BIPHASIC DOSAGE FORMS SUSPENSIONS AND EMULSIONS
UNIT 7

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Suspensions

Heterogenous biphasic dosage form

-- solid is dispersed in liquid medium. Dispersed phase, dispersion medium

PROPERTIES:

--Rapid settling

---Easily redisperdible,pourable

---if parenteral—flow through syringe needle

---if external---spread easily

---Pleasing in colour , odour, appearance.

Types:

---Deflocculated

---Flocculated

PROPERTIES:

---Interfacial property

---Electrical property

- Dispersions containing coarse particles, usually **10 to 50 um** in size, are referred to as **coarse dispersion.**
- Dispersions containing particles of smaller size are termed **fine dispersions (0.5 to 10 um)**

Suspensions

In general sense, Suspension may include:

- **Gels**
- **Lotions**
- **Magmas and Milk**
- **Mixtures**

Reasons for Suspensions

- Certain drugs are chemically unstable when in solution but stable when suspended.
- Suspension insures chemical stability while permitting liquid therapy.
- Many patients prefer liquid form than solid forms for swallowing.
- Convenience in administration
- Safety and convenience of liquid doses for infants and children.
- Disagreeable taste of certain drugs when given in solution is negligible when the drug is administered as undissolved particles of a suspension, **e.g chloramphenicol**

Features Desired in a Pharmaceutical Suspensions

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

Physical Features of the Dispersed Phase of a Suspension

Good pharmaceutical suspensions, the particle diameter is between 1 to 50.

Particle size reduction is generally accomplished by dry-milling prior to the incorporation of the dispersed phase into the dispersion medium.

One of the methods of producing fine drug powders of about 10 to 50 um size is micropulverization.

For still finer particles, under 10 um, the process of fluid energy grinding, sometimes referred to as jet-milling or micronizing.

Dispersion Medium

- Suspending agents are added to the dispersion medium to lend its structure to assist in the suspension of the dispersed phase
- **Examples:**

  Carboxymethylcelulose

  Methylcellulose

  Microcrystalline cellulose

  Polyvinyl pyrolidone,

  Xanthan gum

  Bentonite

SEDIMENTATION

F- Sedimentation volume

Vu-Ultimate volume of suspension

F= Vu/Vo

Vo- orginal volume of suspension.

DEGREE OF FLOCCULATION

Ratio of sedimentation volume of flocculated suspension to the sedimentation volume of deflocculated suspension.

Types:

Suspension containing diffusabile solids

Suspensions containing indiffusible solids

Precipitate forming suspensions

- , polymers.

- Formulation

---use of structured vehicles to keep the deflocculated suspension.

---use the principle of flocculation in order to assure easy redispersion

---Controlled flocculation

by-electrolytes,surfactants

Packaging and Storage of Suspensions

- All suspensions should be packaged in containers having:

1. **Adequate airspace** above the liquid to permit adequate shaking.

2. Should be provided in **wide mouth** containers to permit the prompt and ease of removal of the suspension.

3. Store in **tight containers** protected from freezing, excessive heat and light.

4. Suspensions **should be shaken** before use.

EVALUATION

- Sedimentation method
- Rheological method
- Electrokinetic method
- Micrometric method

EMULSIONS

EMULSIONS

- Introduction
- Types of emulsions
- Emulsifying agents
- Methods of Preparation of Emulsions
- Tests for emulsion types
- Emulsion Stability
- Phase Inversion
- Emulsion Breaking
- General Guidelines

Introduction

EMULSIONS

- An emulsion is a dispersion in which the dispersed phase is composed of small globules of a liquid distributed throughout a vehicle in which it is immiscible.

Classification of emulsions :

- Based on dispersed phase

  Oil in Water (O/W): Oil droplets dispersed in water

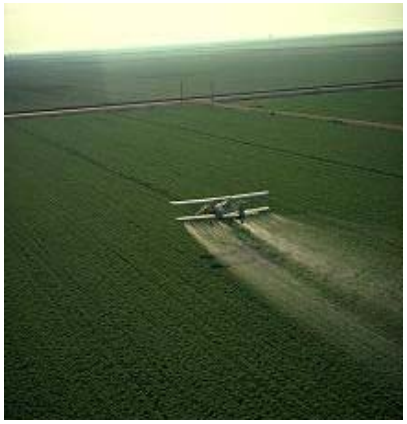
  Water in Oil (W/O): Water droplets dispersed in oil

- Based on size of liquid droplets

  0.2 – 50 mm Macroemulsions (Kinetically Stable)

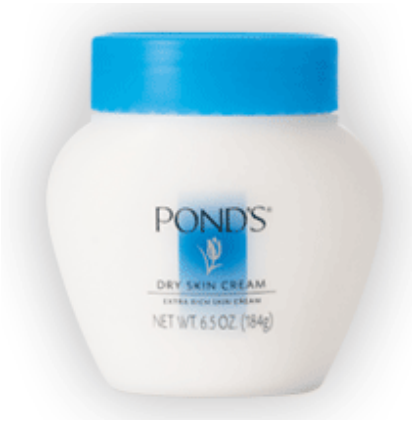
  0.01 – 0.2 mm Microemulsions (Thermodynamically Stable)

Emulsions encountered in everyday life!



