Pharmaceutical suspension
Syllabus content

- Suspensions containing diffusible solids.
- Suspensions containing indiffusible solids.
- Suspensions containing poorly wettable solids.
- Suspensions containing precipitate forming liquids.
- Dispersion of oil in inhalation.
- Suspensions produced by chemical reaction.
Definition

- A Pharmaceutical suspension is a coarse dispersion in which internal phase is dispersed uniformly throughout the external phase.
- The internal phase consisting of insoluble solid particles having a specific range of size which is maintained uniformly throughout the suspending vehicle with aid of single or combination of suspending agent.
- The external phase (suspending medium) is generally aqueous in some instance, may be an organic or oily liquid for non oral use.
Classification

- Based On General Classes
  Oral suspension
  Externally applied suspension
  Parenteral suspension

- Based On Proportion Of Solid Particles
  Dilute suspension (2 to 10% w/v solid)
  Concentrated suspension (50% w/v solid)

- Based On Size Of Solid Particles
  Colloidal suspension (< 1 micron)
  Coarse suspension (> 1 micron)
  Nano suspension (10 ng)
Features Desired In Pharmaceutical Suspensions

- The suspended particles should not settle rapidly and sediment produced, must be easily re-suspended by the use of moderate amount of shaking.
- It should be easy to pour, yet not watery and no grittiness.
- It should have pleasing odour, colour and palatability.
- Good syringeability.
- It should be physically, chemically and microbiologically stable.
- Parenteral/ophthalmic suspension should be sterilizable.
Applications

- Suspension is usually applicable for drug which is insoluble or poorly soluble. E.g. Prednisolone
- To prevent degradation of drug or to improve stability of drug. E.g. Oxytetracycline suspension
- To mask the taste of bitter of unpleasant drug. E.g. Chloramphenicol palmitate suspension
- Suspension of drug can be formulated for topical application e.g. Calamine lotion.
- Suspension can be formulated for parenteral application in order to control rate of drug absorption, E.g. penicillin procaine
- Vaccines as a immunizing agent are often formulated as suspension. E.g. Cholera vaccine
- X-ray contrast agent are also formulated as suspension. E.g. Barium sulphate for examination of alimentary tract
Disadvantages

- Physical stability, sedimentation and compaction can causes problems.
- It is bulky sufficient care must be taken during handling and transport.
- It is difficult to formulate
- Uniform and accurate dose can not be achieved unless suspension are packed in unit dosage form
Suspension containing diffusible solid

- Diffusible solids - light and easily wettable powder, easily dispersed and for long period of time remains in dispersed form upon shaking
- e.g. calcium carbonate, light kaolin, light magnesium carbonate, magnesium trisilicate, rhubarb powder
- General method of preparation
  - Carefully tare the container
  - Finely powered the ingredients
  - Mix insoluble powder in mortar adding in increasing order of bulk
  - Add enough vehicle to produce smooth paste
  - Add in small amount any nonvolatile solid ingredients dissolved in part of the vehicle and mix well
  - If necessary dilute with vehicle until pourable
  - Examine the suspension critically, if it contains particles strain through muslin cloth
  - Strain into tared bottle if the content in the mortar homogenous
  - Add any volatile solid ingredients, previously dissolved in some of the vehicle and mix well
  - Add any liquid ingredients, rinse the measure and mix well after each addition
  - Rinse the mortar and pestle with successive volume of vehicle until they are quite clean, transferring the rinsings to the bottle
  - Make up the volume with the vehicle and shake thoroughly
Containers and storage

- Depend on the class of dispensed medicine
- Very thick wide mouth bottle required
- Physical stability is affected by extreme temperature
- Store in cool place
- E.g. kaolin mixture
Suspensions containing indiffusible solids

- Indiffusible solid: not distributed in a vehicle long enough to ensure the uniformity of dose
- Suspending or viscosity building agents are added (thickening agent)
- This obstruct the collision of particles and slows the fall of particles
- e.g. kaolin mixture, paediatric
Indiffusible solids

- Used internally
  Aspirin
  Chalk
  Aromatic chalk powder
  Phenobarbitalone
  Succinylsulphathiazole
- Used externally
  Calamine
  Hydrocortisone
  Sulphur ppt
  Zinc oxide
  e.g. chalk and opium mixture
Types of thickening agent

