Inter & Intramolecular mixtures as an optimum compromise to enhance solubilization in microemulsions

Jean-Louis Salager, Cesar Scorzza, Josmary Velasquez, Maria A. Arandia, Ana Forgiarini

What is Solubilization?
• it is the ability of a surfactant to produce a monophasic system containing both oil and water

Solubilization Parameters

SP* Solubilization parameter at crossing

SP water in m

SP oil in m

Formulation Scan

At optimum formulation
• Bicontinuous microemulsion

Transparent microemulsion?
• Near R =1 → curvature = 0
• Swollen Micelles → large size
• Surfactant Layer Solubilized Liquid


Formulation Scan

Formulation Scan

Formulation Scan

Formulation Scan
High solubilization = 3φ with turbid microemulsions

<table>
<thead>
<tr>
<th>SP* (ml/g)</th>
<th>γ* (mN/m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>0.01</td>
</tr>
<tr>
<td>10</td>
<td>0.004</td>
</tr>
<tr>
<td>17</td>
<td>0.001</td>
</tr>
<tr>
<td>33</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

Tension-Solubilization Relationship

Solubilization varies as the inverse of interfacial tension

\[ \gamma \times SP^2 = \text{Constant} \]

The constant depends on surfactant (it is the same along the scan)

C. Huh, *J. Colloid Interface Sci.* 71:408-425 (1979)

Winsor’s R Ratio of interactions

\[ R = \frac{Aco}{Acw} \]

interfacial tension - SP

Maximum Solubilization when N = D

\[ R = 1 = \frac{Aco - Aoo}{Acw - Aww} = \frac{N}{D} \]

\[ \frac{2}{2} = \frac{5}{5} = \frac{10}{10} \]

is it the same thing?

Examples

- Alkyl phenol ethoxylates / octane / no alcohol
  - C8 - Ø - 5.3 EO: SP* = 5 ml/g
  - C9 - Ø - 5.7 EO: SP* = 8 ml/g
  - C12 - Ø - 8.3 EO: SP* = 20 ml/g

- N-hexane, 4.5 wt% NaCl, Surf/n-butanol=2/3
  - C12-O-SO3Na: SP* = 5.2 ml/g
  - C18-CH3COONa
    - NHCOCH3: SP* = 15 ml/g

Solubilization increases ... but

But, when chain reaches 18–20 carbon atoms, the surfactant precipitates (Krafft Temperature)

Mixing lipophilic and hydrophilic species

- Extends the reach on both sides
- Avoids precipitation
- Increases packing

Mixture of 2 different Surfactants increases interactions at interface

- Better interactions at interface
- Better packing

High interfacial \( \text{SP}_{\text{int}} \)

\[
\text{SP}_{\text{int}} = \frac{\text{Vol Oil or Water}}{\text{Mass Adsorbed surfactant}}
\]

Example


Beware that adding a short alcohol (balanced) cosurfactant decreases solubilization

- Reduces the average reach on both sides
- Decreases packing

But unbalanced (segregated) additives increases solubilization

- Increases the average reach of surfactant
- Do not decreases packing

LINKER concept
Lipophilic and Hydrophilic Linkers
= thickness + mixture

But fractionation
produce:

- Better match
  (oil does not contact water)
- Continuous polarity variation

Example

= L Linker + Surfactant

<table>
<thead>
<tr>
<th>EO</th>
<th>EO + EO</th>
<th>1 EO + 9 EO</th>
</tr>
</thead>
<tbody>
<tr>
<td>EO</td>
<td>EO + EO</td>
<td>1 EO + 9 EO</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>8</td>
</tr>
</tbody>
</table>

Increasing difference
fractionation

Amphophilic Linker
= thickness + mixture + no fractionning

- It becomes anchored on both sides of interface (low MW diblock polymer)
- There is no precipitation problem only if used at very low concentration
- Considerable enhancement of Solubilization

What may be concluded
as far as solubilization is concerned?

