Formulation of Emulsion

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Topics to be covered ....

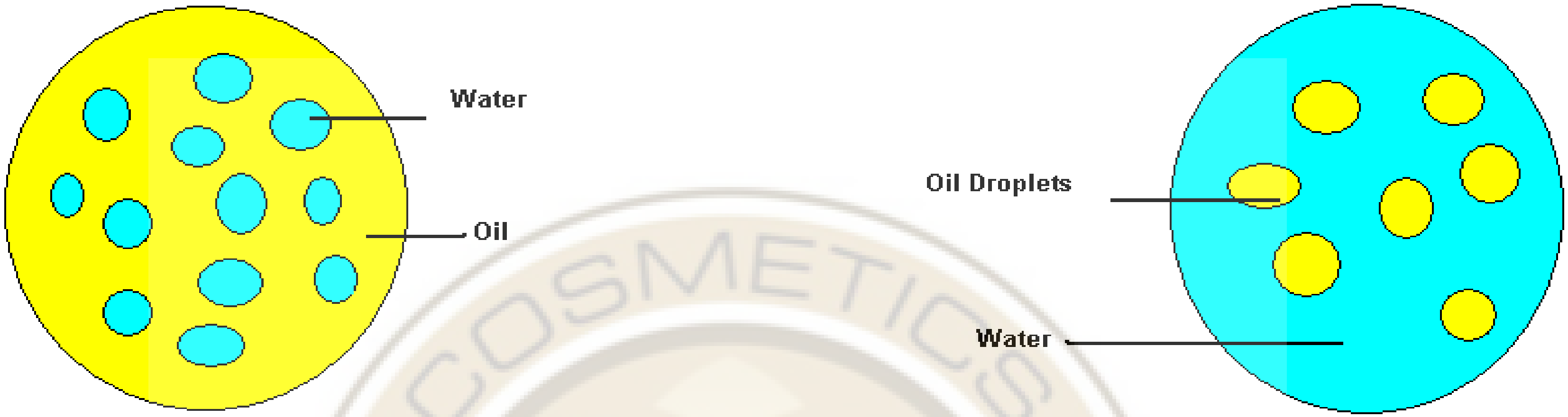
1) Definition
2) Type of Emulsion
3) Pharmaceutical Application of Emulsion
4) Formulation of Emulsion
5) Theory of Emulsion
6) Preservation of Emulsion
7) Preparation of Emulsion
8) Stability of Emulsion

Definition

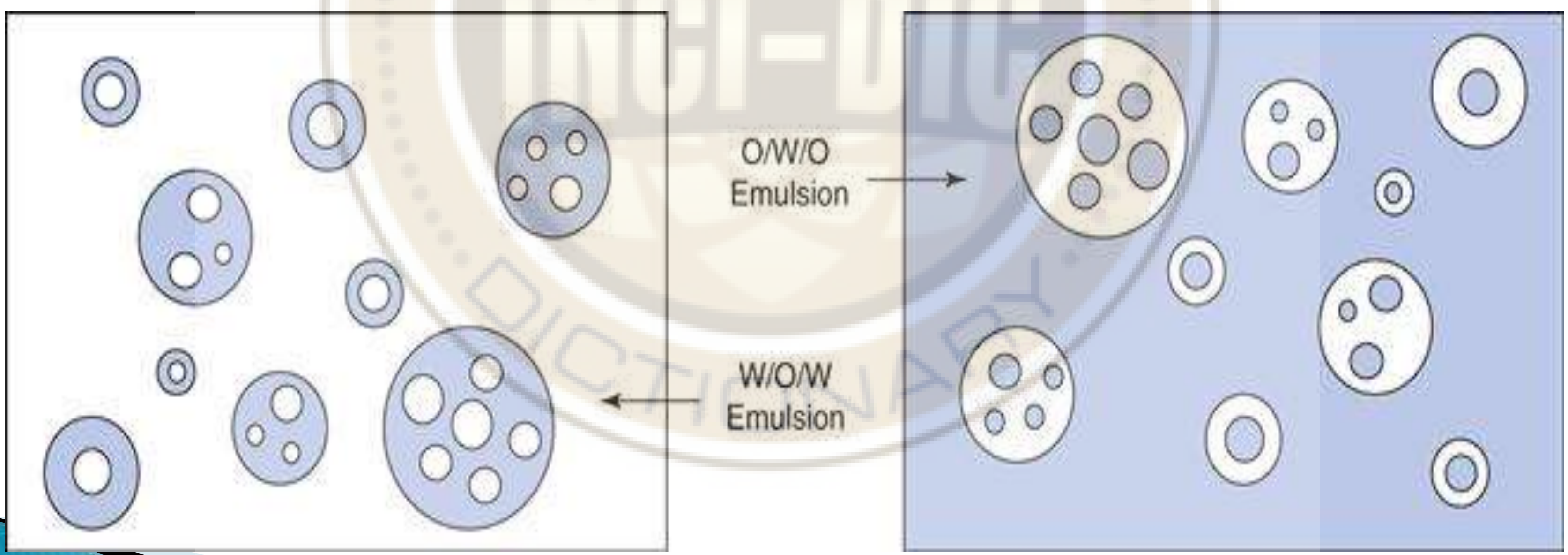
- An emulsion is a two phase system consisting of two incompletely miscible liquids, one of which is dispersed as finite globules in the other. The particle size of the globules range from 0.25 to 25 µm. An emulsifying agent and mechanical energy are needed to join the phases.

