Unit-IV Unit operation - Definition, objective applications, Principles, construction and working of —

Size Reduction

Hammer mill and ball Mill.

Size Separation

Classification of Powders according to I.P, Cyclone Separator, Sieves and standards of sieves

Mixing

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

Filtration

Theory of Filtration, membrane filter and sintered glass filter.

Drying

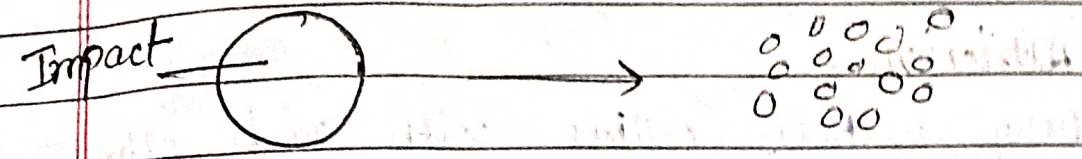
working of Fluidized bed dryer and Procedure of freeze drying.

Extraction

Definition, Classification, Method and applications.

Unit-IV Size reduction

it is the Process in which we convert a drug (bulk particles) into smaller particles through any shape.



Objectives or Importance —

→ For increase Surface area

→ To increase absorption

→ Less energy in mixing

→ Easy to absorption in our body

→ Easy in mixing.

Methods.

① Impact
② Attriction
③ Combined Impact and attriction
④ Cutting
⑤ Compression

1. Impact –
In this, drug molecules convert into small particles through any type impact.
Ex Hammer mill

2. Attriction –
Drug particles collide with each other and reduce there size from large molecules to small particle

Ex – Fluid energy mill

3. Combined Impact and Attriction –
In this method, Impact and attrictio both apply simutaneously.

Ex – Ball Mill

4. Cutting –
In this method, reduce large drug particles into small through cutting it is mostly used for soft and fibrous drugs.

Ex – Cuttermill

⑤ Compression –

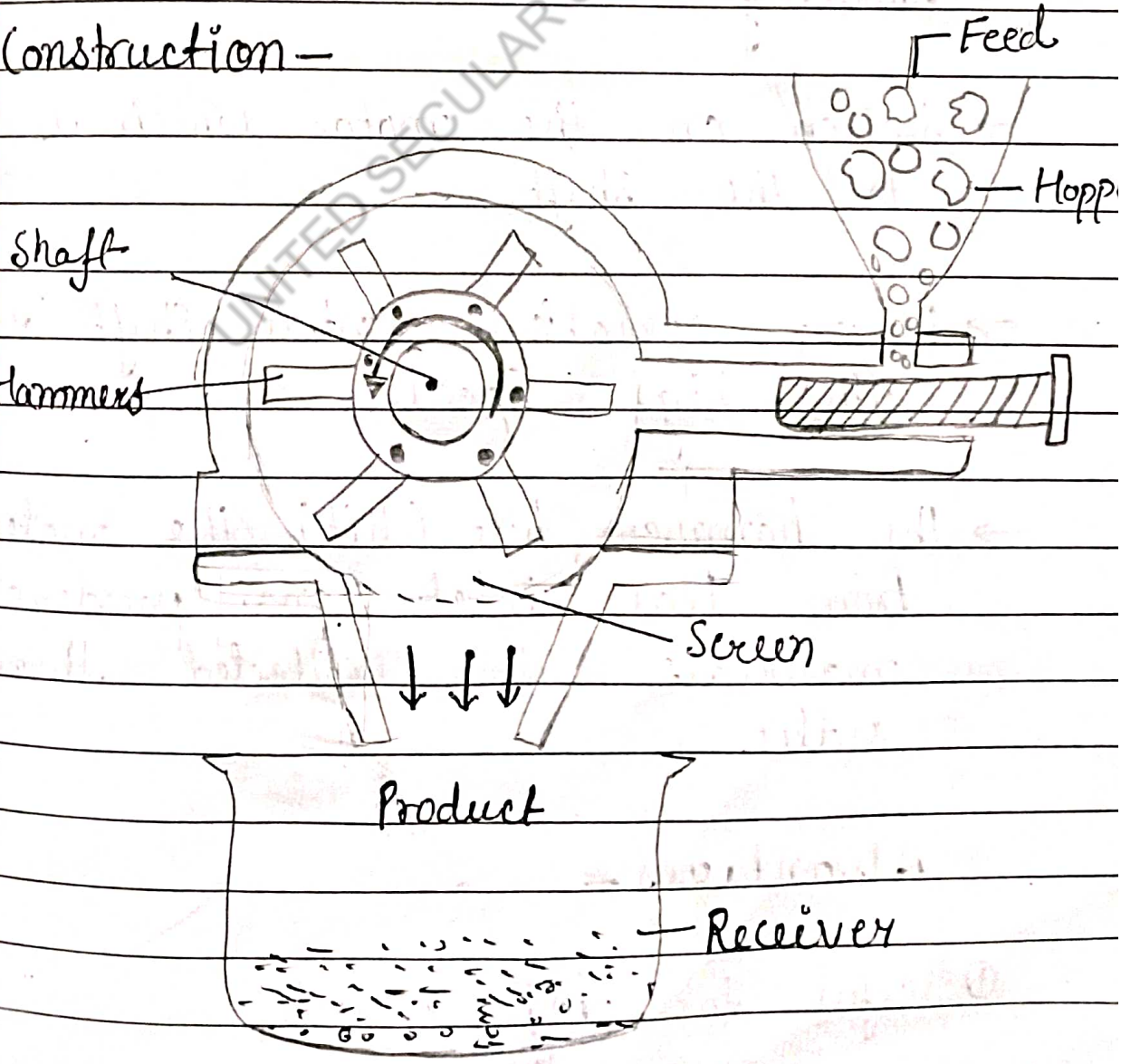
Drug particles reduce through compression or applying pressure on it.
- it is mostly used for hard nature drugs.

Ex- Roller mill.

* Hammer mill *

Principle –
it is based on the principle of Impact.

Construction –



→ it consist of strong metal enclosing central shaft to which hammer are fixed.

→ At the lower there is a screen through which powder passes.

→ There is a Feed inlet on the site of the mill.

→ There is a product outlet.

Working —

→ Switch on the motor which is connected to the shaft.

→ During operation, central shaft rotate with high speed.

→ The hammer bite (hit) the material from feed inlet and powdered materials is collected through outlet.

Advantages —

① Useful for big particles

2. Easy to fast in use.

3. Used to reduce in very small particles through screen.

4. it operate continously

5. its maintenance cost is less.

