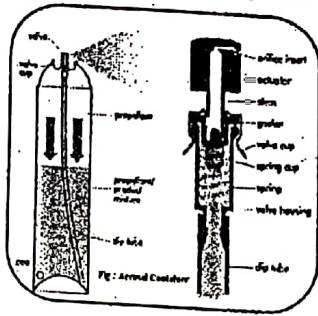
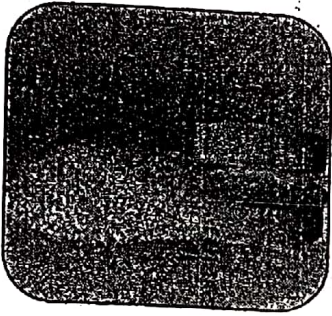
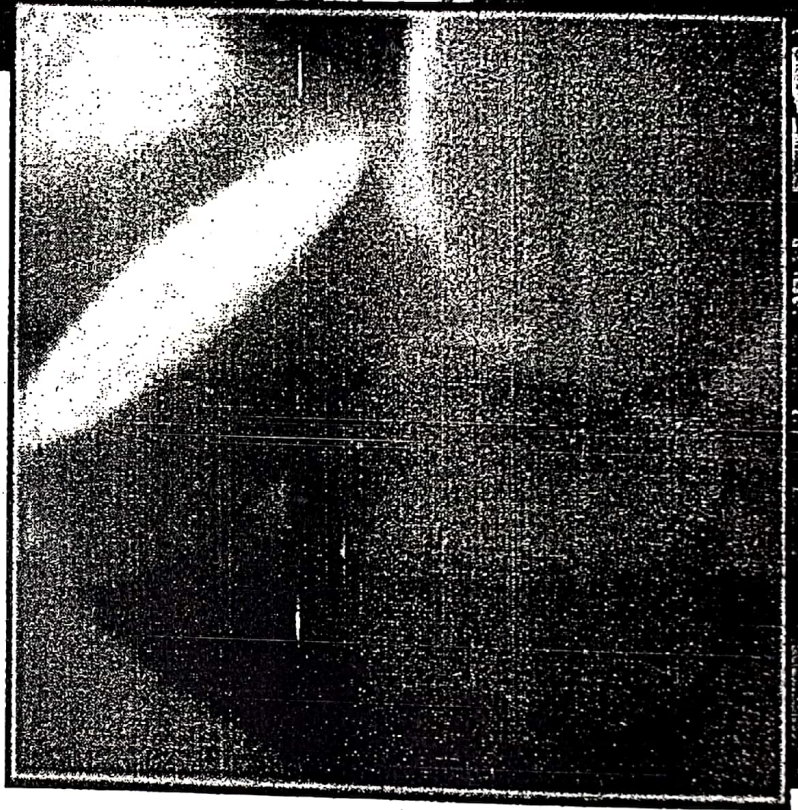




PHARMACEUTICS-I



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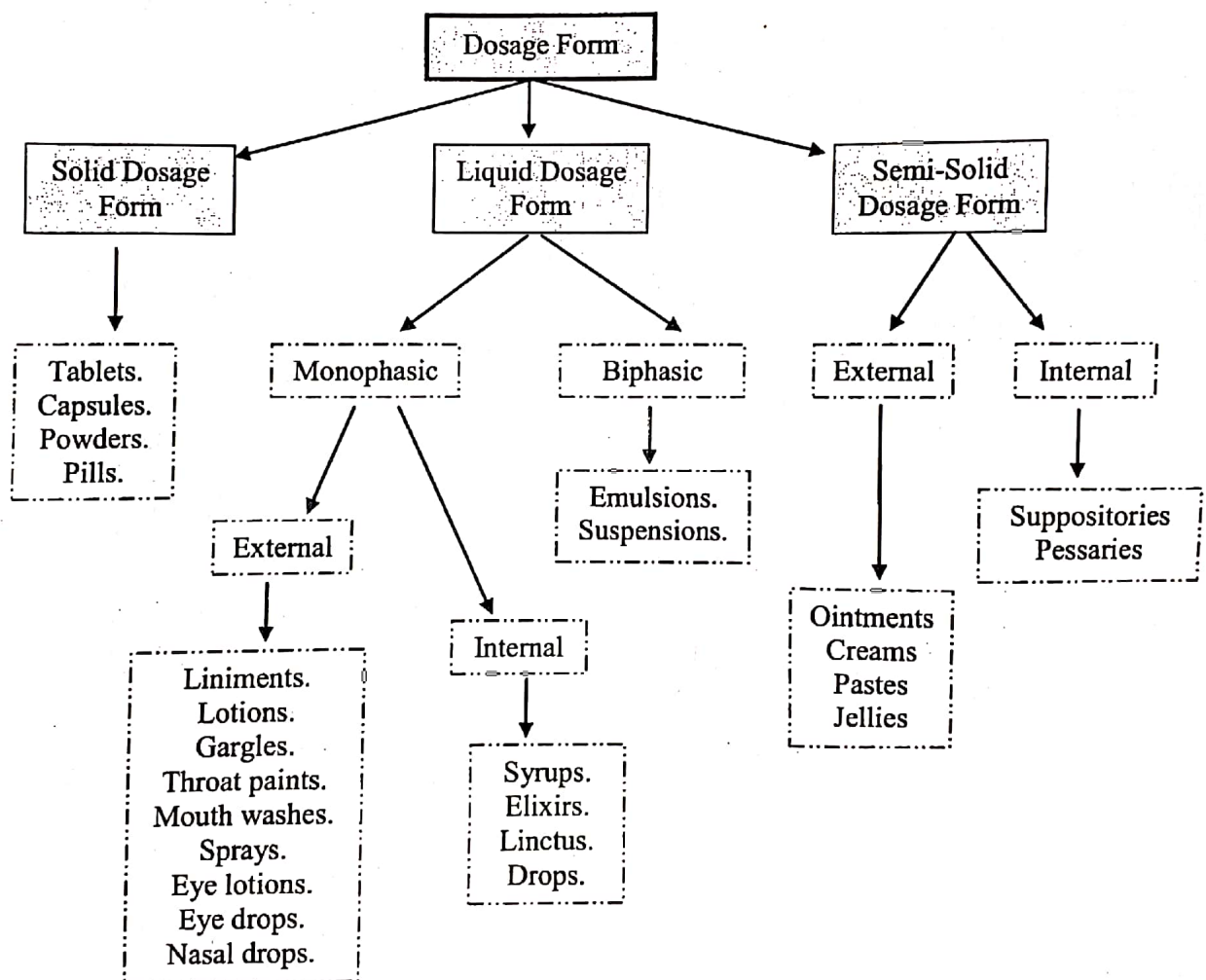
1. DIFFERENT DOSAGE FORMS

◆ DEFINE DOSAGE FORMS AND CLASSIFY DIFFERENT DOSAGE FORM WITH EXAMPLES.

Definition:

A dosage form may be defined as a combination of medicament and non medicament components with mixture of suitable excipients.

CLASSIFICATION OF DOSAGE FORMS:



➤ **Solid Dosage Form:**

The solid dosage forms are available mostly in unit dosage forms (consisting of doses which are taken by numbers) such as tablets, capsules, pills, cachets or powders etc.

➤ **Liquid Dosage Form:**

Liquid dosage forms are meant for internal, parenteral or external use. They are available in monophasic or biphasic form.

➤ **Semi-Solid Dosage Form:**

Semi-solid dosage forms are meant for external application. E.g. ointments, creams, pastes, jelly etc.

➤ **WHAT ARE NEW DRUG DELIVERY SYSTEMS.**

In the last few years, many novel dosage forms (New Drug Delivery Systems) have been developed and are being used now.

Some of the Important New Drug Delivery Systems:

1. Films & Strips: Buccal Strips, Zero order release films, Sprayable bandages.
2. Implants (Magnetically Controlled) eg: Insulin.
3. Nanoparticulates : FITC (Fluorescein Isothiocyanate)
4. Erythrocytes: Allow Drugs to Flow for longer period.
5. Prodrugs: eg: Procaine-Penicillin G.
6. Liposome Drug Carriers: eg: Protein.
7. Controlled Drugs Delivery Modules: eg: Cellulose Esters.
8. Magnetic Microspheres.

2. INTRODUCTION TO PHARMACOPOEIAS

◆ PHARMACOPOEIA & ITS IMPORTANCE.

Pharmacopoeia is a book containing a list of drugs and formula for medicinal preparations, together with descriptions of these substance, tests for identification and purity, and description of method of standardization for each drug either chemical and biology method. The pharmacopoeia is first used in 1580 in a book on drug standards printed in Italy.

◆ IMPORTANCE OF PHARMACOPOEIA:

The importance of pharmacopoeia is to select substances which possess medicinal power, convert them into preparations of suitable composition in order to enhance their power to the maximum advantage. Ex: U.S.P.

◆ LIST OF VARIOUS PHARMACOPOEIAS:

- ✓ Indian Pharmacopoeia (I.P)
- ✓ British pharmacopoeia (B.P)
- ✓ United States Pharmacopoeia (U.S.P)
- ✓ National Formulary (N.F)
- ✓ European Pharmacopoeia
- ✓ International Pharmacopoeia

◆ MONOGRAPH OF I.P.

Main Title

Subsidiary Titles

Chemical Formula, Mol. Wt., Systematic Chemical Name,
Quantity Standards of Purity or Strength

Description

Solubility

Identification of Specific or Non-Specific Tests.

Method of Assay

Methods of Storage and Labeling

Preparations

Action and Use

Doses

◆ **HISTORICAL BACKGROUND OF INDIAN PHARMACOPOEIA.**

In 1946 The Government of India published the Indian Pharmacopoeial list which served as Supplement of British Pharmacopoeia. The Pharmacopoeial list contained about 180 monographs. After Publication of this list, Govt. of India Constituted a Permanent Indian Pharmacopoeial Committee.

In 1948, this committee assigned the work to prepare the Indian Pharmacopoeia to keep it up to date. The first edition of Indian Pharmacopoeia was published in 1955 and a supplement of it was published in 1960.

The work of Version of the Indian Pharmacopoeia as well as the Compliance of New Edition was taken up simultaneously under the chairmanship of Dr. B.N.Gosh, Professor of Pharmacology, R.G.Kar, Medical College, and Calcutta.

The Second Edition of Indian Pharmacopoeia was published in 1966 and a supplement of it was published.

A Working group was constituted by the Committee to Prepare the Monograph, Appendices and general notice that were finalized by the Pharmacopoeial Committee. The same was published in the form of Pharmacopoeia of India in 1985, in two volumes i.e. volume-I and volume-II.

The first Indian Pharmaceutical codex was published in 1953. The codex consists of two parts.

Under the Drugs and Cosmetics Act 1940, The Indian Pharmacopoeia is an official book which contains the standards for drugs and other related substances included in the pharmacopoeia.

◆ **HISTORY OF BRITISH PHARMACOPOEIA.**

The medicinal act of 1858 brought the drastic changes in the medical profession. Under section of this act General Council of Medical Education and Registration enacted and was given this work. The book was named as British Pharmacopoeia. The first British Pharmacopoeia was published in 1864. More useful and successful reprint was published in 1874.

Medicine commission in accordance with the same act reconstituted the British Pharmacopoeia Commission, and Under Section 99 (1) of the Medicine Act. Preparation of the British Pharmacopoeia is the responsibility of British Pharmacopoeia Committee.

The thirteen edition of B.P was published in 1980, 14th in 1988 and 15th in 1993.

3. WEIGHTS AND MEASURES

- ◆ **DEFINE AND CLASSIFY DIFFERENT SYSTEM OF WEIGHTS AND MEASURES FOLLOWED IN PHARMACY WITH SUITABLE EXAMPLES.**

Weights: It is a measure of gravitational force acting on a body and is directly proportional to its mass.

Measures: It is the measurement of volume of any substance.

There are two systems of Weights and Measures. They are:
Imperial system and Metric system.

- ✓ **Imperial System:** The Standard of Imperial system is Pound (lb)
The Imperial system consists of: 1) Avoirdupois System, and
2) Apothecaries System

1) Avoirdupois System of Weights and Measure.

1 Ounce (Oz)	=437.5 Grain (Gr)
1 pound (lb)	=16 ounce (7000 gr)
1 pound (lb)	=7000 grains
1 fluid ounce	=8 fluid drachm (fl dr)
1 fluid drachm	=60 minims
1 pint (pt)	=20 fluid ounce
1 quart	=40 fluid ounce
1 gallon	=160 fluid ounce=4 quart.

GALLON: It is define as the volume occupied by ten imperial standards.

2) Apothecaries System of Weights and Measure.

20 grains	=1 scruple
60 grains	=1 drachm
8 drachm	=1 ounce
12 ounce	=1 pound

Measure of volume is same as avoirdupois system

- ✓ **Metric System:** Standard unit of measures of mass (weight) is kilogram and all other measures of capacity are derived from kilogram.

1 Ton	=1000 Kilogram
1 Quintal	=100 Kg
1 Kilogram	=1000 Grms

PHARMACEUTICS - I

1 Hectogram	=100 Gram
1 Decagram	=10 Gms
1 Decigram	=0.10 Gms
1 centigram	=0.001 gms
1 milligram	=0.0001 gms
1 microgram	=1/1000mg
1 nanogram	=1/1000 microgram
1 picogram	=1/1000 nanogram

Measures of capacity:

Standard unit of measures of capacity (volume) is litre and all other measures of capacity are derived from litre.

1 Litre (lt)	= 1000 millilitre(ml)
1 hectoliter	=100 litre
1 litre	=1000.028 cubic centimeter
1 litre	=33.8 fl. ounce

◆ RELATION OF IMPERICAL SYSTEM WITH METRIC SYSTEM:

4 Millilitre	=1 fluid drachm
1 gram	=15.432 grain
1 kg	=2.2046 pounds
1 ounce	=28.35 gms
1 pound	=453.59 gms
1 grain	=0.064 gms
1 litre	=35.196 fl-ounce
1 ml	=16.9 minim
1 min/im	=0.0592 ml
1 fl-ounce	=28.41 ml

◆ APPROX. EQUIVALENTS:

30 ml	=1 fluid ounce
30 gms	=1 ounce
1 G	=15 grains
1 ml	=15 min
1 teaspoonful	=4 ml
1 desert spoonful	=8 ml
1 table spoonful	=15 ml.

4. PACKAGING OF PHARMACEUTICALS

◆ DEFINITIONS:

- ✓ **Packing** is the process by which the pharmaceuticals are suitably packed so that they should retain their therapeutic effectiveness from the time of their packing till they are consumed.
- ✓ **Container:** A container is a vessel or devices which hold the drugs or pharmaceutical dosage form.
- ✓ **Closure:** The closure is a part of the container. Closure is a device, by means of which the container can be opened and closed.

◆ DESIRABLE FEATURES OF A CONTAINER AND CLOSURE.

✓ Desirable features of container:

1. A container must give sufficient mechanical strength to withstand when emptying, filling, closing, and processing, transport and storage.
2. It must be able to withstand heat during sterilization.
3. It should not react with the product.
4. It should not alter the stability of the medicament.
5. It should protect the preparation from environmental hazards.
6. It should be low in cost.
7. The surface of the container should be uniform for easy labeling.
8. The container must be so designed so as to facilitate withdrawal of dose in a convenient manner as and when required.

☞ Desirable features of a closure:

1. It must give sufficient mechanical strength to withstand when closing, and storage.
2. It must be enough elasticity and hardness.
3. It must be able to withstand heat during sterilization.
4. It should not react with the product.
5. It should not alter the stability of the medicaments.
6. It should be low in cost.
7. It must prevent loss of the product by volatilization.
8. It must prevent loss of the product during transportation and handling.

◆ TYPES OF MATERIAL USED FOR THE CONSTRUCTION OF CONTAINERS.

The following materials are used for the construction of containers. They are used either singly or sometimes in combination with each other.

(1) GLASS (2) PLASTICS (3) METALS (4) PAPER

(1) GLASS:

Glass is mostly produced by heating of silica (SiO_2), soda ash (Na_2CO_3) and lime stone (CaCO_3) in about 1400°C .

Different types of glass used are:

- a) Type I-borosilicate glass
- b) Type II-treated soda-lime glass
- c) Type III-soda-lime glass
- d) Type NP-non-parenteral glass
- e) Colored glass
- f) Neutral glass

(2) PLASTICS:

Plastics are high polymers weight possessing long carbon chains.

There are two types of plastics

(i) Thermosetting Type (ii) Thermoplastic Type

Various thermoplastic polymers used for the manufacture of containers are:

- a) Low density polythene
- b) High density polythene
- c) Polyvinyl chloride (PVC)
- d) Polystyrene
- e) Polypropylene
- f) Poly methylmethacrylate (PMMA)
- g) Polytetrafluoroethylene (PTFE)
- h) Polyamides (nylons)

(3) METALS:

Metals containers are not very popular for packing for pharmaceutical products because they may react with the preparations. For this purpose tin plated steel, stainless steel and aluminium containers are used.

(4) PAPERS:

It is widely used in pharmaceutical industries in one form or the other. Their properties can be modified by treating it with plastic, wax and other materials.

