Pharmaceutical technology

Suspensions

The design of acceptable suspensions

Preparation of suspensions

Types of suspension

By

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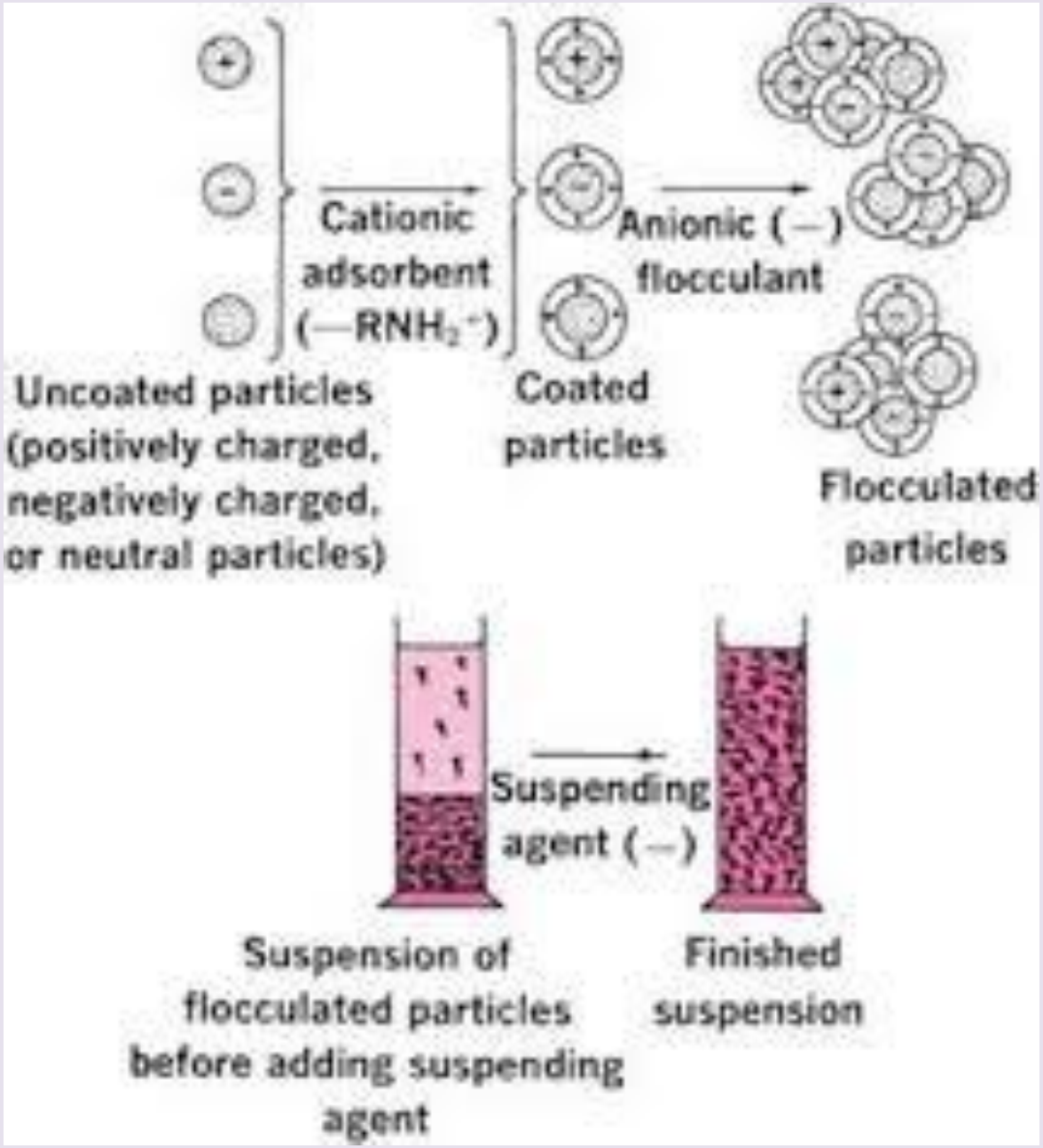
The Design of Acceptable Suspensions

- In practice, a highly flocculated suspension cannot be marketed as such because the particles settle rapidly and ordinarily leave a supernatant layer which is unsightly.
- Consequently, a suspending agent with appropriate rheological properties such as carboxymethylcellulose, bentonite, Carbopol or a combination of these materials is added to produce a final product with sufficient structure to support flocs but not so rigid as to prevent flow when the material is agitated and poured from the container.

- Most suspending agents are belong to the class of negatively charged hydrophilic colloids and when added to suspension containing positively charged flocculating agents they tend to produce an unsightly stringy mass of coagulated suspending agent which settles rapidly and fails in its suspending action.
- Phosphate ions and other negatively charged agents which are used to flocculate positively charged particles are compatible with the commonly used suspending agents and they have no serious problems.

- The difficulty with negatively charged drugs which may be overcome by adsorbing onto the drug particles certain agents which reverse the surface charge from negative to positive.
- ✓ This can be accomplished by the use of fatty acid amines, gelatine at a pH below its isoelectric point or other positively charged molecules, then
- ✓ KH2PO4 or another anionic flocculating agent can bring about the appropriate flocculation.

- These flocculating agents are compatible with the commonly used suspending agents.
- The technique of adsorbing a positively charged substance on suspension particles followed by flocculation with a negative ion and finally stabilization of the product with a negatively charged suspending agent is illustrated in the following Figure.


