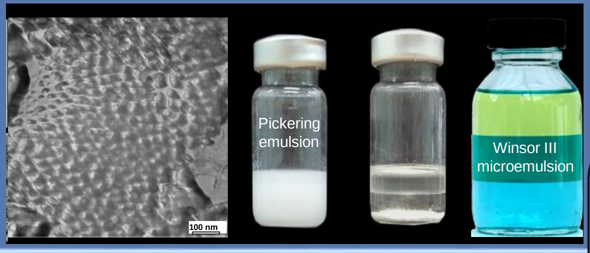
Groupe Chimie Durable – 28 Septembre 2021

LES HYDROTROPES BIOSOURCES : PROPRIETES ET APPLICATIONS A LA SOLUBILISATION ET A L'EXTRACTION

Véronique Nardello-Rataj, Professeur
Centrale Lille Institut, ENSC-Lille

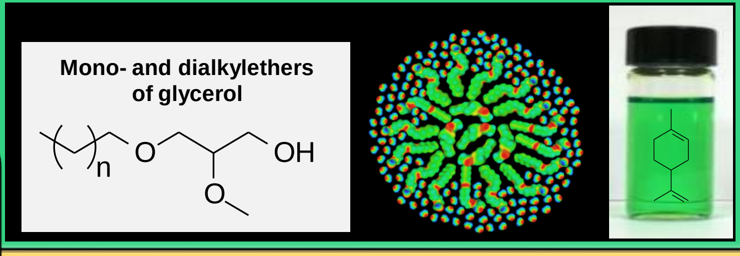
❶ CATALYSE INTERFACIALE

Milieux réactionnels organisés pour l'oxydation



❷ COMPOS2S FONCTIONNELS AGROSOURCES

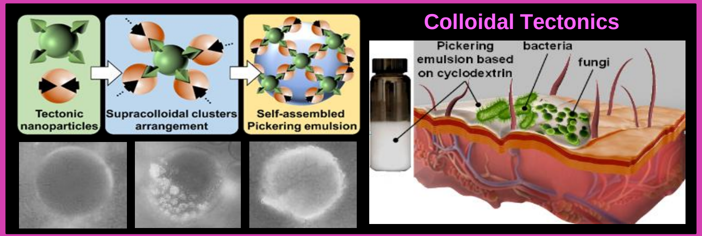
Eco-conception et Propriétés



CISCO2
COLLOIDS
CATALYSIS
OXIDATION

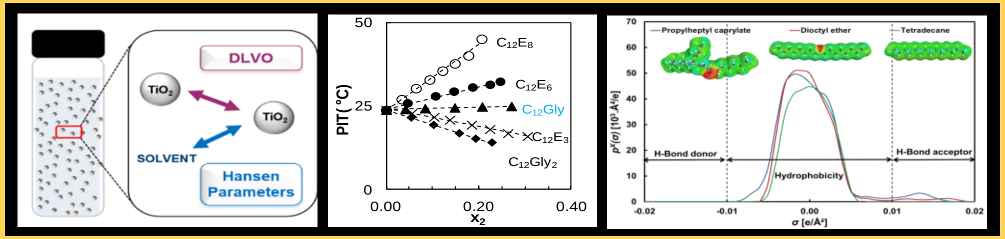
❸ FORMULATIONS COLLOÏDALES

Eco- et biocompatibles



❹ CONCEPTS, OUTILS ET METHODOLOGIES

Pour la formulation



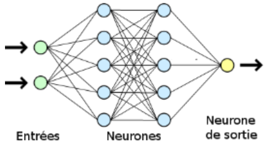
THE HT-SMARTFORMU PLATFORM –

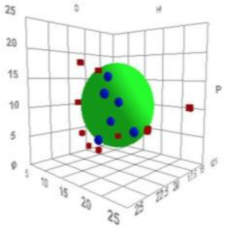
PHYSICO-CHEMISTRY

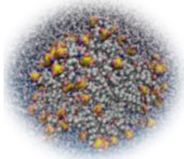
FORMULATION

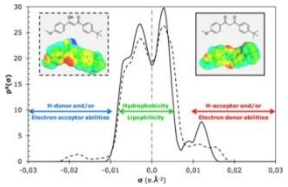
PERFORMANCES

MODELLING









Groupe Chimie Durable – 28 Septembre 2021

Société Chimique de France
Le réseau des chimistes

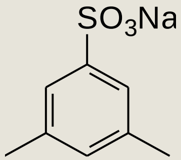
HYDROTROPES

CISCO2 COLLOIDS CATALYSIS OXIDATION · HT SMART FORMU · centralelille ENSCL · SATT NORD · institut Chevreul · Université de Lille · cnrs