◆ **MATERIALS USED FOR THE CONSTRUCTIONS OF CLOSURES:**

- 1) **CORK:** It is essentially a wood obtained from the bark of oak tree. It is used as stoppers for narrow mouth bottles.
- 2) **GLASS:** It is an ideal material for making stopper but these stoppers have the difficulties that they do not provide leak proof closures.
- 3) **PLASTICS:** Plastics closures are becoming more popular day by day because of their ease & convenience.
- 4) **RUBBER:** Natural rubber consists of latex. Rubber closures are mainly used for vials, multidose containers & IV fluid bottles.
- 5) **METALS:** Tin plates and aluminium are most widely used

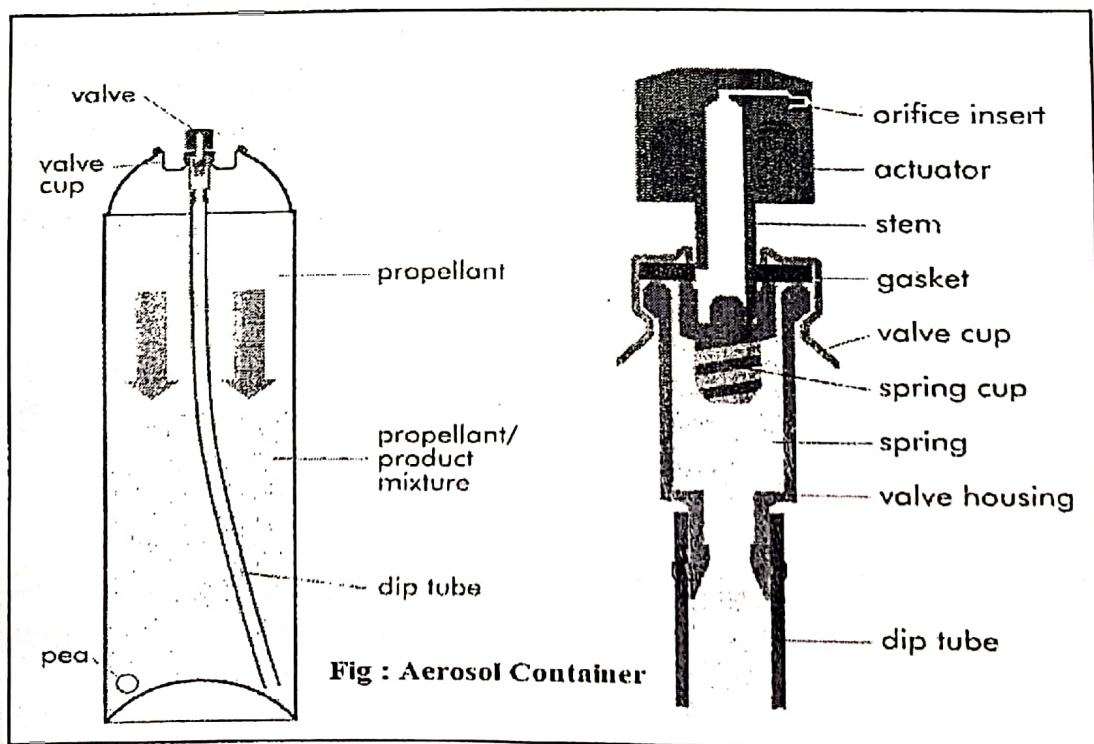
◆ **DEFINE AEROSOL. EXPLAIN CONSTRUCTION & WORKING OF AEROSOL.**

A pharmaceutical aerosol may be defined as the preparation containing the active medicaments dissolved, suspended or emulsified in a propellant or a mixture of solvent and propellant and packaged in a pressurized aerosol container.

Construction of aerosol:

Aerosol is packed in metal containers and glass containers. Aerosol containers can be divided into four parts namely

1. Container
2. Dip tube
3. Valve
4. Actuator



- 1. Container:** Aerosol containers are made from glass, synthetic resins, plastics and metals such as aluminum tin plated steel etc. these containers provide a good mechanical strength and can withstand a high pressure.
- 2. Dip tube:** It is a tube which is attached to the bottom of the valve and leading down to the bottom of the container .whenever the actuator is pressed, the product enter into the dip tube and sprayed.
- 3. Valve:** various types of valves are used in aerosols. In continuous spray valve, the product is expelled until the pressure is completely released .Only a definite quantity is expelled when the actuator is pressed.
- 4. Actuator:** various types of actuator are available and used in aerosol. It is fitted on the valve system. The actuator helps to open and close the valve when required. A fine spray of the product is expelled through the valve orifice and actuator nozzle into the atmosphere.

Working of aerosol:

1. Aerosol is prepared by dissolving the active medicament and other additives such as solvent antioxidant, surface active Agent, flavoring agent are dissolved in propellant. This final product is known as aerosol.
2. The propellants used in liquefied gas or mixture of gases.
3. Aerosols are packed in aerosol containers. The propellants are low boiling substances so that a pressure is excreted within the container even at room temperature.
4. Whenever the actuator is pressed, the valve opens and a fine spray of the contents is expelled through the valve orifice and actuator nozzle into the atmosphere until the pressure is completely released.

◆ ADVANTAGE AND DISADVANTAGES OF AEROSOLS:

Advantage:

1. Aerosol packaging protects the medicaments from light, dust, atmospheric moisture.
2. They protect the medicaments from atmospheric oxidation.
3. They maintain the sterility of the product.
4. Measured doses applied directly into the affected part.
5. It is easier and convenient.

Disadvantages:

1. The cost of the packaging is high.
2. When the container is stored at high temperature, the internal pressure may develop inside the container.

◆ CONTAINERS USED FOR AEROSOLS.

Various materials have been used in the manufacture of aerosol
A container includes:

a) Metal:

- 1) Tin plated steel: side seam (3 pieces) two piece or drawn tin free steel.
- 2) Aluminium: two piece, one piece (extruded or drawn)

b) Glass: un-coated glass, plastic coated glass.

c) Plastics:

- 1) Its adaptability to production methods.
- 2) Compatibility with formulation components
- 3) Ability to sustain the pressure intended for the product.
- 4) Aesthetic appeal on the part of the manufacturer.

5. SIZE REDUCTION

◆ SIZE REDUCTION

Size reduction means to reduce the size of the material. It is defined as the mechanical process by which the drug or any other material is reduced to smaller pieces or coarse powder or fine powder.

◆ MECHANISMS OF SIZE REDUCTION:

1. **Cutting:** The material is cut on small pieces by means of a sharp blade or any other sharp instrument. Eg. Cutter mill.
2. **Compression:** The material is crushed by the application of pressure on the small scale; size reduction is carried out by using pestle or mortar. Eg. Roller mill.
3. **Impact:** It occurs when the material is more or less stationary and is hit by an object moving at high speed and material breaks into small pieces. Eg. Hammer mill and Disintegrator.
4. **Attrition:** In attrition pressure is applied on the material as in the case of compression, but the surfaces are in motion relation to each other, resulting in shear forces which break the particles into still smaller sizes. E.g. Roller mill or motor pestle.
5. **Combined Impact and Attrition:** The mechanism of impact and attrition can be combined in the mill to get better result. Eg. Ball Mill, Fluid-energy Mill.

◆ APPLICATION OF SIZE REDUCTION IN PHARMACY.

OR

OBJECTIVE OF SIZE REDUCTION.

OR

ADVANTAGES OF SIZE REDUCTION.

1. Size reduction is essential to prepare various pharmaceutical dosages forms such as tablets, capsules, injection, etc.
2. It is useful to increase surface area which ultimately increases the rate of solution and absorption.
3. It is useful for exposing tissues for easy penetration in extraction.
4. It helps the processes of drying and mixing.

5. It is useful for easier and economical *manufacture*
6. On reducing the particle size the bulkiness of certain drugs can be increased.

◆ **DISADVANTAGES OF SIZE REDUCTION:**

1. On grinding, the aromatic and volatile constituents of crude drug may be lost due to increased temperature during grinding.
2. Due to increased surface area & if exposed to atmospheric conditions, it may result in oxidation and hydrolysis.

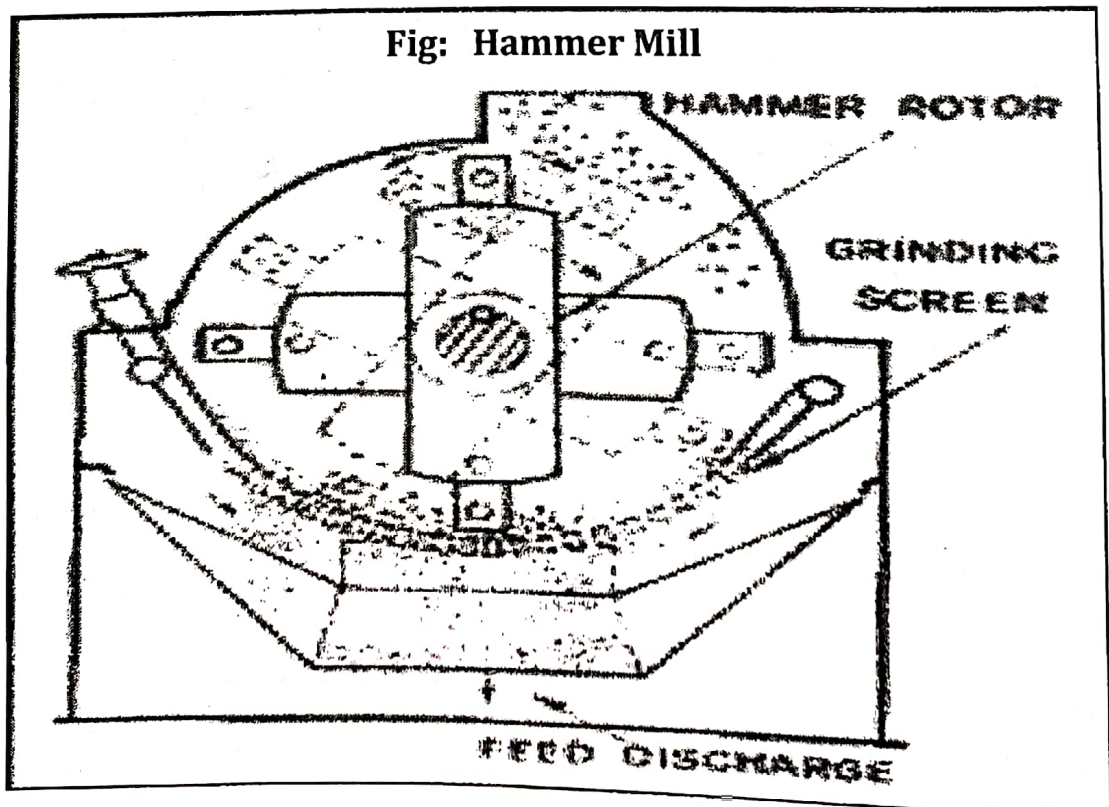
◆ **DESCRIBE THE CONSTRUCTION AND WORKING OF HAMMER MILL**
OR

WHAT IS IMPACT MILL? DISCUSS IN DETAIL THE CONSTRUCTION AND WORKING OF ANY ONE OF THE IMPACT MILL?

Impact Mill: In these methods, material is more or less stationary and is hit by an object moving at high speed, or moving takes place by both the ways.
Eg. Hammer Mill.

Principal: It works on the principle of impact i.e. material is more or less stationary and is hit by an object moving at a high speed.

Construction: It consists of a steel casing enclosing a central shaft, to which four or more swinging hammers are attached. The lower part of the casing consists of a screen, through which material can pass and collected in a suitable receiver, when the desired degree of size reduction is ~~attached~~ *achieved*.



Working: The material is put into the hopper which is connected with the drum. The material is powdered to the desired size, due to fast rotation of hammers and is collected under the screen. This mill has the advantage of continuous operation because the chance of jamming is less as the hammers are not fixed. It can produce coarse to moderately fine powder.

Due to high speed of operation, heat is generated which may affect thermolabile drugs or materials. Moreover, high speed of operation also causes damage to the mill if foreign objects such as stone or metal is present in the feed.

Uses: The hammer is used for producing intermediate grades of powder from almost all types of substances except sticky materials that choke the screen.

◆ PRINCIPAL, CONSTRUCTION AND WORKING OF BALL MILL.

Principal: It works on the principal of Impact and attrition.

Construction: It consists of a hallow cylinder which is mounted on a metallic frame in such a way, that it can be rotated on its longitudinal axis. The cylinder contains balls that occupy 30 -50% of the mill volume. The weight of the balls is kept constant. The ball size depends on the size of the feed and the diameter of the mill. The cylinder and the balls are made of metal.

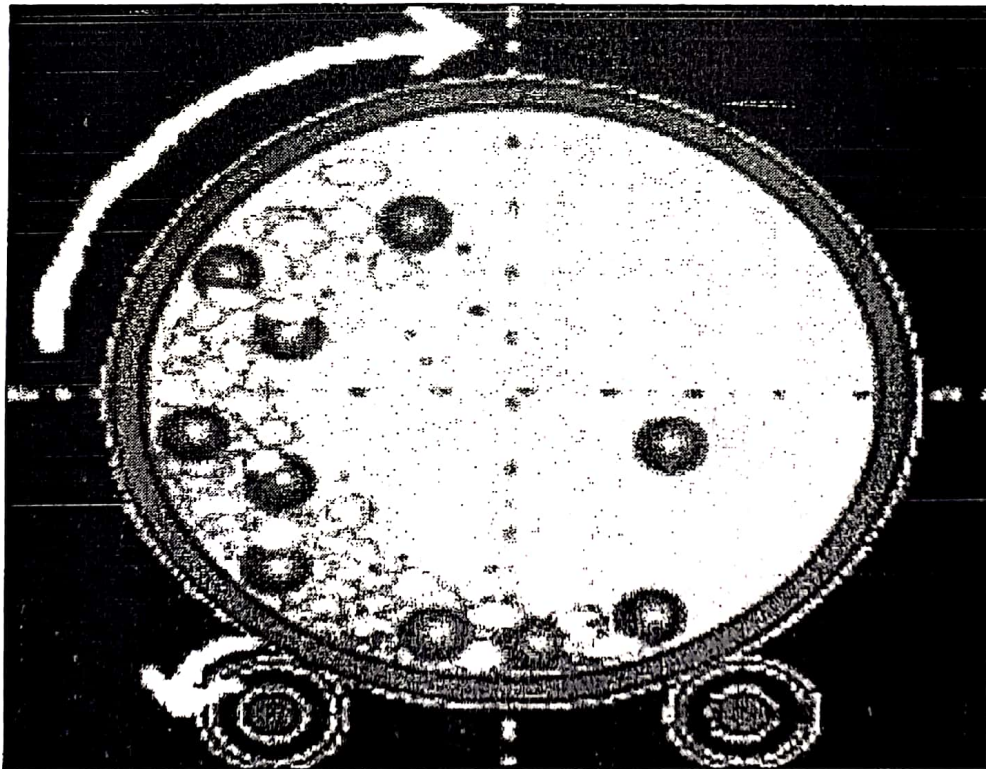


Fig: Ball Mill

Working: The drug to be grind is put into the cylinder of the mill and is rotated. The speed of rotation is very important. At a low speed, the mass of balls will slide or roll over each other and only a negligible amount of size reduction will occur. At a high speed, the balls will be thrown out to the walls by centrifugal force and no grinding will occur. But at about $2/3^{\text{rd}}$ of the speed, the centrifugal force just occurs with the result that the balls are carried almost to the top of the mill and then fall in. By this way the maximum size reduction is effected by the impact of particles between the balls and by attrition between the balls.

After a suitable time, the material is taken out and passed through a sieve to get powder of the required size.

Uses: The mill is used to grind brittle drugs to fine powder.

Advantages:

1. It can produce very fine powders.
2. It can be used for continuous operation, if sieve or classifier is attached to the mill.
3. It is capable of grinding a large variety of materials of different character and of different degree of hardness.
4. It is suitable for both wet and dry grinding processes.
5. It can be used to grind toxic materials as it can be used in a completely enclosed form.

Disadvantages:

1. Ball mill is very noisy machine.
2. Wear occurs from the balls as well as from the casing, which may result in contamination of the product.

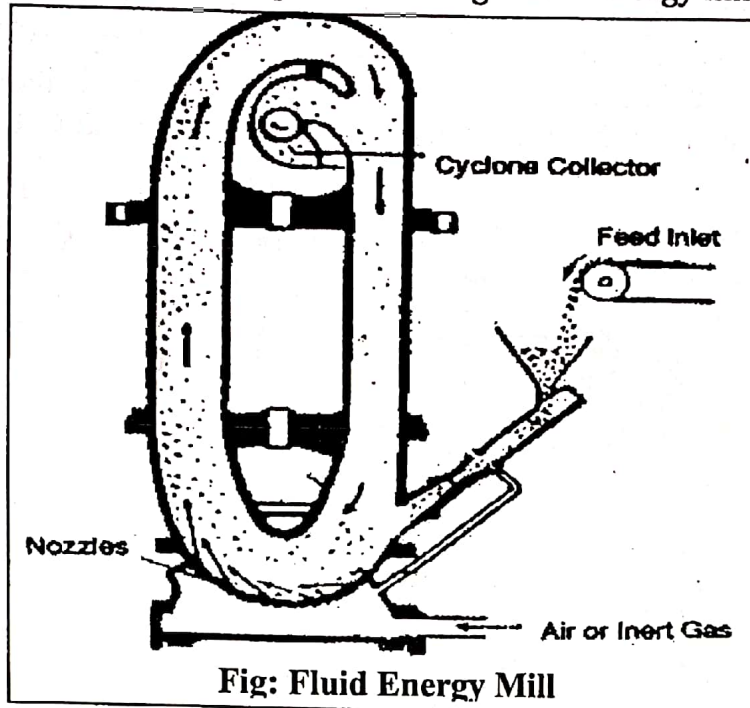
◆ **CONSTRUCTION AND WORKING OF THE FLUID ENERGY MILL.**

Principle: It works on the principle of impact and attrition.

Construction: It consist of a loop of pipe, which has a diameter of 20 to 200 mm, depending on the overall height of the loop, which may be upto about 2m. There is an inlet for the feed and a series of nozzles for the inlet of air or an inert gas. It also has an outlet with a classifier which allows the air to escape but prevent the particles to pass until they become sufficiently fine.

Working: The air or inert gas is introduced with a very high pressure through the nozzles. Solids are introduced into air stream through inlet. Due to high degree of turbulence, impact and attritional forces occurs between the particles. The fine particles are collected through a classifier. Fluid energy mill reduces the particles to 1 to 20 micron. To get a very fine powder, even

up to five micron, the material is pretreated to reduce the particle size to the order of 100 mesh and then passed through fluid energy mill.



