- **Soft gelatin capsules:**

- They are also known as soft shell. These capsules are prepared from gelatin and water to which glycerin sorbitol or a similar polyol has been added as a plasticizer which imports flexibility to the Capsules.
- These capsules are used to fill medicaments, flavours, food concentrate, cosmetics, etc.
- The capsules are used for filling liquids, semi solid, vitamins, etc.
- They are also used for containing ear, eye, nose, and throat preparations.

- **Difference between hard gelatin and soft gelatin capsules:**

| S.No | Hard Gelatin Capsules | Soft Gelatin Capsules |
|---|---|---|
| 1. | They consists of two parts body and Cap | They consists of single unit after sealing the two halves of the capsules. |
| 2. | They are cylindrical in shape | They are round oval and tube like shape. |

| | | |
|---|---|---|
| **3** | **They are prepared from grelatin, titanium dioxide, colouring agent, sugars.** | **They are prepared from gelatin plasticizers and preservatives.** |
| **4** | **They consist of medicaments in the form of powder or granules.** | **They consist of liquids or solid dissolved in suitable excipients to give a paste** |

- Topical preparations - ointments, creams, pastes, gels, liniments and lotions, suppositories and pessaries Nasal preparations, Ear preparations
    - **Topical preparations:**
- Colloids, liniment, lotions, paints, and some, solution are the preparation applied topically to the skin, douches, ear drops, enemas, irrigations, nasal drops, sprays and other solution alternatively are the preparation instilled into body cavities.
- The container and closures used for these preparation should be different from those used for oral preparations, should be different from those used for oral preparations, colour is the only distinguishing feature between bottle and ribbed oval used for mouthwashes.
- The inhalation preparations to be inhaled or sprayed should be packed in colourless fluted bottles, because the drug is delivered to the respiratory tract.
    - **Ointments:**
- Ointments are semi solid preparations for external applications to skin or

mucous membranes.

- The components of an ointments offen but do not melt upon application to the skin.
- They are used topically on a variety of body surface.
- These include the skin and the mucous membranes of the eye (eye ointment), vagina, anus and nose.
- Ointments may or may not be medicated.

- **Therapeutically**:

- Ointments function as skin protective and emollients, but they are primarily as vehicles for the topical application of drug substances.
- It should be chemically and physically stable.
- It should be smooth and free from grittiness.

- **Advantage:**
- They are easy to handle than the bulky liquid dosage forms.
- They are directly applied to the target area avoiding the other body parts.
- Patients sensitive to parenteral and oral route prefer ointment.

- **Disadvantages:**

- They are more bulky than the solid dosage form.
- They required high cost of production.
- They may cause skin irritation.
- They may get contaminated when applied using fingers.

- **Pastes:**

- Pastes are the semi solid preparations meant for external applications to the skin. They contain large amount of finely powdered solids like starch, zinc oxide etc.
- Due to presence of these substances they have viscosity and stiffness and less attractive cosmetically. Since paste are stiff they do not melt at ordinary temparature thus forming and holding a protective coating over the area they are applied.

- **Difference between Ointments and Pastes:**

| Sr.No | **Ointments** | **Pastes** |
|---|---|---|
| 1. | Less Viscous | More Viscous |
| 2. | Less Stiff | More Stiff |
| 3. | More greasy | Less greasy |
| 4. | Contain less conc of solids | More concentrated than ointment |
| 5. | Oleaginous, water soluble water miscible and absorption bases can be used for preparation | Except absorption bases all other bases can be used. |

- **Gels:**

- Gels are aqueous colloidal suspensions of hydrated forms of medicinal substances for oral administration.

- **Example: Aluminium hydroxide gel, etc.**

- **Cold cream:**

- Cold cream is an emulsion which when applied on the skin a cooling effect is produced due to slow evaporation of water present in the emulsion. This are generally prepared by emulsion.
- This are generally prepared by emulsification of oil and water.
- In olden days animals fat vegetable oil was used but vegetable oil have rancid tendency so they replaced by mineral oils.

- **Liniments:**

- They are defined as the liquid or semi solid preparations meant for application to the skin.
- They are applied to the skin with friction and rubbing of the skin.
- A liniments should not be applied to broken skin because it may cause excessive irritation.