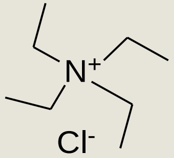
HYDROTROPES AND SOLVO-SURFACTANTS

➩ **Carl Neuberg (1916) :** organic salts like sodium benzoate or salicylate contained in urine are responsible for the solubilisation of hydrophobic compounds in water

➩ **McKee (1946) :** extension to small non-ionic amphiphilic compounds able to ↗ the solubility of oil in water through aggregation



Sodium xylene sulfonate



Tetraethyl ammonium chloride

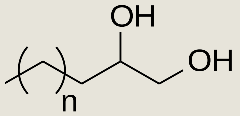
Main features of hydrotropes:

- ✓ **↗ the solubility of organic molecules in water**
- ✓ **Small molecules more or less hindered**
- ✓ **Slightly amphiphilic**
- ✓ **Destabilization of LC phases**

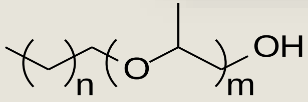
♦ Solvo-surfactants (Kunz 2004) = Volatile & NI hydrotropes = Amphiphilic solvents

➩ **Solvo:** high volatility and solubilizing capacity of solvents

➩ **Surfactant**: surface activity and self-aggregation



1,2-Alkanediol (n ≤ 6)



PPG monoalkyl ether (n ≤ 6, m ≤ 4)

1) Short chain glycerol 1-monoethers: new class of solvo-surfactants. Queste at al. Green Chem., 2006, 8, 822. 2) Dowanol DPnB in water as an example of a solvo-surfactant system. K. Lunkenheimer, W. Kunz, Prog. Colloid Polym. Sci., 2004, 126, 14.

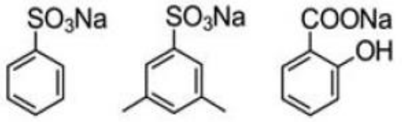
MAIN FAMILIES OF HYDROTROPES

ALIPHATIC

AROMATIC

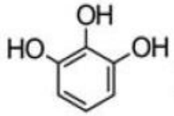
OTHER

Ionic



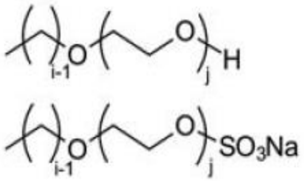
Sodium benzene sulfonate (SBS)
Sodium xylene sulfonate (SBS)
Sodium salicylate (SS)

Non-Ionic



Pyrogallol

Petrosourced

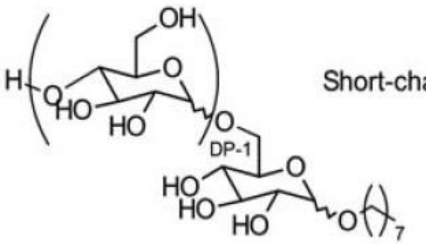


Short-chain glycol ethers

(i=1 to 6, j=1 to 3)

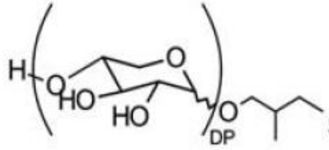
Sulfated short-chain glycol ether

Biosourced

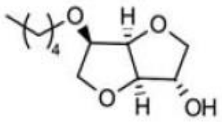


Short-chain Alkylpolyglucosides

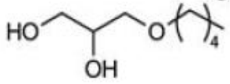
DP=1-3

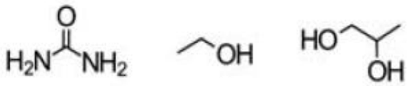


Short-chain Alkylpolypentosides



Short-chain ethers of biosourced polyols





Urea
Ethanol
Monopropylene glycol

V. Molinier et al. « Sugar-based hydrotropes: preparation, properties and applications », Carbohydr. Chem., 2014

EXAMPLES OF REPORTED HYDROTROPES

NATURELS

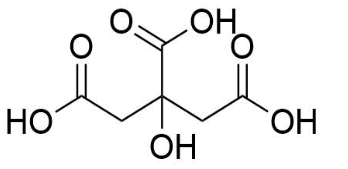
- Urée
- 1,3-Diméthylurée
- Fructose
- Glucose
- Mannitol
- Caféine
- Citrate Trisodique
- Acide citrique
- Tert-butanol
- Sodium Salicylate
- Alginate de sodium
- L-Acide Ascorbique