Types of Emulsion

- Based on dispersed phase
- Oil in Water (O/W): Oil droplets dispersed in water.
- Water in Oil (W/O): Water droplets dispersed in oil.
- Multiple emulsions (e.g. w/o/w emulsions).



Single Emulsion



Multiple Emulsion

Based on size of liquid droplets

- 0.2 – 50 mm Macroemulsions
- 0.01 – 0.2 mm Microemulsions
- 50 – 1000 nm Nanoemulsions

PHARMACEUTICAL EMULSIONS

DIFFERENCE BETWEEN O/W AND W/O EMULSIONS

Oil in water emulsion (o/w)	Water in oil emulsion (w/o)
Water is the dispersion medium and oil is the dispersed phase.	Oil is the dispersion medium and water is the dispersed phase.
Water soluble drugs are more quickly released from o/w emulsions.	Oil soluble drugs are more quickly released from w/o emulsions .
They are preferred for formulations meant for internal use as bitter taste of oils can be masked.	They are preferred for formulations meant for external use like creams.
They are non greasy and easily removable from the skin surface.	They are greasy and not water washable.
They are used externally to provide cooling effect e.g. vanishing cream	They are used externally to prevent evaporation of moisture from the surface of skin e.g. Cold cream.
O/W emulsions give a positive conductivity test as water is the external phase which is a good conductor of electricity.	W/O emulsions go not give a positive conductivity test as oil is the external phase which is a poor conductor of electricity.

Pharmaceutical application of emulsions:

- - Oral, rectal and topical administration of oils and oil-soluble drugs.
- -The unpleasant taste or odor can be masked by emulsification.
- - The absorption and penetration of medicament are enhanced by emulsification.
- - Intramuscular injections of water-soluble drugs or vaccine to provide slow release.
- - The use of sterile stable i.v emulsion containing fats, carbohydrates and vitamins as a potential nutrition.

Formulation of emulsions

Selection of Emulsifying agents (emulsifiers):

- An emulsifying agent is any material that enhances the stability of an emulsion (i.e. Prevention of coalescence and reducing creaming).
- The ideal emulsifying agent is colourless, odourless, tasteless, non-toxic, non-irritant and able to produce stable emulsions at low concentrations.
- Examples of Emulsifying agent

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.

Test for identification of emulsion type

- Dilution test (miscibility test)
- Staining test (dye solubility test)
- Conductivity measurement
- Fluorescence test

THEORY OF EMULSIFICATION

- Film theory or adsorption theory
- Viscosity theory
- Wedge theory
- Interfacial tension theory

Film theory or adsorption theory

- As per this theory, the added emulsifying agent forms a mechanical film by getting adsorption at the interface of the liquid and offers stability to the emulsion. However, this theory could not explain the formation of type of emulsion.

Viscosity theory

- As per this theory, an increase in viscosity of an emulsion will lead to an increase in stability. This theory failed to explain about the milk which shows considerable stability even though its viscosity is less.

Wedge theory

- According to this theory, monovalent soap like sodium stearate give o/w type emulsion and divalent soap like calcium stearate give w/o type emulsion. This was explained by successful accommodation of the soap molecules to give the type of emulsion.

Interfacial tension theory

- In accordance with this theory the added emulsifying agent reduces the interfacial tension between the oil and water phases and thus a stable emulsion is formed. This theory could not explain the formation of type of emulsion.

