

**Topic: Suspension**  
**Subject: Pharmaceutics-II**  
**Class: T.Y. B. Pharm. (Sem.- I)**  
**Academic Year: 2018-19**  
**Programme: 2016-2020**

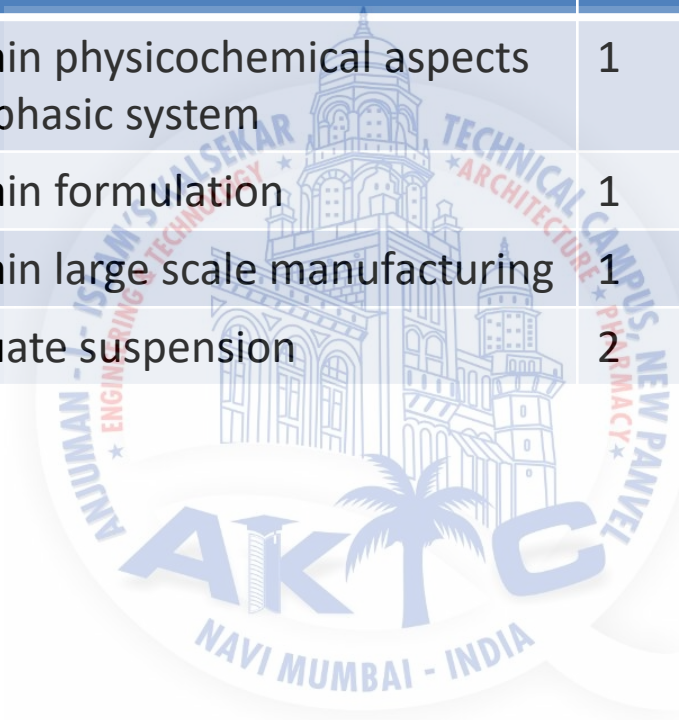


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# Mapping of TLO with Course outcomes (Cos)

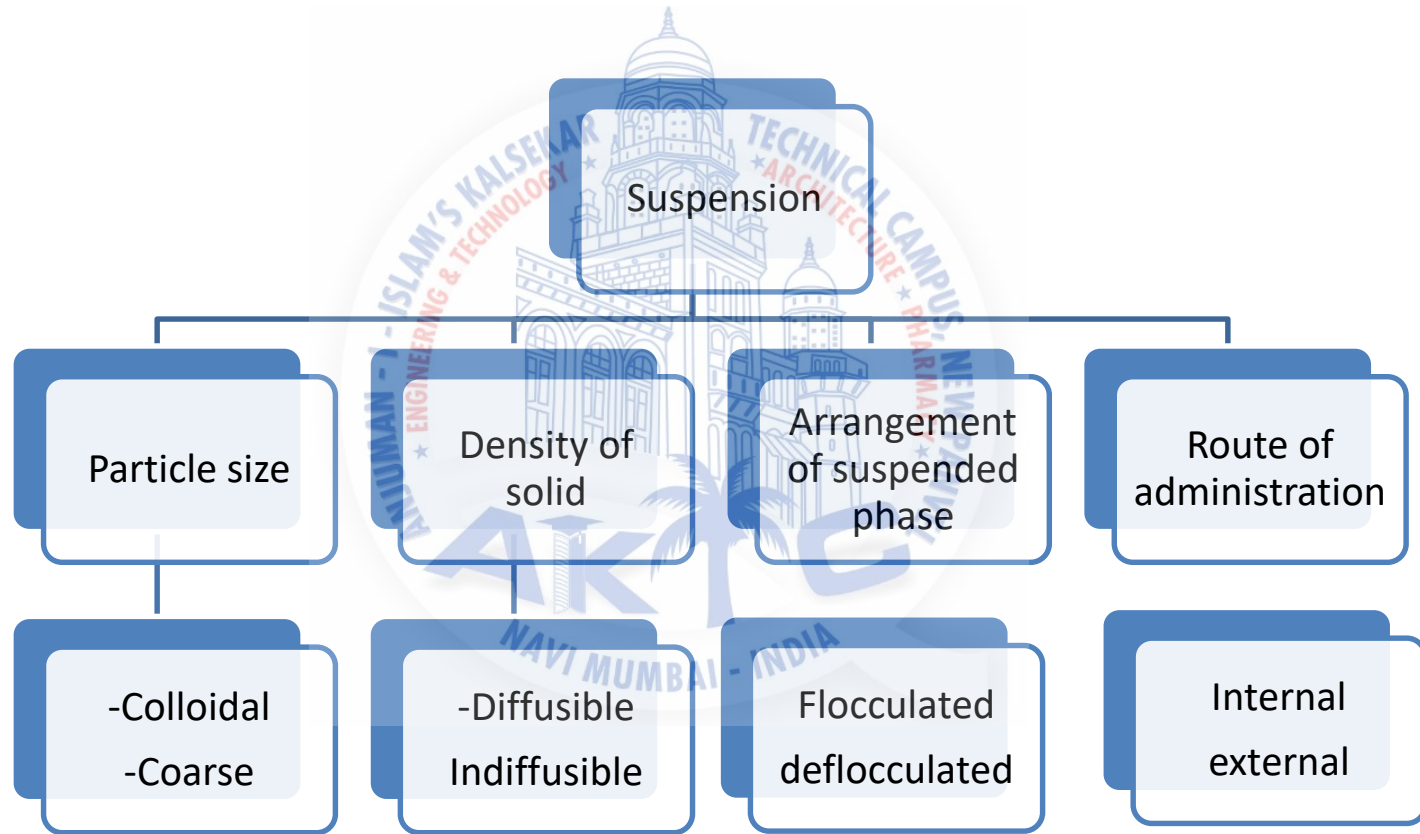
Sr. No	TLO	CO
1	Explain physicochemical aspects of biphasic system	1
2	Explain formulation	1
3	Explain large scale manufacturing	1
7	Evaluate suspension	2