- **Examples : Camphor liniments, soap liniments, etc.**

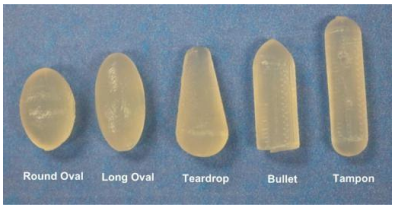
- **Suppositories**

- A Suppositories is a medical solid dosage form generally intended for use into the rectum vagina to a lesser extent the urethra after insertion their melt or saft at body temperature where as vaginal suppositories some time called as peassaries are also made as compressed table that

disintegrate in body fluid.

- **Or**

- Suppository are semi-solid or solid base dosage form of medicament for insertion into body cavity other than mouth and melt into body temperature.
- They are inserted into rectum, vagina or nasal cavity.
- These produce so formulated that after introduce into rectum vagina or nasal cavity.
- These produce so formulated that after introduce the will either melt or dissolve into cavity fluid to release the medicament.
- Suppository available in different sizes and shape.




- **Advantage:-**

- Drugs are rapidly absorbed in rectal mucosa without ionisation.
- Drugs sensitive to acidic pH of can be administered safety.
- Non - Sedating and bitter drugs can be given in this form without difficulties.
- These can easily administered to children old person and to unconscious

patient, who cannot be swallow the drug easily.

- They can be inserted into rectum to rapid active on the rectum.
- These are inserted into rectum to promote evaluation of the bowl.
- Suppository is unit dosage form or drug and no dose variation.
- They have been used to obtained prolonged adion of drug.

- Disadvantage:-

- The irritatant drug can't be administered by this route.
- Absorption of drug through rectum is irregular.
- They are required to be stored self life otherwise throughout there shapes may be destroyed.
- These is leaking problem of material through cavity thus found uncomfortable.
- They should have a maximum desintegration time of 30 minutes.

- **Type of suppository:-**

  - Rectum suppository
  - Vaginal suppository
  - Nasal suppository

- Urethral suppository
- Ear suppository

- **Pessaries:**

- They are solid dosage form of medicament meant for introduction into vagina.
- They either melt or dissolve in cavity fluids to release a medicament and exert a local action.
- **Example: lactic acid, ampicillin, nystatin, etc.**

- **Lotions:**

- Lotions are defined as the liquid suspensions or dispersions meant for external applications to the skin without friction. They usually contain alcohol and glycerin because alcohol fasten drying and produces cooling sensation where as glycerin keeps the skin moist for a sufficient long time.
- **Examples: calamine lotions, salicylic acid and mercuric chloride lotions.**

- **Ear drops:**

- Ear drops are liquid preparations in which drug or drugs are dissolved or suspended in suitable vehicle like water, dilute alcohol, glycerin and are installed into ear with a dropper.
- They are generally used for clearing ear, drying weeping surfaces, softening the wax and for treating mild infections.

- **Examples: hydrogen peroxide ear drops, etc.**

    - **Nasal drops:**

- They are aqueous solutions or liquid paraffin solutions meant for instillation into the nostrills by means of dropper.
- They are commonly used for their antiseptic, local analgesic or vasoconstrictor properties.

- **Examples: Ephedrine nasal drops.**
- Liquid Oral Preparations

    - **Monophasic:-**

- Monophasic dosage form refers to liquid preparation containing two or more components in one phase system it is represent by true solution.
- The component of the solution which is present in a large quantity is known as "solvent" whereas the component present in small quantity is termed as "Solute".