Pesticide

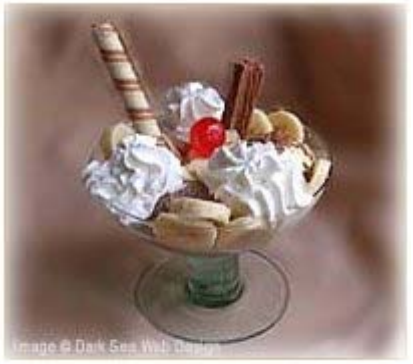
Asphalt



Skin cream

Metal cutting oils

Margarine



Ice cream

Stability of emulsions may be engineered to vary from seconds to years depending on application

General Types of Pharmaceutical Emulsions:

- 1) Lotions
- 2) Liniments
- 3) Creams
- 4) Ointments
- 5) Vitamin drops

Theories of Emulsification:

- 1) Surface Tension Theory:

  - lowering of interfacial tension.

- 2) Oriented-Wedge Theory:

  - mono molecular layers of emulsifying agents are curved around a droplet of the internal phase of the emulsion.

- 3) Interfacial film theory:

  - A film of emulsifying agent prevents the contact and coslescing of the dispersed phase.

Emulsifying Agents:

It is a substance which stabilizes an emulsion .

Pharmaceutically acceptable emulsifiers must also :

- be stable .
- be compatible with other ingredients .
- be non – toxic .
- possess little odor , taste , or color .
- not interfere with the stability of efficacy of the active agent .

Emulsifying Agents:

- 1) Carbohydrate Materials:

  - Acacia, Tragacanth, Agar, Pectin. o/w emulsion.

- 2) Protein Substances:

  -Gelatin, Egg yolk, Caesin o/w emulsion.

- 3) High Molecular Weight Alcohols:

  - Stearyl Alcohol, Cetyl Alcohol, Glyceryl Mono stearate o/w emulsion, cholesterol w/o emulsion.

- 4) Wetting Agents:

  Anionic, Cationic, Nonionic

  o/w emulsion

  w/o emulsion

- 5) Finely divided solids:

  Bentonite, Magnesium Hydroxide, Aluminum Hydroxide o/w emulsion.

Methods of Preparation of Emulsions:

1) Continental or Dry Gum Method:

"4:2:1" Method

4 parts (volumes) of oil

2 parts of water

1 part of gum

2) English or wet Gum Method:

4 parts (volumes) of oil

2 parts of water

1 part of gum

3) Bottle or Forbes Bottle Method:

useful for extemporaneous preparation of emulsion from volatile oils or oleaginous substance of low viscosity.

powdered acacia

\+ Dry bottle

2 parts of oil

This method is not suitable for viscous oils (i.e. high viscosity oil).

Emulsion Type and Means of Detection:

Tests for Emulsion Type (W/O or O/W emulsions)

1) Dilution Test:

- o/w emulsion can be diluted with water.
- w/o emulsion can be diluted with oil.

2) Conductivity Test:

Continuous phase water > Continuous phase oi

3) Dye-Solubility Test:

- water soluble dye will dissolve in the aqueous phase.
- oil soluble dye will dissolve in the oil phase.

4) Refractive index measurement

5) Filter paper test

Emulsions are Kinetically Stable!

Rate of coalescence – measure of emulsion stability.

It depends on:

(a) **Physical nature of the interfacial surfactant film**

For Mechanical stability, surfactant films are characterized by strong lateral intermolecular forces and high elasticity (Analogous to stable foam bubbles)

(b) Electrical or steric barrier

Significant only in O/W emulsions.

In case of non-ionic emulsifying agents, charge may arise due to

(i) adsorption of ions from the aqueous phase or

(ii) contact charging (phase with higher dielectric constant is charged positively)

No correlation between droplet charge and emulsion stability in W/O emulsions

Steric barrier – dehydration and change in hydrocarbon chain conformation.

(c) Viscosity of the continuous phase

(many emulsion are more stable in concentrated form than when diluted.)

Viscosity may be increased by adding natural or synthetic thickening agents.

(d) Size distribution of droplets

Emulsion with a fairly uniform size distribution is more stable

(e) Phase volume ratio

As volume of dispersed phase ↑ stability of emulsion ↓

(eventually phase inversion can occur)

(f) Temperature

Temperature ↑, usually emulsion stability ↓

Temp affects – Interfacial tension, *D*, solubility of surfactant, viscosity of liquid, phases of interfacial film.

Inversion of Emulsions (Phase inversion)

O/W→ W/O

1. The order of addition of the phases

   W →O + emulsifier → W/O

   O →W + emulsifier → O/W

2. Nature of emulsifier

   Making the emulsifier more oil soluble tends to produce a W/O emulsion and vice versa.

3. Phase volume ratio

   Oil/Water ratio↑ →W/O emulsion and vice versa

4. Temperature of the system

   ↑Temperature of O/W makes the emulsifier more hydrophobic and the emulsion may invert to W/O.

5. Addition of electrolytes and other additives.

   Strong electrolytes to O/W (stabilized by ionic surfactants) may invert to W/O

   Example. Inversion of O/W emulsion (stabilized by sodium cetyl sulfate and cholesterol) to a W/O type upon addition of polyvalent Ca.

Emulsion Breaking

Separation of the internal phase from the external phase is called BREAKING of the emulsion. This is irreversible.

- Protect emulsions against the extremes of cold and heat.
- Emulsions may be adversely affected by microbial contamination.

General Guidelines:

1. Type of emulsion determined by the phase in which emulsifier is placed.

2. Emulsifying agents that are preferentially oil soluble form W/O emulsions and vice versa.

3. More polar the oil phase, the more hydrophilic the emulsifier should be. More non-polar the oil phase more lipophilic the emulsifier should be.