CALIFORNIA NORTHSTATE COLLEGE of PHARMACY

To Advance the Art and Science of Pharmacy

Liquid Dosage Form
"Suspensions
&
"Gels and Magmas"

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Key Concepts

- Why do we need Suspension dosage forms?
- How are suspensions formulated?
- Understand the difference between flocculated and deflocculated suspensions.
- What are gels and magmas? How are they formulated?

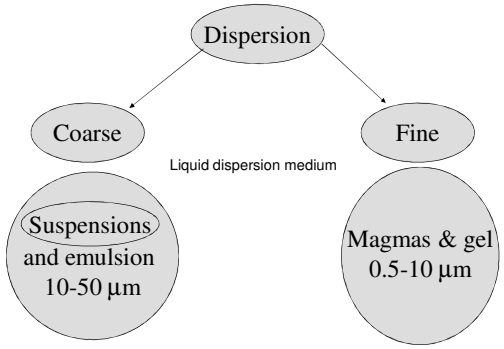
Colloidal dispersions

Particle size — Decreasing size →

Suspensions emulsions | Magmas & gels | microemulsions

Dispersions | **colloids** | **solutions**

Colloidal solutions



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Suspensions

Liquid dosage form containing finely divided drug solid particles (suspensoid) distributed uniformly throughout the vehicle in which the drug exhibits a minimum degree of solubility.

Suspensions are available as

– Ready to use

– Dry powder to be reconstituted

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Suspensions

Purpose of suspensions:

1. Drug is chemically unstable in solution.
2. Preferred over solid (children/elderly) ease of swallowing and larger range of dose adjustment.
3. Disagreeable taste of solution can be masked by suspension.

Example: chloramphenicol (bad taste) and chloramphenicol palmitate (suspension with masked taste).

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Suspension
Desired features

1. Settle slowly and readily re-disperse upon gentle shaking of the container.
2. Particle size should remain fairly constant throughout long periods of undisturbed standing.
3. Pour readily and evenly from the container.

Suspension
Formulation theory

- Sedimentation rate (stokes' law):
- $dx/dt = d^2(\rho_p-\rho_m)g/18\eta$,
- How to ↓ = dx/dt

v = velocity of settling ,
g = acceleration due to gravity,
d = diameter of particle,
ρ_p = density of particle,
ρ_m = density of medium, and
η = viscosity of medium

Suspension formulation

- Particle size: Uniform, acceptable size.
- Very small particles tend to form a cake, very large ones tend to sediment quickly.
- Particle shape is a factor in cake formation.
- Cake formation is an irreversible agglomeration of particles into crystals.
- It is hard to redisperse cake).

Flocculated suspensions

- Highly desirable:
- Floc or floccule: loose aggregation of particles held together by weak Van der Waals forces.
- Formation of flocs is a good way to prevent cake formation.
- Flocs: Settle quickly but incompletely, (large volume of sediment) they easily redisperse.

Suspension

Deflocculated system	***Flocculated system***
Small particles with high repulsive forces (high zeta potential)	Floccules (loose aggregates of particles held together by weak forces)
Suspensoid: Settles slowly Rate of sedimentation is slow.	Flocs settle quickly Rate of sedimentation is high.
Form a cake(closely packed).	Less likely to form a cake.
Small particles fill the spaces between large ones/ turbid supernatant.	High sediment volume/ clear supernatant.


Tight packing


loose packing

Flocculated system

- **Flocculation is achieved by the following:**

1. **Clay** eg bentonite acts as flocculating agent.
2. **pH** adjusted to the region of minimum solubility
3. **Electrolytes** reduce electrical barrier and repulsion between particles
4. **Surfactants** reduce interaction between particles and increase the sedimentation rate

Dispersion medium

- Suspending agents are added to the dispersion medium to increase viscosity and help suspend the suspensoid.
  - Carboxymethycellulose (CMC).
  - Xanthan gum.
  - Bentonite.
  - Microcrystalline cellulose.
  - Problems created by some suspending agents:
    - complexation with drug
    - ↑ viscosity tremendously

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Dispersion medium

- The ability of the dispersion medium to support the suspensoid is dependent on the following factors:

1. Density of the suspensoid.
2. Flocculated vs deflocculated.
3. The amount of material requiring support.

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Preparation of Suspension

1. Reduce particle size.
2. Add wetting agent: alcohol, glycerin, propylene glycol.
   - Displace the air around the particles, disperse the particles and allow penetration of dispersion medium.
3. Add the flocculating agent, clay such as bentonite magma.
4. Dissolve water soluble ingredients in the dispersion medium
5. Add suspending agent to the dispersion medium.
6. Add dispersion medium to wetted particles in portions.

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Extemporaneous compounding

- Stability of the drug in the liquid should be checked.
- Active ingredient source can be from capsule or tablet.
- Neonate: no alcohol, preservative or flavor. (supply as needed).
- Light resistant container, and refrigerated.
- Patient advised to shake well and watch for color change.

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Packaging

- Container with adequate air space for shaking
- Protect from heat, freeze or light.