Disadvantages —

1. Sound produce (Noisy)

2. Very heat produce.

3. Screens may be clogged.

4. It can not be used for low melting sticky or plastic.

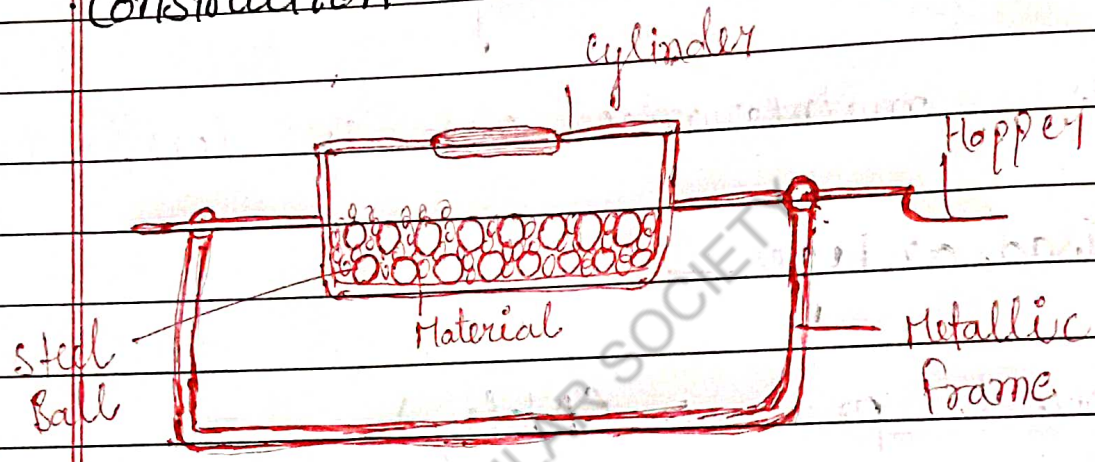
Application —

1. it is used to mill dry materials.

* Ball Mill *

Principle—
it is based on the principle of Impact and Attriction.

Construction—



Ball Mill

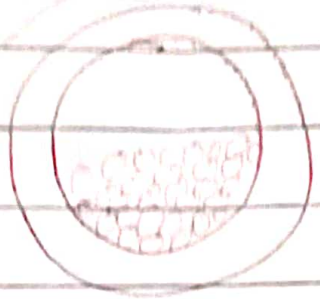
→ it consist of a hollow cylinder which is mounted on a metallic frame in such a way, that it can be rotated on its longitudinal axis.

→ The cylinder contains balls that occupy 30-50% of the mill.

→ The weight of the balls Kept constant

Working:

→ The drug to be ground is put into the cylinder of the mill and is rotated.

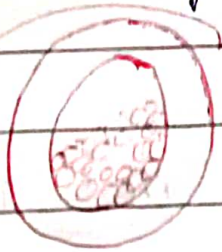


Low Speed

→ At low Speed, the mass of balls will slide or roll over each other and only a negligible amount of size reduction will occur.

High Speed

→ At a high Speed, the balls will be thrown out to the walls by centrifugal force and no grinding will occur.



Correct Speed

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

Size Separation

Size Separation is a process that involves the separation of particles of desired size from the mixture of various particles.

→ Size Separation is also known as sieving, Sifting, Screening.

→ Size reduction and size Separation should be combined to obtain powders of desired size.

Uses of Size Separation —

① To get uniform dosage form.

② To separate undesirable particles.

* In Indian pharmacopoeia, powders are classified as —

Coarse
Moderately coarse
Moderately fine
fine
very fine

The relevant grade of powder and sieve number shown in the table—

Grade of Powder	Sieve through which all particles must pass	Sieve through which not more than 40% of Particles pass
Coarse	10	44
Moderately Coarse	22	60
Moderately fine	44	85
Fine	85	Not Specified
Very fine	120	Not Specified

1. Coarse powder—
it is powder in which all the particles pass through a No. 10 Sieve and not more than 40% through a No. 44 Sieve, this is usually referred to as a 10/44 powder.

2. Moderately Coarse powder—
it is powder in which all the particles pass through a No. 22 sieve and not more than 40% through a No. 60 sieve, this is usually referred to as a 22/60 ~~Sieve~~ Powder.

3. Moderately fine powder –
it is powder in which all the particles pass through a No. 44 sieve and not more than 40% through a No. 85 sieve, this is usually referred to as a 44/85 powder.

4. Fine Powder –
it is powder in which all the particles pass through a No. 85 sieve.

5. Very fine powder –
it is powder in which all the particles pass through a No. 120 sieve

→ when a fineness of powder is describe by a number, all particle must pass through the specified sieve.

* Sieves *

- Sieves are used for size separation.
- Test sieves determine the efficiency of screening devices.
- Most of sieves used for pharmaceutical purpose are of wire mesh type.
- Each sieve is given a definite no. which denotes no. of the meshes present in a length of 2.54 cm or one inch.

Material of Construction —

→ Sieves are woven from wire of brass, bronze, stainless steel. Sieves should not be coated with any material.

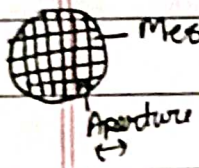
→ Generally iron wire is used to as screen material.

→ Brass, phosphor-bronze and stainless steel are the metal used due to their corrosion resistant, good strength and non-toxic contamination qualities.

→ Non-metals such as nylon & Terylene

are also suitable because they avoid risk of metallic contamination.

→ For special purpose punched plate screen are used.
These sieves are made by drilling holes of varying thickness in metal plates of varying thickness in metal plate.
The holes may be round, rectangular or Square.



Standards of sieve

- Holes in the screen is called Mesh
- Mesh number indicate numbers of holes included in a length of 1 inch.
- Aperture of screen is the clear space between wires of screen opening and it given in term of mm.
- Screen number denotes number of mesh in a linear length of 25.4 mm.
- Nominal aperture size indicates gap b/w two adjacent wires.
- Sieves may be designated by aperture size.

* The common standards used for sieves are —

1. Tyler standard sieve series
2. U.S standard sieve series
3. British Standard sieve series (B.S.S)
4. USASTM
5. German DIN (Deutsche Industrienormein)
6. French Standard sieve (ESS)
7. IP Standard sieve series
8. International Test sieve series (ISO)

1. Tyler Standard sieve Series — it is U.S standard sieve. They are available in mesh number 4-325.

2. U.S Standard sieve series —
it is used in U.S.A.

3. British standard sieve series (BSS) —
it is available in mesh no- 5-300.
it is extensively used in UK.

4. USASTM —
it is "American Society of Testing materials" standard sieve series. it is available in mesh no. 4-325.

5. German DIN (Deutsche Industrienormein) —

it is commonly used in Europe and Germany.