Uses: The mill is to grind heat sensitive materials to fine powder. The mill is used to grind those drugs in which degree of purity is required.

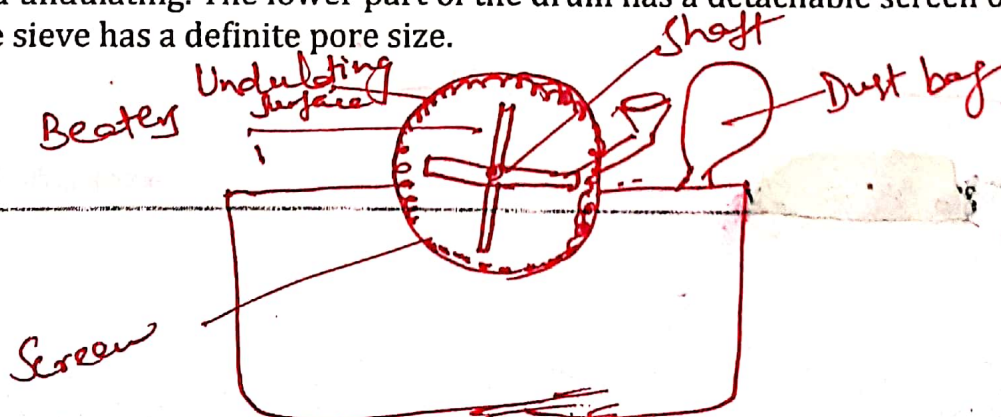
Advantages:

1. The mill is used to grind the material to fine powder.
2. The particle size of the powder can be controlled due to the use of a classifier.
3. There is no wear of the mill and hence there is no contamination of the product.
4. It is useful for grinding heat sensitive substances such as sulphaamides, vitamins.

CONSTRUCTION AND WORKING OF THE DISINTEGRATOR.

Principle: The size reduction in disintegrator is done by impact.

Construction: It consists of a steel drum having a shaft in the centre. The shaft contains a disc, on which four beaters are fixed. The shaft rotates with a speed of 5000-7000 rpm. The side and upper inner surface of the drum is rough and undulating. The lower part of the drum has a detachable screen or sieve. The sieve has a definite pore size.



Working: The beaters are mainly responsible for grinding but are helped by the undulation of the inner surface and roughness of drum. The materials are feed to beaters, through hopper which is fitted to the drum. The material is broken into small particles by impact of the beaters. Due to high velocity of beaters the air velocity inside the chamber is increased. The air is allowed to pass through an outlet on which dust bag is tied, which retains the fine particles of powder.

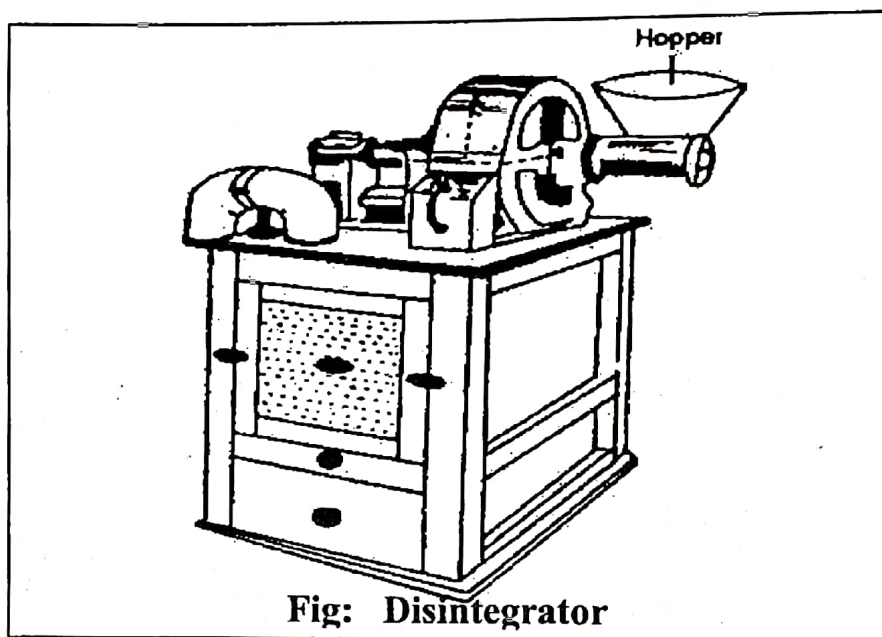


Fig: Disintegrator

Uses: The mill is used to powder all types of drugs including very hard drugs. The drugs should be dried before feeding into the disintegrator to get fine powder. To avoid the jamming of the beaters of the disintegrator, use moderately small pieces.

चर्चनीय नमूने

◆ LEVITATION AND ELUTRIATION.

- ✓ **Levitation:** Levitation is the process of wet grinding. The material is converted into paste with water and then grinding of paste is done in a motor, using a flat headed pestle. In large scale grinding, it is done by using colloidal mill. This process is used for the preparation of light kaolin, chalk etc.
- ✓ **Elutriation:** It is the process of separation of fine particles and coarse particles from a paste obtained after levitation. The paste is mixed is mixed with a large volume of water and the mixture is allowed to stand for a short period and heavy particles settles down at the bottom. The upper liquid is poured off and fine particles are allowed to settle down. The wet paste containing fine particles is then dried. In small scale grinding, conical flask can be used but on large scale, elutriation tanks are used.

6. SIZE SEPARATION

◆ DEFINITION OF SIZE SEPARATION.

Size separation: Size separation process may be applied to the measurement of particle size, in which the portion of each size of particle in a sample is determined and data is utilized to control raw or to maintain the quality of manufacture product.

◆ IMPORTANCE OF SIZE SEPERATION:

1. It is applied to the measurement of particle size, in which the proportion of each size of particle in a sample is determined and the data is utilized to control raw material or to maintain the quality of manufactured product.
2. During the process of size reduction it is not possible to obtain the particles of uniform size hence separation gave the standard for particle size. The degree of coarsens or fineness of a powder can be achieved by size separation process.
3. Size separation increases the rate of absorption of drug and improves the stability of pharmaceutical dosage form such as suspensions.
4. Size separation helps in uniform mixing of drugs, required for preparing different formulations for administration.

◆ NOTE ON OFFICIAL GRADES OF POWDERS OR GRADING OF POWDER.

Grading of powder: In pharmacopoeia the powders are given with different grades based on their sieve numbers and these grades are called as official grades of powders.

The sieve number can be defined as number of meshes or openings included in the length of 2.54 cm in each transverse direction parallel to the wires. Thus sieve no.40 has 40 openings in 2.54 cm in each transverse direction.

The various grades of powders which are official in I.P. are as follows:

1. Coarse powder(10/44): Coarse powder is defined as ,when the powder is passed through sieve number 10,all particles passes through sieve number 10 but not more than 40 percent of particles passes through sieve number 44.

2. Moderately coarse powder (22/60): A powder of which all particles passes through 22 mesh sieve and not more than 40% through 60 mesh sieve.
3. Moderately fine powder (44/85): Moderately fine powder is defined as, when the powder is passed through sieve number 44, all particles passes through sieve number 44 but not more than 40 percent of particles pass through sieve number 85.
4. Fine powder (85): A fine powder of which all the particles passes through 85 mesh sieve.
5. Very fine powder (120): A powder of which all the particles passes through 120 mesh sieve.

◆ 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 remove only coarse particles and allow fine particles to be carried through with the fluid.

Construction: It consists of a cylindrical vessel with a conical base. In the upper part of the vessel is fitted with a tangential inlet and a fluid outlet and at the base it is fitted with solid outlet.

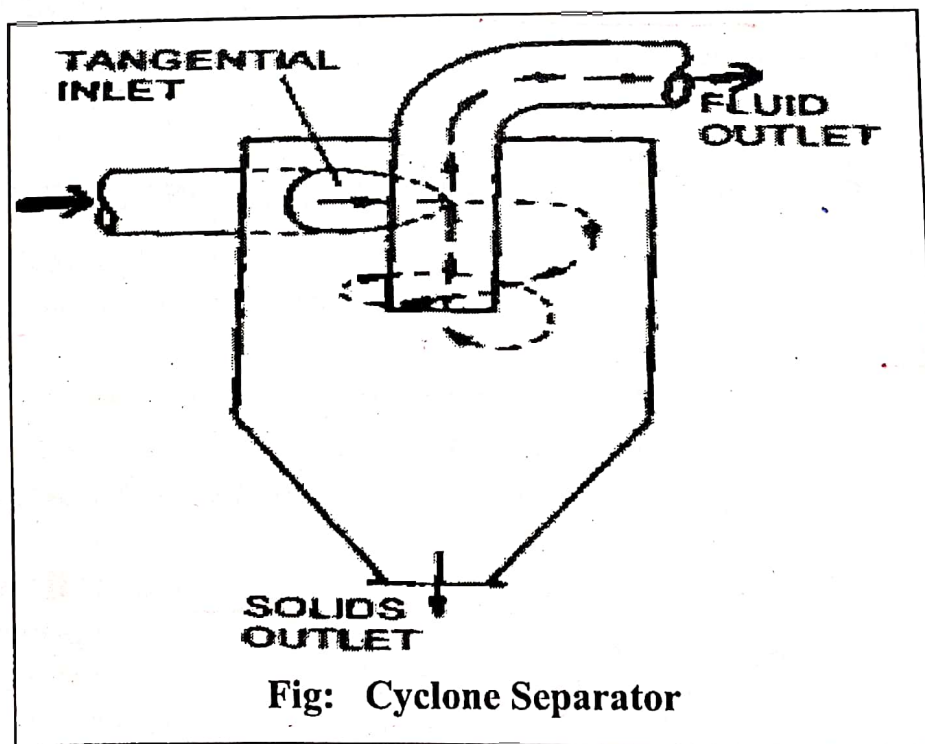


Fig: Cyclone Separator

Working: The suspension of a solid in a 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 rotary flow within the cyclone separator causes the particles to be acted on by centrifugal force. 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.

PROCESS OF SIZE SEPARATION BY ELUTRIATION TANK.

OR

MECHANICAL AIR CLASSIFIER.

Elutriation is a process of size separation of the particles depending on the particle size and density. The process is exclusively applicable to separation of coarse and fine particles on non-hydrating inorganic powders, after the process of levitation. The elutriation is to be carried out in elutriation tank.

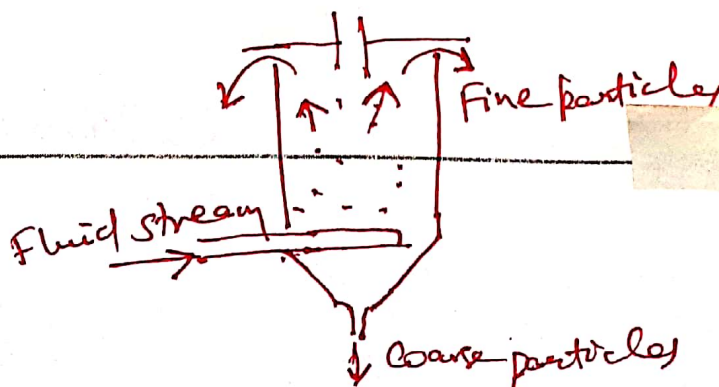
Elutriation method: The apparatus consists of a vertical column with an inlet at the bottom and an outlet at the top. The suspension is passed through the inlet. Depends upon the movement of the fluid, the particle size is separated. Usually two fractions are separated in single vertical column. The coarse particles are collected through the outlet at the bottom. The fine particles are carried along with the fluid which are collected through the outlet at the top.

Advantage:

1. The process is continuous.
2. The apparatus is more compact.
3. The separation is quicker than the sedimentation.

Application of sedimentation and elutriation methods:

- ✓ Both methods are used to separate over size particles and particles of different sizes.
- ✓ These two techniques are applicable to the size separation of insoluble solids such as kaolin or chalk.



7. MIXING AND HOMOGENIZATIONS

◆ DEFINITION OF MIXING AND HOMOGENIZATION.

- ✓ **Mixing:** Mixing may be defined as the process in which two or more components are mixed so that each particle of one component is in contact with each particle of other component.
- ✓ **Homogenization:** Homogenization is the process by which the large globules or particles in a coarse emulsion or suspension or semisolid preparations are broken into smaller globules or particles by passing the sample under pressure through a narrow orifice. As the result, the final product is more stable and uniform.

◆ TYPES OF MIXTURES AND THE FACTORS CONSIDERED IN MIXING PROCESS.

- ✓ **Types of mixtures:** According to the behavior, the mixtures can be divided into three groups-
 1. **Positive mixtures:** When two miscible liquids are mixed or when a soluble solid is mixed in a liquid, positive mixtures is formed. In this case, external force is not required and the mixture is not reversible.
Eg. mixtures containing soluble solids/liquids.
 2. **Negative mixtures:** When two immiscible liquids are mixed or when insoluble solids are mixed with water, negative mixtures are formed. In this case external force is required and the mixture is reversible.
Eg. mixtures containing insoluble solids/liquids.
 3. **Neutral mixtures:** In these types, the substances do not have tendency to mix with each other, but once mixed they do not separate. Ointments, pastes and mixed powders are examples of neutral mixtures.
- ✓ **Factors considered in mixing process:** The following factors are considered in mixing process:
 - a) **Particle size:** It is easy to mix two powders having the same approximate particles sizes. The variation of particle size can do separation also, because the small particles move down ward through the spaces between the bigger particles.
 - b) **Materials density:** It is difficult to mix two powders having different density. This is due to the fact that dense materials always moves

downwards and settles down at the bottom. Therefore for uniform mixing of powders, proper attention should be given to their density.

c) **Particle attraction:** Some particles exert attraction forces due to electrostatic charges on them. This can lead to separation.

d) **Particle shape:** The ideal particle is spherical in shape for the purposes of uniform mixing. The irregular shapes can become interlocked and there are less chances of separation of particles once these are mixed together.

e) **Proportions of materials:** The best result can be achieved if two powders are mixed in equal proportions by weight or by volume in case there is a large difference in the proportion of two powders to be mixed, The mixing of powders is always done in the ascending order of their weights.

◆ EQUIPMENT USED FOR MIXING LIQUIDS.

OR

WRITE THE NOTE ON SILVERSON MIXER?

(Homogenizer)

✓ Construction and working:

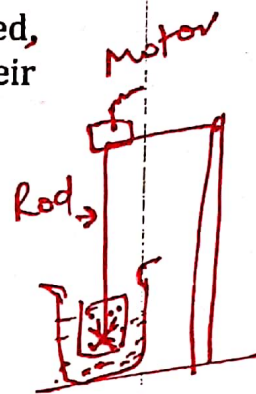
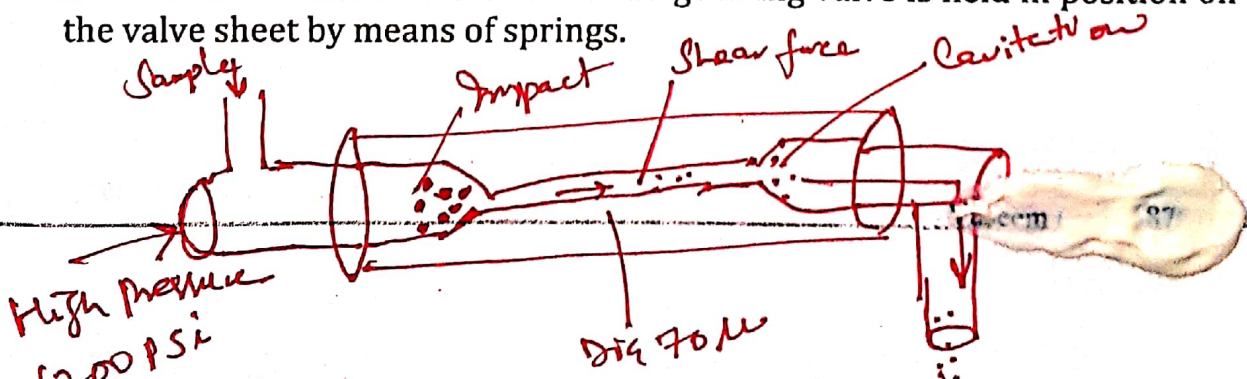
Silverson mixer emulsifier consists of an emulsion head with sharp blades. The head is covered with stainless steel mesh having small holes. Within the emulsor head, numbers of sharp blades are present. The emulsor head is fixed on long rods. There is one central rod which is directly attached to the sharp blades. Motor is fitted at the top.

The coarse emulsion (handmade emulsion) is taken in a suitable vessel. The emulsion head is immersed in the emulsion. The motor is switched on. The long rods along with sharp blades rotate at very high speed. As the result the liquids are sucked and expelled with great force through the small holes and the oil phase is reduced into fine globules by powerful shearing action of rotating blades. Homogeneous fine emulsion is produced.

✓ **Applications:** Silverson mixer emulsifier is used to produce stable emulsion of having oil globules 1.5 to 2 microns.

◆ HOMOGENISER

✓ **Construction and working:** It consists of high pressure pump, a spring scatted valve and an orifice. The homogenizing valve is held in position on the valve sheet by means of springs.



Hand -Made emulsion is passed through the inlet under high pressure. When the high pressure is applied, the springs are compressed. At this point the energy that has been stored in the liquid is released. So the valve sheet rotates at high speed. As a result of shearing action and turbulence motion of the valve sheet, the oily globules are broken into very small globules and stable emulsion is formed. After this first homogenization, the globules may agglomerate. So the homogenization process may be repeated second and third time. In homogenizer, the globule size may be 0.02 micron.

- ✓ **Applications:** Homogenizer is used for preparing stable emulsions and suspensions. It is also used in the manufacture of cosmetic creams and ointments.

