Solubilization in Microemulsions

Principles and Recent Advances with Extended Surfactant (smart) Structures

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What is Solubilization?

- It is the ability of a surfactant to produce a monophasic system containing both oil and water.

![Diagram of solubilization](image)

All phase diagrams contain a monophasic zone

If a formulation variable is changed (along a Formulation scan), how does solubilization change?

Bourrel M., Schechter R. S., Microemulsions and Related Systems, Marcel Dekker, New York, 1988

The “height” of polyphasic zone at fixed oil/water composition (e.g. 50/50) is monitored.


Normal Case (Winsor)

S+A (%)

Bourrel’s gamma (γ) diagram

Formulation (e.g. S)

Minimum S + A

Optimum Formulation

in all cases

- the “cross” locates the point with highest solubilization
Solubilization Parameters

SP\textsuperscript{a} Solubilization parameter at crossing

- SP\textsubscript{water} in m
- SP\textsubscript{oil} in m

At optimum formulation

- Bicontinuous microemulsion

At optimum formulation

- Bicontinuous microemulsion zero curvature structure


Transparent microemulsion?

- Near R = 1, curvature = 0
- Swollen Micelles, large size

Surfactant Layer

Qty. of Surfactant depends on area $\alpha R^2$

Solubilized Liquid

Solubilized Qty. depends on volume $\alpha R^3$

SP $\alpha R^3 / R^2$

valid for micelles and microemulsions

High solubilization = $3\phi$ with turbid microemulsions

<table>
<thead>
<tr>
<th>SP*</th>
<th>$\gamma^*$</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>

m/g

mN/m
Tension-Solubilization Relationship
- Solubilization varies as the inverse of interfacial tension


Solubilization Parameters

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

Winsor’s R Ratio of interactions

\[ R = \frac{A_{co}}{A_{cw}} = \frac{N}{D} \]

R < 1 \hspace{1cm} R = 1 \hspace{1cm} R > 1

Maximum Solubilization when N = D

is it the same thing?


Examples

Alkyl phenol ethoxylates / octane / no alcohol
- C8 – O – 5.3 EO \hspace{1cm} SP* = 5 ml/g
- C9 – O – 5.7 EO \hspace{1cm} SP* = 8 ml/g
- C12 – O – 8.3 EO \hspace{1cm} SP* = 20 ml/g

N-hexane, 4.5 wt% NaCl, Surf/n-butanol=2/3
- C12-O-SO:Na \hspace{1cm} SP* = 5.2 ml/g
- C18-CH < COONa \hspace{1cm} NHCOCH3 \hspace{1cm} SP* = 15 ml/g

Winsor’s Premise

\[ R = 1 = \frac{2}{2} = \frac{5}{5} = \frac{10}{10} \]

- higher interactions
- higher N (or D)
- higher solubilization
In order to change N or D formulation must be changed

To keep R = 1 situation
2 variables (at least) must be changed

Two alternatives
- 2 changes on different sides of interface
- 2 changes on the same side of interface


Solubilization increases
- 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 SP_{int}^*

SP_{int}^* = \frac{Vol \text{ Oil or Water}}{Mass \text{ 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

But mixtures fractionate

Lipophilic species go in oil
Hydrophilic species in water
= preferential partitioning

Only a small % at interface
= Surfactant loss
= Low apparent SP_{app}^*

\[ SP_{app}^* = \frac{\text{Vol Oil or Water}}{\text{Mass Total surfactant}} \]


Example

Lipophilic Linker + Surfactant

Increasing difference in fractionation

<table>
<thead>
<tr>
<th>Additive</th>
<th>SP_{app}</th>
<th>SP_{int}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethoxylated Octylphenol (EON near 5)</td>
<td>4.3</td>
<td>5.5</td>
</tr>
<tr>
<td>Ethoxylated Octylphenol (EON near 5)</td>
<td>5.0</td>
<td>5.5</td>
</tr>
</tbody>
</table>

Caution

- There are (often) opposite phenomena, due to the complexity of the R expression
- Don’t be afraid to go to the EOR literature...