6. F.S.S – it is French standard sieve. it is available in mesh no. 17–32

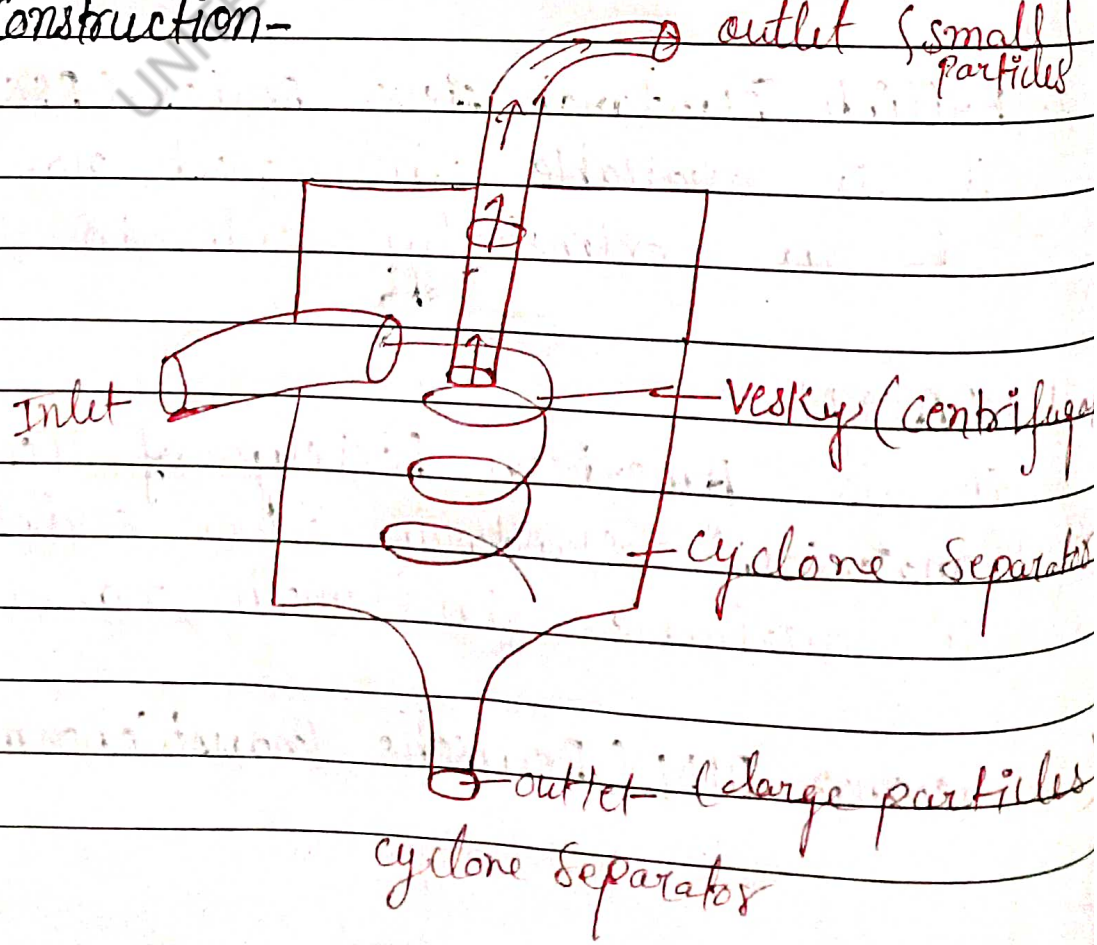
7. IP standard sieve series – it is commonly used in India.

8. International Test sieve series (ISO) – it is used ~~wold~~ world wide.

* Cyclone Separator *

Principle – it is based on the Principle of centrifugation.

Construction –



→ it consist or look like as container, in which, one inlet is present.

→ And two outlet is present in which small particles receive from upper outlet and large particles get from lower ~~outlet~~ outlet

Working –

Firstly, we enter particles (mixed) of different some with some air pressure.

Then, inside it, Air creat centrifugation force and due to this large particles fallen down and get from downside outlet.

Small particles or fine powder expell out from the fluid outlet with air we get.

* Mixing *

Mixing is the most widely used operation in which two or more than two substances are combined together.

The main objectives of mixing may be-

a) Simple physical mixing of materials to form a uniform mixture.

b) To get promote the chemical reaction to get uniform products.

Types of Mixtures-

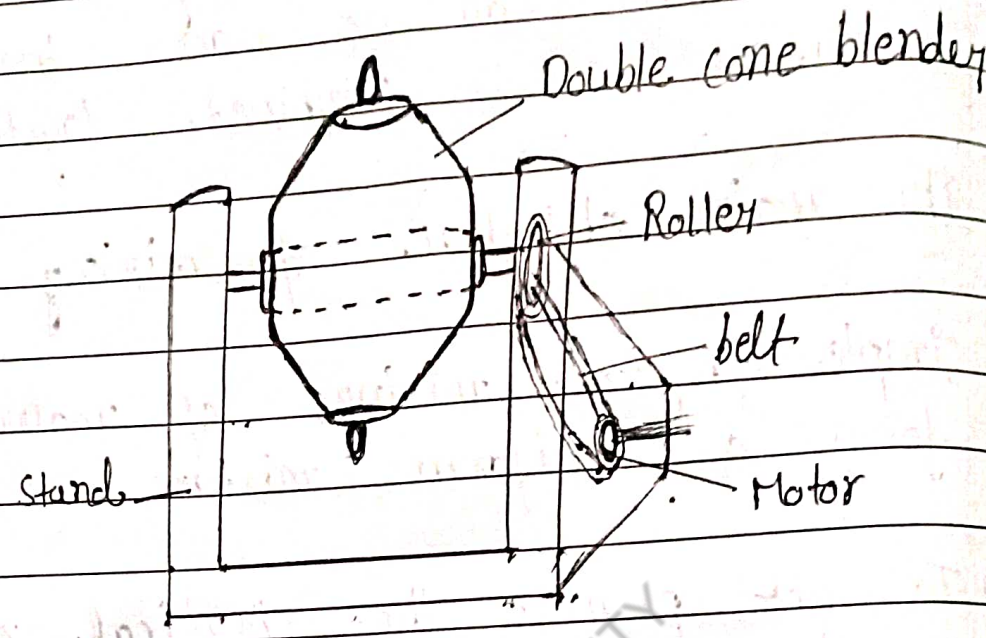
There are 3 types of mixtures

① Positive Mixture
② Negative Mixture
③ Neutral Mixture

1. Double cone blender / Double cone Mixer

Principle- The mixing of Powder in double cone blender is due to tumbling and shearing action with blade

Construction-



Double Cone blender

→ Double cone blender is made of Stainless Steel and is available in different capacity ranging from 5Kg to 200 Kg or even more.

