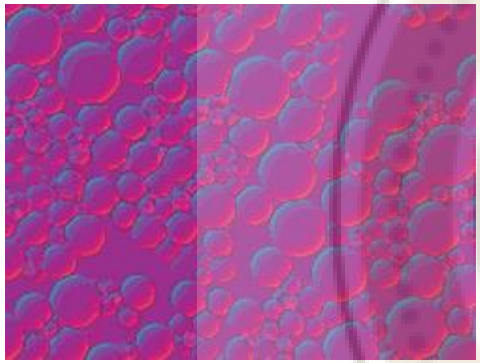
EMULSIONS

Heterogeneous systems consisting of at least one immiscible liquid phase intimately dispersed throughout a second phase in the form of droplets or globules



Thermodynamically unstable mixtures

Dispersed particles range in diameter from 0.1 to 100 □m

Range from lotions with relatively low viscosity to semi-solid ointments and creams

PURPOSE

Oral

- palatabilization of drug of objectionable taste
- absorption of water-insoluble liquids
- enhanced bioavailability of lipophilic drugs

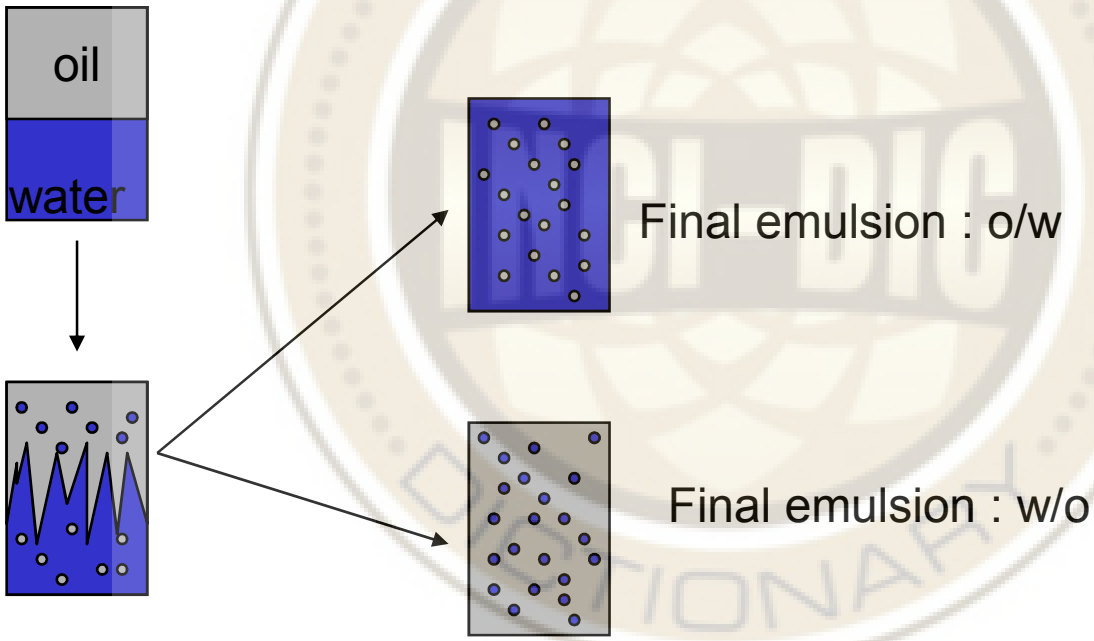
Topical

- oils used as emollients or protectants of skin, when emulsified they feel less greasy
- enhanced transdermal absorption

Emulsification Process

two competing mechanisms

- the dispersion of one liquid throughout another as droplets (energy input, increase □G)
- reduction in □G through coalescence of formed droplets



Emulsifying Agent

added to reduce the rate of coalescence

- stabilizes emulsion

possible mechanisms of action:

- reduces the interfacial tension between 2 immiscible phases
- forms an interfacial film around droplet
- induces steric/electrostatic repulsion

Chemical Types

synthetic

divided into anionic, nonionic

- anionic
  - soft soaps (ex. potassium laurate)
  - hard soaps (ex. Ca-oleate)
- nonionic
  - ex. sorbitan monooleate (Span 80), polysorbate 80 (Tween 80)

natural

- acacia, lecithin
- gelatin
  - type A : pI = 7-9, works best at pH 3
  - type B : pI = 5, works best at pH 8

Auxiliary Emulsifiers

- compounds which are normally incapable of forming stable emulsions alone

- mainly used as thickening agents
  - lipophilic, stabilizing O/W
    - cetyl alcohol, glyceryl monostearate,
  - hydrophilic, stabilizing O/W
    - methylcellulose, NaCMC

Choosing an Emulsifying Agent

HLB: hydrophile-lipophile balance scale

- HLB < 10 : lipophilic
- HLB > 10 : hydrophilic
- for O/W emulsions, want HLB of 8-18
- for W/O emulsions, want HLB of 3-6

- choose an emulsifying agent which has an HLB of the same value as the oil phase
- can combine emulsifying agents to obtain desired HLB
  - HLB values are additive
- be aware of polarity of material being emulsified

- ***required*** HLB
  - the HLB required of a material to be effectively emulsified

HLB values

Emulsifier	HLB
Sorbitan monooleate	4.3
Sorbitan mononstearate	4.7
Gelatin (type A)	9.8
Triethanolamine oleate	12
Polyoxyethylene 20 sorbitan monolaurate	13.3
Polyoxyethylene 20	15

Required HLB

Material	W/O	O/W
Stearic acid	---	17
Cetyl alcohol	---	13
Anhydrous lanolin	8	15
Cottonseed oil	---	7.5
Light mineral oil	4	10-12
Heavy mineral oil	4	10.5
Beeswax	5	10-16

Example

5 g of emulsifying agent is called for in an oil in water emulsion of 50 g liquid petrolatum in water. The total mass of the emulsion is 100g. You decide to use sorbitan monooleate and polyoxyethylene 20 as the emulsifying agents. Determine the amount required of each.