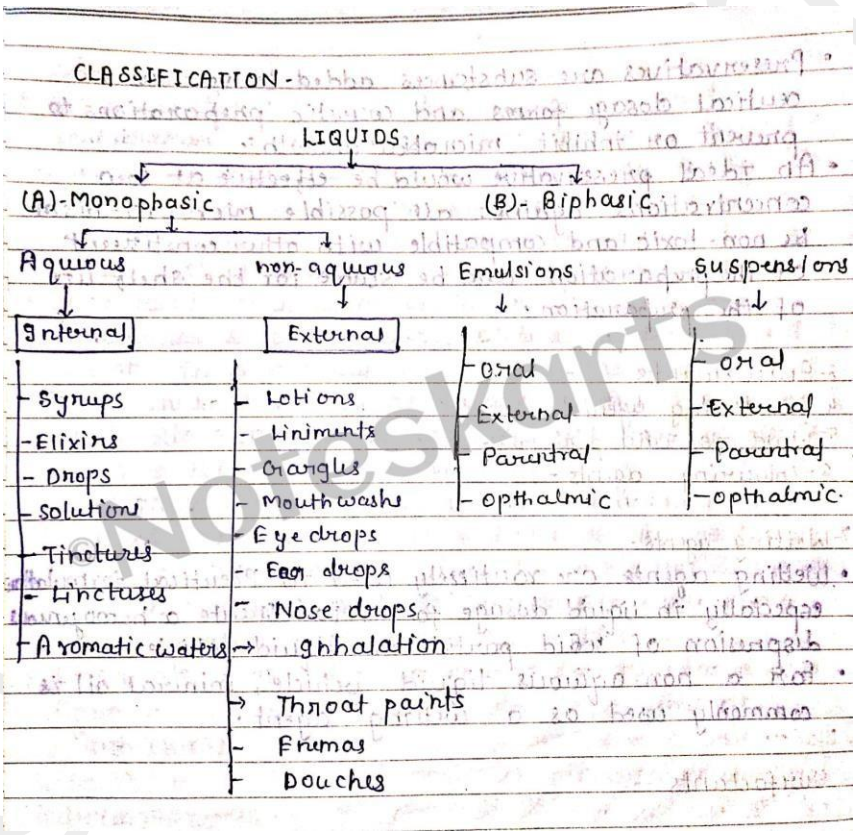
- **Advantage:-**

- It is easy to swallow.
- It absorption is faster than Solid
- It can be administered by various routes: Oral, intramuscular, Enema for rectal use etc.

- **Disadvantage:-**

- They bulky so difficult to transport and store.

- Water is commonly use vehicle which is prone to microbial growth. So addition of preservative is need.
- Drug stability reduce by hydrolysis or oxidation.
- They have shorter expire date than Solid dosage form.
- **Classification of monophasic**




- **Syrup:-**
- They are silent, Viscous, Concentrated solution of sucrose or other sugar in water or any other suitable acques.
- Syrups are concentrated solutions of sucrose or other sugar to which medicament or flavoring agents are often added.

- **Classification of Syrup:-**
- **Simple Syrup**
- **Medicated Syrup**
- **Flavored Syrup Simple syrup**
- Simple syrup is concentrated solution of success in purified water. The concentration of sugar is 66% W/W.
- **Ex- Ginger syrup, Lemon syrup. Preparation of simple syrup**
- According to B.P simple syrup is prepared by adding 1Kg of refined sugar to 500ml of boiling distilled water and heating until it is dessolved and adding Boling distilled water until the weight of the whole is 1.5kg.
- The specific gravity of the Syrup should be 1.33.

- **Medicated syrup**

- They are aqueous solution Containing sugar and at least one water soluble active ingredient.
- The sugar concentration should be between 65-67%
- **Ex- cough syrup, paracetamol syrup**

- **Flavour Syrup**

- It is typically consist of a simple syrup that is sugar with naturally occurring or artificial (Synthesized) flavour that are also dissolved in them.
- Ex- Coffee, Tea, Cake, Ice-cream etc.

- **Elixirs:**
- Elixirs are clear, pleascently, flavoured, sweetened hydro alcoholic liquid preparations for oral administration.
- The main ingredients of elixers are ethanol and water but glycerine, sorbitol, propylene glycol, flavouring agent, sugar and preservatives may be incorporated to the preparation.
- The elixirs may be medicated or non-medicated.
- The medicated elixirs usually contain very potent drugs such as antibiotics and sedatives.
- The bitter and nauseous test of certain drug can be mask by adding flavouring / sweetening agent.
- The non-medicated elixirs are used as flavours and vehicle (Solvent/liquid)

- **Examples are paracetamol elixirs, chloral elixirs.**

- **Storage:**

- Since elixirs contain alcohol and usually some volatile oils which is contaminate of presence of air and light therefore they should be store in tightly closed, light resistance container and in a cool place.

- **Emulsions**
- Emulsion is defined as biphasic liquid dosage form containing a mixture of oil and water and addition of emulsifying agent or emulgent to product emulsion.
- **Classification of emulsion**

- **According to the mode of dispersion:-**
    - **O/W ( Oil in water)-** oil is an internal phase. Water is external phase ex- milk consists of liquid fat particles dispersed in water.
    - **W/O ( Water in oil)-** Water is an internal phase. oil is external phase. Emulsion of water in oil
- Disperse phase is water and the dispersion medium is oil.
- For example, cod liver oil consists of particles of water dispersed in oil.