# Introduction

- A Pharmaceutical suspension is a **heterogeneous biphasic thermodynamically unstable system in which insoluble solid particles** ( as internal/ discontinuous/dispersed phase) is uniformly distributed in liquid phase (external/continuous/ dispersion medium). This may require inclusion of physical stabilizer, suspending agent.

# Classification of suspensions



## Flocculated

- Particle form (loose aggregate) open structure
- Particle forms cluster
- Rate of sedimentation is high
- Sediment is rapidly formed
- Sediment is easy to redisperse
- Sediment is loosely packed and does not form hard cake
- Supernatant liquid is clear
- Floccules stick to the sidewall of bottles
- Suspension is not pleasant in appearance

## Deflocculated

- Closely
- Particle remains as a separate entity packed structure
- Rate of sedimentation is low
- Sediment is slowly formed
- Sediment is difficult to redisperse
- Sediment is closely packed and hard cake is formed
- Supernatant liquid is not clear
- Floccules do not stick to the sidewall of bottles
- Suspension is pleasant in appearance

# Advantages

- Bioavailability of finely dispersed and wet drug is faster than that of solid dosage form
- The large dose of insoluble drug are easy to swallow in the form of suspension than that of solid dosage form eg antacid
- The higher surface area of suspended phase is more effective
- Drugs are chemically more stable in insoluble state than in solution state
- Liquid preparations are easy to swallow and thus more useful for pediatrics and geriatrics
- Insoluble drugs are less unpleasant than the solution eg paracetamol