Hydrophilic colloids
- They have affinity for dispersed phase and dispersion medium and form colloidal dispersion
- Three groups-
  ✓ Polysaccharides
  ✓ Inorganic agent
  ✓ Synthetic compound
1. polysaccharides

- Two types-
- Natural
- Semi synthetic
Natural polysaccharides

- They are the natural products-
  1. Acacia-
     - Dried exudates from *Acacia senegal* and other species of *acacia*
     - Occurs in ovoid, colorless, amber colored tears or white powder
     - Poor thickener as compared to other
     - act as good suspending agent – as is good protective colloid
     - Less satisfactory for suspending heavy particle, Mostly used with other thickeners
     - Used either as compound powder (20% acacia, 15% tragacanth, 20% starch and sucrose) (2 g per 100 ml of mixture) or as mucilage (10 to 20 ml per 50 ml of product)
     - Very sticky so rarely used for external preparations
     - Antimicrobial agent is needed- chloroform, benzoic acid and PABA
2. Tragacanth-
- Dried extract from Astragalus gummifer and other species of Astragalus
  - Occurs as thin, white or yellowish white, ribbon like flakes or as white powder
  - Viscosity depend on concentration
  - Better thickener than acacia due to gelling property
  - Used as powder or mucilage or compound tragacanth powder as suspending agent
- For 100 ml of suspension 0.2 g of pure powder or 2 to 4 g of compound powder or 25 ml of mucilage
- Mucilage used when the vehicle is water or chloroform water
- Less sticky than acacia, suitable for external preparations
- Used in jellies, lotions, pastes, creams
- Contain soluble and insoluble fraction hence with time viscosity increases
- Preservatives are needed
• Starch-
  • High viscosity of mucilage
  • Present in compound tragacanth powder
  • Used with other thickening agent
• Sodium alginates-
  • Sodium salt of alginic acid
  • White or buff powder
  • Forms viscous solution with water
  • Wetting agents are added to prevent lumps e.g. alcohol, glycerin
  • Warming solution is acceptable but should not exceed above 70 C loss of viscosity
  • Should be allowed to stand overnight before use
  • Sodium alginate is an anionic compound and incompatible with cationic antiseptic
• Semisynthetic-
  • Methylcellulose- cellulose-(C₆H₇O₂(OH)₃)n
  • n may be 1000
  • Long chain polymer have high viscosity
  • Methylcellulose 20 BPC
  • Methylcellulose 450 BPC
  • Methylcellulose 2500 BPC
  • Methylcellulose 4500 BPC
  • Number indicate approximate viscosity in centistoke of a 2% mucilage
  • High viscosity used for thickening and dispersing agent
  • Mucilage of them prepared by any of the method –
  1. Hydrate the powder by adding 1/3 of powder, heated to boiling and allow to stand for about 30 min. then rest of water added and product is stirred
  2. Methylcellulose is added 10 times its volume of boiling water, stirring continued for 2 h and rest of the water is added and the mucilage is allowed to stand for 16 hr

Used for both internal and external preparation
Used in conc. Of 0.2 % and 2%
• Hydroxy ethyl cellulose-
• Hydroxy ethyl group present instead of methyl group
• Soluble in hot and cold water
Sodium Carboxymethyl cellulose

- Produces aqueous solutions with viscosities ranging from 6 to 4000 centipoises for 1% solution
- Soluble in hot and cold water
- Used in conc. from 0.25 to 1% of internal and external suspensions
2. Inorganic clay

1. Hydrate easily absorbing many times their own volume of water to produce sol or gels
2. They are thixotrophic, hence hold particles in suspension but upon shaking pourable also
3. Preservative is imp
4. They are anionic in nature incompatible with cationic agent

E.g. bentonite, aluminium magnesium silicate, hectorite, aluminium hydroxide
• Bentonite-
  1. 2% used as suspending agent in external preparations
  2. Must be sterilized before used

• Aluminium magnesium silicate
  3. Used mainly in industry as thickening agent for external and internal preparations (0.5 to 2%)
  4. Heating reduces the viscosity of dispersion

• Hectorite-
  5. Used industrially in suspension for external use (1 to 2%) dispersion
3. Synthetic
   • Carbomer-
     1. High molecular weight polymer of acrylic acid with cross linkages of allyl sucrose
     2. They are low viscosity but when neutralized with sodium hydroxide are converted to highly viscous gels
     3. Less than 1 % produces gel in water
     4. Sensitive to oxidation when exposed to light so incorporating oxidising agent solves the problem
     5. Low conc needed (0.1 to 0.4 %)
     6. Widely used in industry for external and internal preparation

