Pharmaceutical Technology

Coarse Dispersion

Suspensions

Suspensions

- Suspension is a coarse dispersion containing finely divided insoluble material suspended in a liquid medium or available in a dry powder to be distributed in the liquid when desired, this in case the stability of powder is low.
- Suspension consist of two phases; solid dispersed phase and dispersion medium, which is liquid and may be oil or water.
- The particle size of coarse particles usually 10-50 µm in size.
- Suspension could be administer orally, topically, parenterally (except I.V), and for ophthalmic administration.

- Some suspensions preparations are available in:

1. Ready-to use form- that is, already distributed through a liquid vehicle with or without stabilizers and other pharmaceutical additives.
2. Other preparation are available as dry powders intended for suspension in liquid vehicles. This type of product generally is a powder mixture containing the drug and suitable suspending and dispersing agents, which upon dilution and agitation with a specified quantity of vehicle (generally purified water) results in the formation of a suspension suitable for administration.

- This type of preparation is designated in the USP by a title of the **"drug powder for oral suspension".**
- Prepared suspensions not requiring reconstitution at the time of dispensing are simply designated as **"drug oral suspension"**

Examples of suspension preparations

FIGURE 14.2 Commercial antibiotic preparation for oral suspension following reconstitution with purified water. *Left*, dry powder mixture. *Right*, suspension after reconstitution with the specified amount of purified water.

Reasons for suspensions

- There are several reasons for preparing suspensions

1. Certain drugs are chemically unstable when in solution but stable when suspended. In instances such as this, the suspension insures chemical stability while permitting liquid therapy.
2. For many patients, the liquid form is preferred over the solid form of the same drug because of the ease of swallowing liquids and flexibility in the administration of a range of dose. This particularly advantageous for infants, children and the elderly.
3. The disadvantage of a disagreeable taste of certain drugs when given in solution form is overcome when the drug is administered as undissolved particles of an oral suspension.

- Suspension given as intramuscular injection, because absorption from a suspension is normally slower than from solution at the injection site, and thus prolong the time of action of drug.
- By using an oil further slower down absorption and provide sustained or prolong action.
- Externally used suspension are either formulated in aqueous or oily vehicle depending on the intended of their use.
- For parenteral and ophthalmic use suspension should be sterile, and smaller particle size (less than 10µm)

Features desired in a pharmaceutical suspension

1. A properly prepared pharmaceutical suspension should settle slowly and should be readily redispersed upon the gentle shaking of the container.
2. The characteristics of the suspension should be such that the particle size of the suspensoid remains fairly constant throughout long periods of undisturbed standing.
3. The suspension should pour readily and evenly from its container.

What are the properties of ideal suspension

- The properties of acceptable ideal suspension are:

1. It should have a uniform particle size so that each particle acts as other particles producing constant behavior for the suspension as a whole.
2. No particle-particle interaction (no aggregation) and no clamping should occur; such suspension is called monodispersed suspension.
3. Their should be no sedimentation, the particles should either be stationary or moved randomly through out the dispersion so that there is always uniform dispersion of the drug.
4. The suspension should not be too viscous and pour freely.
5. It should have an agreeable odor, color, and taste.
6. It must not be decomposed or support microbial growth during storage.

- In other words suspension must provide a uniform therapeutically active pleasant dose that is convenient to take by the patient.
- The properties or parameters that could be controlled in an attempt to reach ideal behavior are:

1. Particle size: it is desirable to have small particle size.

➢ In colloidal system Brownian movement keeps the particles movement, while in coarse dispersion as in suspension the particle size are too large for the terminal energy to keep them suspended and their will be always some degree of sedimentation.

- The terminal velocity with which particles settle in a coarse dispersion is expressed by stokes law:

$$\frac{dx}{dt} = V = \frac{d^2(\rho - \rho_0)\, g}{18\,\eta}$$

- Where, V is the terminal velocity or sedimentation rate of fall of an average particle in the dispersion (perfectly spherical particles).
- d is the mean particle diameter.
- ρ is the density of the particles
- ρ_0 is the density of the dispersion medium.
- G is acceleration constant due to gravity
- η is the viscosity of the dispersion medium.