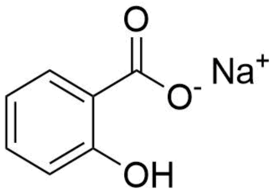
BIOLOGIQUES

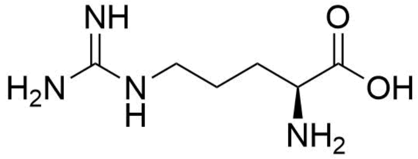
- L-Nicotinamide
- L-Niacine
- L-Proline
- L-Arginine
- Acide Malique
- Sodium Pyroglutamate
- L-Arabinitol
- Adénosine Triphosphate

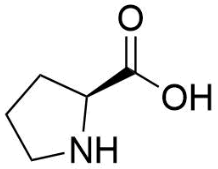
BIOSOURCES

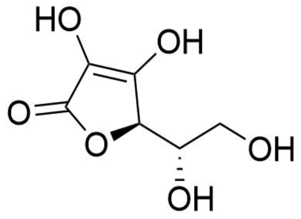
- Méglumine
- Esters de carnitine
- Alkyl Poly Glucoside
- Cyrène
- Isosorbide et dérivés

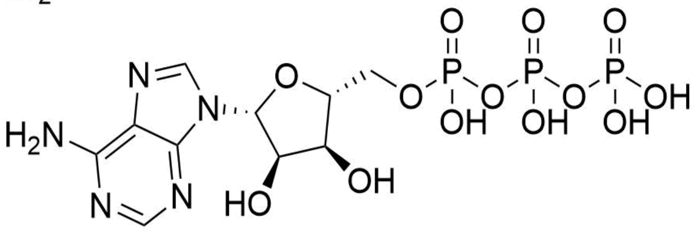


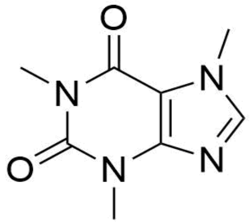


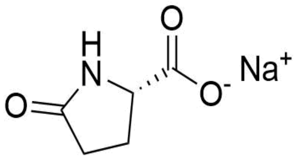