◆ **HAND HOMOGENISER.**

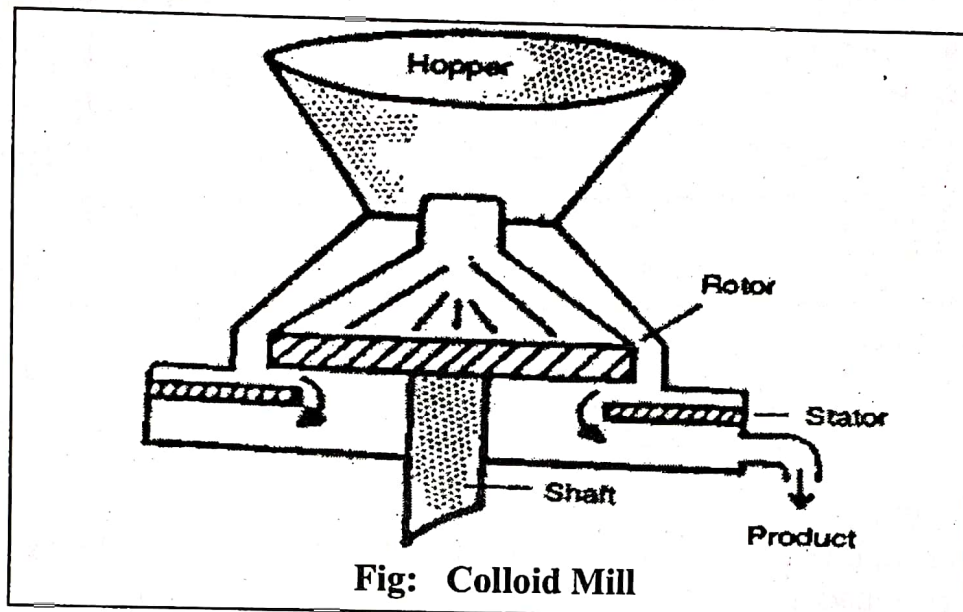
- ✓ **Construction and working:** It consists of a hopper and a fine orifice. The hand-made emulsion is taken in the hopper. This homogenizer operates with hand. The handle is moved up and down .By this way, the emulsion is forced to pass through the fine orifice continuously and thereby the oil globules are broken into fine globules of uniform size.

◆ **PROPELLER MIXER.**

- ✓ **Construction and working:** It consists of a number of blades, fixed in a long shaft. The liquids to be mixed are taken in a vessel. The shaft is allowed to rotate at high speed. As the blades rotate, a moderate radial and tangential flow occurs above and below the blades. It brings the liquids from all regions of the tank and thereby mixing is affected. During mixing, the blades are kept deep in the liquid to avoid aeration. During the process of mixing, there are chances of formation of vortex and entrapment of air. These defects can be avoided by the following ways:
 - 1) By using the propeller offset from centre.
 - 2) By using the propeller in inclined position
 - 3) By using the propeller from the side.
 - 4) By using a push-pull type propeller.
- ✓ **Disadvantage:** Propeller mixers are not suitable for mixing viscous liquids like glycerin, liquid paraffin.
- ✓ **Application:** Propeller mixer is used for mixing liquids of low viscosities.

◆ **COLLOIDAL MILL**

- ✓ **Principal:** The size reduction is affected due to shearing, when the material is passed between the narrow gap of milling surfaces of rotor and stator.

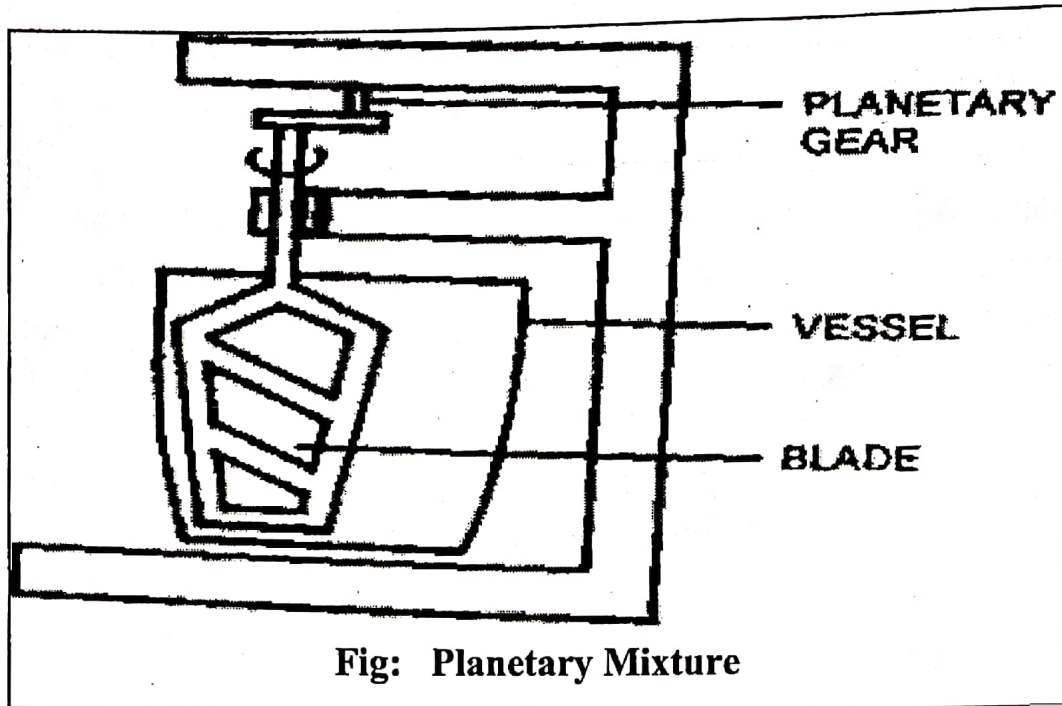


- ✓ **Construction:** Colloidal mill consists of a rotor and a stator. The rotor rotates at a speed of 3000 to 20000 rpm. The stator has conical milling surfaces between which there is an adjustment clearance between 0.002 to 0.03 inches.
- ✓ **Working:** The materials E.g. Emulsion and suspension is placed into the hopper of the mill. It is then passed through the narrow gap between the rotor and stator and thus reduced to fine particle size.
- ✓ **Uses:** Colloidal mills are capable of producing particles in micron size. These are commonly used to prepare pharmaceutical suspensions and emulsions having particle size less than one micron.

◆ **PLANETARY MIXER.**

- ✓ **Construction and working:** It consists of a high speed impeller blades fixed on a vertical cylindrical rod. The samples to be mixed are taken in a mixing tank. The cylindrical rod with impeller blades is allowed to revolve at high speed. When it rotates on its own axis, the planetary movement of the tank helps uniform mixing of the samples.
- ✓ **Advantages:**
 - 1) It provides uniform mixing.
 - 2) It serves to break down agglomerates rapidly.

(शुद्धि हेतु)



✓ **Disadvantages:**

- 1) It requires high voltage to operate the equipment.
- 2) Heat is produced during operation.

✓ **Application:**

- ✓ 1) Planetary mixer is used for mixing semisolids such as ointments, pastes and creams.
- ✓ 2) It is also used for mixing liquids and powders.

◆ **TRIPLE ROLLER MIXER OR TRIPLE ROLLER MILL.**

- ✓ **Principle:** Triple roller mill is used for milling (reducing the particle size) and for mixing. The principle of working triple roller mill is attrition.
- ✓ **Construction and working:** It consists of three stainless steel rollers mounted horizontally with a very small gap between them. The gap can be adjustable. The rollers revolve at different speeds. The speed can be adjustable. The sample to be mixed is introduced through the inlet. The rollers are allowed to revolve at optimum speed. When the sample passes through the gap between the rollers, it is crushed and mixed by means of revolving rollers. The crushed and mixed product is transferred from the slower to the faster roller so that the sample is mixed thoroughly.
- ✓ **Applications:** Triple roller mill is used for milling and mixing suspensions, ointments, creams etc.

8. CLARIFICATION AND FILTRATION

◆ Define the terms filtration, clarification Straining.

- ✓ **Filtration:** It may be defined as the separation of solids or suspended matter in a liquid or gas by passing through a porous medium which retain the solids but allows the fluids to pass.
- ✓ **Clarification:** It is the process by which finely divided solids and colloidal materials are separated from liquids with the help of clarifying agents such as paper, pulp, talc etc.
- ✓ **Straining:** Filtration is to remove large visible particles by using coarse filtering medium such as muslin and cotton wool is known as straining.

◆ FILTER MEDIA.

- ✓ **Filter media:** The surface upon, which solids are retained in the process of filtration is known as 'filter medium'.
- ✓ **Various filter media used in filtrations:**
 1. Filter press
 2. Filter cloth
 3. Cotton wool
 4. Glass wool
 5. Asbestos
 6. Membrane filters
 7. Sintered glass filter
- ✓ **Properties of an ideal filter medium:**
Filter medium should be:
 - 1) Chemically inert
 - 2) Should have high retentive power
 - 3) Should offer filter resistance?
 - 4) Should be mechanically strong
 - 5) Should be resistant to corrosive actions of fluids
 - 6) Economical, reusable, should not absorb or adsorb dissolved material.

◆ FILTER AIDS.

✓ **Filter Aids:** These are the substance which reduces the resistance of the filtrate to flow. These are added to the preparation in concentration from 0.1 to 0.5 percent before filtration. An ideal filter aid should possess the following qualities:

1. It should be able to remain suspended in the liquids.
2. It should be free from impurities.
3. It should be inert to the liquid being filtered.
4. It should be low specific gravity.
5. It should form a porous cake

✓ **Various filter aids used in pharmacy are:**

1. Talc
2. Kieselguhr
3. Charcoal.

◆ FACTOR AFFECTING THE RATE OF FILTRATIONS:

1. Area of filter surface: Rate of filtrations is directly proportional to area of the filtered surface. Greater the filtering surface greater will be the rate of filtration.
2. Particle size of solids to be removed: Rate of filtrations is directly proportional to the particle size of solids to be removed.
3. Pore size of the filter media: Rate of filtration is directly proportional to the pore size of the filter media.
4. The resistance of the filter cake and filter media: The rate of flow will be greatest at the beginning of the process because there is minimum resistance but as the process proceeds the filter cake is formed which goes on increasing and adding thickness to the cake which slow down the rate of filtration but this cake also act as a secondary filter medium.
5. Viscosity of the liquid to be filtered: The rate of filtration is inversely proportional to the viscosity of the liquid to be filtered.
6. Temperature: Increased temperature reduces the viscosity of thick liquids such as syrup, glycerin etc thus they can be filtered quickly.
7. Pressure difference across the filter: The rate of filtration is directly proportional to the pressure difference across the filter bed. The rate of filtration can be increased by increasing the pressure on the liquid to be filtered or by reducing the pressure under the filter media i.e. in the receiver (vacuum filtration).

◆ EQUIPMENT USED IN FILTRATION PROCESS.

✓ Filter press:

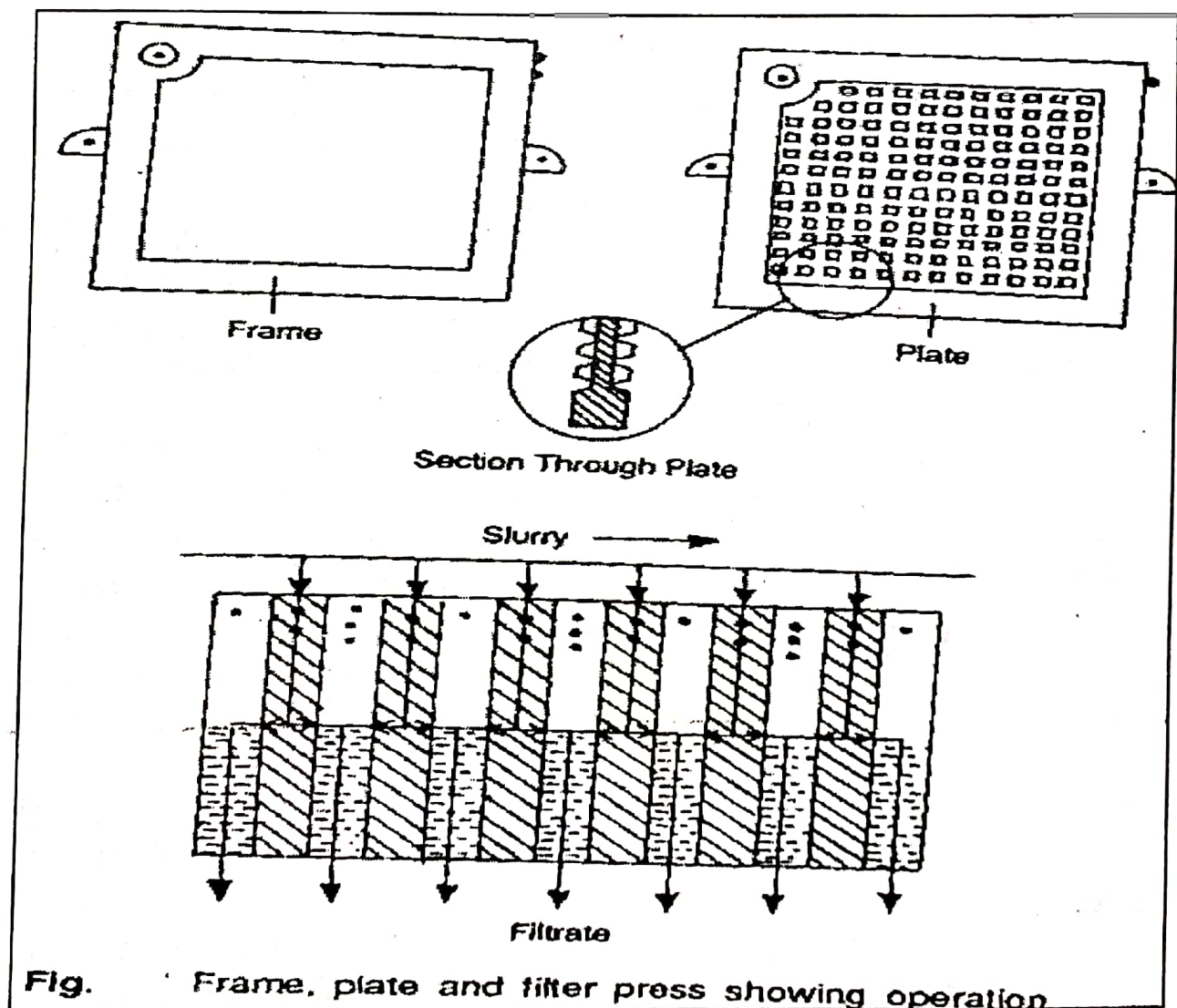
Principle: The rate of filtration is increased by increasing the pressure on the liquid to be filtered.

Various types of filter presses are used for large scale filtration but the plate and frame press is widely used in pharmaceutical industries.

As the name indicates this filter press consists of a number of hollow frames and solid plates. Plates have grooved surface. Each plate is having a central inlet and an outlet for the filtrate. The plates and frames are assembled alternatively and each set works as a unit.

Liquid to be filtered is allowed to enter the frame under pressure, the filtrate passes through the filter medium on the surface of the plate while the filter is retained in the frame. Filtrate drains out through the outlet.

The operation is continued till the frame is filled with the filter cake. When the process is stopped, the filter cake is removed from the frame and the process is restarted.



Advantages of Filter press:

1. The filtering media can be used repeatedly.
2. Operation and maintenance is simple.
3. It requires less space.
4. It provides a large surface for filtration.
5. Efficient washing of cake is possible.

Disadvantages of Filter press:

1. It is not a continuous process.
2. It is used where the proportion of solid in the liquid to be filtered is about 5% or less.
3. Costlier, leakage between plates may take place through faulty assembly.

9. EXTRACTION PROCESS AND GALENICALS

◆ **EXTRACTION:** Extraction may be defined as the process in which the plant or animal tissues are treated with solvent, whereby medically active constituents are dissolved.

◆ **GALENICALS:** The various preparations which are prepared by extraction process are known as Galenicals.

◆ **MENSTRUUM:** The solvent used for extraction is called as Menstruum.

◆ **SOLVENTS USED IN EXTRACTION PROCESS:**

1. **Water:** It is a solvent for protein, coloring matter, gums, glycosides, sugars, enzymes etc.

Waxes, fats, fixed oils and most alkaloids are insoluble in water.

2. **Alcohol:** It is a solvent for volatile oils, resins, glycosides, alkaloids etc.

◆ **EXTRACTION PROCESS.**

Various methods used for the extraction of drugs include:

- 1. Infusion
- 2. Decoction.
- 3. Maceration.
- 4. Percolation.
- 5. Digestion.

1. Infusion:

This method is used for those drugs which are soft in nature so that water may penetrate easily.

It consist of pouring water over the drugs and then allowing it to keep in contact with water for the stated period, usually 15 minutes, with occasional stirring and finally filtering off the liquid. The marc is not pressed. The boiling water is commonly used as a solvent, since it has a greater solvent action than cold water.

Apparatus: Coffee pot or a teapot is the simplest form of apparatus used for preparation.

Types of Infusion:

- a) Fresh Infusion.
- b) Concentrated infusions.

2. Decoction:

It is the process in which the water soluble and heat stable constituents of hard and woody crude drugs are extracted out.

In this process, the drug is boiled with water for a stated period usually 10 minutes. After boiling the liquid is strained and water is passed through the content of the strainer to make the required volume.

This process is mainly used for vegetable drugs of hard and woody nature having thermolabile water soluble constituents.

3. Maceration:

(a) Simple maceration for organised drugs:

- ❖ Organised drugs are those drugs which have a specific cell structure like roots, stems, leaves, flowers etc.
- ❖ Solid Drugs (crushed, cut small or moderately coarse powder)
- ❖ Whole menstruum is closed in a vessel for 2-7 days with occasional stirring.
- ❖ Liquid is strained and marc is pressed.
- ❖ Add the expressed liquid to the strained liquid.
- ❖ Combined liquid are Clarified by Decantation or Filtration.
- ❖ Final volume is not adjusted
- ❖ Water or alcohol is used as Menstruum.
- ❖ Generally closed vessel is used to prevent evaporation of Menstruum.
- ❖ Drug and Menstruum is used in the ratio 1:10.

Examples: i) Tincture of Orange.

ii) Tincture of Lemon.

