Disperse Systems - Emulsions

Objectives:

After reading this topic, the student will be able to:
-Define the pharmaceutical emulsions

-Distinguish between the different types of pharmaceutical emulsions based on their physical state

-Differentiate between the different types of pharmaceutical emulsions based on their intended uses.

-Compare and contrast emulsification theories: surface tension, oriented wedge, and Interfacial film.

-Compare and contrast various types of emulsifying agents

-Identify the methods and techniques employed in preparing of stable pharmaceutical emulsions.

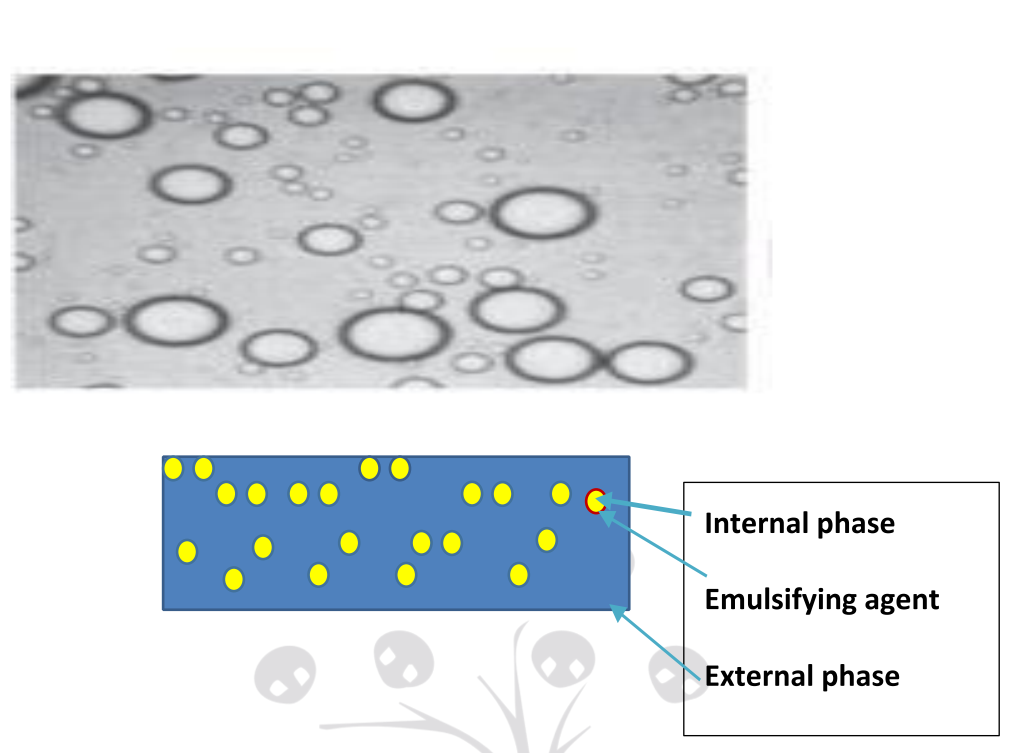
-Identify the factors that affect the stability of emulsion, such as temperature and environmental conditions.

Emulsions

Emulsion is a thermodynamically unstable disperse system consisting of two immiscible liquids, one of which is distributed throughout the other in minute globules (droplets).

-In emulsion terminology, the dispersed phase is the internal phase, and the dispersion medium is the external or continuous phase.

Generally, to prepare a stable emulsion, **a third phase, an emulsifying agent**, is necessary.



◇ Emulsion Types

1- **Oil-in-Water (o/w) Emulsions:**

- In **o/w** emulsions, the internal phase consists of an oleaginous or oily component, dispersed within an aqueous external phase.

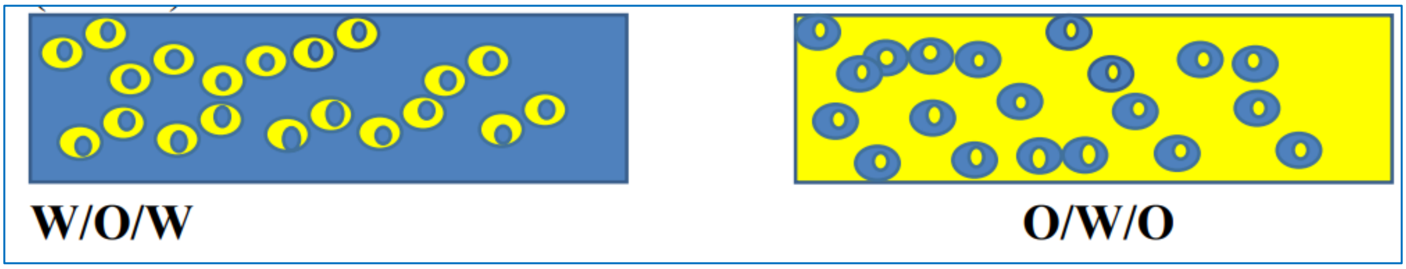
2-Water-in-Oil (w/o) Emulsions:

-In **w/o** emulsions, the internal phase consists of water or an aqueous component, dispersed within an oleaginous external phase.

Because the external phase of an emulsion is continuous. An o/w emulsion may be diluted or extended with water or an aqueous preparation and a w/o emulsion, with an oleaginous or oil-miscible liquid.

3-Multiple emulsions:

Multiple emulsions have multiple layers of dispersed and continuous phases, including both oil-in-water-in-oil (**o/w/o**) and water-in-oil-in-water (**w/o/w**) structures.



Macroemulsions vs. Microemulsions

Microemulsions can be formed spontaneously by agitating oil and water phases with carefully selected surfactants.

-The type of microemulsion produced depends on the properties of the oil and surfactants used.

-Microemulsions have significantly smaller droplets compared to macroemulsions, with diameters ranging from 100 Å to 1,000 Å.

-In contrast, macroemulsions have larger droplets, around 5,000 Å in diameter.

-Both o/w (oil-in-water) and w/o (water-in-oil) microemulsions can be formed based on the oil and surfactant properties.

Microemulsions offer advantages in oral drug delivery, providing more rapid and efficient absorption compared to solid dosage forms.

Microemulsions enhance transdermal drug delivery by facilitating increased diffusion into the skin. -The small droplet size of microemulsions promotes efficient absorption through the skin barrier

Macroemulsion	Microemulsion
Size: around 5,000 Å	Size: 100 Å to 1,000 Å
White opaque appearance	Cloudy –Translucent or Transparent
Thermodynamically unstable	Thermodynamically stable
Requires a substantial input energy for production	Forms spontaneously

Determination tests of the emulsion type

1-Miscibility test

o/w emulsion remain stable upon dilution with water, but will not remain homogenous upon addition of oil and vice versa

---

2-Staining test

Addition of oil soluble stain to the emulsion of unknown type on a glass slide under microscope

-Staining globules and colorless medium= o/w emulsion

-Staining background and colorless globules = w/o emulsion

3-Conductivity test

Water conduct electricity, hence an emulsion in which water forms the continuous phase acts as a conductor. Oil is a non-conductor and emulsion in which forms the external phase act as non-conductor.

Classification of emulsions according to the physical state

Emulsions can be formulated as:

-**Liquid**
-**Semisolids**

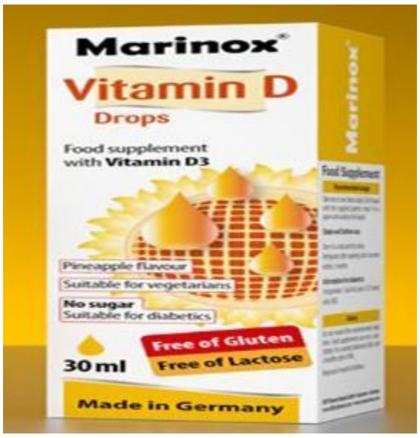
According to the route of administration

Based on the constituents and the intended application - **Liquid emulsions may be employed**:

-Orally: o/w for example, castor oil emulsion
-Topically: for example lotion
-Parenterally: (I.V. o/w) (I.M. and S.C. may be w/o)

-Semisolid emulsions

• Topically: for examples, lotions, creams and liniments



The choice between o/w and w/o emulsions depends on many factors such as:

1-The nature of therapeutic agents,
2-Desired effects,
3-The intended route of administration

Purpose and Benefits of Emulsions

Improved Drug Administration:

Emulsification allows the pharmacist to create stable mixtures of two immiscible liquids, enabling the administration of a liquid drug in the form of minute globules (introducing of many ingredients in different phases as liquid dosage form).