→ The efficiency of the blender depends mainly on the speed of rotation.

→ The rate of rotation should be optimum which depends on the size and shape of Tumbler as well as nature of material to be mixed.

Working-

→ The material to be blended is loaded approximately 50–60% of the total capacity of the blender.

→ The common range is 30–100 r.p.m.

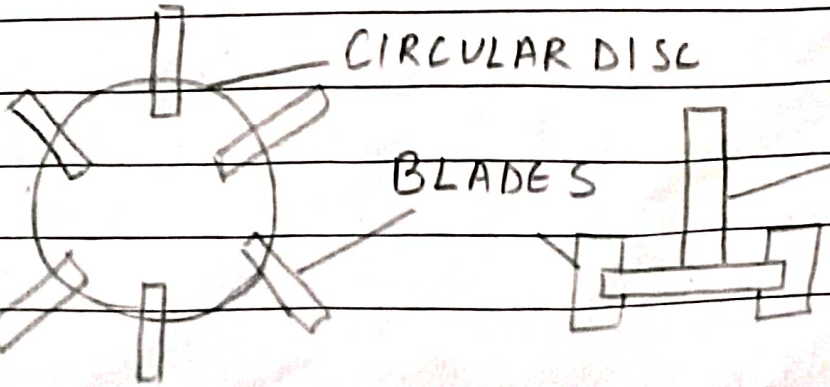
→ As the blender rotates the material undergo tumbling motion and mixes the material ~~that~~ thoroughly.

→ The double cone blender is an efficient design for mixing powders of different densities and is used mainly for small quantity of powders.

2. * Turbine Mixer *

Principle – it work on the principle of Shearing force.

Construction –

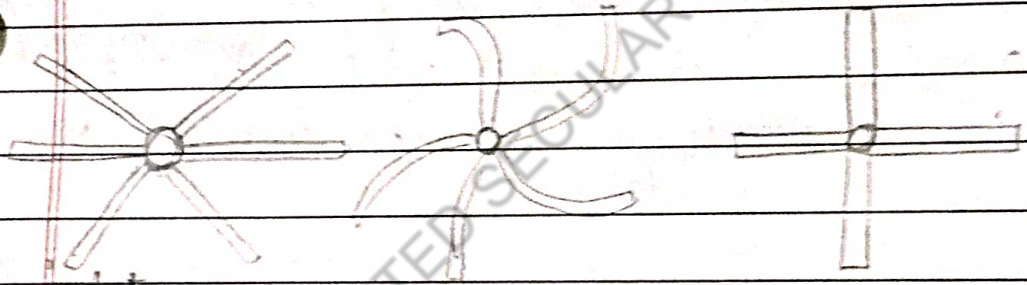


→ A Turbine consists of a circular disc to which a number of short blades are attached.

→ Diameter of turbine range from 30 to 50% of diameter of the vessel.

→ it rotates at a lower speed 50-200 Rpm.

→ The blades may be Straight, curved, pitched or vertical.



Straight Vertical Curved Pitched

Working —

→ The liquid to be mixed is placed into the vessel.

→ turbines are placed into the vessel and Shaft the rotation.

→ After certain period when liquid are mixed, removed from the vessel.

3. * Triple Roller Mill *

Principle- Shear force created by 3 horizontally positioned rolls rotating in opposite directions different speeds relative to each others.

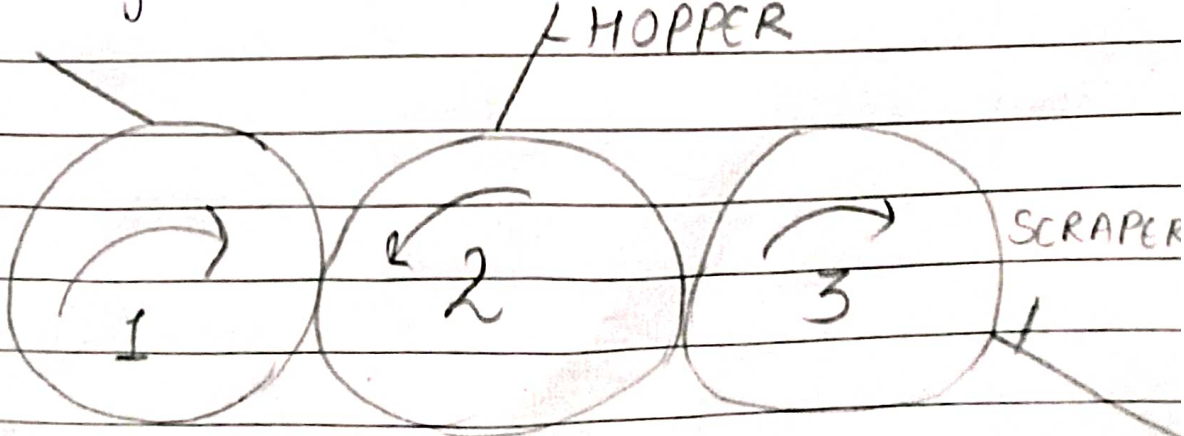
Construction-

→ The mill consist of 3 rollers which are made of a hard abrasion-resistant material.

→ These roller are arranged in such a way that they come very close to each other.

→ The rollers are rotated at different rates of speed.

→ The material coming between the rollers is crushed depending on the gap between them and the difference in rates of movement of the 2 surfaces.



Triple Roller Mill

Working —

→ The material after passing through hopper comes between roller 1/2 and is reduced in size in the process.

→ The gap between roller 2/3 usually less than that between 1 and 2, further crushes and smooth the mixture which adhere to roller 2.