(b) Simple maceration for unorganised drugs:

- ❖ Unorganised drugs are those drugs which have no cellular or tissue structure and are obtained from plants.

Extraction of drugs is carried out as follows:

- ❖ Drug is kept in contact with $\frac{4}{5}$ th of menstruum in a closed vessel for 2-7 hours with occasional stirring.
- ❖ Clear liquid is decanted or filtered and marc is not pressed.
- ❖ Volume is adjusted by passing remaining $\frac{1}{5}$ th menstruum through the marc.

Examples: i) Tincture of Tolu.

ii) Tincture of Myrrh.



(c) Multiple maceration:

- ❖ Multiple maceration process is carried out in the same way as simple maceration process, but the menstruum used is divided into two parts in double maceration process and into three parts in triple maceration process.

❖ Double maceration:

During this process the maceration of drug is carried out twice and total volume of menstruum to be used is divided in two parts in such a way that same quantity of menstrum is used for each maceration.

$$\begin{array}{l} \text{Volume of} \\ \text{menstrum to be} \\ \text{used for first} \\ \text{maceration} \end{array} = \frac{\text{Total volume} \\ \text{of menstruum}}{2} - \frac{\text{Volume of menstruum} \\ \text{retained by the drug}}{2} + \text{Volume of} \\ \text{menstrum} \\ \text{retained by} \\ \text{the drug}$$

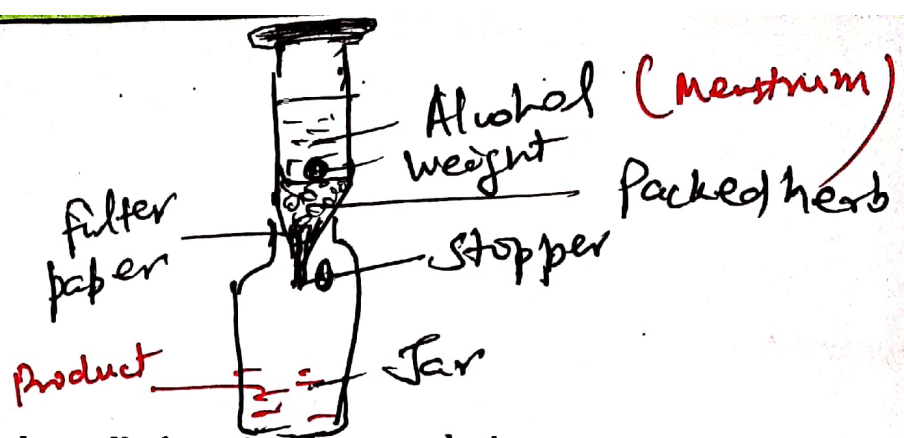
❖ Triple maceration:

Triple maceration process is sometimes used where the marc cannot be pressed.

In case of triple maceration, the menstruum is divided into three parts and maceration is done thrice.

$$\begin{array}{l} \text{Volume of} \\ \text{menstrum to be} \\ \text{used for first} \\ \text{maceration} \end{array} = \frac{\text{Total volume} \\ \text{of menstruum}}{3} - \frac{\text{Volume of menstruum} \\ \text{retained by the drug}}{3} + \text{Volume of} \\ \text{menstrum} \\ \text{retained by} \\ \text{the drug}$$

$$\begin{array}{l} \text{Volume of} \\ \text{menstrum required} \\ \text{for 2}^{\text{nd}} \text{ and 3}^{\text{rd}} \\ \text{maceration} \end{array} = \frac{\text{Total volume} \\ \text{of menstruum}}{2} - \frac{\text{Volume of menstruum} \\ \text{used for 1}^{\text{st}} \text{ maceration}}{2}$$



4. Percolation:

- ❖ Percolation is also called as simple percolation.
- ❖ This method is used in the preparation of tinctures & liquid extract.

Extraction of drugs is carried out as follows:

- ❖ Drug + Menstruum are packed in a percolator.
- ❖ Drug is allowed to remain in contact with the menstruum for 24 hours, then more menstruum is added and percolation is started.
- ❖ Required volume is collected, marc is pressed and expressed liquid is added to the percolate.
- ❖ The required volume is produced by adding more of menstruum, and mixed liquid is clarified by denaturation or by filtration.

Examples: i) Tincture of Ginger.

ii) Tincture of Cardamom.

- ❖ The entire percolation process is explained by dividing it into following stages:
 - i. Size reduction or comminution of drug.
 - ii. Imbibitions.
 - iii. Packing.
 - iv. Maceration.
 - v. Percolation.

5. Digestion:

- ❖ Drug is extracted by heating at a particular pressure; this will increase penetration power of the menstruum.
- ❖ Apparatus known as "Digester" is used for the extraction of drug by this method.
- ❖ It is a vessel made up of metal.

◆ SOLVENTS USED IN EXTRACTION PROCESS:

- i. Nature of drug.
- ii. Cost of drug.
- iii. Stability of drug.
- iv. Therapeutic value of drug.
- v. Nature of solvent.
- vi. Concentration of the product.

10. HEAT PROCESS

◆ HEAT PROCESS:

The important heat processes used in pharmaceutical manufacturing are:

- 1) Evaporation.
- 2) Sublimation.
- 3) Exsiccation.
- 4) Desiccation.
- 5) Fusion.
- 6) Calcination.
- 7) Ignition.
- 8) Distillation.
- 9) Freeze drying.

◆ EVAPORATION:

Evaporation means the free escape of vapours from the surface of liquid below its boiling point.

Vapour pressure is maximum at the boiling point of liquid. Vapour pressure of a liquid is equal to the atmospheric pressure at its boiling point.

◆ FACTORS AFFECTING EVAPORATION:

Following are the factors which affect the rate of evaporation of a liquid.

1. **Temperature:** Rate of evaporation is directly proportional to the temperature of the liquid.
2. **Temperature and time of evaporation:** Exposure to a relatively high temperature for a short period of time may be less harmful to the active principles of a drug than a lower temperature with exposure for a longer period.
3. **Agitation:** During evaporation, formation of upper layers takes place which lowers the rate of evaporation. Therefore it becomes necessary
4. **Surface area:** Rate of evaporation is directly proportional to the surface area of the vessel exposed to evaporation.
5. **Atmospheric pressure:** Rate of evaporation is inversely proportional to the atmospheric pressure on the surface of the liquid.
6. **Types of product required:** On evaporation of the liquid the concentrated liquid, semi-solid and solid are formed. A type of product required depends upon the selection of method and equipment.

◆ EVAPORATORS:

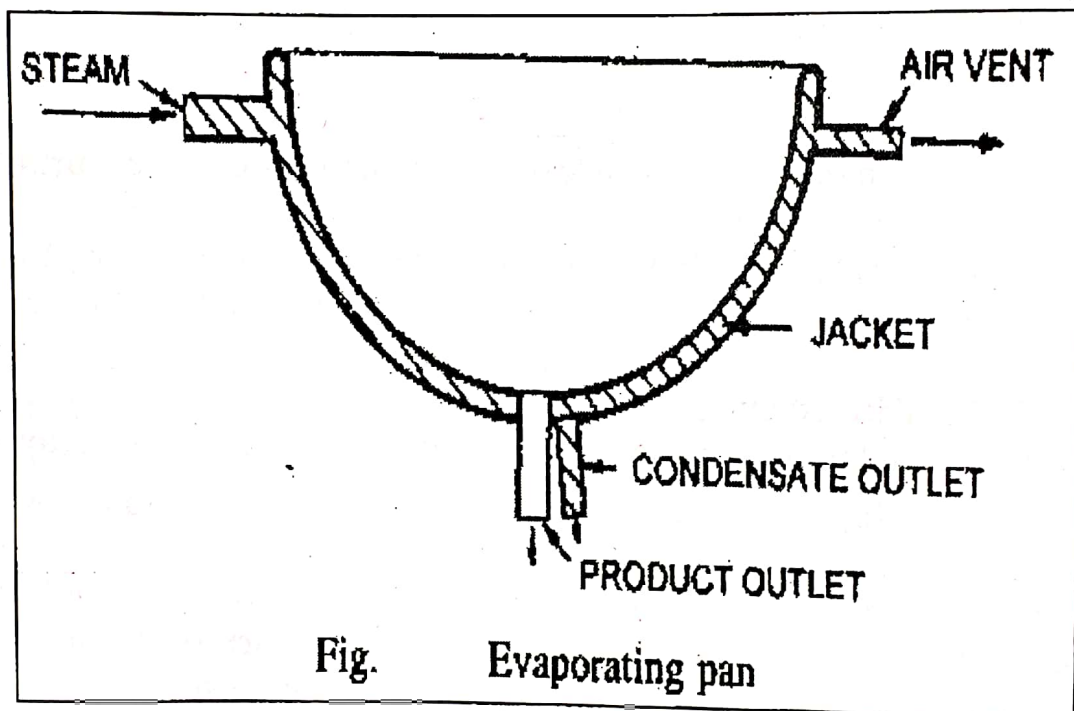
The equipment used in the process of evaporation is called evaporators.

Different evaporators used are described below:

- (1) Evaporating pans.
- (2) Evaporating stills.

◆ EVAPORATING PANS:

- ☞ It is made up of copper or stainless steel and surrounded by steam jacket.
- ☞ Hemispherical shape provides a large surface area for evaporation.
- ☞ The emptying of the pan is done from the product outlet.
- ☞ The evaporating pans are heated by steam which passes through a steam jacket.



Advantages:

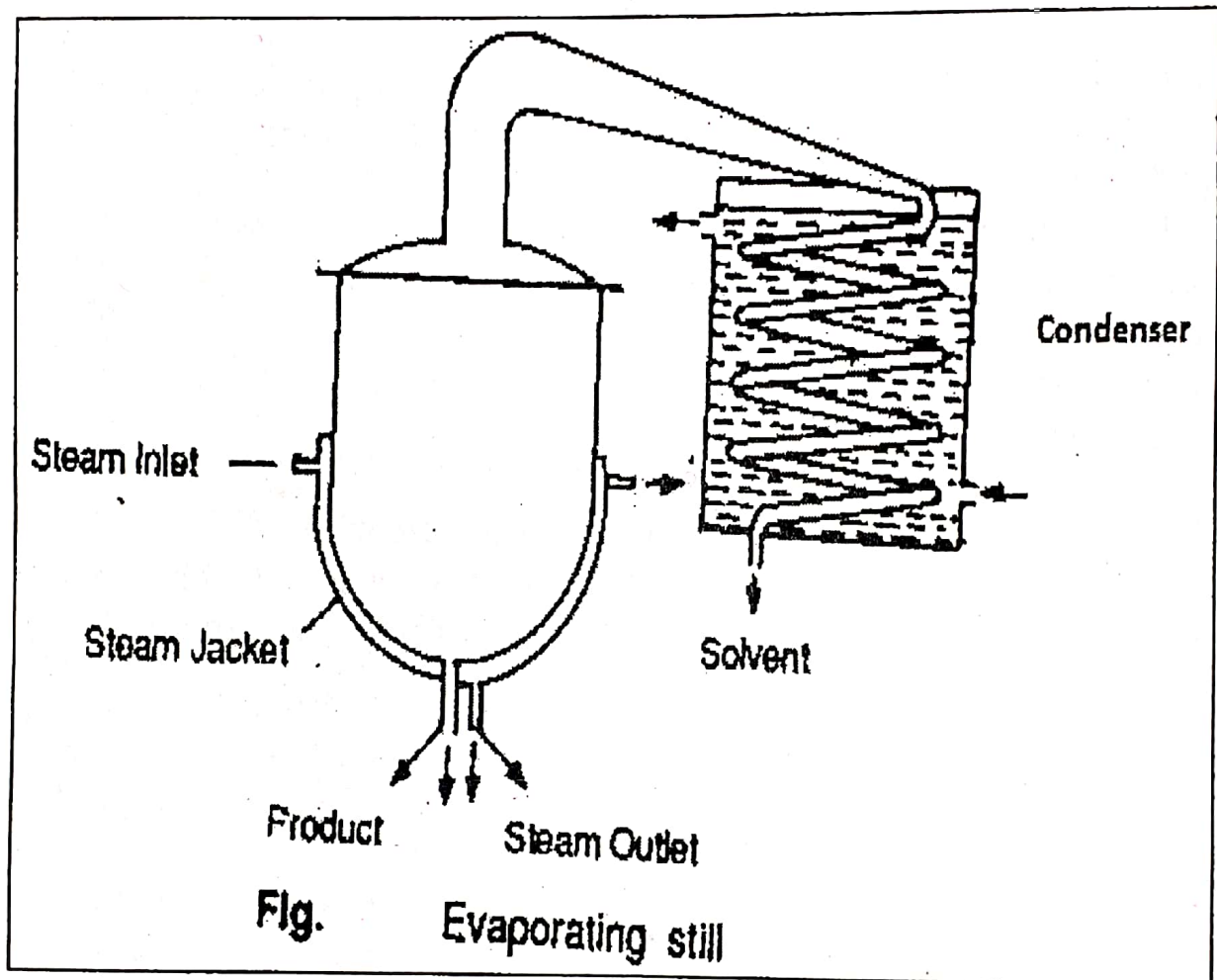
- i. Simple and easy to construct.
- ii. Easy to use and clean.
- iii. Stirring of evaporating liquids can be done easily.
- iv. Economical.

Disadvantages:

- i. Whole liquid is heated at a time.
- ii. Layers are rapidly formed, which decreases evaporation.
- iii. Cannot be used for organic solvents like alcohol.
- iv. Not suitable for thermolabile materials.

◆ EVAPORATING STILL:

- ☞ It is commonly known as still because the evaporating pan is covered and connected to the condenser.
- ☞ Condenser converts the vapours into liquids.
- ☞ Liquid is distilled off and collected.



Advantages:

- i. Simple in construction.
- ii. Easy to clean and maintain.
- iii. Vapours are condensed in it.
- iv. Increases the speed off evaporation.
- v. Good for evaporation under reduced pressure.

Disadvantages:

- i. Heating surface is limited.
- ii. Not suitable for thermolabile materials.
- iii. Heat transfer coefficient is poor.

CHAPTER. 11 DISTILLATION

Q.1 Define Distillation and write the different types of distillation.

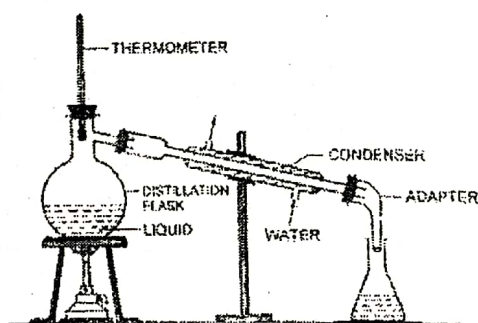
Ans: Def: It is the process of converting liquid into its vapours by heating and reconvert it again into liquid by condensing the vapours. It is a method of separating substances which differ in their vapour pressure.

Types of distillate process:

1. Simple Distillation.
2. Distillation under reduced pressure.
3. Steam Distillation.
4. Fractional Distillation.
5. Destructive Distillation.

Q.2 Explain the simple distillation .Give its application.

1. Simple Distillation: Simple distillation is a process of converting a liquid into its vapour in a distillation still, transferring the vapour to another place and condensing it again into liquid.



It consists of a distillation flask with a side arms sloping downward which is connected to a condenser. The condenser vapour is collected in a flask called receiver. The whole apparatus is made of glass. The distillation flask should be of such a size that it can contain half to two-thirds of the liquid to be distilled. The thermometer is fitted in the distillation flask to note down the temperature at which the vapours are distilled. Bumping is avoided by adding small pieces of porcelain before distillation.

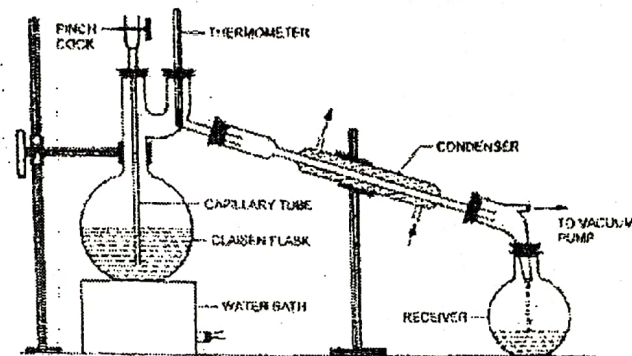
Application:

1. It is used for the preparation of distilled water and water for injection.
2. Many volatile oils and aromatic water are prepared by simple distillation.
3. Organic solvents are purified by distillation.
4. Ether, spirit of nitrous ether is prepared by simple distillation.

5. Concentration of liquid and to separate non-volatile solid from volatile liquids such as alcohol and ether

2. Distillation under reduced pressure or Vaccume Distillation:

It is the process of distillation which involves application of vaccume due to which the liquid boil at relatively lower temperature when compare to their actual boiling point this is called as distillation under reduced pressure.



It consists of a double neck distillation flask known as claisen flask. In one of its neck a thermometer is fitted and in the second neck a capillary tube is fitted which prevents bumping of the ~~heat~~ liquid. The capillary tube should be so fine as to permit only a slow stream of bubble which can controlled with a pinch cock.

Thick walled glass apparatus with under changeable standard glass joints are used for vaccume distillation. The claisen flask is connected to a receiver through condenser vaccume pump is attached to the receiver to attain the desired degree of vaccume. Heating of claisen flask is not started until the desired vaccume has been obtained.

Application:

1. It is used for thermo liable substance.
2. It is used for evaporation of the menstrum in the preparation of extracts.
3. To separate volatile constituents from the vegetable drugs.