   • Colloidal silicon dioxide
     7. Used as thickening agent
     8. 1.5 to 4 % sufficient to stabilize suspension
Suspension containing poorly wettable solids

- Are both insoluble in water and poorly wetted by it
- E.g. sulphur, hydrocortisone
- To ensure satisfactory wetting, suitable wetting agent must be added to reduce the interfacial tension by getting adsorbed on the surface of liquid and solid
- Wetting agent-e.g. polysorbates (oral), alcohol, glycerin, glycerol
- E.g. sulphur lotion, compound (alcohol, glycerol)
Suspension of ppt forming liquids

- Liquid preparations contain resinous matter that is ppt on addition of water
- e.g.
  1. compound benzoin tincture
  2. Myrrh tincture
  3. Tolu tincture
- To prevent ppt, a protective colloids are added in vehicle before tincture
- Tragacanth mucilage or compound tragacanth can be used as protective colloid
• Method using compound tragacanth powder-
  a. Finely powder any insoluble solid and mix with gum
  b. Triturate the mixture with vehicle to form smooth cream and dilute to about 50% of final volume
  c. Measure the ppt forming liquid in dry measure and pour in slow stream in centre of the suspension stirring rapidly
  d. If preparation contains an electrolyte-
     1. Should not be added until resin has been protected
     2. It should be well diluted
     3. Use about half of the remaining vehicle
     4. It should be added slowly with constant stirring
     5. Strain, if necessary make up to volume and mix
• Method using tragacanth mucilage-
  1. Mix the mucilage with an equal volume of vehicle in a beaker
  2. Measure the ppt forming liquid in a dry measure and pour slowly into the centre of mucilage with constant stirring.
  3. Dissolve any electrolyte, dilute well and as above
• Dispersion of oils in inhalations—
  1. Used for suspension containing volatile oils
  2. To ensure uniform distribution of oil, diffusible solid (magnesium carbonate) used to adsorb some of oil and finely divided the remainder
  3. The powder does not interfere with free vaporization of the oil when the inhalations are added to water at about 65 °C for use
  4. If quantity is not mentioned 1 g of light magnesium carbonate for each 2 ml of oil or 2 g of volatile solid gives satisfactory result
  5. E.g. menthol and eucalyptus oil inhalation
Suspension produced by chemical reactions:
1. Insoluble active constituents are formed by chemical reaction
2. The reacting substances should be dissolved separately in half volume of vehicle and two parts are mixed
3. Finer Ppt formed is diffusible and no suspending agent is necessary
4. E.g. zinc sulphide lotion B.P.C.
   a. Sulphurated potash (mixture of potassium polysulphides and other sulphur containing potassium compounds)
   b. Zinc sulphate
   c. Con. Camphor water
   d. Water
Dissolve both the ingredients separately in half the qty of water
Add potash solution slowly to zinc sulphate solution with constant stirring
add camphor water in small amount with shaking adjust the volume and mix
( a and b reacts to form zinc sulphite)
• Most suspending agents perform two functions i.e. besides acting as a suspending agent they also imparts viscosity to the solution. Suspending agents form film around particle and decrease interparticle attraction.

• A good suspension should have well developed thixotropy.

• At rest the solution is sufficient viscous to prevent sedimentation and thus aggregation or caking of the particles. When agitation is applied the viscosity is reduced and provide good flow characteristic from the mouth of bottle.
• **Ideal Requirements of Packaging Material**

  • It should be inert.
  • It should effectively preserve the product from light, air, and other contamination through shelf life.
  • It should be cheap.
  • It should effectively deliver the product without any difficulty.
Types of suspensions

- Mixtures
- Lotions
- Injections
mixtures

• An oral suspensions are convenient means of administering:
  1. An insoluble medicament, when difficulties with swallowing
  2. Drug with an unpleasant test
  3. Bulky insoluble powders intended to absorb toxin from intestine in diarrhea
• Oral suspension- three types-
  1. Prepared entirely by dispensing pharmacist
  2. Readymade proprietary suspensions that are dispensed
  3. Proprietary suspensions supplied as granules or powder to which pharmacist add vehicle at time of dispensing
• Lotions- when applied to skin solvent evaporates leaving a light deposit of medicament on the surface

• Preparations for use on broken surfaces should be prepared hygienically to minimize the risk of infection