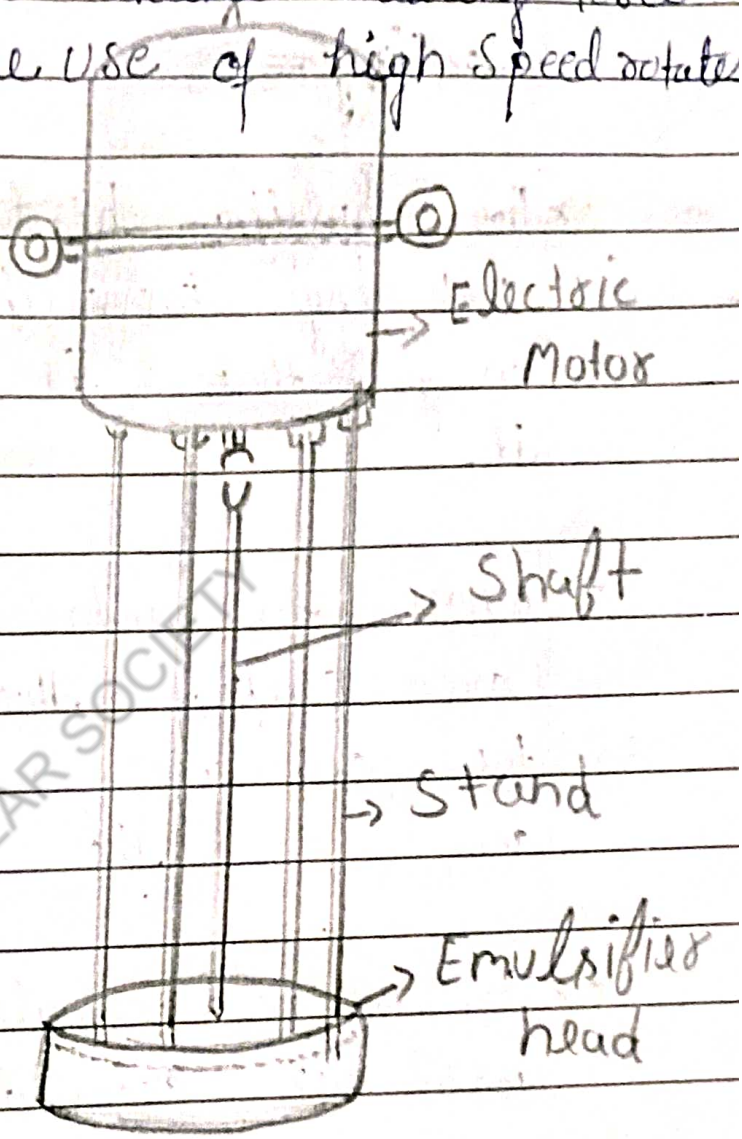
→ A Scraper is arranged in such a way, that it can remove the mixed material from the roller no. 3 does not allow the material which has not passed between both sets of the rollers to reach the Scraper.

Emulsifier

4. * Silverson mixer homogenizer *

Principle – it produce intense shearing force and turbulence by the use of high speed rotate

Construction –



→ it consist of an emulsifier head which is covered with fine meshed stainless steel sieve

→ The emulsifier head consist of number of blades which rotate at a very high speed, in order to produce a powerful shearing action.

→ The blades are rotated by using an electric motor fitted at the top.

Working –

→ The emulsifier head is placed in the vessel containing immiscible liquids, in such a way that it should get dipped into it.

→ When the motor is started, the liquids are sucked through the fine holes and the oil is reduced into fine globules due to the rotation of the blades.

→ So, a fine emulsion is produced which is then expelled out.

→ The intake and expulsion of the mixture set up a pattern of circulation.

* Filtration *

Filtration is the process, where by solid particles are separated from the liquid by passing it through a porous medium which retains the solid but allows the fluid to pass.

Theory of Filtration-

The Theory of filtration gives an idea about the factors influencing the mechanism by which the particles are retained.

→ The factor affecting the rate of filtration were studied by a scientist named Darcy and he expressed it in the form of an equation, which is known as "Darcy's Law".

The eqn is.

$$V = \frac{K A \Delta P}{\eta L}$$

Where,

V = Volume of filtrate

K = Permeability coefficient and is dependent on the nature of the precipitate to be filtered and the filter medium

A = Area of filter bed

ΔP = Pressure difference on the liquid and below the filter medium

η = viscosity of the fluid

l = Thickness of filter cake

* Membrane Filter –

Membrane filters operate as a barrier between contaminants and water, or they remove the contaminated particles.

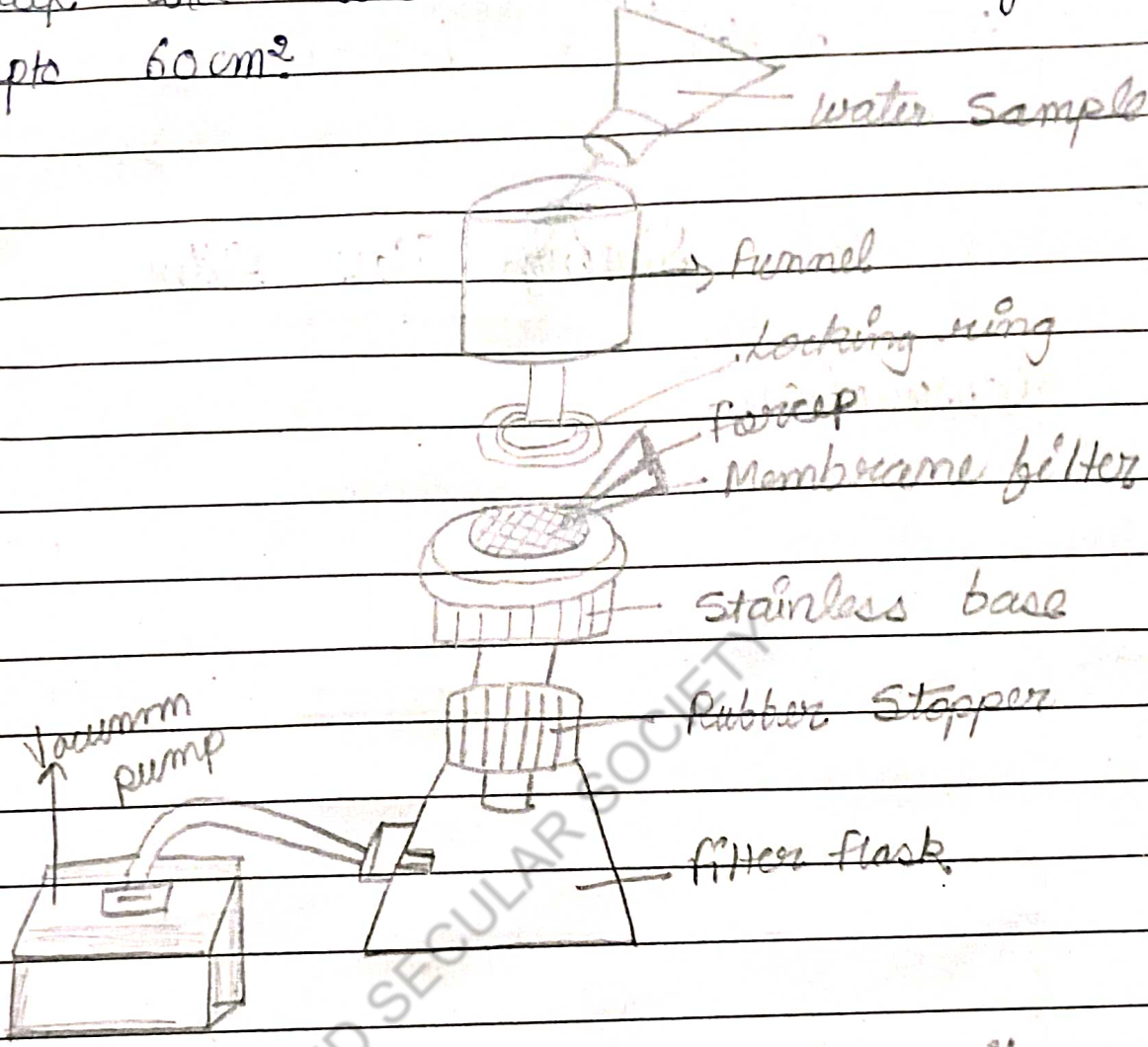
→ Membrane are used in reverse osmosis, ultrafiltration and nanofiltration.