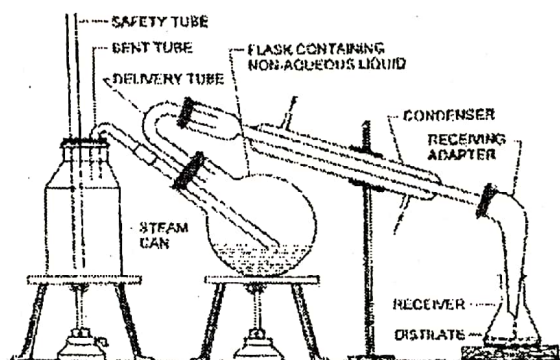
3. Steam Distillation:

Q. Draw a diagram for steam distillation and explain the principle underlying steam distillation.

Ans: When two immiscible liquids are heated together, then the mixture boils when the sum of the vapour pressure equals to the atmospheric pressure. The temperature at which mixture boils is lower than that of either of the liquids.

i.e., the boiling point of the mixture is lower than that of the liquid with the lower boiling point. The temperature at which the mixture boils remains stationary until one of the liquids has been completely removed from the still.

It consists of a 'steam can' fitted with a cork having two holes. Through one of the holes passes a bent tube leading the steam to the flask containing the non aqueous liquid. This tube should reach almost to the bottom of the flask. Another long tube which passes through the other hole reaches almost to the bottom of the steam can. This tube acts as a safety tube, so that in case the pressure inside the steam can becomes too much, it is relieved by forcing water out of it.



When steam starts coming out from the safety tube, it indicates that the steam can is almost empty. The delivery tube carrying vapours from the flask is connected to the condenser to convert it into liquid which gets collected in the receiver.

The non aqueous liquid is placed in the flask. A small quantity of water is added to it. The steam can and the flask are heated simultaneously, so that a uniform flow of steam passes through the boiling mixture.

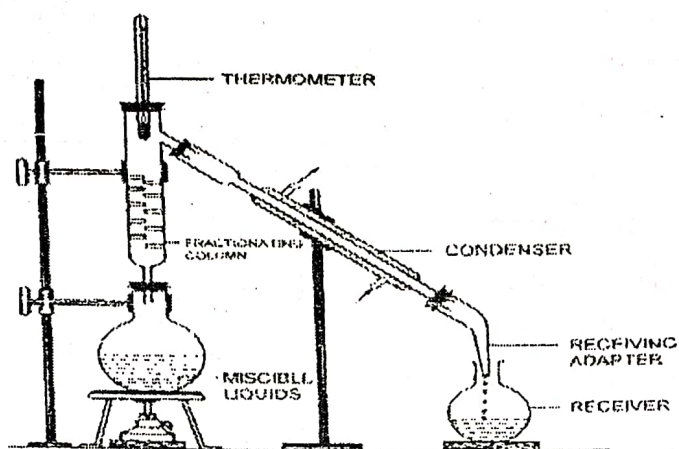
Distillation is continued until all the non aqueous liquid has distilled over. The distillate is then collected in Florentine receiver where oil is completely separated from water.

Application:

1. It is used for the preparation and extraction of volatile oil such as rose, clove, eucalyptus etc. from the crude drugs.
2. This process is used to prepare aromatic waters.
3. It is used for the distillation of liquids which are immiscible with water.

4. Fractional Distillation:

Fractional distillation is the process employed to separate two miscible liquids having different boiling points. When two miscible liquids are heated together. The mixture boils when the sum of their partial pressure is equal to the atmospheric pressure. When two liquids are heated, lower boiling point liquid is distilled rapidly than the higher boiling point liquid.



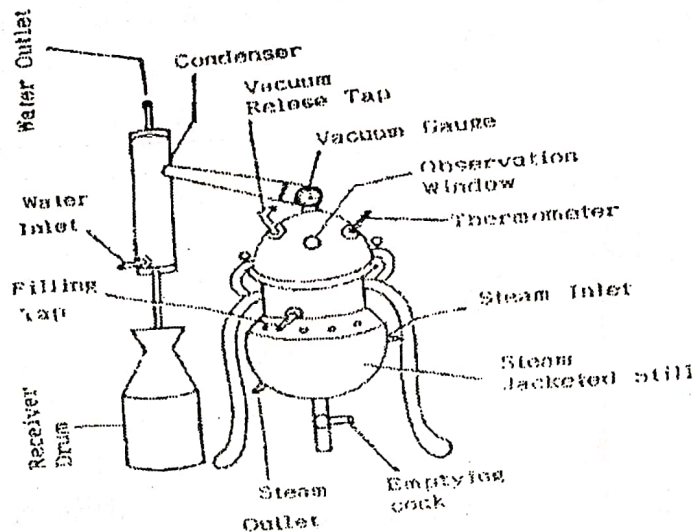
Method: The mixture of miscible liquids is taken in a distillation flask. The flask is fitted with a fractionating column. The flask is heated and the distillation process is carried out. The vapours are allowed to pass through a fractionating column where less volatile part gets condensed in the fractionating column and re enters into the distillation flask. The more volatile part of vapours go to condenser and gets condensed. The condensed liquid i.e, distillate is collected in a receiver. The distillate contains higher percentage of more volatile liquid and lower percentage of less volatile liquid.

Application:

1. It is used for the separation of miscible liquids such as alcohol and water, acetone and water, chloroform and benzene.
2. This process is used in the manufacture of ethyl alcohol.

VACCUME STILL

It consists of a steam jacketed copper still. The liquid to be distilled is the steam jacketed still through the filling tap. Steam is passed through the inlet and the liquid to be distilled gets heated and the liquid is evaporated. The observation window is used to observe the progress of the distillation.



The vapour passes through the condenser and the distillate is collected in the receiver drum. During the distillation process vacuum is applied by means of vacuum pump.

Advantage: Heat sensitive medicaments can be separated from the liquid mixture.

Application:

1. This method is used for separating substances which undergoes decomposition when boiled under normal atmospheric pressure.
2. It is used for concentrating and drying of the extracts, when low temperature is necessary to prevent the decomposition of active constituents.

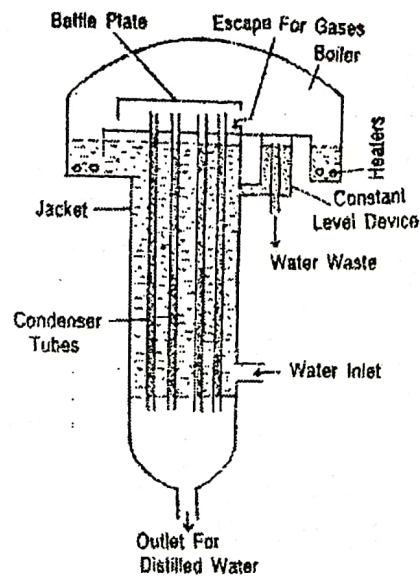
PREPARATION OF PURIFIED WATER I.P

Ordinary drinking water contains traces of salts such as calcium, magnesium etc and some gaseous impurities. Hence purification of water is necessary to remove all these impurities.

Method of preparation:

Purified water is prepared by distillation method. Purified water prepared by distillation method is also called distilled water. Purified water or distilled water is prepared by stokes still.

Construction and working:



It consists of a boiler. The condenser tubes are arranged inside the jacket. A constant level device is attached to the boiler to avoid excessive concentration of salts. A baffle plate is present over the condenser tubes. The baffle plate prevents entrainment of liquid droplets into the condenser tubes. The tap water is passed into the jacket through the inlet. The water reaches the boiler where it is heated by the heaters. The vapour arising from the boiling water enter into the condenser tubes. The vapour gets condensed and the distilled water is collected through the outlet. The dissolved gases in the water are escaped from the jacket.

PREPARATION OF WATER FOR INJECTION I.P:

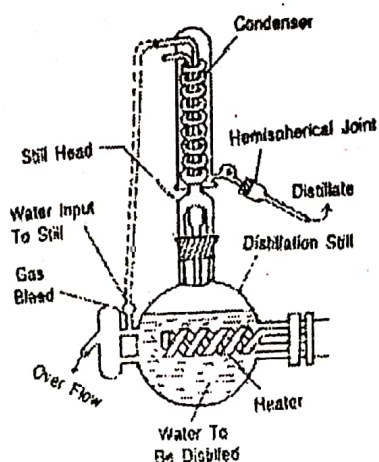
Sterilized distilled water free from pyrogen and other impurities is known as water for injection.

Method of preparation: Water for injection I.P is prepared by distillation method.

Construction and working:

The apparatus used for the preparation of water for injection consists of a stainless steel or glass still. The apparatus is first cleaned by rinsing with chromic acid to destroy any pyrogen attached to their surfaces and then washed with distilled water.

Water to be distilled is taken in the distillation still and closed with a condenser. The water is heated by chromium plated immersion heater. The vapour arising from the boiling water enter into the condenser. The vapour gets condensed and water for injection is collected through the outlet.



Water for injection is collected in a pyrogen free container. When the container is full, it is sealed at once and sterilized immediately. During the preparation of water for injection. The first part of the distillate and the last part of the distillate should be rejected. The first part of the distillate may contain dissolved air and the last portion of the distillate may contain volatile substances. So the first part and the last part of the distillate should not be collected, otherwise they will contaminate the distillate.

CHAPTER 12 DRYING PROCESS

Q.1 Define drying process and classify driers.

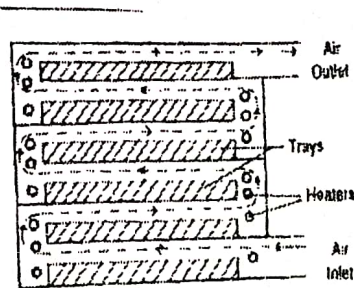
Ans: Drying is defined as the final removal of moisture from solids by thermal vaporization. It is generally used to prevent the product more soluble and to prevent deterioration of the product.

Classification of dryers: It may be classified into:-

- 1) Dryers used for drying solutions and suspensions ex: drum dryer, spray dryer.
- 2) Conduction dryer ex: tray dryer, fluidised bed dryer.
- 3) Convection dryer ex: vacuume dryer, freeze dryer.
- 4) Radiant heat dryer ex: U.V. lamp, I.R. lamp, electric rods, hot plates etc.

Q.2 Write the construction and working of tray dryer.

Ans: Tray dryer is also called as compartment dryer or shelf dryer. Tray dryer consists of a number of trays arranged alternatively on the shelves. The material to be dried is placed in the trays and the trays are kept in a cabinet or hot air oven. The cabinet is provided with heaters. Air is passed through the inlet. This air heated by means of heaters. The hot air flows in the direction as shown by the arrow mark.

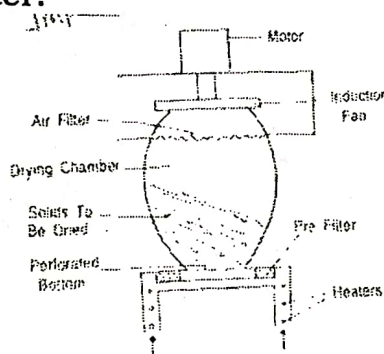


The hot air circulates around the cabinet. As the hot air passes over each tray. Certain amount of heat is given up to provide latent heat of evaporation which is essential for drying. As the result the material is dried and finally the dried material is removed.

Application: Tray dryer is used for drying crude drugs, chemicals, powders, tablet granules etc.

Q.3 Write the construction and working of Fluidised bed dryer.

Ans: It consists of a stainless steel. Conical shaped vessel containing drying chamber with a perforated bottom. The powder material to be dried is packed in the drying chamber. Air is passed through the inlet. This air is heated by means of heaters. The dust particles are removed from the hot air by means of pre-filter.



The motor is switched on and so the induction fan rotates. As the induction fan rotates, hot air is drawn into the drying chamber through perforations. As the hot air enters into the drying chamber, it carries the powder particles along with it and the particles are suspended in the hot air and thus the powder material is dried. Air filter prevents the escape of powder particles from the drying chamber. Finally the dried material is removed.

Advantage:

- i) Drying time is very shorter.
- ii) The individual powder particles are dried.
- iii) The temperature of the fluidized bed is uniform and can be controlled accurately.

iv) It produces free flowing powder. It helps in the process of tablet manufacture.

Disadvantage:

- i) The turbulent motion may cause damage to the individual particles.
- ii) The vigorous movement of particles in hot dry air may lead to the generation of electricity and therefore suitable precautions must be taken.

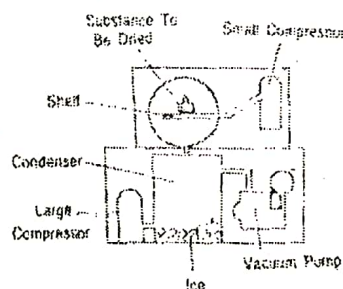
Applications:

- i) The fluidised bed dryer can be used for drying any powdered material.
- ii) A special application is the drying of tablet granules.

Q.4 Write the principle involved in freeze drying.

Principle: Freeze drying is also called as lyophilisation or elisiccation. Freeze dryer is one of the equipment used for drying liquids. Freeze drying is the process of drying in which water vapour is removed from a frozen solution by sublimation. Usually freeze drying is carried out at a temperature of -10°C to -40°C . The material to be dried is first frozen at a temperature below -40°C . The water vapour is removed from the drying chamber by means of condenser. Then the material is subjected to heat under high vacuum so that frozen liquid sublimates and leaving dry solid.

Working: The aqueous product to be dried is placed on the shelf in the drying chamber. The product is frozen at -40°C by circulating refrigerant from the small compressor through pipes within the shelf.



After freezing is complete, the chamber is evacuated by means of vacuum pump. Then water vapour is removed from the chamber by means of a condenser. Heat is then introduced from the shelf to the product by means of electric sources or by circulating hot water until the product is dried. During heating, Vacuum is applied. The container is then removed and sealed under aseptic conditions.

Advantages:

- i) Biological and pharmaceuticals which are unstable when dried by some other methods can be processed.
- ii) The samples can be dried without elevated temperature.
- ii) Freeze drying products are more soluble and more stable.

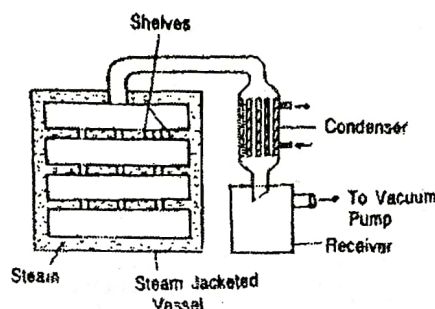
Disadvantages:

- i) Cost of the preparation is high.
- ii) It requires more time for processing.

Applications:

- i) Freeze drying is used for preserving human tissues.
- ii) It is used for drying blood serum, plasma, antibiotics, hormones etc.
- iii) In food industry, freeze drying is used for preservation.

VACUUM DRYER OR VACUUM OVEN



It consists of a steam jacketed vessel which is provided with a number of shelves. The oven is connected to a vacuum pump through a condenser and receiver. The materials to be dried are spread into the trays and the trays are kept on the shelves. The oven is then closed by a door. The trays are heated by passing steam into the steam jacketed vessel. As the result, the materials are dried. During operation, vacuum is applied. The remaining steam condenses in the condenser and the condensate is collected in the receiver.

Advantages:

- i) Vacuum dryer is useful for drying thermo labile materials such as penicillin, vitamin etc.
- ii) It is also useful for drying dry extracts.

**CHAPTER. 13
STERILIZATION**

Q.1 Define and classify sterilization process.

Definition: It is the process of removing or killing all the micro-organisms and their spores. A product is said to be sterile when it is free from living micro-organisms. *or their spores.*

Methods of Sterilization processes:

1) Physical method:

- i) Dry heat Sterilization Ex: Hot air oven
- ii) Moist heat Sterilization Ex: autoclave
- iii) Radiation Sterilization Ex: Ultra violet rays

Ionizing radiation

2) Chemical method:

i) Sterilization by heating with bactericide Ex: Benzyl chromium chloride
Phenyl mercuric nitrate. etc.

ii) Gaseous Sterilization Ex: Ethylene oxide
Formaldehyde

3) Mechanical method Ex: Ceramic filter
Sintered glass filter
Membrane filters .etc.

Sterilization by physical method:

i) Dry heat Sterilization: In this method the micro-organisms and their spores are killed by oxidation of essential cell constituents. In this process sterilization is affected by heating at a temperature of 160°C for 2 hrs.

Q. Write a note on Hot air oven.

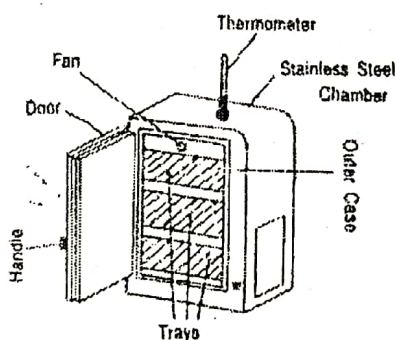
Ans; Principle and method:

1) In this process the micro-organisms are killed by the oxidation of the bacterial cell.

2) In which heat is transmitted from its source to the materials to be sterilised by radiation and conduction.

3) The materials are exposed to 100°C for 1hr to destroy all bacteria and to 140°C for 3 hrs.

Construction and working:



- 1) It consists of an aluminium or stainless steel chamber and a hollow door.
- 2) The door is filled with insulation and carries an asbestos gasket that provides a tight seal. It also provide with an handle
- 3) The outer case of the stainless steel chamber contains glass fibres insulation and heaters.

4) The materials to be sterilized are placed in trays and the switch is on. The temperature is maintained for sufficient time to ensure complete sterilization.

5) The materials to be sterilised are exposed to 100°C for 1hr to destroy all bacteria and to 140°C for 3 hrs to destroy all the bacterial spores.

Advantages:

- 1) It is suitable for substances which are destroyed by moisture Eg. Dry powder, oily substances.
- 2) It is suitable for sterilization of glass wares like flask, test tubes, pipettes, syringes.
- 3) It is not so damaging to glass and metal equipments as moist heat.

Disadvantage:

- 1) This method is not suitable for surgical dressings.
- 2) This method is also not suitable for plastic materials.