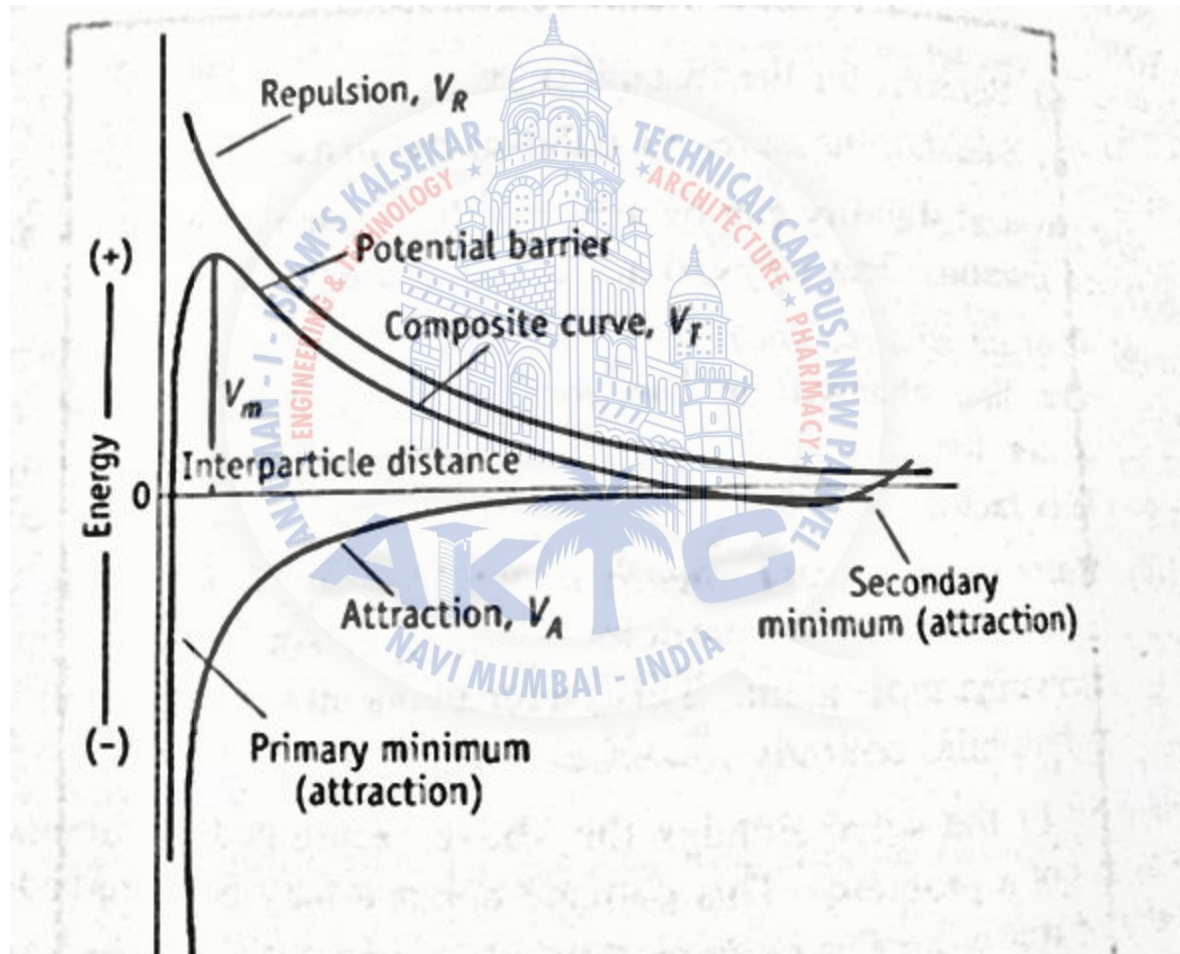
# Disadvantages

- A no of drugs have **some solubility in commonly used solvent and this could lead to physical instability** of suspension
- Due to higher surface area the fine drugs can **adsorbs added flavours and made system difficult to formulate**
- In case of **adsorption of presevatives by suspended phase, liquid systems needs addition of higher concentration of preservative**
- The **rate of absorption is slower** than solution

# DLVO

- Stability of dispersion is explained by DLVO theory Derjaguin, Landau, Verway and overbeek
- According to this theory **distance between two dispersed particles influence particle-particle interactions**.. In colloidal dispersion, the brownian movement results in frequent collision between particles. Such interaction responsible for stability of colloids. There are two types of interactions, **namely attractions and repulsions**. When **attractions** predominate, the particles **adhere** after collision. When **repulsion** predominate, the particle rebound after collision and remain **individually dispersed**.
- The potential existing at the surface of particle can be expressed in term of zeta potential . In presence of high zeta potential repulsive forces is more than attractive forces and the system turns into deflocculated suspension . Zeta potential is lowered by addition of some flocculating agent which tend to increase in attractive forces and system become flocculated.
- The potential energy versus interparticle distance for particles in a dispersion is given