Cationic
adsorbent
(—RNH$_2$$^+$)
Anionic (–)
flocculant
Uncoated particles
(positively charged,
negatively charged,
or neutral particles)
Coated
particles
Flocculated
particles
Suspending
agent (–)
Suspension of
flocculated particles
before adding suspending
agent
Finished
suspension

- The steps in this scheme are as follows:

1- The particles irrespective of their charge are coated with a (+ve) agent which must be checked for lack of toxicity before use.

2- The particles are flocculated by the use of a (-ve) agent to bring the product into the noncaking zone.

3- Finally, a minimum amount of a suspending agent is added and the suspension is again observed for optimum flocculation and freedom from caking.

Preparation of suspensions

- In the preparation of a suspension, the pharmacist must be familiar with the characteristics of both the intended dispersed phase and the dispersion medium.
- In some instances, the dispersed phase has an affinity for the vehicle to be employed and is readily wetted by it. Other drugs are not penetrated easily by the vehicle and have a tendency to clump together or to float on the vehicle.
- In the latter case, the powder must first be wetted to make it more penetrable by the dispersion medium. Alcohol, glycerin, propylene glycol, and other hygroscopic liquids are employed as wetting agents when an aqueous vehicle is to be used as the dispersion phase.

- In large-scale preparation of suspensions, wetting agents are mixed with the particles by an apparatus such as a colloid mill; on a small scale in the pharmacy, they are mixed with a mortar and pestle.
- Once the powder is wetted, the dispersion medium (to which have been added all of the formulation's soluble components, such as colorants, flavorants, and preservatives) is added in portions to the powder, and the mixture is thoroughly blended before subsequent additions of vehicle.
- A portion of the vehicle is used to wash the mixing equipment free of suspensoid, and this portion is used to bring the suspension to final volume and ensure that the suspension contains the desired concentration of solid matter.
- The final product is then passed through a colloid mill or other blender or mixing device to ensure uniformity.

- Whenever appropriate, suitable preservatives should be included in the formulation of suspensions to preserve against bacterial and mold contamination.
- An example formula for an oral suspension is the antacid aluminum hydroxide, the preservatives are methylparaben and propylparaben, and syrup and sorbitol solution provide the viscosity and sweetness.
- Aluminum hydroxide compressed gel 326.8 g
- Sorbitol solution 282.0 mL
- Syrup 93.0 mL
- Glycerin 25.0 mL
- Methylparaben 0.9 g
- Propylparaben 0.3 g
- Flavor qs
- Purified water, to make 1,000.0 mL

Types of suspension

I. **According to route of administration:**

1. Oral suspensions should be taken by oral route and therefore must contain suitable flavoring and sweetening agents.
2. Topical suspensions meant for external application and therefore should be free from gritty particles
3. Parenteral suspensions should be sterile and should possess property of syringability.
4. Ophthalmic suspensions should be sterile and should possess very fine particles
5. Otic suspension
6. Rectal suspension

II. According to the size of solid particles

1. Coarse suspension (> 1 µm)
2. Colloidal suspension (< 1 µm)
3. Nano suspension (10-100 nm)

III. According to nature of sediment:

1. Flocculated suspension
2. Deflocculated suspension

IV. According to proportion of solid particles

1. Diluted suspension (2 to 10% w/v solid), e.g., predinsolone acetate suspension
2. Concentrated suspension (50% w/v solid), e.g., zinc oxide suspension

V. According to nature of dispersed phase and methods of preparation: The suspensions are classified as suspensions containing

1. diffusible solids,
2. indiffusible solids,
3. poorly wettable solids,
4. precipitate forming liquids
5. Dispersion of oils in inhalations
6. products of chemical reactions.

- A suspension containing diffusible substances:

1. They contain insoluble but easily dispersible solids
2. These solid are light and easily wettable substances
3. Readily mixed with water and on shaking diffuse evenly throughout the liquid long enough to ensure even distribution and a dose to measure.
4. The sediment forms slowly

- Examples: light kaolin, magnesium tri silicate, light calcium carbonate, magnesium carbonate

- Suspensions containing indiffusible solids

1. These solids are insoluble powders and will not remain evenly distributed in a vehicle long enough to ensue uniformity of dose

➢ For example zinc oxide, calamine powder, aspirin and phenobarbitone

2. The sediment too rapidly forms and requires the addition of other materials to reduce sedimentation rate to an acceptable level.

➢ For example thickening agent to increase viscosity, decrease sedimentation rate and avoid collision of particles.

- Suspensions containing poorly wettable substances

1. The particles are both insoluble and poorly wettable in water.

➢ Examples: sulfur and hydrocortisone

2. The interfacial tension between particles and water is high, i.e., not diffusible in water.
3. Wetting agents (e.g., surfactants) are added to decrease interfacial tension, thus affinity of the particles to the surrounding environment is increased and the interparticulate force is decreased.

- Suspensions of precipitate forming liquids

1. Resinous materials when mixed with water become precipitated.

➢ Examples: compound benzoin tincture, Tolu tincture

2. This type of suspension requires addition of protective colloid (thickening agent) .

Ingredients for formulation of suspensions

1. Wetting agents: these agents are added to disperse solids in continuous phase.
2. Flocculating agents: these agents are added to floc the drug particles
3. Thickeners: these agents are added to stabilize the suspension.
4. Buffers and pH adjusting agents: these agents are added to adjust the suspension to a desired pH range.
5. Osmotic agents: these agents are added to adjust osmotic pressure comparable to biological fluid.
6. Coloring agents; these agents are added to impart desired color to suspension and improve elegance.
7. Preservatives: these agents are added to prevent microbial growth.
8. External liquid vehicle: these agents are added to construct structure of the final suspension.