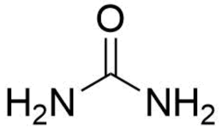












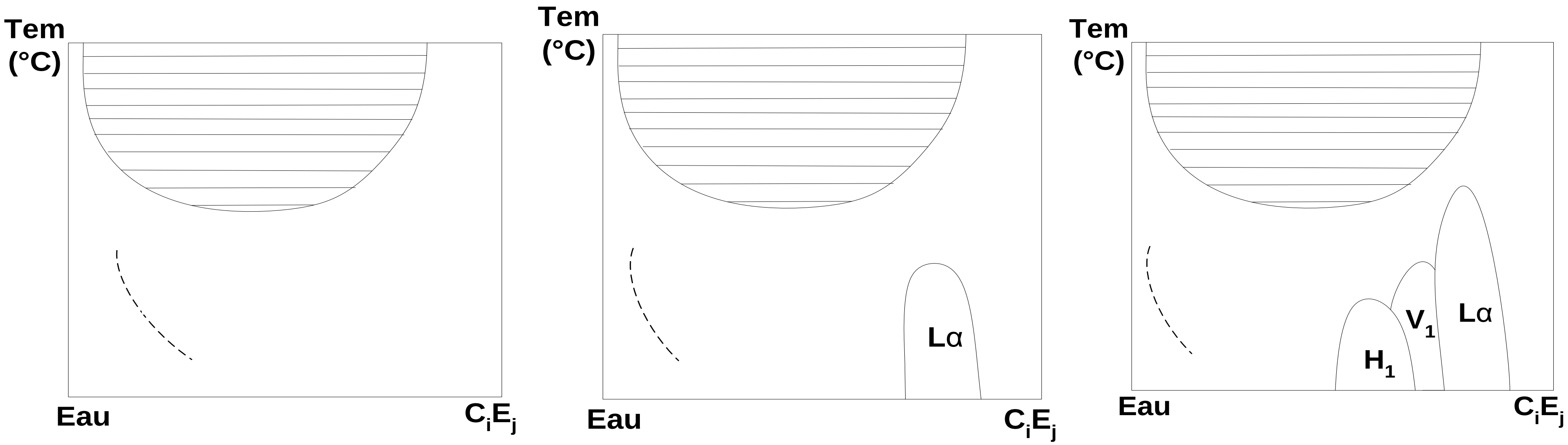
Aqueous Behaviour of Hydrotropes

Low amphiphile → C_4E_1

Medium amphiphile → C_8E_3

Strong amphiphile → $C_{12}E_6$

i and j ↗ ⇨ Amphiphily ↗



Hydrotropes & Solvo-surfactants

⇒ agreggation = ? dimers, trimers, weak interactions

“True” surfactants

⇒ micelles then liquid crystals

Mechanisms of Solubilization of Hydrotropes

3 Hypotheses

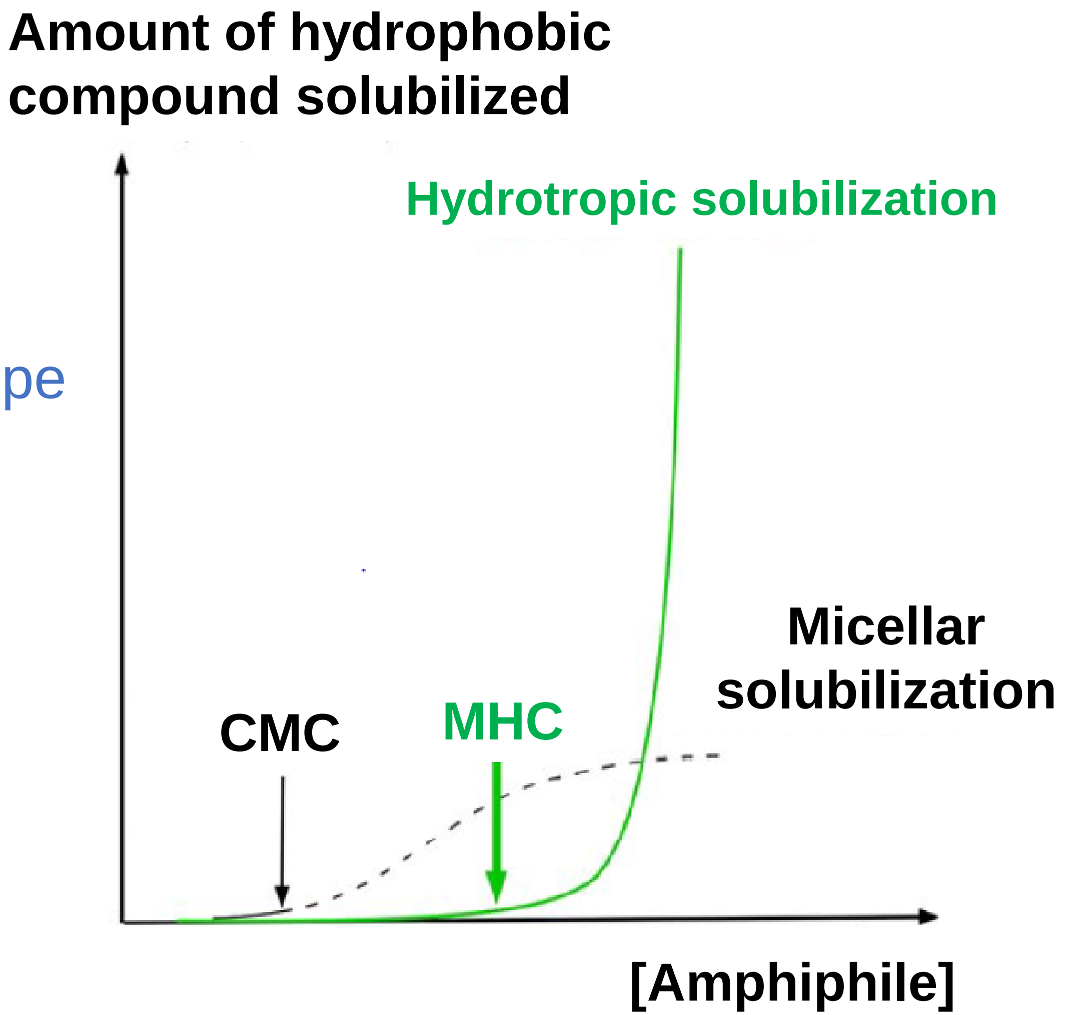
❶ Self-aggregation of hydrotrope molecules