Application: This method is used for the sterilization of glass wares, stainless steel

ii) Moist heat Sterilization:

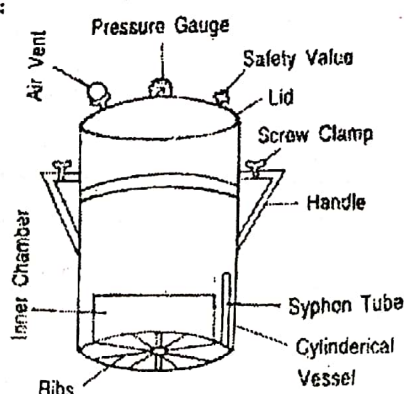
It is more effective than dry heat sterilization because the steam is having more penetration power than dry heat and even the thermal capacity of steam is also more. This method is useful even to destroy microbial spores by coagulation of cellular proteins.

Q.4 Explain the construction and working of an Autoclave.

Ans: Principle and method:

1. In this process, the micro organisms are killed by the coagulation of cellular proteins.
2. Sterilization of moist heat is carried out by means of an autoclave or steam sterilizers.
3. In this method, the materials to be sterilised are exposed to 115°C for 30min or 121°C for 15min at 15-17 pound pressure.

Construction and Working:



1. It consists of an aluminium or stainless steel vessel fitted with a lid. The lid is held in position by means of screw clamps.
2. The inner chamber is partially filled with water. The materials to be sterilized are wrapped in paper kept in a wire basket which is then placed in the inner chamber. The switch is on and water in the inner chamber is started heating.
3. Steam is allowed to escape from the air vent for 5 min in order to expel air from the chamber and then air vent is closed. When the required pressure is attained, the safety valve is closed. The syphon tube should be closed otherwise water will come out when the pressure develops inside the chamber.
4. The temperature and pressure are maintained for sufficient time to ensure complete sterilization.
5. The air vent and safety valves are opened that the temperature and pressure falls to atmospheric temperature and pressure. Then the lid is opened and the sterilised articles are taken out.

Advantages:

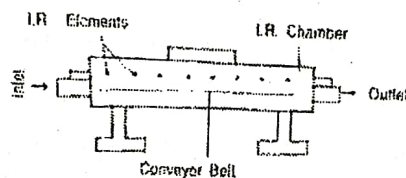
1. The steam is having high penetration power than dry heat and the micro-organisms and their spores get destroyed more effectively in lesser time and even low temperature compared to dry heat sterilization.
2. Large sizes of autoclave are having more space for the materials to be sterilized.
3. Solutions packed in sealed containers, such as ampoules can be effectively sterilized by this method.
4. Bulk parenterals solutions, glass wares, surgical instruments, eye drops can be sterilized by this method.

Disadvantages:

1. This method is not suitable for thermo sensitive material and dosage form which cannot withstand heating temperature of more than 115°C.
2. This method is not suitable for formulation containing oils and fats, ointments, creams, powders.

3. Containers should properly sealed before sterilization.
4. Water should be maintained at required level to provide effective production of steam.

iii) Radiation Sterilization: It is also a physical method of sterilization which is also called as sterilization by radiations. Here high speed electrons from a accelerator or gamma rays from a radio isotope can be used for sterilization. When UV-radiation or gamma radiations are passed over the material to be sterilized brings about ionisation within the bacterial cells thus destroyed them effectively.



Radiations chambers are used where the radiations are emitted from their source and come in contact with any object to get sterilization.

Advantages:

1. Vaccines and some other thermo labile medicaments can be sterilised Ex. Gamma radiations and U.V radiations.
2. No aseptic handling is required Ex. Gamma radiations.
3. Rise in temperature is very fast and sterilisation time is short Ex. I.R radiations.

Disadvantages:

1. Cost of the instrument is high Ex. Gamma radiations.
2. Eye and skin are affected by exposing the radiations.
3. The radiations produce undesirable changes in many medicaments.

Application:

1. I.R radiations are used for sterilization of glass containers, bottles, glass syringes, aluminium caps etc.
2. U.V radiations are used for sterilization of air in an aseptic room. It is used for sterilization of surfaces or table tops etc.
3. Gamma radiations are used for sterilization of plastic syringes, rubber catheters, scalpel, needles, adhesive dressings, surgical catgut etc.

2) Chemical method:

i) Sterilization by heating with a bactericide:

Here liquid dosage form such as injections can be sterilised by heating with certain bactericidal chemical agent to destroy the micro-organisms.

Ex: Benzyl benzoate, thiomersal, phenyl mercuric nitrate, phenol, Benzalkonium chloride.

Bactericide should possess the following properties:

1. It should be non toxic.
2. Compatible with medicaments.
3. Stable and active at various PH.
4. Stable during heating and storage.

Application: It is used for the sterilisation of injections. Eye drops can be sterilised by this method.

Q. Give an account of Gaseous Sterilization.

Ans: Gaseous Sterilization:

The articles which are thermo labile an surgical instruments, laboratories, operation theatre, rooms, wards can be successfully sterilised by using certain gases. This method is also called as fumigation. Here the objects to be sterilised or exposed to gases to destroy the micro-organisms. Ex: Sulphur dioxide, Ethylene oxide, Formaldehyde.

Advantages:

1. This method is suitable for thermo labile substances.
2. The penetrating power is more.

Disadvantages:

1. It is a slow process. It requires long exposing time, So that this method cannot be used in emergency.
2. Some gases are irritating to the respiratory tract Ex: Formaldehyde.

Applications:

1. Thermo labile powders such as penicillin, tetracycline, erythromycin can be sterilised by this method.
2. Thermo labile articles like plastic materials, rubber items, blankets etc. can be sterilised by this method.

Q. Write in brief on filters used for sterilization.

Ans: Mechanical method:

Principle: In this method, thermo labile solutions such as injections, ophthalmic solutions etc. can be sterilised by passing the solution through bacteria proof filters. The micro-organisms are entrapped into the pores and are removed from the solutions.

Procedures: Bacterial filtration method is only suitable for medicaments which are in solution form. The solution to be sterilised is filtered through a bacteria proof filter medium. Then the filtered solution is filled into the final containers and the containers are sealed. All these procedures should be done under aseptic conditions. Even though these procedures are done

under aseptic conditions, there are much chances of contamination. There sterility test must be performed after bactericidal filtration

Ex: Filter candles, membrane filters, sintered glass filters, Meta filters, Seitz filters, asbestos pads.

Advantages:

1. The operation is very simple.
2. Thermo labile liquids such as injections, ophthalmic solutions are sterilized.
3. It is very economical.

Disadvantages:

1. Sometimes fragment of fibres may be found in the filtrate.
2. Sometimes the drug may be absorbed by the filters.
3. Suspensions, oily preparations and solid medicaments cannot be sterilised.

Application: Bacterial filtration is useful for the sterilization of thermo labile injections such as vitamins, hormonal preparations and ophthalmic solutions.

CHAPTER. 14

TABLETS

Q.1 Define tablets and write advantages and disadvantages of tablet.

Definition: Tablet may be defined as a solid unit dosage form, containing one or two drug with or without non-drug component called excipients or additives. Tablets are prepared either by compression or moulding method. They may be either circular, flat or biconvex in shape.

Advantages:

1. The tablets are easy to be administered.
2. They are easy to be dispensed.
3. These are more stable dosage forms.
4. They maintain the accuracy of dosage.
5. Bitter and nauseous substances can be given easily in tablet form after giving easily in tablet form after giving a suitable coating to the tablets.
6. They are the lightest and the most compact of all dosage forms.
7. Tablets are easiest and the cheapest as regard packing and transport.
8. These are an economical dosage form.

Disadvantage:

1. Manufacturing of tablets needs labours and machines.
2. The onset of action is slow compare to liquid dosage form.
3. Potent drugs are difficult to convert into tablets.

4. The bioavailability is less compare to liquids and parenterals.
5. The drugs which get decomposed by gastric juices and enzymes cannot be formulated as tablets.
6. The drugs which are sensitive to light and moisture requires coating.

Q. 2 Classify tablets according to their route of administration.

Ans: Types of tablets:

Tablets are classified according to their route of administration or function. The following are the four main classification groups:

I) Tablets ingested orally:

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

II) Tablets used in the oral cavity:

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

III) Tablets administered by other routes:

1. Implantation tablets
2. Vaginal tablets

IV) Tablets used to prepare solution:

1. Effervescent tablets
2. ~~Dispensing~~ tablets *Dispersing*
3. Hypodermic tablets
4. Tablet triturates

Q.3 Explain the various tablet adjuvants with suitable example.

Ans: In addition to the active medicament, each tablet contains some additives or excipients.

1) Diluents: If the medicaments is in small quantity, so an inert substances is added to increase the bulk in order to make the tablet a suitable size for compression.

Ex: Lactose, Dicalcium phosphate, calcium sulphate.

2) Binders or Granulators: It gives the cohesiveness to the powdered materials so that the powder can be converted into granules. Binders are used in 10% concentration.

Ex: Acacia, starch, starch mucilage.

3) Lubricants: Lubricants are substances which improve the rate of flow of granules, prevent adhesion of granules to the surface of the dies and punches and facilitates the ejection of tablets from the die cavity used in 1% concentration.

Ex: Talc, magnesium stearate, calcium stearate.

4) Glidant: It improves the flow properties granules from the hopper. It is used in 1% concentration.

Ex: magnesium stearate, calcium stearate.

5) Disintegrators: A disintegrator is a substance or a mixture of substances included in tablet formulation to facilitate the disintegration of the tablet after administration. It is used in 5-15% concentration. **Ex:** Starch, cellulose, gums.

6) Colouring agents: It gives elegant appearance to the tablet. **Ex:** Amaranth, tartrazine, sunset yellow.

7) Flavouring agents: It gives good flavor to the tablet. They are mixed with dry granules by spraying the flavours on the granules before compression. 0.5% volatile oils are used.

8) Sweetening agent: It masks the bitter taste of the medicaments.

Ex: Dextrose, lactose, mannitol, saccharin.

Method of preparation of Tablet/Processing of Tablet:

Tablets are prepared by three methods:

- 1) Wet granulation method.
- 2) Dry granulation method.
- 3) Direct compression method.

Q. Explain the wet granulation technique for the manufacture of tablet:

Ans: 1) Wet granulation method:

1. Weighing and mixing: The required quantities of the ingredients are weighed. The active medicament, diluents, colouring agent and disintegrating agent are mixed well and passed through a sieve to remove lumps.

2. Granulation: The powder mixture is wetted with liquid binding agent and mixed well until a coherent mass is formed.

3. Screening the damp mass: The wet mass is passed through a sieve by hand.

4. Drying: The moist granules are placed on large sheets of paper on wire trays. The trays are placed in hot air oven and the granules are dried at 60°C.

5. Dry screening: After drying, the dried granules are once again passed through a smaller mesh screen (16 or 20 mesh). During this screening the granules size will be more uniform.

6. Lubrication and compression: After dry screening the granules are mixed with lubricating agent. If necessary flavouring agent and sweetening agent can also be mixed with dry granules before compression finally the granules are compressed.

2) Dry granulation method: This method is also known as slugging method or double compression method or pre compression method. This method is suitable, when the ingredients are sensitive to moisture and heat and also when the ingredients have cohesive or binding properties.

1. Weighing and mixing: The active medicament, diluents, disintegrating agent and part of the lubricating agent are weighed, mixed and passed through a sieve to remove lumps, binding agent is not necessary.

2. Slugging: The powder mixture is then compressed into large tablets. These large tablets are known as slugs.

3. Dry screening: The compressed slugs are then broken into suitable sized granules in an oscillating granulator machine and then passed through the sieve to obtain uniform sized granules. Drying by heat is not necessary.

4. Lubrication and compression: After dry screening, the granules are mixed with the remaining lubricating agent and compressed into tablets.

Ex: Acetyl salicylic acid, thiamine hydrochloride, ascorbic acid, magnesium hydroxide etc.

3) Direct compression method: There are certain medicaments which are available in crystalline form or in the form of granules having its own binding property. Such medicaments are passed through sieve no. 20 or any other specified sieve and then mixed with any additional excipients.

Ex: Aspirin, sodium bromide, potassium chlorate and dried yeast etc.

Q. Write in brief about manufacturing defects of tablets.

Ans: Defects in Tablets or Processing problems:

1. Capping, Lamination and Chipping: Capping is the partial or complete separation of the top or bottom of the tablet. Lamination means the tablet breaks into two or more layers.

Chipping occurs due to breaking the edge of the tablet.

These defects may be due to:

a. Imperfect punches and dies.

b. By applying too much pressure.

2. Picking and Sticking: Picking is the adherence of the granules to the punches and sticking is the adherence of the granules to the die wall.

These defects may be due to:

- a. Excessive moisture present in the granules.
- b. Insufficient quantity of lubricants mixed with the granules.

3. Mottling: It is an unequal distribution of colouring agent on the surface of the tablet. It may be due to the migration of colouring agent in the granules during drying.

4. Double Impression: The punch moves some distance freely before the tablets are ejected. During its free movement, the punch mark impression on the tablet. So that double impression is formed on the tablet.

Q. Describe the quality control tests for tablets.

or

Write evaluation tests for tablets.

Ans: Quality control tests for Tablets are as follows:

1. Shape and appearance of tablet: The shape and appearance of tablet always depends on dies and punches during compression any default in the thickness, shape and diameter should be controlled. Thickness and diameter was determined by using slide caliber.

2. Weight variation: 20 tablets are weighed individually and the average weight is calculated. The weight of 2 tablet is not more than and also not deviate from the average weight percentage given in the standard table.

Standard weight variation table:

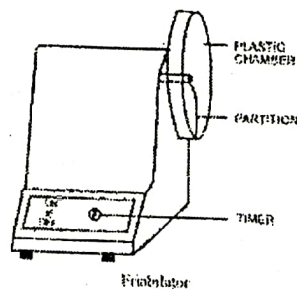
Average weight of tablets	Percentage deviation
120mg or less	± 10
More than 120mg and up to 300mg	± 7.5
More than 300mg	± 5

3. Tablet thickness: If the tablets are thicker than the specified size, they cause problems during packing, therefore thickness or diameter of the tablets is determined with a screw gauge. 5% deviation may be allowed depending on the size of the tablet.

4. Content uniformity test: This test is performed to ensure that every tablet must contain the stated amount of medicaments within the prescribed limits given in the pharmacopoeia.

30 tablets are selected. 10 tablets are assayed individually. At least 9 tablets must be within $\pm 15\%$ of the prescribed limits and none may exceed $\pm 25\%$. If more than 2 tablets exceed $\pm 15\%$ of the prescribed limits, another 10 tablets are taken and assayed.

5. Friability test: Friability test is carried out to assess the ability of the tablet to withstand abrasion in packaging, handling and transportation.



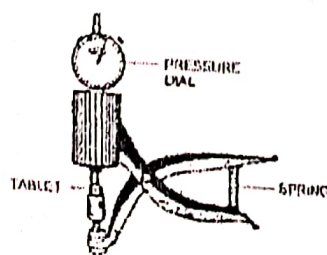
Roche friabilator is used to measure the friability of the tablet. 20 tablets are weighed and placed in this apparatus. It is allowed to revolve for 4min at 25rpm. When the apparatus revolves, the tablets fall from top to bottom of the apparatus. After 4min the tablets are weighed. The tablets pass the test if the loss is less than 0.5-1% of their original weight.

6. Hardness test: Tablets require certain amount of strength or hardness to withstand mechanical shocks of handling in manufacture, packaging and transportation. If the tablets are too hard, they may not disintegrate within the prescribed time. If it is too soft, they will not withstand mechanical shocks of handling in manufacture, packaging and transportation.

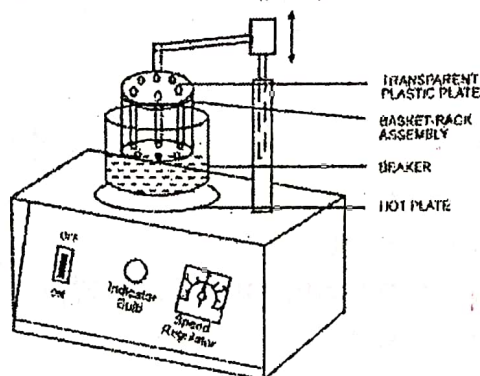
Hardness of the tablet can be determined by using 2 testers.

1. Monsanto hardness tester.
2. Pfizer tablet hardness tester.

Pfizer tablet hardness tester: Tablet is placed in between jaws of the instrument and it is pressed with the help of handle until the tablet breaks. The force required to break the tablet is recorded on a dial. The force is expressed in kilograms or pounds. If the tablet withstands a force of about 4kg, it is considered as a good tablet.

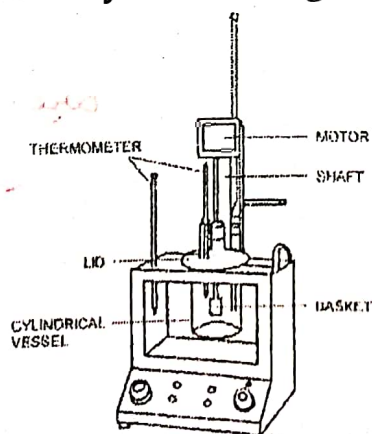


7. Disintegration test: Disintegrator of a tablet means to break the tablet into smaller particles after swallowing. The time required to disintegrate the tablet is called 'Disintegration Time'.



The test is carried out using disintegration tester. A basket supporting with 6 cylindrical glass tubes with 6 holes having the diameter as the tubes. The Tubes are fitted with a motor in such a way that they move up and down motion. The bottoms of the tubes are covered with 10 mesh screen. Six tablets are placed in the tubes. The motor is switched on. The tubes are moved up and down motion into the distilled water. The temperature of the distilled water is maintained at 37°C . If all the particles from the tablets pass through the wire mesh within 30 min, it indicates that the tablet passes the test. For coated tablet is 1hr.

8. Dissolution test: This test is done for measuring the amount of time required for a given percentage of the drug substances in a tablet to go into solution under specified condition in vitro. It consists of a stainless steel basket. The bottom of the basket is covered with 40 mesh screen. 1 tablet is taken in the basket and it is immersed in the dissolution fluid which is maintained at the temperature of 37°C . The basket is allowed to rotate at specified speed. The samples of the dissolution fluid are removed at specified intervals of time and analysed the drug content.