Bourrel M., Schechter R.S., Microemulsions and Related Systems, Marcel Dekker, New York 1988
Huh C., Interfacial tensions and solubilizing ability of a microemulsion phase that coexists with oil and Brine. J. Colloid Interface Science, 71: 408-426 (1979)

In some cases Winsor’s model does not explain the observed increase in solubilization

Lipophilic Additive increases solubilization
Lipophilic Linker effect

Proposed Mechanism

The Lipophilic Linker increases interactions on the oil side by “ordering” the molecules deeper inside the oil bulk phase

The Lipophilic Linker

- does not adsorb at interface
  (it is not a cosurfactant)
- is a slightly polar oil
  (or a very lipophilic amphiphile)
- is located inside oil phase near interface
  (interfacial segregation)
- gets oriented perpendicular to interface
- "stretches" the reach of surfactant in oil
  (without producing precipitation)

The LIPOPHILIC LINKER effect is due to the SEGREGATION of the most polar substances in the oil phase which concentrate near interface.

The other phase and the surfactant only "see" the most superficial layer of the oil phase
(similar to a chocolate covered candy)

Interesting for applications!

Examples of Lipophilic Linkers

- Long chain n-alcohols (> 8)
- Long chain alkylphenols (> 8)
- idem slightly ethoxylated (EON < 2)
- Single chain esters (ethyl oleate)
- probably other linear lipophilic amphiphiles

Gracia A. et al., Improving Solubilization in Microemulsions with Additives - Part II: Long chain Alcohol as Lipophilic Linkers, Langmuir 9: 3371 (1993)

Alcohols as Lipophilic Linkers

Lipophilic Linker effect adds up to surfactant effect

0.02 M Ethoxylated Alkylphenol
T = 26 °C
0.0325 M n-alcohol Isocane
WGR = 1

Mixing LL improves solubilization = Longer LL

Alcohol (LL) Mixture
The Lipophilic Linker is ...  
... a very lipophilic amphiphile
- or a polar oil ...  
... which acts at very low concentration
- because it locates itself ...  
... near interface

It is not a case of adsorption ...  
... but of **segregation**

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**Interfacial Segregation**

- Take a oil mixture...
  ... (same molar volume oils)
  - Hexadecane —> non polar (ACN=16)
  - Ethyl Oleate —> polar (EACN=6)

- Measure or evaluate
  - interfacial tension
  - optimum formulation
  - oil composition near interface

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**Interfacial Segregation**

Everything happens as if the “interfacial” oil were “pure” polar oil, when there is 50% of this oil in the mixture (green arrow)

= polar oil segregation near interface

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**Hydrophilic Linker**

- Similar role on the water side although much less

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**Lipophilic and Hydrophilic Linkers**

= thickness + mixture

- produce:
  Better match
  (oil does not contact water)

- Continuous polarity variation

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Amphiphilic Linker
\[ \text{thickness} + \text{mixture} + \text{no fractionation} \]

- 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?

Favorable factors are:
- Continuity in interfacial transition
- And a good match on both sides
- No partitioning

What should be done?

- Far away reach
- Thick intermediate zone but no precipitation (mixture + intermediate polarity)
- Good hydrophilic interaction
- Easier to get a good interaction with water

Extended Surfactants (1st Generation)

- Dodecyl
- Poly-propylene oxide (variable length) = mixture feature
- Ethoxy (2EO)
- Sulfate sodium salt


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

= Intramolecular mixture

Extended Surfactant Properties

- Depend on Propylene Oxide Number (PON)

When PON increases
- CMC decreases
- Cloud Point is lowered
- Optimum Salinity (3φ) decreases

Conclusion:
- When PON increases ...
- Surfactant becomes more lipophilic...
- But does not precipitate (mixture)
Usual behavior of anionics

\[ \ln S = k ACN + \ldots \]