❷ Modification of the water structure by hydrotrope

❸ Formation of hydrotrope/solute complexes

Thermodynamic considerations ⇒

Fluctuation Solution Theory (FST)



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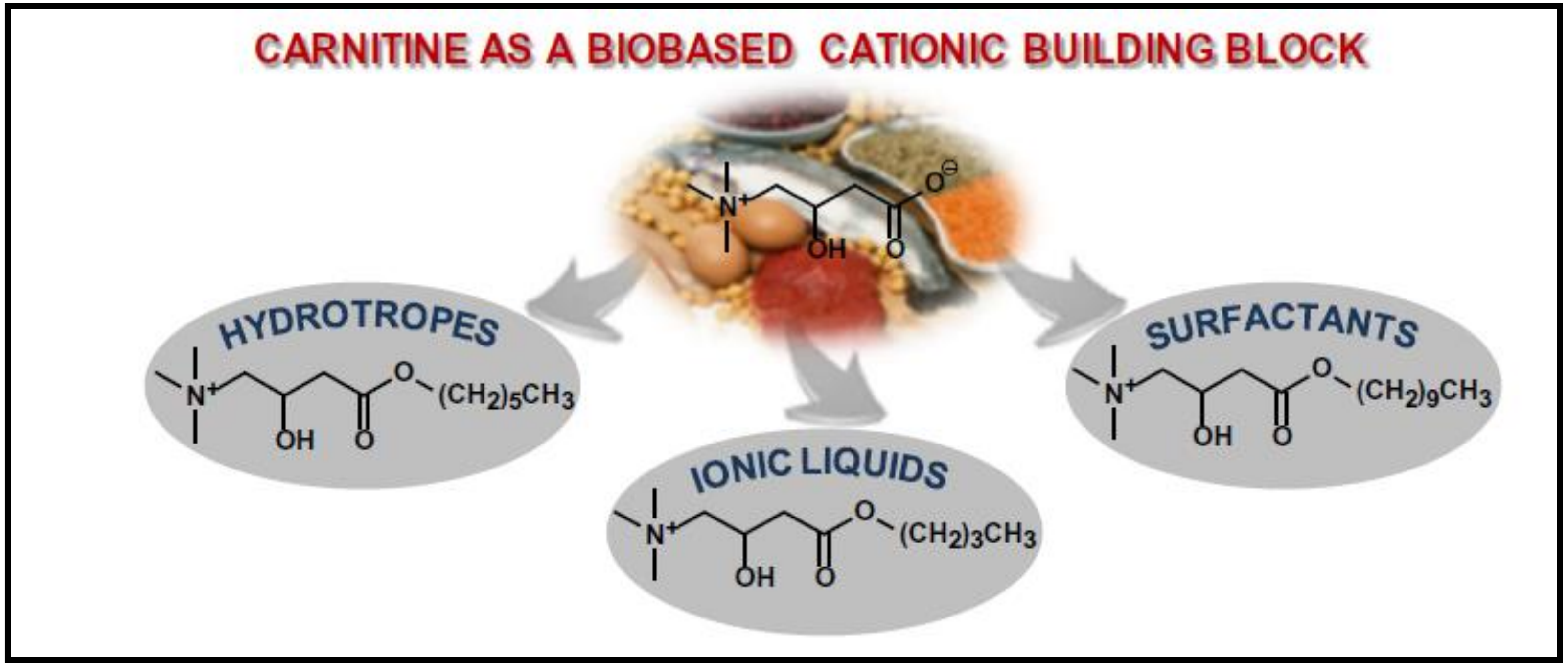
journal homepage: www.elsevier.com/locate/jcis