The HLB (Hydrophilic lipophilic balance system) of emulsifying agents:

- An HLB number (1-20) represents the relative proportions of the lipophilic and hydrophilic parts of the molecule.
- High numbers (8-18) indicate a hydrophilic molecule, and produce an o/w emulsion.
- Low numbers (3-6) indicate a lipophilic molecule and produce a w/o emulsion.
- Oils and waxy materials have a 'required HLB number' which helps in the selection of appropriate emulsifying agents when formulating emulsions.
- Liquid paraffin, for example, has a required HLB value of 4 to obtain a w/o emulsion and 10.5 for an o/w emulsion.

HLB Scale

- HLB ca. 1 to 3.5: Antifoams
- HLB ca. 3.5 to 8: Water-in-Oil Emulsifiers
- HLB ca. 7 to 9: Wetting and spreading agents
- HLB ca. 8 to 16: Oil-in-Water Emulsifiers
- HLB ca. 13 to 16: Detergents
- HLB ca. 15 to 40: Solubilizers

HLB Values of Selected Emulsifiers

Chemical Designation	HLB Value
Ethylene glycol distearate	1.5
Sorbitan sesquioleate	3.7
Diethylene glycol monostearate	4.7
Sucrose diolate	7.1
Polyoxyethylene (4) lauryl ether	9.5
Polyoxyethylene (6) cetyl ether	10.3
Polyxyethylene (20) sorbitan tristearate	10.5
Polyxyethelene (9) nonyl phenol	13.0
Sodium Oleate	18.0
Polyxyethylene (100) Stearate	18.8
Potassium Oleate	20.0

Criteria For The Selection of Emulsifying Agents

- An ideal emulsifying agent should posses the following characteristics:
- It should be able to reduce the interfacial tension between the two immiscible liquids.
- It should be physically and chemically stable , inert and compatible with the other ingredients of the formulation.
- It should be non irritant and non toxic in the conc., used.
- It should be organoleptically inert i.e. should not impart any color , odour or taste to the preparation.
- It should be able to produce and maintain the required viscosity of the preparation.
- It should be able to form a coherent film around the globules of the dispersed phase and should prevent the coalescence of the droplet of the dispersed phase.

Packaging, Labelling and Storage of Emulsions

- Depending on the use, emulsions should be packed in suitable containers. Emulsions meant for oral use are usually packed in well filled bottles having an air tight closure.
- Light sensitive products are packed in amber colored bottles.
- For viscous emulsions, wide mouth bottles should be used. The label on the emulsion should mention that these products have to be shaken thoroughly before use.
- External use products should clearly mention on their label that they are meant for external use only.
- Emulsions should be stored in a cool place but refrigeration should be avoided as this low temperature can adversely effect the stability of preparation.

Preservation of Emulsions

- **Microbial contamination may occur due to:**
- contamination during development or production of emulsion or during its use.
- Usage of impure raw materials
- Poor sanitation conditions
- Invasion by an opportunistic microorganisms.
- Contamination by the consumer during use of the product..
- **Precautions to prevent microbial growth ;**
- Use of uncontaminated raw materials
- Careful cleaning of equipment with steam .

Antimicrobial agents

- **The preservative must be :**
- Less toxic
- Stable to heat and storage
- Chemically compatible
- Reasonable cost
- Acceptable taste, odor and color.
- Effective against fungus, yeast, bacteria.
- Available in oil and aqueous phase at effective level concentration.
- Preservative should be in unionized state to penetrate the bacteria.
- Preservative must no bind to other components of the emulsion

Antimicrobial agents

- **Examples of antimicrobial preservatives used to preserve emulsified systems include**
- parahydroxybenzoate esters such as methyl, propyl and butyl parabens,
- organic acids such as ascorbic acid and benzoic acid,
- organic mercurials such as phenylmercuric acetate and phenylmercuric nitrate,
- quaternary ammonium compounds such as cetrimide,
- cresol derivatives such as chlorocresol
- and miscellaneous agents such as sodium benzoate, chloroform and phenoxyethano

The ideal antioxidant should be:

- Nontoxic, nonirritant,
- effective at low concentration under the expected conditions of storage and use,
- soluble in the medium and stable.
- Antioxidants for use in oral preparation should also be odorless and tasteless.

Example of Antioxidants

- Gallic acid, Propyl gallate - pharmaceuticals and
- cosmetics - Bitter taste
- Ascorbic acid – Suitable for oral use products
- Sulphites - Suitable for oral use products
- L-tocopherol - pharmaceuticals and cosmetics - Suitable for oral preparations e.g. those containing vit A
- Butylated hydroxyl toluene - pharmaceuticals and cosmetics - Pronounced odor, to be used at low conc.
- Butylated hydroxylanisol - pharmaceuticals and cosmetics

Preparation of Emulsion

The methods commonly used to prepare emulsions can be divided into two categories

A) Trituration Method

This method consists of dry gum method and wet gum method.