Idem but \( k \) depends on PON

Extended Surfactant Properties

- ES Produce a high SOLUBILIZATION and LOW TENSION particularly with natural oils
- Soya oil = natural triglyceride

Extended Surfactant Properties

- ES produce \( 3 \phi \) with HIGH SOLUBILIZATION and LOW TENSION with polar oils
- Ethyl oleate
- Miglyols
- Soya Oil

Extended Surfactant Properties

- Micellar aggregation of extended surfactant
- Large volume in which polar oil can be solubilized

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
    - At PON=10 \( SP^* \) does not vary with ACN

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


Extended Surfactant Properties

Usual mixing rule vs formulation

Mixing rule of ES with nonionics

Obey HLD = $\beta - kACN + bS - f(A) + c_1$ (T-25)

With $\beta = \alpha - EON$ for CSEON

Extended Surfactant Properties

As far as $SP^*_{ext}$ 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!

ANIONICS

Other POs are not!

First 2–3 PO groups are wet by water!

Extended Surfactant Properties

Current availability ... poor

Some samples of alkyl PolyPO (EO) sulfates have been prepared by three surfactant manufacturers (Seppic, Sasol, Huntsman) and some studies reported.

Recent Publications

- SORRENZ C. et al., As an other new family of ‘‘extended’’ glucidoamphiphilic Synthesis and Surfactant Properties for different Sugar head Groups and Spacer Arm lengths, J. Surfactants Deterg. 5: 357 (2002)
- HUANG L. et al., Effect of the temperature on solubilization performance of extended surfactants containing a carboxylic or sulfate polar group, J. Surfactants Deterg. 8: 167 (2005)
Optimize nature and size of the 3 pieces:
- Adjust structure to oil nature
- New generation of extended surfactants: Biocompatible “green” polar groups
- Determine mixing rules
  Conventional + extended surfactants

2nd Generation of extended surfactants for biocompatible applications
- sugar polar group
- tailored spacer arm
- Fatty acid derivative (hydrophobic tail)

Physico-chemical Properties of theses Products are under study

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
  - ethoxy-sulfate
  - carboxylate
  - ethoxy-carboxylate
  - C6 sugars
  - xylitol (C5 sugar)
  - di-xylitol
  - ethoxy-xylitol
  - carboxylate & xylitol
  - carboxylate & glucose

Extended soaps

Extended alkyl monoglycoside

Extended mono-di-xylitol a non-cyclic glycoside
Current best solubilization:
1 g of high performance extended surfactant can solubilize almost 40 g of hexadecane or ethyl oleate and 15 g of C18 triglyceride.

Potential Applications
- Microemulsions to be directly injected in blood stream (Drugs are generally oil soluble)
- Soak-only Detergents (no stirring required)
- Solvent like extraction (e.g. edible oil in pressing residue)
- Transdermic transfer (pharmaceuticals and cosmetics)
- Crude Oil dehydration (ext. surf. combine with asphaltenes)

For some applications, the used surfactants must be completely biocompatible, biodegradable, non-toxic, “green”… etc…!

Just a slight improvement in solubilization and the original R&D goal (1987) may be attained.

Solubilization may be increased by increasing the thickness of the polar-apolar transition zone:
- Increasing the surfactant size
  - up to a limit > precipitation
- Using a mixture of Lipo-/Hydrophilic amphiphiles
  - up to a limit > partitioning
- Using an intramolecular mixture with spacer arm of intermediate polarity = extended surfactant...
  - probably better if intermediate is a mixture (polyPO)
  - up to a limit ... to be found!

A Comment on this Research Progress

Understanding according to Winsor

LIPOPHILIC LINKER

EXTENDED SURFACANT

Understanding properties

New structures, Biocompatibility issues

innovation

annoyancy
diagnostic

PROGRESS

TIME

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Thank you for your Attention