Regular Article

Carnitine alkyl ester bromides as novel biosourced ionic liquids, cationic hydrotropes and surfactants

Katharina Häckl [c], Andrea Mühlbauer [a], Jesús F. Ontiveros [a], Sinisa Marinkovic [b], Boris Estrine [b], Werner Kunz [c,*], Véronique Nardello-Rataj [a,*]

[a] Univ. Lille, CNRS, Centrale Lille, ENSCL, Univ. Artois, UMR 8181-UCCS-Unité de Catalyse et Chimie du Solide, F-59000 Lille, France
[b] ARD Agro-Industrie Recherches et Développements, Route de Bazancourt, 51110 Pomacle, France
[c] Institute of Physical and Theoretical Chemistry, University of Regensburg, Universitätsstraße 31, D-93053 Regensburg, Germany



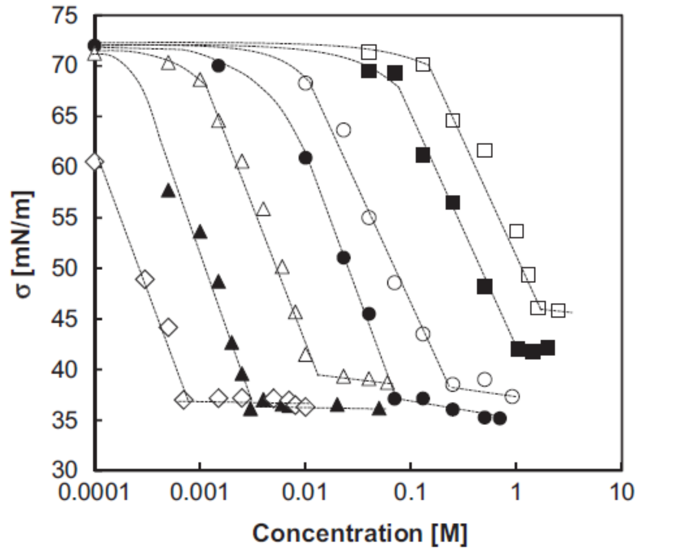


Fig. 3. Surface tension curves of **[C_nCar]Br** compounds with n = 2 (□), 4 (■), 6 (○), 8 (●), 10 (△), 12 (▲) and 14 (◇).

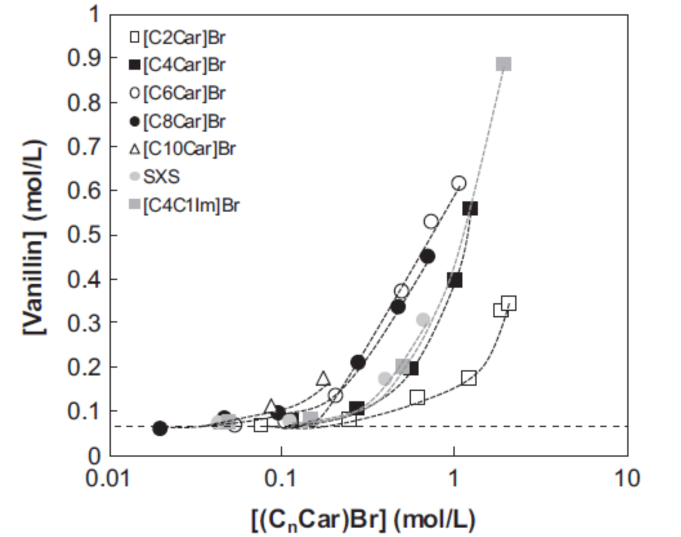


Fig. 6. Solubility of vanillin at room temperature in aqueous solutions of **[C_nCar]Br**. For sake of clarity, only the curves for n = 2–10 are shown in comparison with **SXS** and **[C_4C_1Im]Br.** Curves for n = 12, 14, DTAB, CTAB and L-carnitine can be seen in Supporting Information (Fig. S4). Dotted line indicates water-solubility of vanillin in water.