- Dry Gum Method

In this method the oil is first triturated with gum with a little amount of water to form the primary emulsion. The trituration is continued till a characteristic 'clicking' sound is heard and a thick white cream is formed. Once the primary emulsion is formed, the remaining quantity of water is slowly added to form the final emulsion.

This method consists of

"4:2:1" formula

4 parts (volumes) of oil

2 parts of water

1 part of gum

- Wet Gum Method

As the name implies, in this method first gum and water are triturated together to form a mucilage. The required quantity of oil is then added gradually in small proportions with thorough trituration to form the primary emulsion.

Once the primary emulsion has been formed remaining quantity of water is added to make the final emulsion.

This method consists of

"4:2:1" formula

4 parts (volumes) of oil

2 parts of water

1 part of gum

Mortar and Pestle

Homogeniser

B) Bottle Method

- This method is employed for preparing emulsions containing volatile and other non-viscous oils. Both dry gum and wet gum methods can be employed for the preparation.
- As volatile oils have a low viscosity as compared to fixed oils, they require comparatively large quantity of gum for emulsification.
- In this method, oil or water is first shaken thoroughly and vigorously with the calculated amount of gum. Once this has emulsified completely, the second liquid (either oil or water) is then added all at once and the bottle is again shaken vigorously to form the primary emulsion. More of water is added in small portions with constant agitation after each addition to produce the final volume.

Mechanical equipment for emulsification (Agitation)

- Mechanical stirrers
- Propeller type mixers
  - -Turbine mixers
  - - Homogenizers
- Colloid mills
- Ultrasonifiers

Mechanical stirrers

Colloidal mill

Stability of Emulsion

- An emulsion is said to be stable if it remains as such after its preparation , that is the dispersed globules are uniformly distributed through out the dispersion medium during its storage. The emulsion should be chemically stable and there should not be any bacterial growth during it shelf life.
- Emulsion instability may either reversible or irreversible and manifest in the following ways:-

1) Cracking (irreversible instability)
2) Flocculation
3) Creaming
4) Phase inversion

1) Cracking:-

- Cracking means the separation of two layers of disperse and continuous phase , due to the coalescence of disperse phase globules which are difficult to redisperse by shaking.
- Cracking may occurs due to following reasons:-