- **In case of consistency:-**
    - **Liquid emulsion-** usually O/W type and used parenterally orally and externally.
    - **Semi solid emulsion-** this type of emulsion used for external purpose.

- **According to partical size:-**
    - **Coarse emulsion**
    - **Micro emulsion**
    - **Fine emulsion**

- **Type of emulsion:-**
- **Water in Oil emulsion (W/O):-** In these emulsion rufer to water in oil. If the dispersed phase in water and dispersion medium is oil
- **Oil in water emulsion (O/W):-** These type of emulsion rufer to water oil in oil water in these dispersed phase is oil and dispersion medium is water.

| ○ **Different between o/w and w/o emulsion.** | |
|---|---|
| ▪ (O/W) | ▪ (W/O) |
| • 1) Water is the dispersion medium and oil is the dispersed phase. | • Oil is the dispersion medium and water is the dispersed phase. |
| • 2) non greasy and easily removable from the skin. | • Greasy and not water washable. |
| • 3) Preferred for internal use as bitter taste of oils can be masked. | • Preferred for external use like creams. |

- **Formulation of emulsions:-**
- Following ingredients are included in the formulation of emulsion.
- **Oil phase :-** This phase medicament or vehicle is mode up of fixed oil mineral oil, volatile oil or also resin type that is used for preparation of

emulsion.

- **Aqueous phase:-** Due to increased risk of microbial contamination freshly boiled and cooled purified water are used.
- **Antioxidant:-** It prevents the oil form getting oxidising during Its shelf like hence It enhance the stability of the oil phase in the emulsion.
- **Flavouring agent:-** It enhances the palatability of the final product pineapple, orange, chocolate, and mint flavours are commonly used.
- **Colouring Agent:-** It is used for identifying the preparation and enhancing its aesthetic appeal. Erythrosine tartrazine etc. Colours approved by the food Drug and cosmetic act are used as Colouring Agent.
    - **Biphasic liquid dosage form**

- **Suspension:-** It is a dispersed system in which our substance is distributed in discrete unit throughout a second substance Phase.

- Or

- A course dispersion in which insoluble solid are suspended in a liquid medium with the help of the suspending agent known as pharmaceutical suspension.
- **Advantage:-**
    - Improve chemical stability
    - Higher rate of bioavailability

- Drug can be dispense as suspension

- **Disadvantage:-**
  - Physical unstable
  - Sedimentation
  - Uniform drug delivery difficult to achieve
  - Stability is poor
  - Suspension containing diffusible solid and liquid and their preparation.
  - Diffusible suspension comprising of light powder that are insoluble are sprengil soluble in the vehicle.

- **Following of the steps involved in the preparation of suspension containing diffusible solid**
  - The solubility of all solid vahical is checked in the mixture.
  - Then the amount of vahical is calculated which is required to dissolved any soluble solid.
  - All solid weight on a electronic balance.
  - Then a small braker all the soluble solid are dissolved in the vahical.
  - Vahical is added in small quantity mixed with solid in motor and postal to yield a smooth paste. Other vehicles is added in small amount and mix properly.
  - Then the motor is the washing are added to the conical mesered.
  - Now the remaining liquid ingredients are added to the mixture in the conical mesered this is because some of this ingredients are

volatile which may less while being mixed in the mortar.

- The final volume is made up with the vahical after storing generally the resent is transfer to abottal which is labels and despensensed to the patient.

- **Dry Powder For Reconstitution:**
- You will frequently have the opportunity to reconstitute or compound drugs that are in a dry powder form. These are usually drugs such as antibiotics, which lose their potency in a short period of time after being prepared in a liquid dosage form.
    - Establish how much of a drug is contained in a vial or bottle.
    - Calculate the powder volume displacement of a reconstituted drug.
    - Solve problems related to dry powders.

## • Powders :

- A pharmaceutical powder is a mixture of finely divided drug and or chemicals in drug form.
- These are solid dosage form of medicament which are meant for internal and external use.
- They are available in crystalline or amorphous form.
- The particle, chemical and biological properties of the dosage forms.
- There is a relationship between particle size of powder and dissolution absorption and therapeutic efficacy of drugs.