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The volume of dissolution fluid is maintained constant by adding a volume equal to that removed for analysis. The test is repeated with another five tablets. If 1 or 2 tablets fail to meet the requirements, the test is repeated on 6 additional tablets, not less than 10 out of 12 tablets must meet the requirements.

Tablet Coating: Coating of the tablet was done for the following ^{reasons} ~~reactions~~

1. To mask the unpleasant taste and odour.
2. To improve the appearance of the tablets
3. To prevent the medicaments from atmospheric effects.
4. To control the site of action of drugs.
5. To produce the sustained released product.

Types of tablet coating:

- 1) Sugar coating
- 2) Enteric coating
- 3) Film coating

Imp - Q. Write a note on sugar coating of tablet.

Ans: It was done to cover the entire surfaces of the tablet using a thick sugar solution. This can mask the bitter taste of medicaments.

Various stages of sugar coating:

1. **Sieving:** The tablets were shaken in a sieve to remove fine powder or broken pieces of tablets.
2. **Sealing:** Here water insoluble substances such as shellac or cellulose, ^{are} ~~was~~ dissolved in alcohol and coated several time using pan. This gives water proof surface to the tablet.
3. **Sub-Coating:** The sub-coating solution is applied on the tablets and the tablets are allowed to roll. When the tablets are uniformly wet, the sub-coating powder is dusted uniformly on the tablets until the tablets roll freely. 3-4 sub-coatings are usually given. The tablets are dried between each coat. After sub-coating, the tablets are dried.
4. **Syrup coating:** A thick sugar syrup solution was coated to give opacity, white colour and sweet surfaces several coats of sugar ^{are} ~~was~~ applied.
5. **Finishing:** 3-4 coats are done with syrup in rapid session without using dusting powder and a cold air was circulated before each coat.
6. **Polishing:** Polishing was done to give glossy surface to the tablets. Here beeswax dissolved in organic solvents. The tablets were transferred to a polishing pan made up of canvas lined and rotated at high speed.

Q. Write a note on Enteric coating of tablet.

Ans: Enteric coating is a type of coating which does not permit the release of drug in acid medium of the stomach but it releases the drug in alkaline medium of the intestine.

Enteric coating was done by following reasons:

1. When the medicament decomposed in stomach by the acids Ex: Ranitidine.
2. When delayed action is need Ex: Enteric coated aspirin tablet
3. When medicament produces gastric irritation. Ex: Aspirin, Ibuprofen
4. When the action of the medicament is needed in the intestine. Ex: Anthelmintics and Amoebicides.
5. Require to get absorb from the intestine for maximum effect.

Q. Write a note on Film coating.

Ans: Film coating has got some advantages over sugar coated tablets. In film coating, the coating time is reduced; the cost of production is less, more resistance to chipping and cracking. The tablets are taken in a coating pan. Film coating solution is dissolved in volatile solvents such as chloroform or acetone. Then it is applied or sprayed on the tablets and the pan is allowed to rotate. If the tablets are to be coloured, the dyes are dissolved in the solvent and sprayed over the tumbling tablets.

Several coatings are applied and the tablets are dried between each coat. Finally the tablets are allowed to dry in warm air so as to form a permanent film over the tablets.

CHAPTER 15

CAPSULE

Q.1 Define capsule and classify it.

Ans: Capsules are a solid dosage form in which the drug substance is enclosed in a water soluble shell or an envelope. A capsule shell is made from gelatin.

Types of capsules:

1. Hard gelatin capsule.
2. Soft gelatin capsule.

Q. 2 Define and list out the advantages of capsule.

Ans: Hard gelatin capsules are solid dosage form in which medicaments are enclosed in either a hard or soft shell of a suitable form of gelatin. It consists of 2 parts. The lower part is known as body and the upper part is known as cap.

Advantages:

1. It protects the medicaments from environmental hazards.

- ✓ 2. Elegance in appearance.
- ✓ 3. Bitter and unpleasant taste of drugs can be administered in a tasteless form.
- ✓ Capsule number and its approximate capacity:

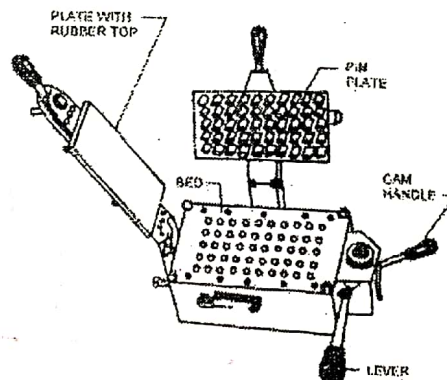
Capsule number	Approximate capacity in mg
000	950
00	650
0	450
1	300
2	250
3	200
4	150
5	100

↑ +300
200 +
+150
50
↓

✓ Q. Explain the filling of hard gelatin capsules.

Ans: Methods of filling the hard gelatin capsules: The capsules can be filled either by hand or Semi-automatic device or by an automatic filling machine.

Hand operated machine:



The empty capsules are filled in the loading tray and it is placed over the bed. The powder tray is placed in a proper position and filled with an accurate quantity of powder with scraper. The excess of powder is collected on the flat form of the powder tray. The pin plate is lowered and the filled powder is pressed by moving the pin downwards. After pressing, the pin plate is raised and the remaining powder is filled into the bodies of the capsule. The powdered tray is removed after its complete filling. The cap holding tray is again placed in position. The plate with the rubber top is lowered and the lever is operated to lock the caps and bodies. The loading

tray is then removed and the filled capsules are collected. With a 200 hole machine, about 5000 capsules can be filled in one hour, where as in a machine having 300 holes, about 7500 capsules can be filled in one hour.

Cleaning of capsules: All capsules, whether they have been filled by hand or machine, will require cleaning. Small quantities of capsules can be wiped individually with soft cloth. But in case of large quantities, capsules are rotated or shaken with crystalline sodium chloride. The capsules are then rolled on cloth covered surfaces.

Sealing of capsules: The capsules are then sealed, to ensure that the medicaments may not come out of the capsule due to rough handling. This can be done by banding them with molten gelatin, laid around the joint in a strip and dried. Capsules can be sealed by spot welding, by means of a heated metal pin, pressed against the cap and fusing it to the body.

2. Soft gelatin capsules: Soft gelatin capsules are solid dosage forms in which powder, paste or liquid medicaments are enclosed in a soft, globular gelatin shell. They may be round, oval or oblong in shape.

Advantages:

1. Ointments, pastes, creams and liquids can be formulated in soft gelatin capsules.
2. It protects the medicaments from environmental hazards.
3. Elegance in appearance.
4. Bitter and unpleasant taste of drugs can be administered in a tasteless form.

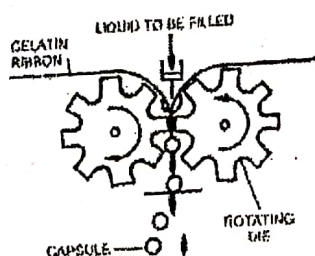
Q. Explain the filling of ^{Soft} ~~hard~~ gelatin capsules.

Ans: Methods of filling the soft gelatin capsules: Soft gelatin capsules are prepared by 2 methods namely: 1. Plate process

2. Rotary die process.

✓ **1. Plate process:** In this method, a set of plates (lower plate and upper plate) having number of depressions are used. A molten sheet of gelatin is laid over the lower plate. A measured quantity of liquid medicament is poured over it. Then another sheet of gelatin is poured on it, over this upper plate is placed. Then pressure is applied on both plates. As a result soft gelatin capsules are formed. Then the capsules are removed from the plates and cleared by washing with hexane and then dried.

✓ **2. Rotary die process:** Gelatin, glycerine, water, preservative and colourants are mixed and heated at 70°C for 2hrs. The gelatin mass is formed, air is removed from the gelatin mass. The gelatin mass is poured into air cooled rotating drum so that gelatin ribbons of controlled thickness are formed.



Two gelatin ribbons from opposite directions are fed between a pair of revolving dies and an injection wedge. The 2 dies are revolving in an opposite directions. The dies are maintained at controlled temperature. As the gelatin ribbons enter in between the dies, they cut out into two hollow forms of gelatin pieces.

The medicament to be encapsulated flows from the fill tank through the metering pump into the hollow forms of gelatin pieces. The metering pump forces a measured quantity of medicament into one half shell of the capsules and filled into it. On further movement of dies, the other half shell of the capsule is sealed and then the complete capsule comes out. The unwanted material adhering to the capsules are cut off by the knives. The capsules are then washed thoroughly in hexane and then dried. Depending upon the capacity of the machine and capsule size, about 20,000 to 30,000 capsules per hour can be manufactured.

Q. Differentiate between hard and soft gelatin capsules:

Ans:

Hard gelatin capsules	Soft gelatin capsules
The hard gelatin capsule shell consists of 2 parts 1) body 2) cap	The soft gelatin capsule shell becomes a single unit after sealing the two halves of the capsules.
They are cylindrical in shape.	They are available in round, oval and tube like shapes.
The contents of a hard gelatin capsule usually consist in the form of powder, beads and granules.	The contents of soft gelatin capsules usually consist of liquids or paste like consistency.
These are prepared from gelatin, titanium dioxide, colouring agent and plasticizer.	These are prepared from gelatin, plasticizer and preservative.
Capsules are sealed after they are filled to ensure that the medicaments may not come out of the capsule.	Filling and sealing of soft gelatin capsules are done in a combined operation on machine.

CHAPTER.16

IMMUNITY AND IMMUNOLOGICAL PRODUCTS

Q.1 Define and Classify Immunity.

Def: Immunity is defined as the power of resistance to diseases or infections. Immunological products are biological products mainly used for the prevention of diseases. And they are also used for the treatment of diseases and for diagnostic purpose.

Types/classification of Immunity:

1. Natural Immunity:

2. Acquired Immunity:

i) Active Immunity: a. Naturally acquired Immunity

b. Artificially stimulated Immunity

ii) Passive Immunity: a. Naturally acquired Immunity

b. Artificially stimulated Immunity

1. Natural Immunity: By nature our body possess some power of immunity, this is known as natural immunity.

1. Age: Majority of children in the age group between 2-5 years are susceptible to diphtheria disease, where as adults are immune to it.

2. Species: Men are susceptible to typhoid fever, where as mice are immune to it.

3. Individuals: Some persons are more resistance against cold and skin diseases than other.

2. Acquired Immunity: When natural immunity is not sufficient to protect against diseases, immunity can be induced by artificial methods, this is known as acquired Immunity. It is classified into two types : i) Active Immunity ii) Passive Immunity

i) Active Immunity: When natural immunity is not sufficient to protect against diseases, immunity can be induced by giving antigen containing preparations which are known as vaccines.

a. Naturally acquired Immunity: This immunity is produced after occurrence of certain infections. Ex: small pox, typhoid.

b. Artificially stimulated Immunity: This type of immunity develops by giving antigen containing preparation which stimulates the production of antibodies and as a result immunity develops.

Edward Jenner - Vaccine

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ii) Passive Immunity: When natural immunity is not sufficient to protect against diseases, immunity can be induced by giving antibody containing preparations. This is known as Passive Immunity.

a. Naturally acquired Immunity: For example children under 9 months are generally immune to certain infectious diseases such as diphtheria, measles. This type of immunity develops due to the presence of antibodies received from the mother. *(Transplacental)*

b. Artificially stimulated Immunity: This type of immunity develops by administering the preparations containing the ready-made antibodies, which are also known as antiserums. *or immunoglobins*

Q.2 Differentiate between active immunity and passive immunity:

Ans:

Active immunity	Passive immunity
Antigen containing preparations produce active immunity.	Antibody containing preparations produce passive immunity.
Immunity develops slowly and remains for a long time.	Immunity develops quickly and remains for a short period.
It is used for the long time prophylaxis.	It is used for both prophylaxis and curative.

e.g. Vaccination

e.g. Tetnus antibodies, Rabies antibodies (ATS), (ARS), Antisnake Venom Serum (AVS)

SMALLPOX VACCINE

Q. Describe the preparation of smallpox vaccine.

Definition: This preparation was formerly known as vaccine lymph or cowpox vaccine. It is a viral vaccine containing living organisms used for active immunisation.

Method of preparation: It is prepared by 2 methods they are:

1. From the Sheep or Calf
2. From the Eggs

1. From the Sheep or Calf:

i) Selection of animals: Healthy sheep or calves are selected and quarantined for 10-14 days and examined thoroughly for the absence of any infectious diseases. Only those proved to be healthy and free from diseases are selected.

- ii) **Inoculation:** The abdomen portion of the sheep or calf is selected for the preparation for smallpox vaccine. The abdomen portion is shaved, scrubbed, and disinfected. Then the shaved area is scarified with a scalpel. The area is then rubbed or inoculated with virus suspension.
- iii) **Incubation:** After inoculation the animals are taken to a special room and kept for 7-9 days. During this period the viral organisms grows and multiplies rapidly and pustules or vesicles form along the lines of scarification.
- iv) **Harvesting:** The animals are then killed and a post-mortem is done on the animal's carcase to confirm the absence of any infectious diseases. The abdomens are then washed with sterile water and the serous matter in the pustules is withdrawn by means of a special spoon known as Volkmann's spoon with aseptic precautions.
- v) **Purification:** The serous matter that withdrawn is purified by mixing with equal of glycerine. Then it is chilled and finally ground to form a homogenous mixture. This product is smallpox vaccine.

2. From the Eggs:

- i) Eggs are incubated for 12 days. On 13th day, the eggs are examined for its fertility. All the non fertile eggs and dead embryos are discarded.
- ii) The selected eggs are examined in front of the lamp and a triangle is marked on the egg shell at a place where chorioallantoic membrane is well developed. The triangle is then cut out and the triangular shell flap is gently lifted with sterile forceps so that the chorioallantoic membrane is exposed.
- iii) Then the chorioallantoic membrane is infected by rubbing a little of the virus suspension over the surface. The flap is then replaced to its original position and sealed with a little melted paraffin wax.
- iv) The inoculated eggs are incubated for 3 days. During this period the organisms are multiplied and a characteristic lesion is developed on the membrane.
- v) Using aseptic precautions the shell is removed, the membrane is separated and placed in a sterile mortar containing sterile saline. 50% glycerol is added to this and the material is ground to produce a homogenous suspension. The resulting product is smallpox vaccine.

B.C.G VACCINE

(Live attenuated)

Q. Explain the preparation of B.C.G Vaccine.

Ans: B.C.G Vaccine is a bacterial vaccine used for active immunity. It is a suspension of living cells of Mycobacterium tuberculosis. It is also known as Bacillus Calmette-Guerin Vaccine. The organisms have been attenuated by

cultivation on a suitable medium and repeated sub culturing over many years and thereby they lost their pathogenicity but retain their antigenicity.

Method of Preparation:

A suitable liquid medium is taken in a number of sterile containers. The organisms *M.tuberculosis* are grown on this medium for 14 days. The culture is transferred to sterile containers containing liquid medium and the organisms are allowed to grow for 1-2 months. Once again the culture is transferred to sterile containers containing liquid medium and the organisms are allowed to grow for several months. Thus the sub culturing process is repeated up to 1-2 yrs. By this repeated sub culture, the organism loses its pathogenicity but retains its antigenicity. The resulting product is centrifuged, washed and suspended in a sterile liquid that preserves the viability and antigenicity of the organisms. The resulting liquid vaccine is transferred to sterile glass containers and sealed. B.C.G vaccine is also available in powder form.

DIPHTHERIA ANTITOXIN

Q. Explain the preparation of Diphtheria Antitoxin.

Ans: Diphtheria antitoxin is an antibody containing preparation used for passive immunity.

Method of Preparation:

- i) **Selection of animals:** Horses are chosen for the preparation of diphtheria antitoxin because they are easy to handle and they are big in size, therefore considerable volume of blood can be taken and so the yield of the preparation is high.
- ii) **Preparation of animals for immunisation:** The healthy horses are selected and quarantined for 7 days. During this period they are examined for infectious diseases such as glanders. This infection is detected by injecting the reagent called mallein to the animals. If any animals suffering from glanders, mallein produces inflammation and oedema. Such animals are rejected and only healthy animals are selected.
- iii) **Immunisation of the horses:** 5 ml of diphtheria formal toxoid is injected initially into the neck muscles of the horse. Then the dose is gradually increased up to 600-1000ml for a period of 2-3 months. During this period, the concentration of antibody level in the blood is attained maximum.
- iv) **Bleeding of horse:** 8 litres of blood is withdrawn aseptically from the jugular vein of the horse. The blood is collected in bottles containing anticoagulant solution. The bleeding is repeated twice over the next 8 days. After that the horses are given rest for 10 days. Afterwards the animals are administered Alum precipitated toxoid to stimulate further antibody production. Again the bleedings are repeated 4-5 times.

v) Separation of serum: The blood thus collected is stored in refrigerator until the cells are settled. The supernatant fluid plasma is separated. Calcium chloride is added to the plasma to induce clotting. It is set aside for some time. The clear supernatant fluid serum is separated from the clot by filtration. The filtrate is crude antitoxic serum.

vi) Purification of serum: The filtrate serum contains high concentration of proteins which produces hypersensitive reactions when injected. So the serum should be purified.

It is purified by the following method:

The crude antitoxic serum is treated with ammonium sulphate. The gamma globulin is precipitated which is separated and discarded. Excess of ammonium sulphate is then added. The beta globulin together with antitoxin is precipitated. The precipitate is separated by filtration and collected in a cellulose bag. The cellulose bag is suspended in tanks containing water. The beta globulins and excess of ammonium sulphate passes out through the cellulose bag. The antitoxin remaining in the bag is made into solution with normal saline. 0.3% tricresol is added to this solution which is then filtered through a bacteria proof filter. The filtrate is diphtheria antitoxin. It is then packed in sterile containers.