Emulsions

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Background of Emulsions

- Emulsions are a heterogeneous, metastable system of two immiscible liquid phases, in which one phase is dispersed in the other as drops of microscopic of colloidal size.[1]
- Emulsions can be classified as oil in water (o/w) or water in oil (w/o).[2]
- Emulsion formation requires the presence of emulsifying agents or surfactants that decrease the overall interfacial tension through favourable interactions between the different phases.[3]

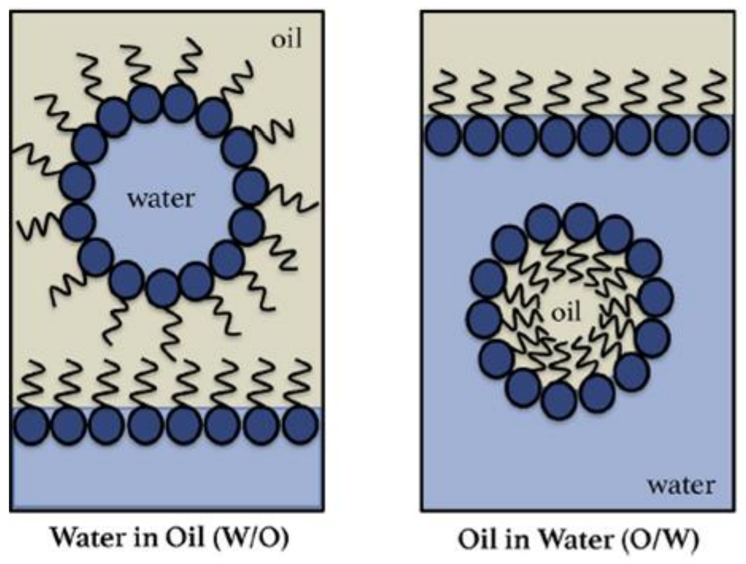


Figure 1: [2] Schematic representation of w/o (left) and o/w (right) emulsion systems.

Types of Emulsions: [4]

- **Macroemulsions (MAE)**: visually opaque with particles >400 nm (0.4 µm)
  - Thermodynamically unstable because phases coalesce then separate due to high interfacial tension and it costs energy to increase the interfacial area.[5]
- **Microemulsions (ME)**: transparent dispersions with particles <100 nm (0.1 µm)
  - Thermodynamically stable due to decrease in of interfacial tension by surfactant and large dispersion entropy due to phase mixing in the form of many small droplets.

$$\Delta G_f = \gamma \cdot \Delta A - T \cdot \Delta S$$

G_f = free energy of formation
γ = surface tension of oil water interphase
Δ**A** = change in interfacial area
Δ**S** = change in entropy of the system
T = temperature

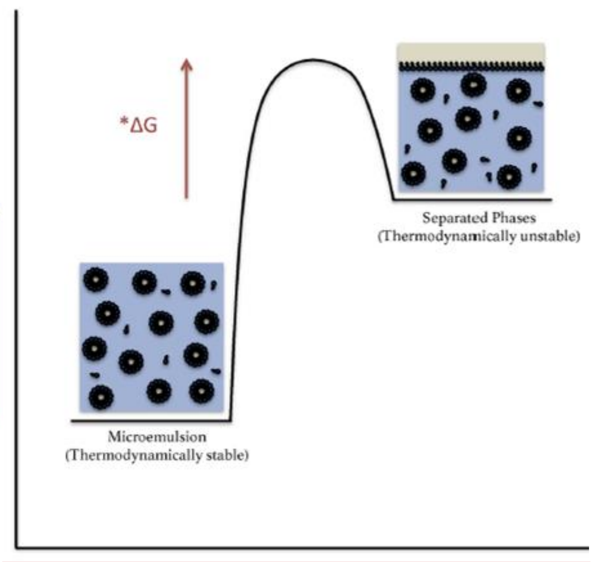


Figure 2: [2] Schematic of the energetics involved in a typical ME system.