Construction –

→ Membrane filters are made of thin and flat membranes of cellulose derivatives, such as cellulose acetate and cellulose nitrate.

→ These filters are brittle when in dry condition and can be stored for an identify period.

→ The Filters are between 50 and 150 μ thick and are available in sizes upto 60 cm².



Membrane Filter Unit

Working-

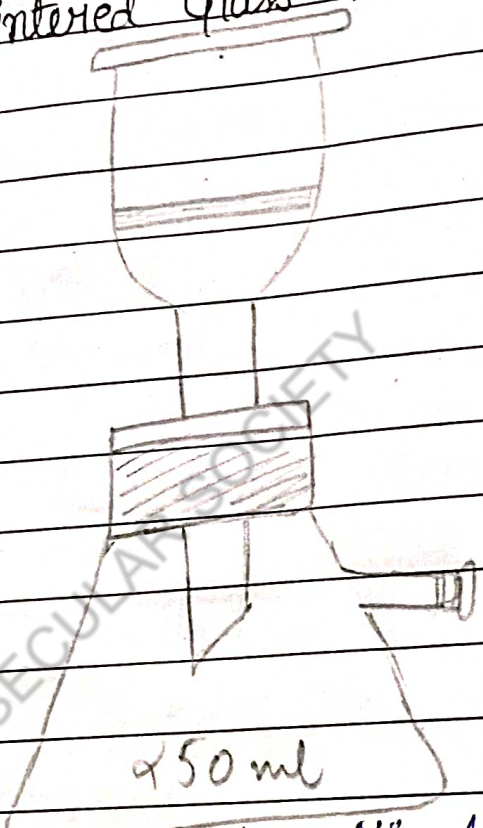
→ A membrane filter has 400 to 500 million pores per square centimeter of filter surface, which are all the same size and account for around 20% of the filter volume.

→ Pre-filtration is frequently required to avoid membrane closing.

→ The type of membrane filter to use for a specific application is determined by the particles to be removed.

Sintered Glass Filter

Construction-



- These are made of borosilicate glass.
- Borosilicate glass is finely powdered, sieved and particle of desired size are separated.
- it is then packed into a disc mould and heated to a temp. at which adhesion takes place between the particles.

- The disc is then fused to a funnel of suitable shape and size.

Working –

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

* Drying *-

Defination-
it is the process of removal of small amount of liquid (water, moisture) by application of heat to obtain dry solid or solid product.

These are two ways to remove water by drying-

① Thermal process- it involves the application of heat

② Non-Thermal process- it involves-

→ Squizing- remove water by Squeezing of wet substance).

Ex- Spongy material.

→ Adsorption- in which dessicant particle absorb all water from surface of wet substance)

Ex- Silica gel

→ Extraction- (wet remove by extraction from wet Solid.

- The equipments which are used from drying are known as dryer.

Objective and Applications-

- Preservation of drug products
- Improved handling
- Improved characteristics.

Fluidized bed dryer

Principle-

it is most widely used technique for drying pharmaceutical powders and granules.

- In FBD hot air is passed at high pressure through a perforated bottom of the container. The granules are lifted from the bottom and suspended in the steam of air, this condition is called as Fluidized state. The hot gas or air surrounding every granules completely dry them.

Construction -

- The dryer is made up of stainless steel or plastic.

- A detachable perforated bowl is placed at the bottom of the dryer which

is used for charging and discharging of material.

- A fan is mounted in the upper part for circulating hot air.
- Fresh air inlet, pre-filter and heat exchanger are connected serially to the required temperature.
- Bag filters are placed over bowl for recovery of fines.