Favorables factors are:

- Continuity in interfacial H ↔ L transition
- Larger size + a good match on both sides
- No precipitation and no fractionation

What should be done?

Far away reach
Thick intermediate zone but no precipitation
(mixture + intermediate polarity)
Good hydrophilic interaction

Surfactant+linker effect could be attained with a single “extended” surfactant ! = intramolecular mixture

Extended Surfactant

Surfactant + Linker

hydrophobic chain

hydrophilic group

Spacer arm is hydrophobic but slightly polar

POLY-PROPYLENE OXIDE

Extended Surfactant (1rst Generation)

dodecyl

poly-propylene oxide (variable length)

= mixture feature

ethoxy (2EO)

sulfate sodium salt


Extended Surfactant Properties

depend on \( \rightarrow \) Propylene Oxide Number (PON)

When PON increases

- CMC decreases
- Cloud Point is lowered
- Optimum Salinity (3\( \phi \)) decreases

Conclusion:

- When PON increases ...
  ... surfactant becomes more lipophilic
  ... but does not precipitate (mixture)

Extended Surfactant Properties

Usually SP* decreases as ACN increases

At low PON it does too!

At high PON it increases with ACN

Good for LONG ALKANES

Depends on PON and EACN


Extended Surfactant Properties

produce 3 \( \phi \) with HIGH SOLUBILIZATION and LOW TENSION with POLAR OILS

Ethyl oleate

Miglyols

Soya Oil

Depends on PON and EACN

Salager J.L et al., 7th Word Surfactant Congress CESIO, Paris, June 2008
Extended Surfactant Properties

Usual mixing rule of 2 AI surfactants

Mixing rule of ES with nonionics

Obey: $HLD = \beta - kACN + bS - f(A) + cT - (T-25)$

with $\beta = \alpha - EON$ for C9EO3.

Miñana-Pérez M. et al., 4th World Surfactant Congress. Barcelona Spain, June 1996

As far as SP'MIX is concerned the rule is (only) approximately linear for polar oils and dependent only on extended surfactant mixture feature does not work the same way!

Extended Surfactant Properties

ES with PPO less hydrophilic as Temp increases

First 2–3 POs are wet by water!

ES with PPO Independent of PON

Optimize nature and size of the 3 pieces:

- Adjust structure to oil nature
- New generation of extended surfactants:
  - Biocompatible “green” polar groups
- Learn how to use mixing rules
  - Conventional + extended surfactants

What’s next?

- Optimize nature and size of the 3 pieces:
  - Adjust structure to oil nature
- New generation of extended surfactants:
  - Biocompatible “green” polar groups
- Learn how to use mixing rules
  - Conventional + extended surfactants
**Extended Alkyl Monoglycoside**

![Extended Alkyl Monoglycoside Diagram](image)


**Polar Heads (Simple or Combined)**

Currently synthesized and tested

- Linear C12-C18 chain attached at end or center, saturated or unsaturated
- Different kinds of spacers you could think about

**Different Head Groups**

- Sulfate
- Phosphate
- Carboxylate
- Ethoxy-Sulfate
- Ethoxy-Carboxylate
- Polyethoxylate
- C6 sugars
- Xylitol (C5 sugar)
- Di-Xylitol
- Ethoxy-Xylitol
- Carboxylate & Xylitol
- Carboxylate & Glucose

**Current Best Solubilization:**

1 g of high performance extended surfactant might solubilize 33 g of hexadecane or ethyl oleate and 15 g of C18 triglyceride

**Conclusions**

Solubilization may be increased by increasing the thickness of the polar-apolar transition zone:

1. Increasing the surfactant size (both sides) up to a limit > precipitation
2. Using a mixture of Lipo-/Hydrophilic amphiphiles up to a limit > fractionation
3. Using an intramolecular mixture with spacer of intermediate polarity = extended surfactant
   - Even better if intermediate is a mixture (PPO) up to a limit ... yet to be found!

Visit us at [www.firp.ula.ve](http://www.firp.ula.ve)

Thank you for your Attention