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PHARMACEUTICS – I

UNIT 3

TOPIC :

- **Biphasic liquids :**
- **Suspensions :** Definition, advantages and disadvantages, classifications, Preparation of suspensions; Flocculated and Deflocculated suspension & stability problems and methods to overcome.

Biphasic liquids

→ Biphasic liquid dosage forms are heterogeneous systems composed of two immiscible phases, typically a dispersed phase and a continuous phase. These preparations require shaking before use to ensure uniform dosing.

→ They are used when the drug is insoluble in the vehicle or needs to be stabilized in a two-phase system.

Advantages

- ✓ Can deliver insoluble drugs
- ✓ Mask bad taste of oily drugs (emulsions)
- ✓ Provide localized action (e.g., on skin)
- ✓ Some allow for sustained or controlled release

Disadvantages

- Require shaking before use for dose uniformity
- Risk of physical instability (e.g., caking or creaming)
- Shorter shelf life
- May need special storage (e.g., avoid freezing)
- More complex formulation

Suspensions

→ Suspensions are biphasic liquid dosage forms in which insoluble solid drug particles are dispersed uniformly in a liquid vehicle. These are not true solutions, and particles settle on standing but can be redistributed on shaking.

Advantages

- Suitable for poorly soluble drugs
- Can mask unpleasant taste
- Preferred for children, elderly who cannot swallow solids
- Allows controlled or slow release in some injectable forms

Disadvantages

- Physical instability (settling, caking)
- Requires shaking before use
- Less accurate dosing if not well mixed
- Bulkier and less stable than tablets/capsules

Preparation of Suspensions

1. **Wetting the Drug**:
   Insoluble powders are mixed with a wetting agent (like glycerin, Tween 80) to allow dispersion in the vehicle.
2. **Dispersion into Vehicle**:
   Slowly add vehicle (usually water) while stirring.
3. **Addition of Suspending Agent**:
   Agents like CMC, bentonite, tragacanth are added to reduce sedimentation.
4. **Homogenization (Optional)**:
   For uniform particle size and better suspension.
5. **Flavoring, Sweetening, Coloring (for oral)**:
   For palatability and patient compliance.

6. **Preservatives**:
   To prevent microbial growth (e.g., parabens, sodium benzoate).
7. **Filling and Packaging**:
   Store in wide-mouthed amber bottles labeled: "Shake well before use".

Classification

1. Based on general classes:

Oral Suspensions :

e.g. Paracetamol suspension

Antacid suspension

Antibiotic suspension

Anthelminitics suspension

Laxative suspension

Topical suspensions : (Externally applied)

e.g.- Calamine lotion.

Parenteral suspension :

e.g. Cholera vaccine, insulin, Zinc suspension.

2. Based on proportion of solid:

Dilute suspension : (2 to 10% w/v solid)

E.g. Cortisone acetate, Prednisolone acetate.

Concentrated suspension : (50% w/v)

E.g. Zinc oxide suspension.

3. Based on deteriorate nature of solid particles

1. Flocculated

2. Deflocculated

1. Flocculated Suspension

- A flocculated suspension is a type of biphasic suspension in which the insoluble particles form loose, fluffy aggregates known as flocs, held together by weak van der Waals forces or electrostatic interactions. These aggregates settle rapidly but can be easily redispersed by shaking.

2. Deflocculated suspension

- A deflocculated suspension is a biphasic liquid system in which insoluble drug particles remain dispersed individually in the dispersion medium. These particles do not form aggregates or flocs, and thus settle slowly, but may form a hard, compact cake that is difficult to redisperse.

Flocculated suspension	Deflocculated suspension
1. Particles exist as loose aggregates.	1. Particles exist as separate entity.
2. Rate of sedimentation is high.	2. Rate of sedimentation is low.
3. Sediment formed rapidly.	3. Sediment formed slowly.
4. Consist of loosely packed particles possessing a Scaffolding like structure a hard dense cake does not form and the sedimentation can easily redispersed.	4. Sediment becomes very closely packed as the repulsive forces between the particles are overcome a hard cake is formed which is difficult to redisperse.
5. Elegant preparation are obtained due to uniform distribution of loosely bonded flocs.	5. Unsightly preparation result due to the formation of sedimentation.

Stability Problems in Suspensions

1. **Sedimentation**
   - Particles settle at the bottom due to gravity.
   - Leads to uneven drug distribution.
   - Solution: Reduce particle size, add suspending agents, increase viscosity.
2. **Caking**
   - Hard, compact sediment formed after prolonged standing.
   - Difficult or impossible to redisperse.
   - Solution: Use flocculating agents, avoid over-reducing particle size.
3. **Crystal Growth (Ostwald Ripening)**
   - Small particles dissolve and redeposit on larger ones.
   - Increases particle size and risk of caking.
   - Solution: Use uniform particle size, add stabilizers, store at stable temperature.
4. **Poor Redispersibility**
   - After settling, particles do not mix uniformly upon shaking.
   - Leads to inaccurate dosing.
   - Solution: Form flocculated suspensions, use proper suspending agents.
5. **Flocculation/Deflocculation Imbalance**
   - Over-flocculation: quick sedimentation
   - Under-flocculation: hard cake formation
   - Solution: Optimize zeta potential, adjust pH and electrolyte concentration.
6. **Microbial Contamination**
   - Bacterial or fungal growth in aqueous suspensions.
   - Causes spoilage, turbidity, or odor.
   - Solution: Use preservatives, follow aseptic processing, proper storage.

Methods to Overcome Stability Problems in Suspensions

1. **Reduce Particle Size**
    - Use micronization or ball milling.
    - Slows sedimentation and improves uniformity.
2. **Use Suspending Agents**
    - Increase viscosity to reduce settling.
    - Examples: Carboxymethylcellulose (CMC), methylcellulose, xanthan gum, bentonite.
3. **Add Flocculating Agents**
    - Promote loose aggregation of particles to prevent caking.
    - Examples: Electrolytes (NaCl, KCl), polymers (gelatin), surfactants (Tween 80).
4. **Ensure Uniform Particle Size Distribution**
    - Prevents Ostwald ripening (crystal growth).
    - Improves stability and prevents caking.
5. **Control Temperature During Storage**
    - Prevents solubility fluctuations that cause crystal growth.
    - Store at recommended room temperature or cool conditions.
6. **Add Preservatives**
    - Prevent microbial growth in aqueous base.
    - Examples: Methylparaben, sodium benzoate, benzoic acid.
7. **Use Proper Packaging**

- Amber-colored, wide-mouthed bottles with airtight caps.
- Label with "**Shake well before use**" to ensure patient compliance.