-Orally administered emulsions, are always in the form of o/w emulsions. They can improve the palatability of drug administration by dispersing it in a sweetened, flavored aqueous vehicle (taste masking).

o/w emulsion act as carrier for lipophilic drugs, enabling the oil soluble drug to dissolved in the dispersed phase and potentially enhance oral bioavailability

-**Sterile I.V. o/w emulsions** are used for administration of nutritive oil and oil soluble vitamins to the patients unable to ingest food. Intravenous emulsions must be o/w.

-Intramuscular and subcutaneous injections can be formulated as w/o emulsions. In such oily emulsions, the drug's effects are prolonged, as the drug must diffuse from the aqueous dispersed phase through the external oil phase to reach the tissue fluids.

-Emulsions for topical use can be either o/w or w/o, depending on the nature of therapeutic agents, the desired effects, and skin conditions.

-An o/w emulsion is more easily removed from the skin with water, making it suitable when easy removal is required. Medicinal agents that irritate the skin generally are less irritating in the internal phase of an emulsified topical preparation than in the external phase.

-w/o emulsions are more softening to the skin, resisting drying and removal by contact with water.

-The diminished particle size of the internal phase in emulsions can enhance **percutaneous absorption** (absorption through the skin), making them a valuable choice for dermatological formulations.

The acceptable emulsion is characterized by the following:

1-The globules of dispersed phase must be remain uniformly distributed throughout the continuous phase

2-The formulation should have a pleasing appearance and texture

3-For oral administration, the flavor must be appropriate

4-For external application, the formulation must be easily spread over the affected area
5-Physically stable (shows no signs of flocculation, creaming, sedimentation and coalescence)

6-Absence of deterioration by microorganisms

Disadvantages of emulsions

1. Pharmaceutical emulsions, being thermodynamically unstable, require careful formulation to prevent the separation of their two phases.

2. Before measuring a dose, it is essential to shake the emulsion thoroughly. Even with efficient shaking, the accuracy of the dose is likely to be lower compared to solutions.

3-Storage conditions may affect the disperse system, potentially causing creaming or cracking

4-There is a possibility of microbial contamination, which can further lead to cracking issues

5-In comparison to solid dosage forms, liquid dosage forms, such as emulsions, tend to be more bulky

---

Gibbs free energy in an emulsion

$$\Delta G = \Delta A \gamma$$

A is the total surface area of dispersed particles **γ** is the interfacial tension ,

Stable emulsions must have a large "A" and a small "G" concurrently for consistent and uniform dosing. This is done by decreasing "γ," which will decrease "G," which will decrease self-attraction of dispersed phase particles

---

Theories of Emulsification

There are many theories of emulsification:

1. Surface Tension Theory:

All liquids tend to minimize their surface area by forming spherical shapes, which is the shape with the least surface area.

Surface tension measures this tendency and is a force that resists the formation of smaller droplets when two immiscible liquids come into contact.

-Emulsifying agents, often called surfactants or wetting agents, reduce interfacial tension and diminish the liquids' attraction to their own molecules (reducing the repellent force between the liquids and diminishing each liquid's attraction for its own molecules).

-This theory suggests that emulsifiers lower the interfacial tension between immiscible liquids, thus, the surface-active agents facilitate the breaking up of large globules into smaller ones, which then have a lesser tendency to reunite or coalesce

---

◇ 2. Oriented-Wedge Theory:

-This theory is based on the idea that emulsifying agents form monomolecular layers around the droplets of the internal phase. The theory is based on the assumption that certain emulsifying agents orient themselves about and within a liquid in a manner reflective of their solubility in that particular liquid.

-In a system containing two immiscible liquids, probably the emulsifying agent is preferentially soluble in one of the phases and is embedded more deeply in that phase than the other. Because many molecules of substances have a hydrophilic or water-loving portion and a hydrophobic or waterhating portion, the molecules position or orient themselves into each phase.

-Emulsifying agents with a greater hydrophilic character tend to promote o/w emulsions, while those with a more hydrophobic character favor w/o emulsions.

-The phase in which the emulsifier is more soluble becomes the continuous phase of the emulsion.

◇ 3. Plastic or Interfacial Film Theory:

This theory places emulsifying agents at the interface between the immiscible liquids, forming a thin film adsorbed on the surface of internal phase droplets.

-The film acts as a barrier, preventing contact and coalescence of the dispersed phase.

-The stability of the emulsion depends on the toughness and flexibility of this film.