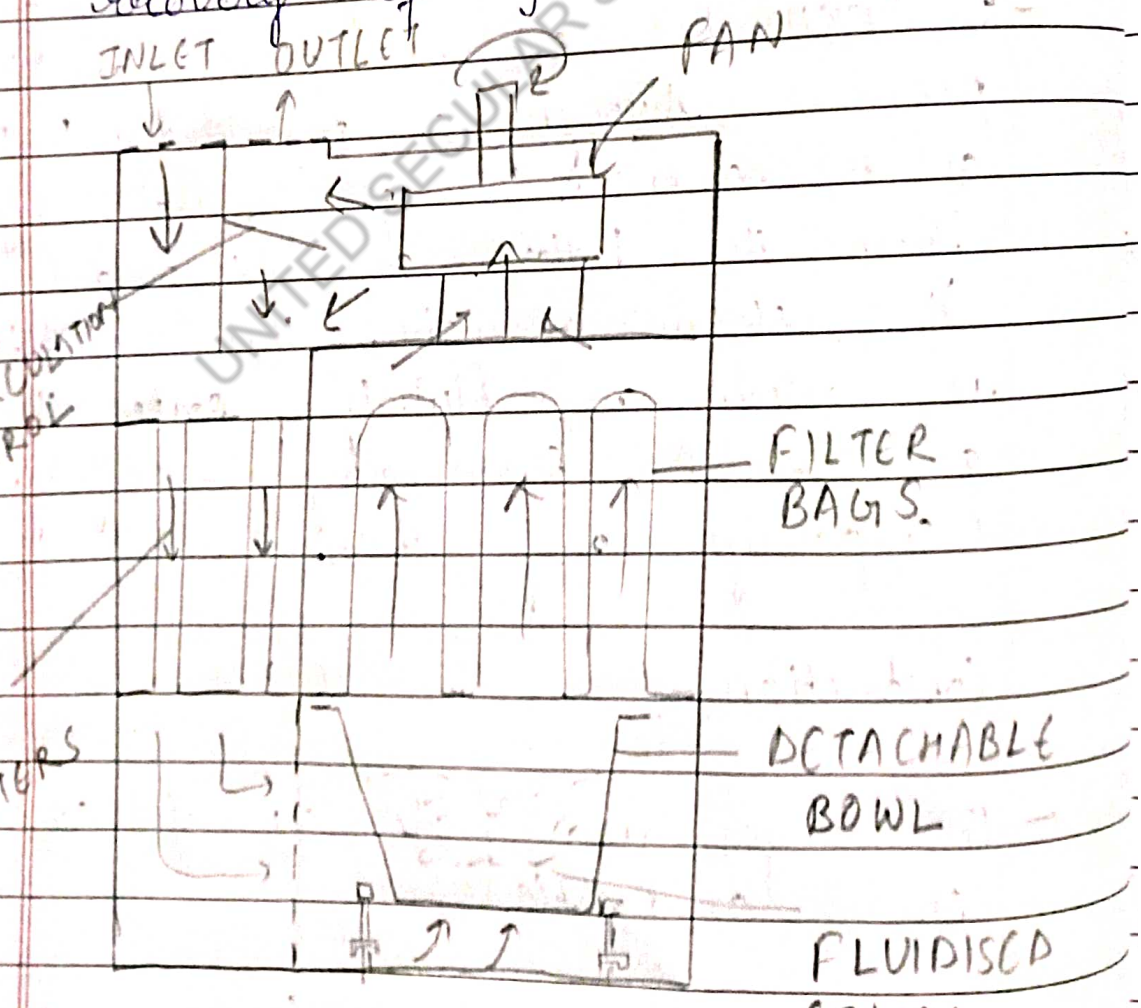


Fig- Fluidized bed dryer

Working:-

- The wet granules to be dried are placed in the detachable bowl, the bowl is pushed into the dryer.

- Fresh air is allowed to pass through a pre-filter which get heated up.

- The hot air flows through the bottom of the bowl and fan is allowed to rotate.

- The velocity of the air is gradually increased. when the velocity of the air is greater than setting velocity of the granules, granules remains partially suspended in the gas steam.

- After sometime a point of pressure reached at the frictional drag is equal to the force of gravity.

- The granules rises in the container because of high velocity gas and after fall back in a random boiling motion.

This condition is said to be fluidised state.

- The gass surrounding every granules to completely dry them.
- The air leave the dryer by passing through the filter bag.
- The entrained particles remain adhere to the inside surface of the bag.
- The bags are shaken to remove the entrained particles.

Freeze dryer

Freeze-dryer is a method of removing water by sublimation of ice crystals from frozen material.

- Freeze drying, also known as Lyophilisation Lyophilization or cryodesiccation is a dehydration process typically used to preserve a perishable material.

Principle-

- The main principle involved in freeze drying is a phenomenon called Sublimation, where water passes directly from solid state (ice) to the vapour state without passing through the liquid state.

- Sublimation of water can take place at pressure and temperature below triple point.

Construction-

Freeze dryer is consist of-

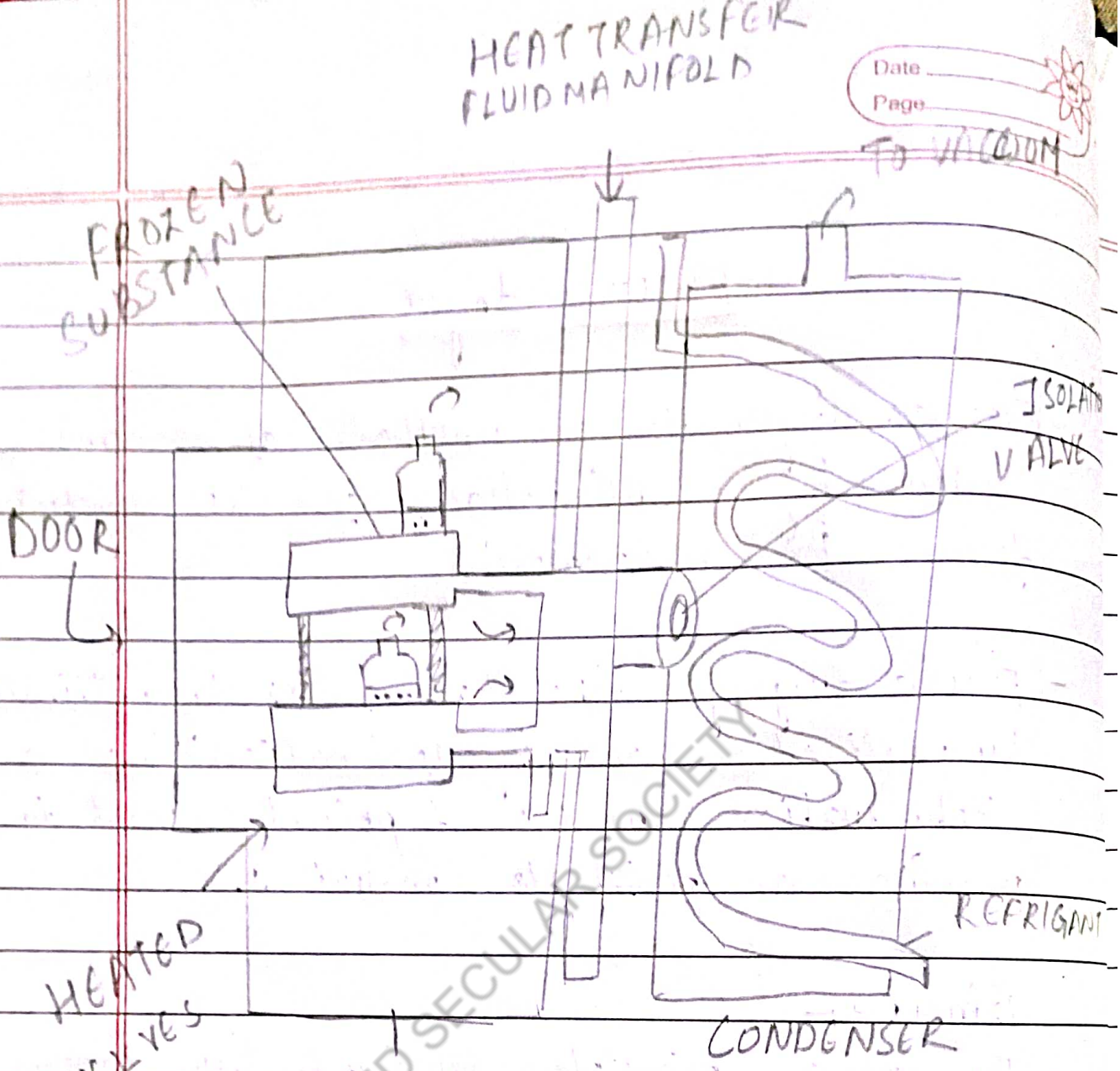


Fig- Freeze dryer

- Drying chamber in which tray are loaded.
- Heat Supply in the form of radition.
- Vapour condensing or adsorption System
- Vaccum pump or steam jacket or both.