- Videos to watch

1. http://pharmlabs.unc.edu/video2.php?legacy/2001_susp1.flv
2. http://pharmlabs.unc.edu/video2.php?legacy/2001_susp2.flv

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Gels and Magmas

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Gels

- Gels are semisolid systems made using substances (called gelling agents) that when hydrated and dispersed in dispersing medium or dissolved undergo a high degree of cross-linking or association.
- This cross-linking or association of the dispersed phase will alter the viscosity of the dispersing medium(↑) and confer rigidity to the dispersion.
- Please watch video in the following link:

http://pharmlabs.unc.edu/labs/gels/gel.htm

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Colloid=dispersed phase

Lyophilic colloids
solvent loving
disperse readily

Lyophobic colloids
solvent hating
must be "encouraged" pulverization, chemical reaction
Association or Amphiphilic colloid
Is formed by grouping or association of molecules that exhibit both lyophilic and lyophobic properties.

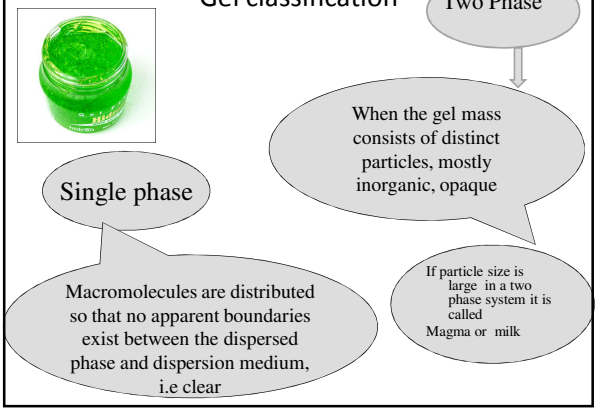
Colloid may be lyophilic or lyophobic depending on dispersion medium (solvent)

Increasing concentration of colloidal phase

sol → gel

Liquid sol

Semisolid
Or
solid dipersion



Properties of gels

Linked to unique molecular and physical structure

Thixotropy

Imbibition

Swelling

Syneresis

Thixotropy
Change from semisolid to liquid state with increase in shear stress(agitation) or increased temperature. Will resume their solid state after remaining undisturbed for a period of time.

Imbibition
Taking up of a certain amount of liquid i.e incorporation of dispersion medium without noticeable increase in volume.

Swelling
Taking up of a liquid /Incorporation of dispersion medium with noticeable increase in volume.

Syneresis (weeping)
Separation of dispersion medium as a result of gel contraction. Due to interaction of dispersed phase particles. Form of instability.
Xerogel
Gel framework from which dispersion medium has been removed

Common Gelling agent

- Gelatin
- Acacia
- trgacanth
- alginic acid
- bentonite
- Carbomers (Carbopols®)
- carboxymethyl cellulose (CMC),
- ethylcellulose (EC),
- Methylcelluslose (MC)
- hydroxyethyl cellulose,
- poloxamers (Pluronics®),
- Each gelling agent has its unique properties, but there are some generalizations that can be made:

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Gelling agents

1. Problem: Powdered substances that absorb water but do not dissolve. They are prone to clumping

- Solution: sieve the agents onto the surface of the medium a little at a time as the medium is stirred. Using glycerin or other wetting agent will sometimes minimize clump formation.
- Question: What are examples of wetting agents?

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Gelling agents

2. Some gelling agents are more soluble in cold water than in hot water.

- **Methylcellulose and poloxamers**
  Dispersed in **cold** water then **heated**.

- **Gelatin, bentonite and sodium carboxymethylcellulsoe**
  Dispersed in **hot** water then **cooled** to form gels
  Or moistened with organic liquid followed by addition of hot water
- Carbomers, tragacanth, and alginic acid gels are made with tepid water.

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Gelling agents

3. Gelling agents such as (carbomers) require a "neutralizer" or a pH adjusting chemical to create the gel after the gelling agent has been wetted in the dispersing medium.

- e.g of pH adjusters: sodium hydroxide or triethanolamine.

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Gelling agents

4. Most gelling agents require 24 to 48 hours to completely hydrate and reach maximum viscosity and clarity.

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Gelling agents

5. Gels are usually prepared by adding the active drug before the gel is formed if the drug doesn't interfere with the gel formation.
6. Gelling agents are used in concentrations of 0.5% to 10%, depending on the agent.

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Gel preparation

- Please watch the video in the following link

http://pharmlabs.unc.edu/video1.php?lidocaine_gel.flv

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Example of Magmas

1. **Bentonite magma NF**
2. **Aluminum Hydroxide gel, USP**
3. **Milk of Magnesia**

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Bentonite magma NF

- 5% bentonite(colloidal hydrated aluminium silicate) in water
- Bentonite can swell x 12 its volume
- Swelling test is required by USP
- Used as suspending agent or flocculating agent.
- Thixotropic gel above 4%

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Aluminum Hydroxide gel, USP

– Antacid for hyperacidity and peptic ulcers

– Interacts with tetracycline (chelation) and may adsorb some drugs.

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Milk of Magnesia

– 7-8.5% magnesium hydroxide

– Prepared by chemical reaction NaOH + $MgSO_4$ or direct hydration of magnesium hydroxide

– Water may separate upon standing

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