Microemulsions in Enhanced Oil Recovery (EOR)

Scope: overcome capillary forces (Pc) to displace oil from solid surface: results from pressure difference across aqueous and organic interface.[6]

$$P_c = \gamma \cdot C = \frac{2\gamma \cos\theta}{R} \quad (1)$$

How: Injecting fluid composed of water and surfactant (amphiphilic molecule) which forms a ME with organic component

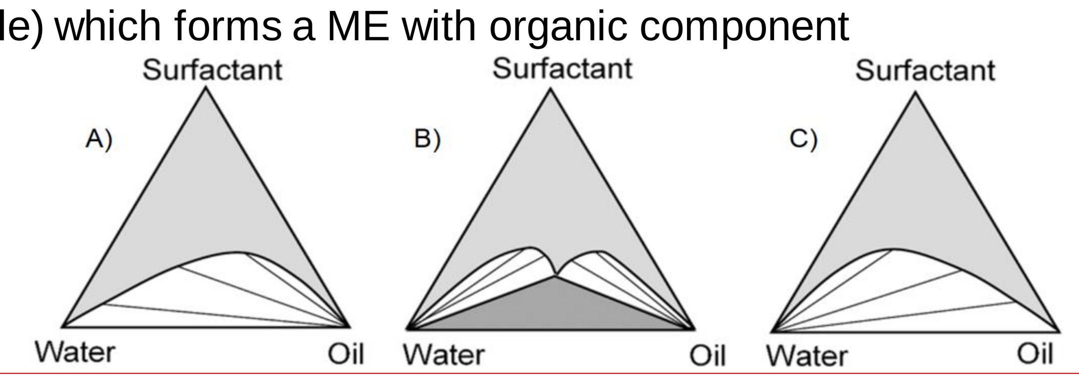


Figure 3: Overall ME composition: O/W ME in equilibrium with the oil excess phase, W/O ME in equilibrium with the water excess phase, and ME in equilibrium with both water and oil excess phase.[7] **A**: Winsor I two-phase states for a ME in equilibrium with an organic phase (oil). **B**: Winsor III three-phase states of a microemulsion in equilibrium with both an organic and aqueous phase. **C**: Winsor II two- phase states for a microemulsion in equilibrium with an aqueous phase.[8]

- Increased mobility from increased solubilization capacity for both components from decreased interfacial energy.[9]
- Controlled with ME slug to form stabilized oil-water bank

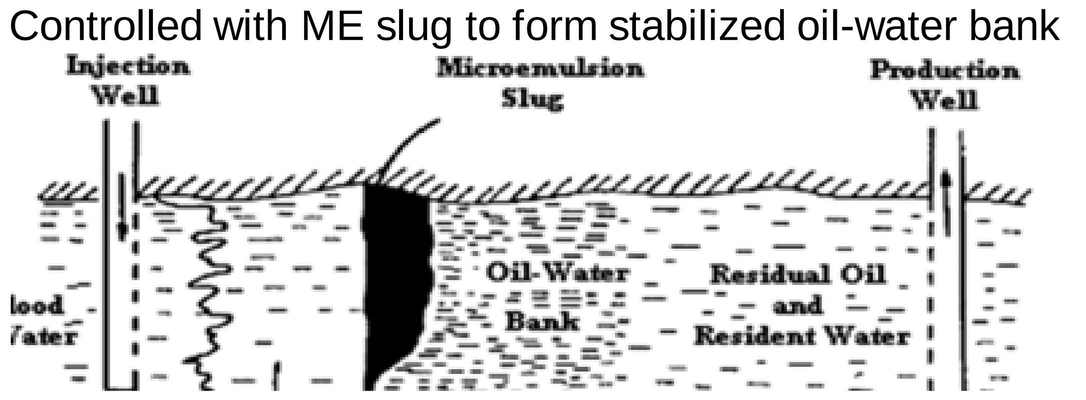


Figure 4: Microemulsion EOR process.