- **Classification of powders:**
- Bulk power for external use
- Bulk power for internal use
- Simple and compound powders
- Effervescent granules
- Cachets
- **Bulk power for external use:**
    - External bulk powders contain non potent substances for external applications.
    - These powder are dispensed in glass, plastic wide mouth bottles and also in cardboard with specific method of application.
    - **Bulk power for external used are of following types:**
- Dusting powder
- Insufflation
- Snuffs
- Douche powder
- **Dusting powder:**
    - Dusting powder usually contain substance such as zinc oxide, starch and boric acid or natural mineral substances, such as kaolin or talc.
    - Talc may be contaminated with pathogenic micro-organisms such as clostridium tetani, etc. And hence it should be sterilized by dry heat.
    - Dusting powders should not be applied to broken skin if desired powders should be micronised or passed through a sieve 80 or

100.

- Dusting powders should have adsorption and adsorption capacity.
- They provide protection to the skin against irritation caused by friction moisture or chemical irritations.

- **Insufflation:**
  - Insufflations are a class of powders meant for application to body cavities
  - Eg. Ear, nose, vagina etc.
  - The powder has to be extremely fine and must find an entry to the cavity deep enough to bring about its action the site.
  - It is delivered to the effected part in a stream with the help of the device called an insufflators, which blow the powder to the site.
  - Pharmaceutical industry packages the insufflations in pressurized from
  - Eg. Aerosols.
  - Aerosols contain the medication in a stout container with a suitable value the delivery of the powder being accomplished by a liquefied or compressed gas propellant of a very low bioling points.
  - On pressing the actuator of the value the propellant delivers the medication in a stream.
- **Advantage of powders:**
  - These are the oldest dosage form used both internally and externally.
  - These are more stable than liquid dosage form.

- It is convenient for the physician to prescribe a specific amount of powdered medicament depending upon the need of the patient.
- They are portable.
- The large quantity of drug can be administered easily by dissolving the powdered in an appropriate liquid.

- **Disadvantages of Powders:**
  - Drugs having bitter bauseous and unpleasant taste cannot be dispensed in powdered form.
  - Deliquescent and hygroscopic drugs can't be dispensed in powder form.
  - Drugs which get affected by atmospheric conditions are not suitable for dispensing in powder forms.
  - The dispensing of power is a time consuming.
  - Quantity less than 100mg or so cannot be weight convenienty or dispensing balance.

  - **Effervescent Powder:**
  - Effervescent powders create a carbonated drink when added to room-temperature water.
  - **Example: Eno, etc.**
  - This dosage form is useful for patients who don't tolerate capsules/tablets, who need a high dose of the active ingredient & who need are more palatable flavour for the drug. The combination of the carbonation & the flavour (i.e. mango, passion fruit or raspberry) can override the negative taste of the active ingredient.

- **Effervescent granules:**
- Granular solid dosage form consisting of one or more active medicament in a dry mixture usually composed of sodium bicarbonate, citric acid and tartaric acid when added to water the acid and base react to liberate carbon dioxide resulting in effervescences and are administered as carbonated solutions.

- **Formulation:**
  - Active medicaments **ex:** Antacids, Laxatives, Antibiotics, Antipyretics etc.

- **Citric acid and trataric acid. Sweetening agent:** Sucrose and aspartame
- **Colouring agent:** Titanium dioxide, tumeric etc.
- **Flavouring agent:** Peppermint oils, lemon oil etc.

  - The effervescent granules (salts) are prescribed to the dispensed in bulk form, no granulation is necessary.
  - The ingredients are mixed uniformly and directions stated on the label to add the prescribed quantity to water before use.
  - **Advantage of granules:**

- They also remove or control dust. They increase the compressibility.
- They have good flowability than powders. This feature helps in supplying drug materials easily from the hopper (feeding container) to the die cavities of tablet compression machine.
- Their physical and chemical stability is much more than powders

because they have a smaller surface area.

- Sterile formulations – Injectables, eye drops and eye ointments

- **Sterile formulations**
- Sterile dosage forms containing therapeutic agents do not present any viable microbes parenteral, opthalmic and irrigating preparations are the prime sterile dosage product among which the parenteral products are unique as they are injected in the internal body carities through the skin or mucous membranes.

Or

- Sterile dosage forms are those which are free from any microorganisms, dust, fibres, and foreign particles, and should be isotonic.
- Parenteral preparations as name suggests (par+enteral) are those which are administered other than enteral routes.