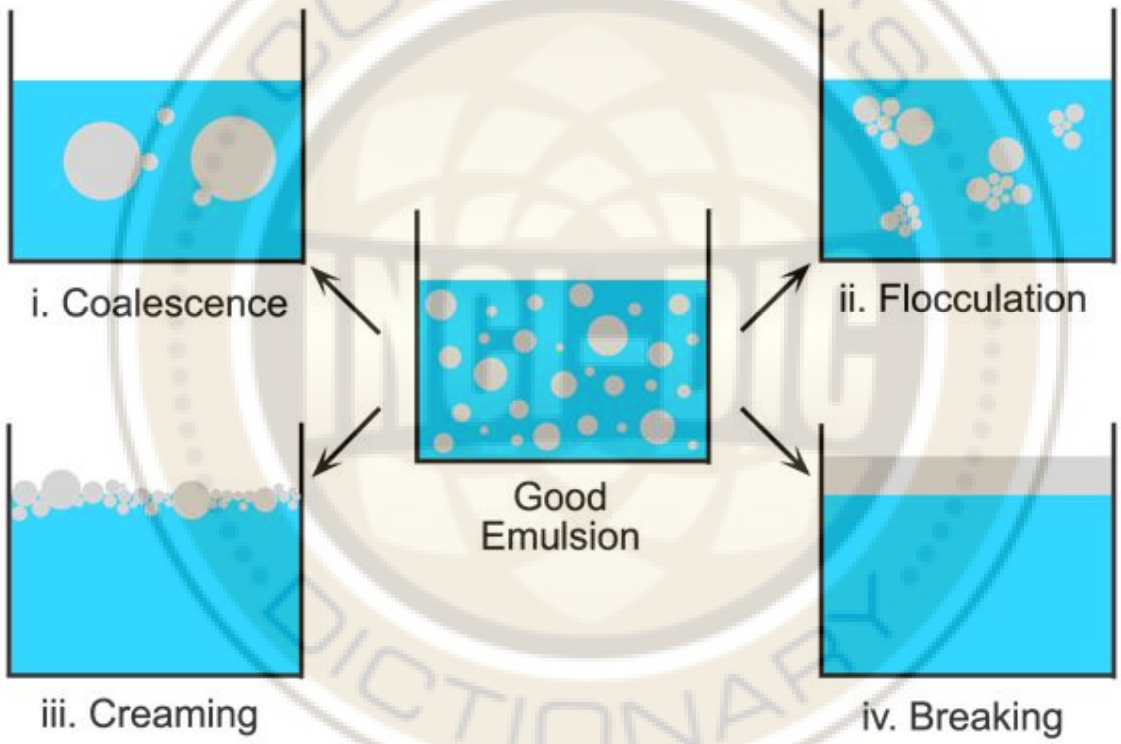
Example

Determine the amounts of emulsifying agent to prepare the following oil-in-water emulsion :

light mineral oil	31%
beeswax	5 %
cottonseed oil	2 %
polyoxyethylene 20 sorbitan monolaurate sorbitan monostearate	7 %
water	55%

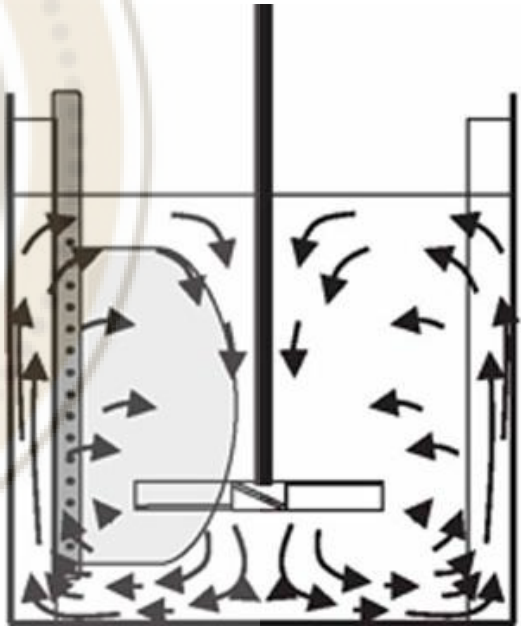
Physical Stability

Emulsions can be de-stabilized in different ways:



Preparation

- oil phase and water phase components heated separately
- pump one phase into other phase with agitation
  - mechanical stirrers
  - homogenizers
  - colloid mills
- cool emulsion, then homogenize
- package



Droplet Size

For mechanical mixers, there are a number of correlations that have been developed based on the Weber number, We, to use to estimate the average droplet size of the dispersed phase.

$$We = \frac{\rho_c n^2 D_a^3}{\gamma}$$

6-bladed turbine:

$$\frac{D_p}{D_a} = 0.058(1 + 5.4\psi)We^{-0.6}$$

4-bladed turbine:

$$\frac{D_p}{D_a} = 0.056(1 + 10.97\psi)We^{-0.6}$$

Example

An oil-in-water emulsion formulation has been developed as a subcutaneous injectable depot where the drug is in the oil phase. The volume fraction of oil phase present is 0.45. You are asked to change the droplet size during manufacturing so as to achieve a 50% increase in the release rate. The emulsion is manufactured using a 6-bladed turbine. Estimate by how much the impeller speed must be increased during the emulsification stage to achieve this objective. Assume release occurs at steady-state, that the rate-limiting step during release is diffusion from the oil phase into the aqueous environment, and that the tissue represents an infinite sink.