Wang et. al Methods:

- 3 ME with Δw% of SDBS, n-butanol, NaCl, and crude oil
- 5 different temperatures (Δ10°C)

Increased recovery rate with increased temperature: reduces interfacial viscosity by increased collision frequency and droplet coalescence.[10]

Dantas et. al Methods:

- 4 ME of Alkonant L90, n-butanol, kerosine, and Δw% HCl
- ME injected into Limestone plugs

Increased percent recovery with increased acid molarity: flow channel formation by solid dissolution connecting isolated zones(increase permeability of low permeability zone) causing more wettable surface.[11]

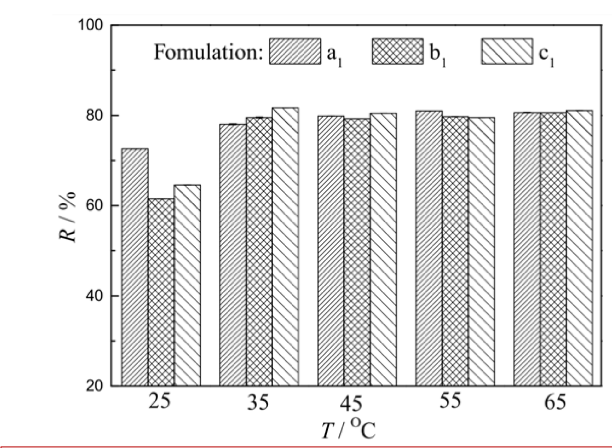


Figure 5: Influence of temperature on recovery rate (R/%).

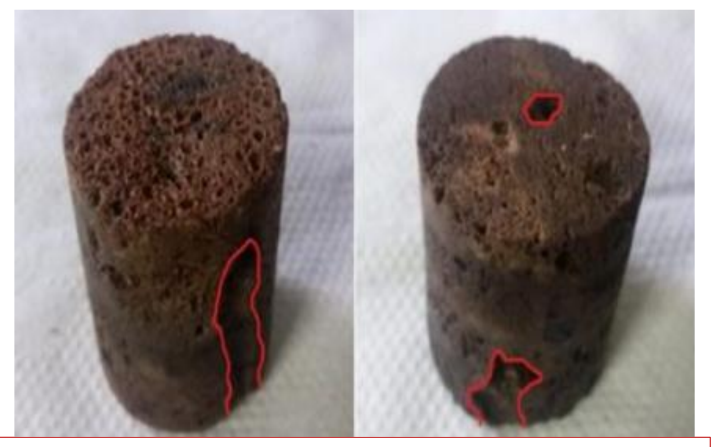


Figure 6: Influence of increasing acidic concentration of HCl(10%, 15%) on solid surface.

Microemulsions in Cosmetics

Background:

- Recent research has shifted focus from MAE to ME to formulate consistent skin products that deliver maximum benefits from functional ingredients.
- Many ME have cosurfactants to improve emulsification by ensuring flexibility of interfacial layer, thus reducing interfacial tension.
- Song et al. (2019) used cosurfactant 1,3-butylene glycol (1,3-BG) to stabilize lavender oil (LO), an antioxidant, within ME skin cosmetics.[12]

MAE Sunscreen Consistency Methods and Results:[13]

- Two sunscreens with different mean particle sizes (MPS) were heated then cooled to 22.0 ± 2.0 °C with agitation.

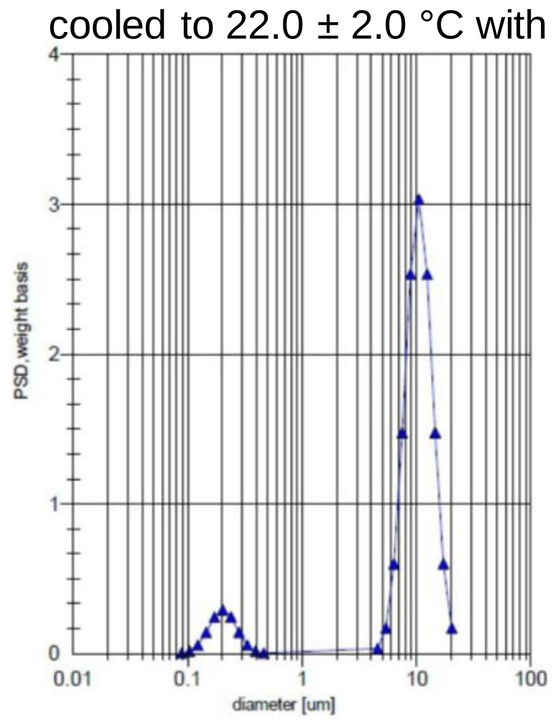


Figure 7. MAE1 Bimodal particle size distribution with means of 202nm (9%) and 10.4µm (91%).