- Diameter is important factor because it is raised to the 2nd power.
- So by reducing the diameter by reducing particle size using mortar and pestle the terminal velocity is decreased. Thus decrease sedimentation of particles.

- Mills is used for hard substances like crystals.

2. Particle movement and density and viscosity of medium.

A. If the density of solid equal the density of the dispersion medium then the rate of sedimentation V equal zero, which means ideal condition; **but this condition is hard to get, because**

- it is difficult to prepare a suspension with density great enough to match the density of a solid.
- Also the density of a solution is affected by the temperature, so density matching is useful only at control temperature.

B. Viscosity adjustment is better control of movement of sedimentation that by increasing it to a certain extent will decrease the sedimentation rate because there is an inverse proportion between them referring to Stokes' law, and this done by

- adding a thickening or suspending agent to increase the viscosity of the dispersion medium.
- Hydrophilic colloids are commonly used specially gums; cellulose, clays.

Example

- A powder has a density of 1.3 g/cc and is available as a powder with an average particle diameter of 2.5 microns (assuming the particles to be spheres). According to stokes Equation, this powder will settle in water (viscosity of 1cps assumed)at a rate of:

$$V = \frac{(2.5 \times 10^{-4})^2 (1.3 - 1.0)(980)}{18 \times 0.01} = 1.02 \times 10^{-4} cm/sec$$

- If the particle size of the powder is reduced to 0.25 μ and water is still used as the dispersion medium, the powder will now settle at a rate of:

$$V = \frac{(2.5 \times 10^{-5})^2(1.3 - 1.0)(980)}{18 \times 0.01} = 1.02 \times 10^{-6} cm/sec$$

- As is evident, a decrease in particle size by a factor of 10 results in reduction in the rate of settling by a factor of 100,
- This enhanced effect is a result of the “d” factor in stokes’ equation being squared.

- Now, if a a different dispersion medium, such as glycerin is used in place of water, a further decrease in settling will result.
- Glycerin has a density of 1.25g/cc and a viscosity of 400 cps. The larger particle size powder (2.5 μ) will settle at a rate of:

$$v = \frac{(2.5x10^{-4})(1.3 - 1.25)(980)}{18\ x\ 4} = 4.25\ x\ 10^{-8}\ cm/sec$$

- The smaller particle size (0.25μ) powder will now settle at a rate of:

$$v = \frac{(2.5x10^{-5})(1.3 - 1.25)(980)}{18\ x\ 4} = 4.25\ x\ 10^{-10}\ cm/sec$$

- A summary of these results is shown in the following table:

Condition	Rate of settling (cm/sec)
2.5µ powder in water	1.02×10^{-4}
0.25µ powder in water	1.02×10^{-6}
2.5µ powder in glycerin	4.25×10^{-8}
0.25µ powder in glycerin	4.25×10^{-10}

- As is evident from this table, a change in dispersion medium results in the greatest change in the rate of settling of particles. Particle size reduction can contribute significantly to suspension stability. These factors are important in the formulation of physically stable suspensions.

3. Concentration of solid:

- High concentration of solid increase the possibility of particle-particle collision, but will also promote particle-particle interaction.
- The concentration of solid is usually fixed in prescription and can not be changed to affect the stability purpose.

4. Particle-particle interaction

- Particle-particle interaction controls the deflocculation and flocculation system. Particle-particle interaction must be avoid because the aggregation of small particle will behave as single large particle and tend to settle at increase rate of flocculation.
- If particle have similar electric charge then they preventing from coming together. It is usually for solid particles dispersed in aqueous media to carry the same type of charge.

- There are varies ways where charge can developed:

1. Ionization of groups on solid surface.
2. Adsorption of surfactant on solid surface.
3. Adsorption of electrolyte from solution.

- The last two methods are the most common. The sign of charge develop on the surface of particle can be predicted if the charge result from adsorption of sodium lauryl sulphate on the solid will make the solid carry negative charge.
- The sign of charge which develop from electrical charge adsorption depend on the ion adsorption from the solution and it is difficult to be predicated.
- The magnitude of charge is define as: the difference in electrical potential between the charge of solid surface and bulk of the solution.