# Sedimentation in suspension

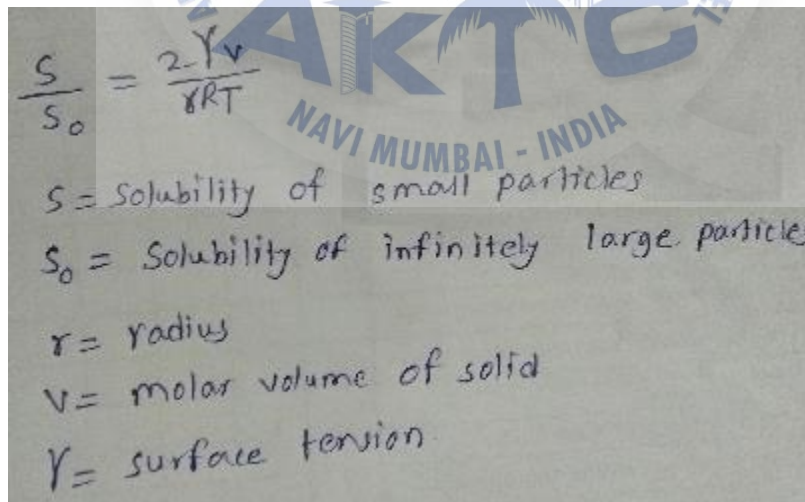
- The velocity in sedimentation is expressed by stoke's law.

$$v = \frac{d^2(\rho_s - \rho_0)g}{18\eta_0}$$

- $v$ : Velocity of sedimentation
- $d$  = Diameter of particle
- $\rho_s$  and  $\rho_0$ : Density of dispersed phase and dispersion medium
- $g$  = Acceleration due to gravity
- $\eta_0$  = Viscosity of dispersion medium

# Crystal factors

- The **size distribution of dispersed system increases during ageing** i.e. storage, due to three principle mechanism
- i) Ostwald ripening
- ii) polymorphic transformation
- iii) Temperature cycling
- i) Ostwald ripening: Kelvin equation is applied to the equilibrium solubility of small particle.



$$\frac{S}{S_0} = \frac{2\gamma V}{rRT}$$

$S$  = Solubility of small particles  
 $S_0$  = Solubility of infinitely large particles  
 $r$  = radius  
 $V$  = molar volume of solid  
 $\gamma$  = surface tension

# Formulation of suspension

- 1. Flocculating agent: The dispersion can be improved by adding surfactant or protective colloid which act as a flocculating agent. The flocculating agents act by reducing surface tension and thereby improving dispersion of solid. Eg. SLS, tweens, spans and carbowaxes
- 2. Thickening agents: These are hydrophylic colloids which form a colloidal dispersion with water and increasing the viscosity of the continuous phase, so that the solid particles remain suspended, polysaccharides, inorganic agents and synthetic compounds
- A) Natural; polysaccharide
- Gum acacia: It is good protective colloid and suspending agent. It is effective when used as a compound tragacanth powder contains 20% acacia, tragacanth 15% , starch 20% and sucrose. It is used 2% . CTP is always used when the vehicle is other than water or chloroform water
- Tragacanth: It forms more viscous solution or gel. It is used in 0.2% with 2-4% of CPT and 25 ml of mucilage for 10 mL of final mixture.
- Starch: Starch alone is not satisfactory suspending agent. It is combined with other suspending agent to enhance the viscosity
- Sodium alginate:
- It forms viscous solution with water; used in 1%. Since it is anionic compound it is incompatible with cationic antiseptic like cetrimide and also incompatible with heavy metals, calcium salt

- Semisynthetic suspending agent:
- Methyl cellulose: High viscosity grade like 2500 and 4500 centistokes are used as thickening agent. They form viscous liquid in cold water but insoluble in hot water. It requires preservative to protect microbial growth like PMN(0.001%)
- Hydroxyethyl cellulose:
  - Soluble in cold and hot water
  - Sodium carboxy methyl cellulose: It dissolves in cold hot water to a greater extent. It is incompatible with strong acids and heavy metal ions
- Microcrystalline cellulose: It is dispersible in hot and cold water



- Clays:
- Bentonite: 2% is used as suspending agent for indiffusible solidseg calamine lotion. Since it is naturally obtained must be sterilized by heating  $160^{\circ}\text{C}$  for 1 h.
- Aluminium magnesium silicate: “Veegum”..  
10% aluminium magnesium silicate
- Synthetic
- Carboxyvinyl polymer 1 to 4%