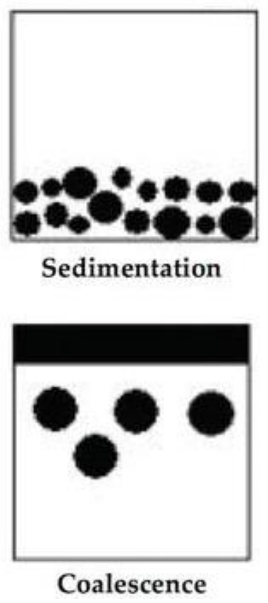
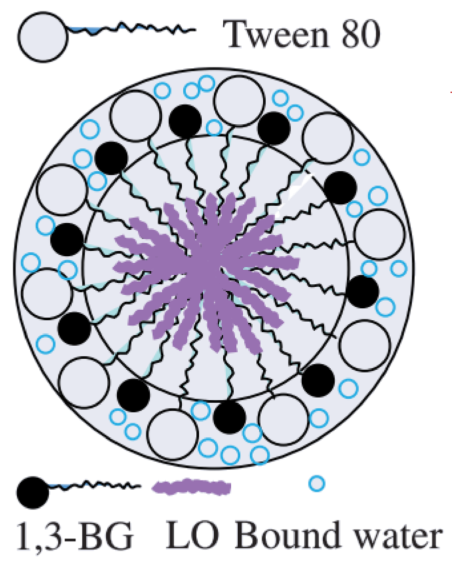


Figure 8: Coalescence in thermodynamically unstable MAE1.

- White MAE1 had MPS of 202 nm and 10.4 µm. Unstable after 48 hours.
- Glowing blue MAE2 had MPS of 10 nm and 4.5 µm. Stable after 48 hours.
- Larger particles (MAE1)
  - Gravity
  - Sedimentation
  - Coalescence
- Smaller particles (MAE2)
  - Stayed suspended

Lavender ME Methods and Results:[12]

- Radical scavenging activity increased as ME water content increased (Fig 9).
- Water accelerated LO interaction with radicals
- The 1,3-BG cosurfactant, amongst others, gave the highest existence of ME.
- ME in cosmetics solubilize poorly water-soluble essential oils to deliver functional ingredients into a stable carrier and optimize antioxidant power.