Working - it involves 5 stages -

i) Preparation and pretreatment
ii) Prefreezing to solidify water
iii) Primary drying
iv) Secondary drying
v) Packing

i) Preparation and pretreatment —

- it is essential process, which reduces the actual drying by 8 - 10 times.
- The solution is pre-concentrated under normal tray drying, final products becomes more porous.
- Liquid or solid dessicants are also used for this.

ii) Prefreezing to solidify water —

- Vials, ampoules or bottle in which the solution is packed are frozen cold shelves (about -50°C).
- During this stage, cabinet is maintained at low temperature and atmospheric pressure.

iii) Primary drying -

- The material to be ~~dried~~ dried is spread as much large surface as possible for sublimation.

- The temp. and pressure should be below the triple point of water, that is 0.0098°C and 0.583 kiloposcale (4.58mmHg) for the sublimation.

- Vaccum is applied to the of about 3mmHg on the frozen sample. The temp. linearly increased to about 30°C in the span of 2 hrs.

- All the things has to controlled in such a manner so as to get highest possible water vapour at its surface, without melting the material.

- Primary drying stages removes easily removable moisture. (98% to 99% water is remove)

- Still process of moisture is present in the sample.

iv) Secondary drying –

- During this stages, process of moisture is removed.

- In this, the rate of drying is very low and it takes about 10-20 hrs.

v) Packing –

After vaccum is replaced by inert gas, the bottles and vials are sealed or closed.

X X

* Extraction *

it defined as the treatment of the plant or animal tissues with solvent, where by the medicinally active constituents are dissolved and most of the inert matter remains undissolved.

- The solvent used for extraction is known as 'menstruum' and the inert insoluble material that remains after extraction is called "marc".

Types of Extracts –

Dry extract (Tablet, capsules)
Ex- belladonna Extract

Soft (ointment, suppository)
Ex- Glycerrhiza extract

Liquid –
As tincture

Ideal prop. of Solvents–

1. Not react with the extracted compound or with other compound in the plant materi

2. Have a low price.
3. Should be harmless man and to the environment
4. Should not mix up with water
5. Should have minium viscosity.

- Classification of Extraction –
Classification of Extraction process is based on two different categories–

1 Classification based on operation –
Batch process
continuous Process

2 Classification based on Types & Phases –
- Liquid - Liquid Extraction – Sample phase Liquid
- Extract phase (Liquid) Basis of Separation (Partitioning)
- Solid phase extraction or – Sample phase (Gas, liquid)
- Micro - extraction Extract phase (Liquid, Solid, stationary phase) Basis for separation (Partitioning or adsorption)
- Leaching or Solid Liquid – Sample phase (Solid)
- Extraction Extract phase (Liquid) Basis for Separation (Partitioning)
- Supercritical Fluid – Sample phase (Solid, Liquid)
- Extraction Extract phase (Supercritical Fluid) Basis for separation (Partioning with applied heat)

2. Have a low price.
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Various methods of Extraction–

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

1. Infusion –

- it consist of pouring water over the drug and then allowing it to keep in contact with water for the stated period, usually 15 min., with occasional stirring and finally filtering off the liquid.

- Drug is placed at the bottom of the pot.

- water is added and it is well stirred 3 or 4 times.

- Infusion can also be prepared by enclosing the drug in a muslin bag and then suspending it just below the level of the water in a beaker.

- Stirring is not required because water slowly circulate due to increase in

Specific gravity of water near the drug.

- When water comes in contact with the drug, it dissolves API and become havier.

- Special pots known as Infusion pot used for preparation of infusion.

These are two types of Infusion-

a. Fresh infusion

b. Concentrated infusion

2. Decoction-

- Decoction is the extraction of hard and woodly crude medicines' water soluble and heat stable ingredients.

- The medication is sliced into little pieces and cooked with the menstruum for 10-15 minutes.

- After the liquid has been boiled, cooled and filtered, more water to pumped through the marc to get the desired volume.
For example- Tea, coffee.

3. Maceration-

Maceration Term derived from Latin word "macerate" meaning to Soak.

- it is a process in which the properly comminuted drug is permitted to soak in the menstruum until the cellular structure is softened and penetrated by the menstruum and the soluble constituents are dissolved.

- Maceration is usually conducted at a temp. of 15°C - 20°C for 3 days or until the soluble matter is dissolved.

Examples- Compound Benzoin, Sweet orange Peel Tincture, Tolu Balsam Tincture.

Method- Plant material is cut into small piec

↓

Placed in a closed vessel with menstr

↓

Sending for specified time with occasional Shaking

↓

Liquid is strained off and clarified

↓

Evaporation and concⁿ

4. Percolation –

The term percolation, from the Latin Per meaning through and colare meaning to strain.

– it may be described generally as a process in which a comminuted drug is extracted of its soluble constituents by the slow passage of a suitable solvent through a column of the drug.

– The drug is packed in a special extraction apparatus termed a percolator, with the collected extractive called the percolate. Most drug extractions are performed by percolation.

– In the process of percdation the flow of the menstruon over the drug column is generally downword to the exist orifice, drawn by the force of gravity as well as the weight of the column of liquid.

Method of Percolation -

Prep. of the dried crude drug for percolation
a. powdering b. Moistening

↓

Packing the percolator

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Period of Maceration

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Percolation and collective of Percolate

↓

Adjustment of conc^{n} of percolation as required.

5. Digestion

- This is a modified version of maceration in which the medication is extracted by heating it at a specific pressure.
- The will boost the menstruum's penetration capability, allowing for complete medication extraction.

Process -

The 'Digestor' apparatus is a metal vessel.

- The entire medicine is deposited in the digestor's body, which is then covered and bolted shut with nuts.

- Menstruum is used to treat the medicine for a set period of time under specific temp. and pressure conditions.

Example - Extraction of Morphine

Application of Extraction -

- Essential oils and Lipids dietary supplements are examples of nutraceutical extracted from plants.

- The observed total yield and saponin yield increased by 15-30% respectively after extracting saponin from ginseng.

- Rice bran oil extraction using basic aqueous sol^n was found to be efficient in 30 min. under high ~~intensity~~ intensity ultrasound

- Depending on temp., ultrasound-assited extraction rates of carvone and Limonene were 1.3-2 times faster than traditional extraction.

4-Unit Completed