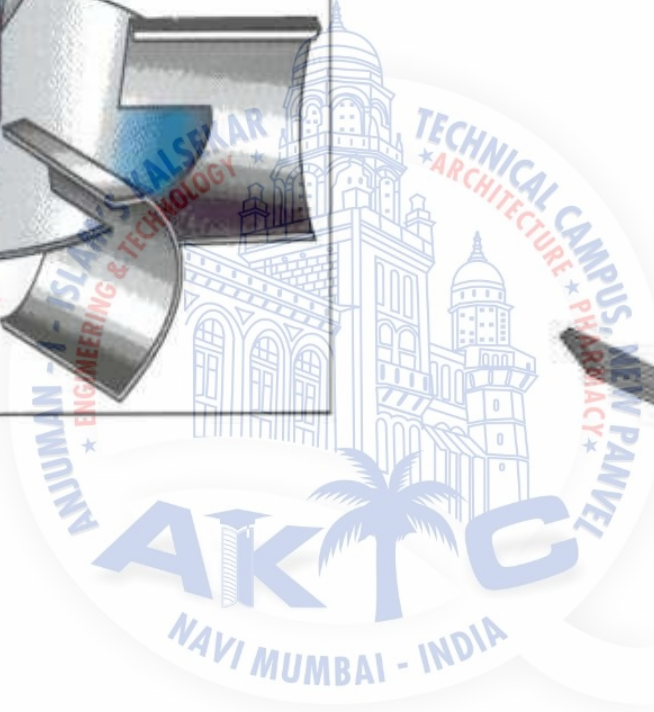
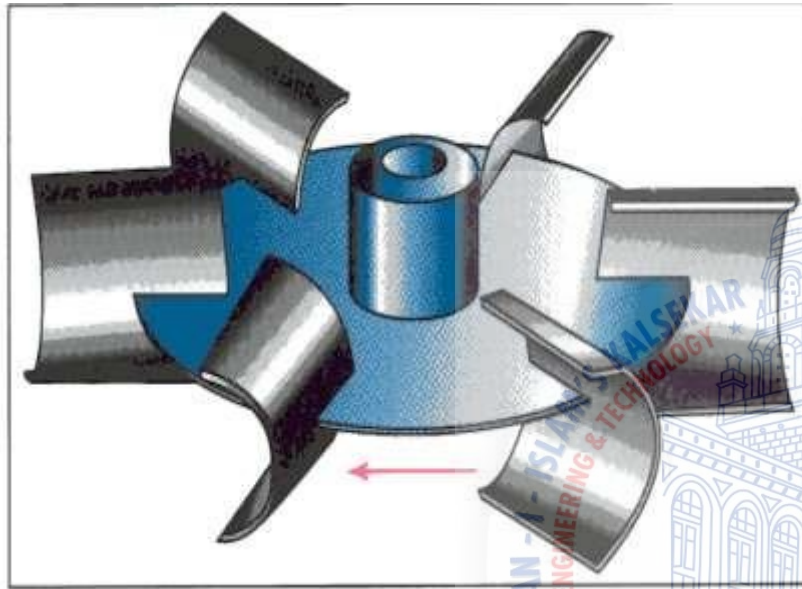
# Methods of suspension preparation

## a) Precipitation method

- i) Organic solvent precipitation
  - ii) Precipitation effected by change in pH
  - iii) Double decomposition
- ## B) Dispersion method
- Small scale: mortar and pestle
  - Large scale: Colloidal mill

# PROPELLER MIXERS





# HIGH SPEED DISPERSER

- It is also called as saw blade disperser.
- This machine consists of a **variable speed shaft connected** to an impeller with a serrated edge.
- The impeller should be **located at the bottom of vessel**
- It can **deagglomerating particles** when the viscosities between 10,000 to 20,000cps.
- **Application:**
- It is used for **pigment dispersion, dye stuffs**

# COLLOIDAL MILL

- It is used to disperse the solids into liquids and to emulsify liquid-liquid systems.
- These generally used as polishing machines for suspensions because they produce fine particle to enhance a products stability.
- They are operated at speed of 3600 rpm