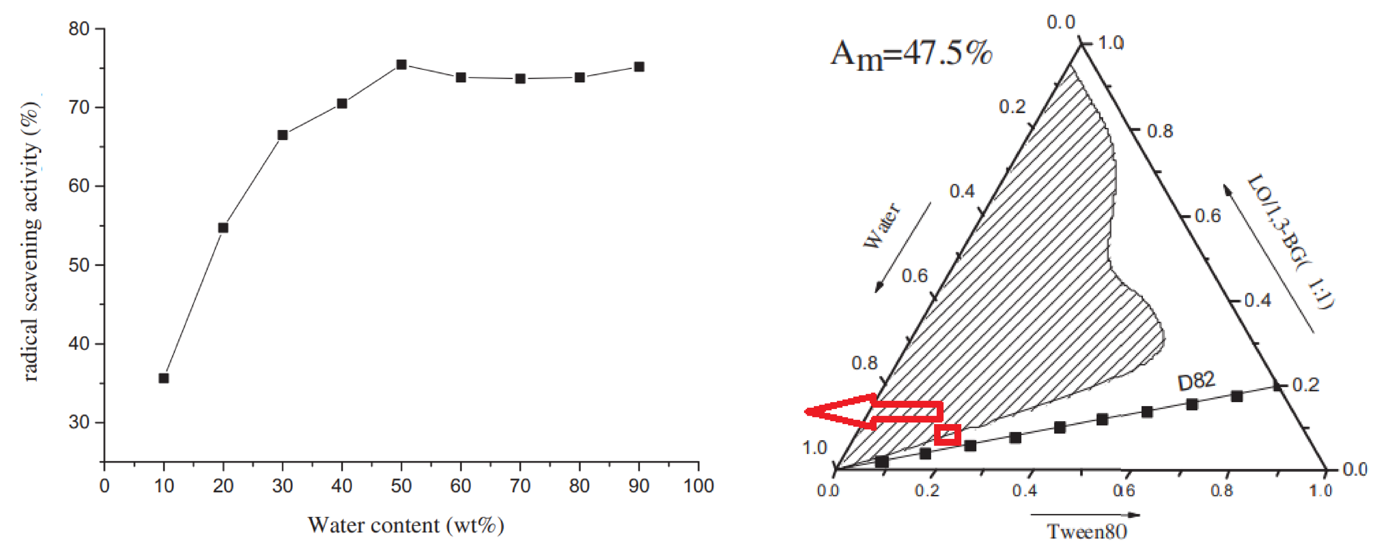


Figure 9: [12] Pseudoternary phase diagram (right) indicating ME existence (A_m = 47.5%) in gray for various ratios of water, Tween80 and LO/cosurfactant (1:1). D82 represents an effective dilution line. Radical scavenging activity in ME of various water content % (left). Radical scavenging activity increased from 35% to ~75% as water content increased from 10% to 90%.

LO's solubilization and antiradical properties were structurally dependent on the presence of 1,3-BG and higher water content in ME.

Microemulsions in Drug Delivery

Background:

- ME are widely used in the pharmaceutical industry as drug carriers to enhance drug solubility and absorption.
- Self-microemulsifying drug delivery systems (SMEDDS) contain mixtures of oils, surfactants, cosurfactants that produce o/w emulsions when introduced into the gastrointestinal tract.
- Zhu et. al (2012) develop a SMEDDS to improve the oral bioavailability of berberine hydrochloride (BBH), an anti-diabetic and cholesterol-lowering drug.[14]

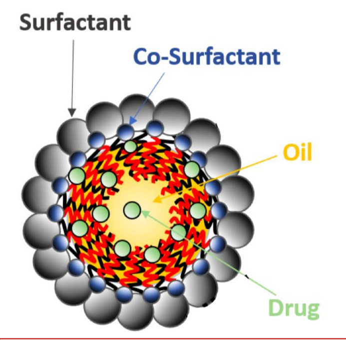


Figure 9:[15] O/W emulsion with encapsulated drug

SMEEDS Formation Methods and Results[14]

- Screening of oils and surfactant type and ratio based on solubility of BBH and formation of pseudoternary phase diagrams.
  - Optimal formation: 40% (w/w) of ethyl linoleate and oleic acid (2:1), 35% (w/w) Tween-80 and 25% (w/w) glycerol.

	Vehicles	Solubility (mg/mL)
Oils	Oleic acid	0.69 ± 0.05
	Ethyl linoleate	0.70 ± 0.06
	Soybean oil	0.12 ± 0.01
	Olive oil	0.11 ± 0.01
Surfactants	Tween-20	1.0 ± 0.09
	Tween-60	1.27 ± 0.10
	Tween-80	1.55 ± 0.11
	Cremophor EL	0.87 ± 0.07
	Cremophor RH40	0.85 ± 0.07
	Labrasol	4.94 ± 0.23
Co-surfactants	Ethanol	5.31 ± 0.32
	Isopropanol	16.88 ± 1.20
	Propylene glycol	53.27 ± 3.37
	Glycerol	162.34 ± 10.14
	PEG-400	67.62 ± 4.25