## Injectables:

- Injectables are used to relax facial wrinkles and folds (such as “smile lines”), contour the body (such as reducing the appearance of a “double chin”) and
- improve the signs of facial fat loss by creating structure, framework and volume to the face and lips.

- **Eye drops:**

- These are the aqueous or oily solution or suspension that are installed into the conjunctival sac of the eye.
- These are used as anaesthetics, anti-inflammatory agents, antiseptics, diagnostic agent, mitotics, mydriatics and artificial tears.
- **Examples:**
- Atropine sulphate eyedrops
- Physostigmine eyedrops
- Hyoscine eyedrops

- **Eye ointment:**

- These are placed in the conjunctival sac or applied to the margins of the eyelids. Ointments are thicker than drops and that means they can stay in your eye longer.
- They are used when the medicine needs to work directly in your eye to relieve or treat eye conditions.
- **Eg: Bacitracin, ophthalmic ointment.**

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

- **Immunological products:**
- Immunology is the study of the immune system. The immune system is a host defence system comprising many biological structures and

processes within an organism that protects us from infection and disease causes bacteria.

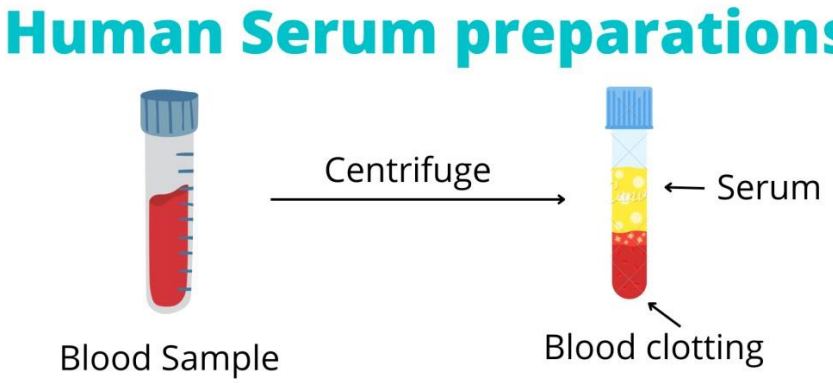
- Immunization is the process whereby a person is made immune or resistant to an infectious disease, typically by the administration of a vaccine.

### ○ SERA: (Serum)

- The clear, pale yellow liquid that separates from the clot in the coagulation of blood.
- Sera does not contain bacteria or toxins. It contains anti formed in another animal.
- Sera acquired immune immediately and remain a short time. Specific animal by immunization, whole blood collected in, but the serum is a nonspecific mixture obtained after centrifugation.

- **SERA manufacturing methods**
- **Human Serum preparations**

### ○ Plasma - Clotting factor = Serum




- **Antotoxic SERA**

- Sera may be Anti-toxic, Anti-viral, Anti-bacterial. Anti-toxic sera more effective than Anti-viral, Anti-bacterial
- **Example 1.**
- **DIPHTHERIA ANTITOXIN:-**
- It is sterile, nonpyrogenic solution containing specific antitoxic antibody from healthy horse.
- They neutralize the toxin produce by C-diphtheriae Preparation. (c diphtheriae is Corynebacterium diphtheriae. a pathogenic bacterium that causes diphtheria).

- **VACCINE :**

- Vaccine is an antigenic substance prepared from the causative agent of a disease or a synthetic substitute, used to provide immunity against one or several diseases.
- It Contains dead bacteria or weak bacteria or toxins.
- Vaccine stimulates the body to make antioxidants.
- Vaccines are preparations of antigenic materials, which are administered with the objective of inducing in the recipient specific and active immunity against infectious microorganisms or toxins produced by them.
- They contain living or killed microorganisms, bacterial toxoids or antigenic material from the particular parts of bacterum, rickettsia, or virus

- **Types of Vaccines**
    - Inactivated vaccines.
    - Live-attenuated vaccines.
    - Messenger RNA (mRNA) vaccines.
    - Subunit, recombinant, polysaccharide, and conjugate vaccines.
    - Toxoid vaccines.
    - Viral vector vaccines.

    - **Toxoid Vaccines**
- Some bacteria release toxins (poisonous proteins) when they attack the body, and it is the toxins rather than the bacteria itself that we want to be protected against.
- The immune system recognises these toxins in the same way that it recognises other antigens on the surface of the bacteria, and is able to mount an immune

response to them.

- Some vaccines are made with inactivated versions of these toxins.
- They are called ‘toxoids’ because they look like toxins but are not poisonous.
- They trigger a strong immune response.