# Fine suspension and size reduction equipments

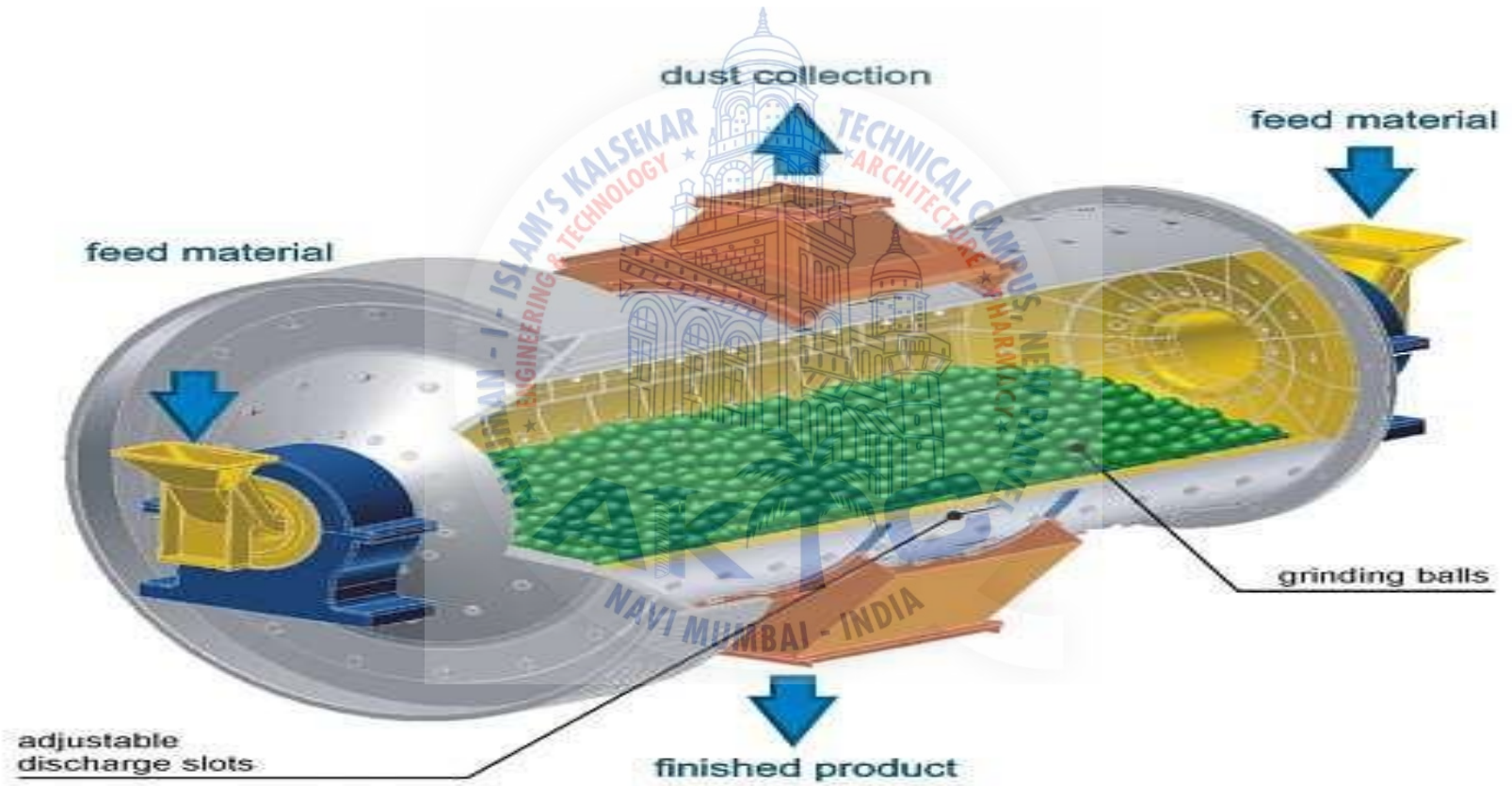
- Triple roll mill
- Ball mill





# BALL MILL

- It is used for **size reduction fine solid discrete particles or for deagglomeration** of very tightly bound agglomerates.
- The machine consists of **cylindrical drum into which a charge of heavy spherical balls usually metal or ceramic** is loaded along with the components of the dispersion.



# Packaging

- Ideal requirements of packaging material:
- It should be inert.
- It should effectively preserve the product from light, air, and other contamination.
- It should effectively deliver the product without any difficulty.
- It should be cheap.

# Labelling

- **Shake well before use**
- **Do not freeze**
- **Protect from direct light (for light sensitive drugs)**
- **In case of dry suspensions powder the specified amount of vehicle to be mixed may indicated clearly on label.**

# References:

- “The Theory & Practice Of Industrial Pharmacy” by Leon Lachman
- , H.A.Lieberman.
- Remington’s “The Science & Practice Of Pharmacy” 21<sup>st</sup> Edition,  
Volume-I.



# **Review questions to ensure attainment of TLOs/ Cos**

- 1) Define suppository and describe advantages and disadvantages for same**
- 2) Elaborate on bases of suppository Method of manufacturing of aerosol**
- 3) Packaging material used for aerosol**
- 4) Evaluation tests for suppository**