Figure 10: Solubility of BBH at 37ºC in various vehicles

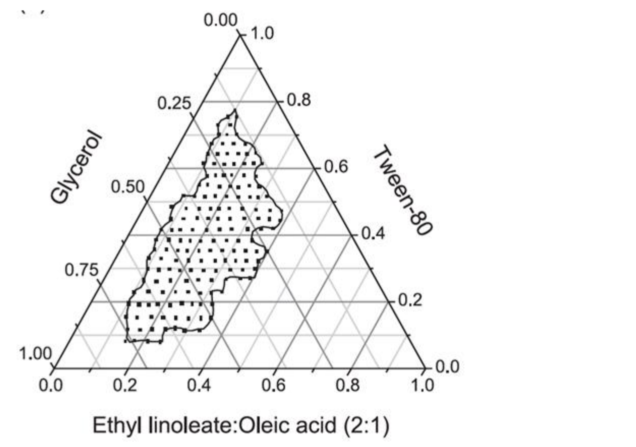


Figure 11: Pseudoternary phase diagram indicating the efficient self-microemulsification region

Bioavailability Study Methods and Results[14]

- Comparison of BBH dissolution from SMEDDS and commercial tablet in various dissolution media (pH 6.8 phosphate buffer, dist. water, 0.1N HCl)
- Comparison of BBH plasma concentration in rats following oral administration of BBH SMEDDS and commercial tablet.

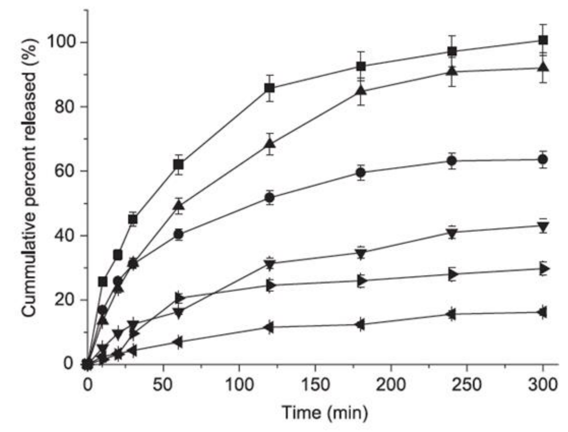


Figure 12: *In vitro* profiles of BBH from SMEDDS and commercial tablet formulation in various dissolution media at 37°C (—■—, pH 6.8 Phosphate buffer, SMEDDS; —▲—, distilled water, SMEDDS; —●—, 0.1N HCl, SMEDDS; —▼—, pH 6.8 Phosphate buffer, commercial tablet; —▶—, distilled water, commercial tablet; —◀—, 0.1N HCl, commercial tablet).

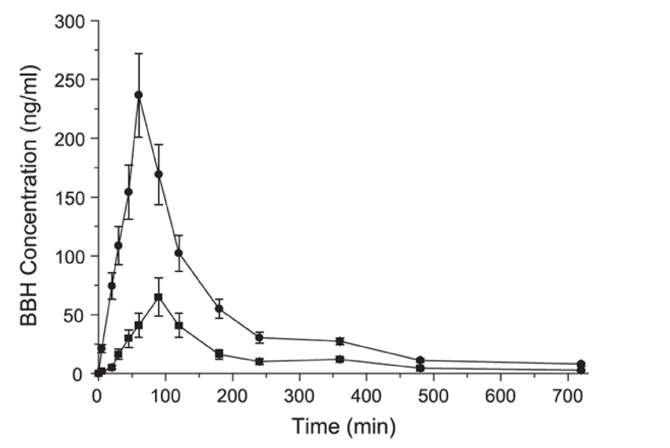


Figure 13: Plasma concentration profiles of BBH after oral administration of SEMDDS (•) and the commercial tablet (■) in rats (n = 6 and 25 mg/kg).

- **Results:** Understanding the physicochemical behavior and stabilization mechanisms of SMEDDS

Conclusions

- Surfactants and cosurfactants control interfacial tension by altering the surface chemistry to stabilize emulsions.
- ME smaller droplet surface area (lower, negative ΔG) makes ME favorable as it is thermodynamically stable in comparison to MAC which have larger droplet surface area (higher, positive ΔG).
- ME have thermodynamic stability that permit widespread industrial applications.

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