-The degree of solubility of the emulsifying agent in the two phases determines whether o/w or w/o emulsions are formed.

Preparation of Emulsions

Factors Affecting Emulsion Formation:

The stability and characteristics of an emulsion are influenced by the following factors:

-Emulsifying agents
-pH
-The ratio of internal to external phases.

The success of emulsions depends on the careful selection of emulsifying agents and understanding their properties. The initial step in preparation of an emulsion is selection of the emulsifier.

Criteria for Selecting Emulsifying Agents:

1-Compatibility:
Emulsifying agents must be compatible with other formulation ingredients and should not interfere with the stability or efficacy of the therapeutic agent.

2-Stability:
Emulsifying agents should be stable and not deteriorate during the preparation or storage of the pharmaceutical product.

3-Safety:
Emulsifiers should be nontoxic and safe for consumption by the patient, and they should possess minimal odor, taste, or color.

4-Promotion of Emulsification:
A crucial role of emulsifying agents is to promote emulsification, ensuring that the two immiscible phases are dispersed effectively.

Common Types of Emulsifying Agents

1. Carbohydrate Materials:

-Naturally occurring agents like acacia, tragacanth, agar, chondrus, and pectin are used. These materials form hydrophilic colloids. They typically form o/w emulsions.

-Acacia is often used in extemporaneous emulsions. Tragacanth and agar are commonly employed as thickening agents in acacia-emulsified products.

Microcrystalline cellulose is employed in a number of commercial emulsions as a viscosity regulator.

2. Protein Substances:

-Gelatin, egg yolk, and casein are examples of protein-based emulsifiers that produce o/w emulsions.

-Gelatin, while effective, can lead to emulsions that become more fluid over time.

---

3. Molecular Weight Alcohols:

- Substances like stearyl alcohol, cetyl alcohol, and glyceryl monostearate are primarily used as thickening agents and stabilizers for o/w emulsions in external applications.

-Cholesterol and cholesterol derivatives may also be employed in externally used emulsions to promote w/o emulsions

---

4. Wetting Agents:

-These agents can be anionic, cationic, or nonionic and contain both hydrophilic and lipophilic groups. In anionic agents, the lipophilic portion is negatively charged, but in the cationic agent, it is positively charged.

-Anionic and cationic agents tend to neutralize each other and are considered incompatible, while nonionic emulsifiers show no inclination to ionize.

Depending on their individual nature, certain members of these groups form o/w emulsions and others w/o emulsions.

-Anionic emulsifiers include various monovalent, polyvalent,

-Organic soaps, such as triethanolamine oleate,

-Sulfonates, such as sodium lauryl sulfate.

-Cationic emulsifier, such as Benzalkonium chloride (known primarily for its bactericidal properties)

-Nonionic emulsifiers, such as span and tween

5. Finely Divided Solids:

-Colloidal clays like bentonite, magnesium hydroxide, and aluminum hydroxide can form o/w emulsions when the insoluble material is added to the aqueous phase if there is a greater volume of the aqueous phase than of the oleaginous phase.

If the powdered solid is added to the oil and the oleaginous phase volume predominates, a substance such as bentonite is capable of forming a w/o emulsion.

-The relative volume of internal and external phases is critical for their effectiveness.

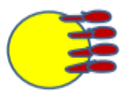
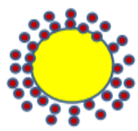
Auxiliary emulsifying agent

-Lipophilic

-High molecular Weight Alcohols Substances like stearyl alcohol, cetyl alcohol, and glyceryl monostearate are primarily used as thickening agents and stabilizers for o/w emulsions in external applications.

-Hydrophilic

Tragacanth and agar are commonly used as thickening agents in acacia – emulsified products

Type	**Example**	**Mechanism**	
Mono-molecular	Potassium laureate Tween 80	Coherent flexible film formed by SAA. (Lower interfacial tension) and stabilize the emulsion	
Multi-molecular	Acacia, Gelatin	Strong rigid film formed mostly by hydrocolloids, which produce O/W emulsions. Stability due mainly to strength of interfacial film (forming a coherent multi-molecular film which is strong and prevent the coalescence)	
Solid particles	Bentonite Magnesium hydroxide	Film formed by solid particles that are small in size compared to the droplets of the dispersed state Particles wetted by both phases to some extent in order to remain at the interface and form a stable film (form a particulate film that prevent the coalescence)