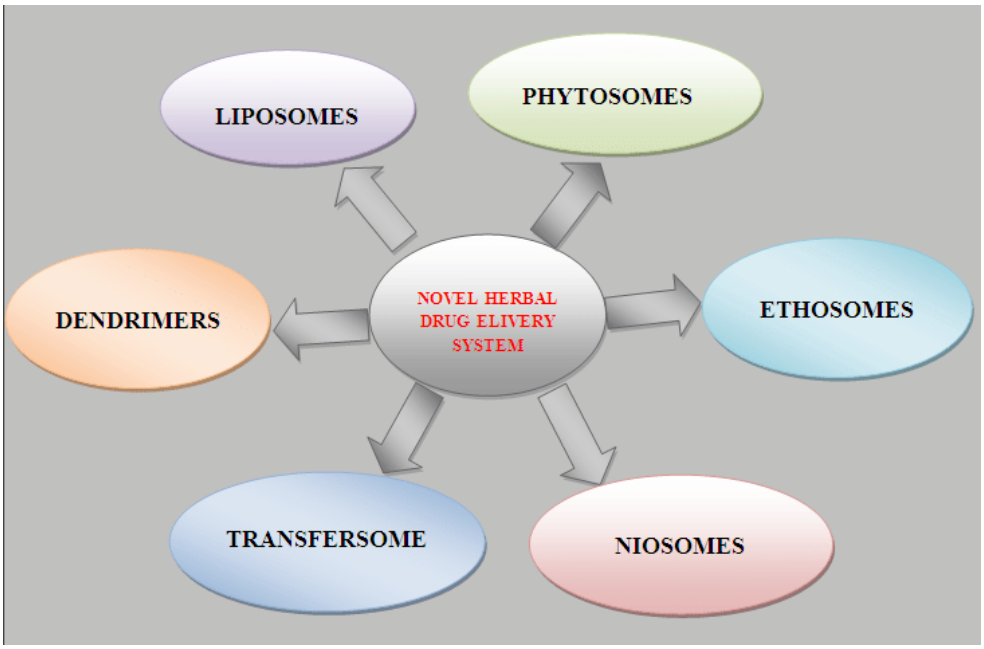
## Novel Drug Delivery Systems:

- **Introduction:**

- The method by which a drug is delivered can have a significant effect on its efficacy.
- A novel drug delivery systems (NDDS) can be defined as a new approach that combines innovative development, formulations, new technologies, novel methologies for delivering pharmaceutical compounds in the body as needed to safety achieve its desired pharmacological effects.
- The new ideas on controlling the pharmacokinetics, pharmacodynamics, non-specific toxicity biorecognition and efficiency of drugs were generated.
- These new strategies is called drug delivery systems (DDS)
- Drug Delivery Systems (DDS) are based on interdisciplinary approach that combines polymer science, pharmaceutics, bioconjugate chemistry, and molecular biology.
- To minimize drug degradation and loss to prevent harmful side effects and to increase drug bioavailability and the fraction of the drug accumulated in the required zone various drug delivery and drug targating system are currently under development.

- Some drugs have an optium concentration range within which maximum benefit is derived and concentrations above or below this range can be toxic or produce no therapeutic benefit at all.
- On the hand the very slow progress in the efficacy of the treatment of severe disease has suggested a growing need for a multidisciplinary approach to the delivery of therapeutic to targets in tissues.

    - **Classification Of Novel Drug Delivery System**




- **Advantage:**
- Improve patient compliance
- Accurate dosing
- Enhanced efficacy and safety
- Decreased toxicity/side effects
- Controlled delivery by maintaining desired drug concentration and contralled rate.

- Deneficial to patients with improved comfort and standard of living.
- Reduction in drug accumulation with chronic therapy.
- **Disadvantages:**
- Less patients compliance.
- Repeated dosage is necessary.
- Large amount of drug deliver.

### Challenge of novel drug delivery systems (NDDS):

- Problems involved and overcoming challenges in the delivery of poorly soluble drugs
- Novel approaches in the delivery of poorly soluble drugs
- Overcoming bioavailability hurdles for poorly soluble clinical candidates
- Rationale formulation design for poorly soluble compounds
- Overcoming challenges in protein drug delivery
- Challenges in pediatric and geriatric drug delivery
- Overcoming addictive nature of drugs