i. By addition of emulsifying agent of opposite type

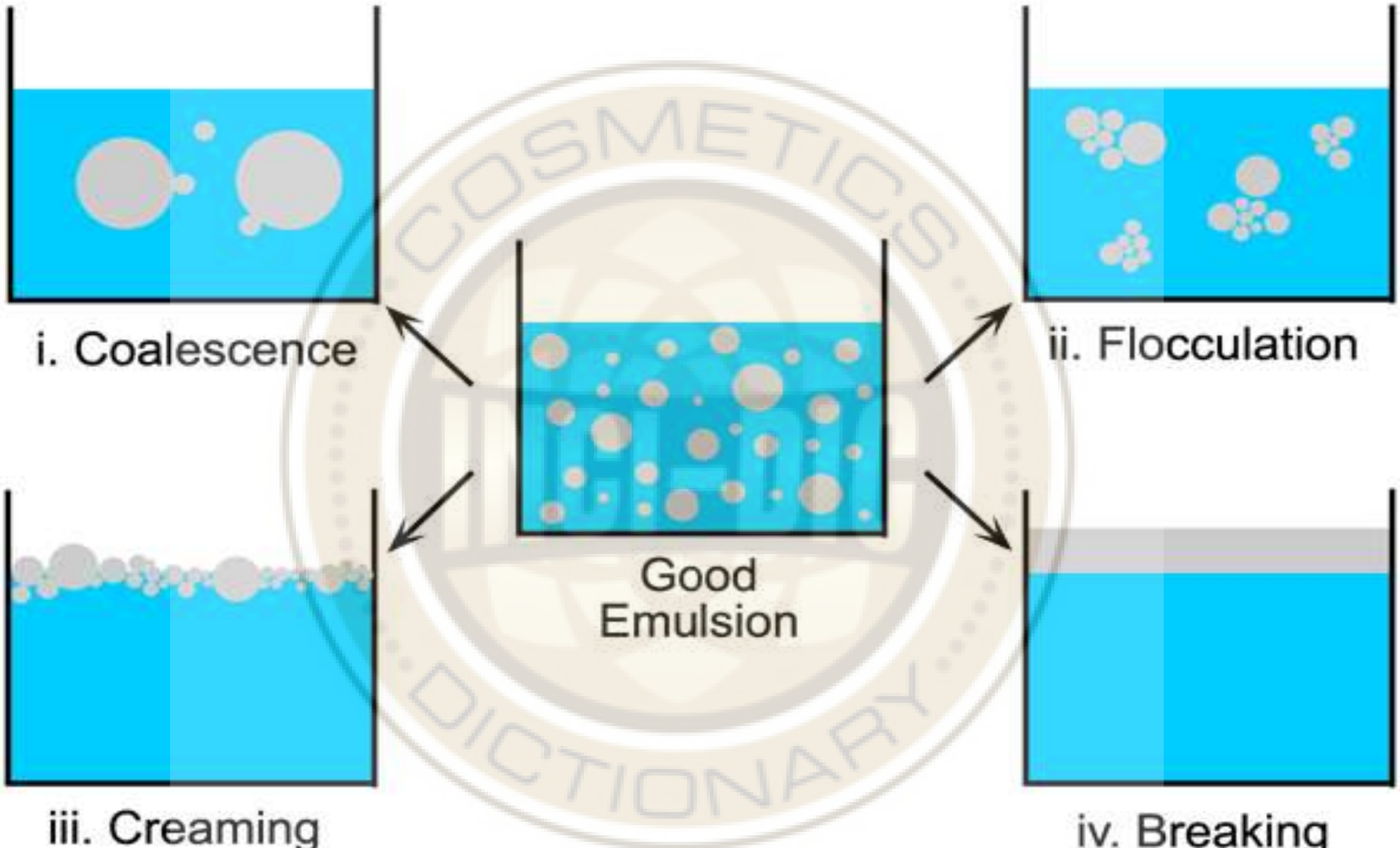
ii. By decomposition or precipitation of emulsifying agent

iii. By addition of common solvent

iv. By microorganisms

v. Change in temperature

vi. By creaming


i. Coalescence
ii. Flocculation
Good
Emulsion
iii. Creaming
iv. Breaking
COSMETICS
DICTIONARY

2) Flocculation :-

- In flocculated state the secondary interaction (van der waals forces) maintain the droplets at a defined distance of separation.
- Application of shearing stress to the formulation (shaking) will redisperse these droplets to form a homogeneous formulation.
- Although flocculation may stabilise the formulation, there is also possibility that the close location of droplets would enable droplet coalescence to occur if the mechanical properties of the interfacial film are compromised.

3) Creaming:-

- Creaming may be defined as the upward movement of dispersed globules to form a thick layer at the surface of emulsion.
- Creaming is temporary phase because it can be re-distributed by mild shaking or stirring to get again a homogenous emulsion.
- The factors affecting creaming are described by stoke’s law:

$$V = 2r^2 (d_1 - d_2)\, g / 9\eta$$

- Where V= rate of creaming
- r=radius of globules
- d_1= density of dispersed phase
- d_2= density of dispersion medium
- g= gravitational constant
- η = viscosity of the dispersion medium

The following approaches can be used for decreasing Creaming

a. Radius of globules

b. Difference in density of disperse phase and continuous phase

c. Viscosity of dispersion medium

d. Storage condition

4) Phase inversion:-

- Phase inversion means the change of one type of emulsion into other type, that is oil in water emulsion changes into water in oil type and vice-versa.

Due to following reasons the phase inversion takes place:-

i. By the addition of an electrolyte

ii. By changing the phase-volume ratio

iii. By temperature change

iv. By changing the emulsifying agent

- The phase inversion can be minimised by keeping concentration of disperse phase between 30 to 60 % , storing the emulsion in cool place and using a proper emulsifying agent in adequate concentration.

Points to be considered during formulations of emulsions:-

- Stability of the active ingredient
- Stability of the excipients
- Visual appearance
- Color
- Odor (development of pungent odor/loss of fragrance)
- Viscosity, extrudability
- Loss of water and other volatile vehicle components
- Concentration of emulsifier
- Particle size distribution of dispersed phases
- pH
- Temperature of emulsification
- Method and rate of cooling
- Texture, feel upon application (stiffness, grittiness, greasiness, tackiness)
- Microbial contamination/sterility
- Release/bioavailability (percutaneous absorption)
- Phase distribution, Phase Inversion (homogeneity/phase separation, bleeding)

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Thank you…