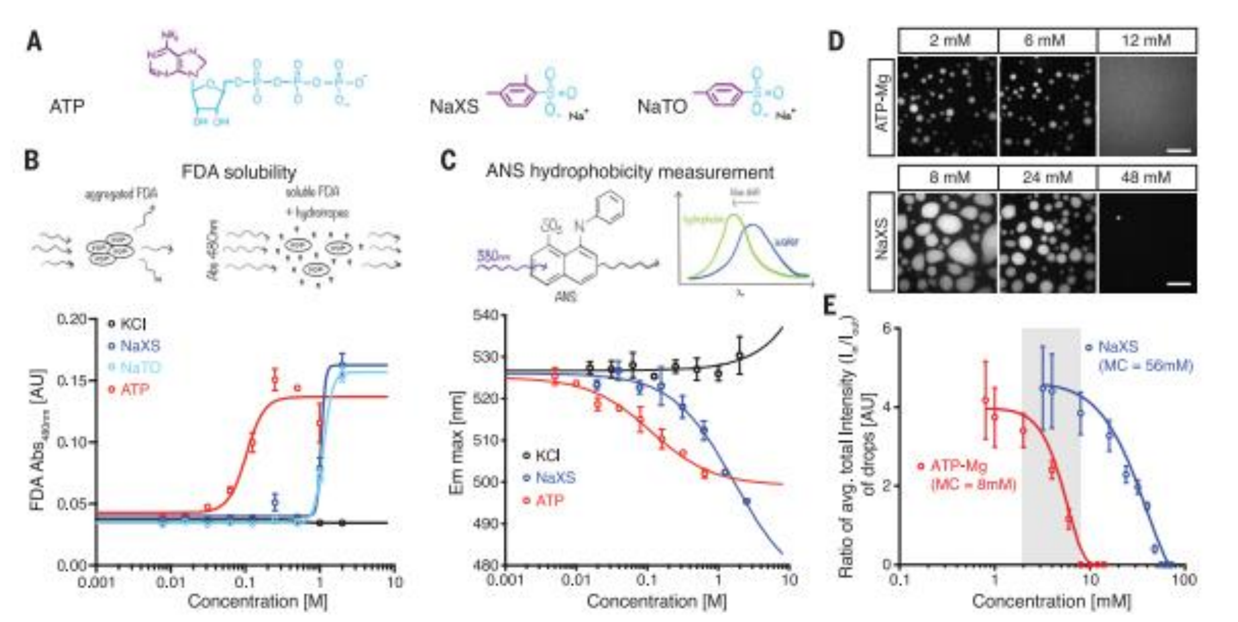
RESEARCH

BIOCHEMISTRY

ATP as a biological hydrotrope

Avinash Patel,[1*] Liliana Malinovska,[1*] Shambaditya Saha,[1] Jie Wang,[1] Simon Alberti,[1] Yamuna Krishnan,[2†] Anthony A. Hyman[1†]

Hydrotropes are small molecules that solubilize hydrophobic molecules in aqueous solutions. Typically, hydrotropes are amphiphilic molecules and differ from classical surfactants in that they have low cooperativity of aggregation and work at molar concentrations. Here, we show that adenosine triphosphate (ATP) has properties of a biological hydrotrope. It can both prevent the formation of and dissolve previously formed protein aggregates. This chemical property is manifested at physiological concentrations between 5 and 10 millimolar. Therefore, in addition to being an energy source for biological reactions, for which micromolar concentrations are sufficient, we propose that millimolar concentrations of ATP may act to keep proteins soluble. This may in part explain why ATP is maintained in such high concentrations in cells.



Patel et al., Science 356, 753–756 (2017)

ACS Sustainable Chemistry & Engineering

Research Article

Cite This: ACS Sustainable Chem. Eng. 2019, 7, 7878−7883

pubs.acs.org/journal/ascecg

Geminal Diol of Dihydrolevoglucosenone as a Switchable Hydrotrope: A Continuum of Green Nanostructured Solvents

Mario De bruyn,[*,†,‡] Vitaliy L. Budarin,[§] Antonio Misefari,[§] Seishi Shimizu,[∥] Heather Fish,[∥] Martin Cockett,[∥] Andrew J. Hunt,[⊥] Heike Hofstetter,[#] Bert M. Weckhuysen,[‡] James H. Clark,[§] and Duncan J. Macquarrie[§]

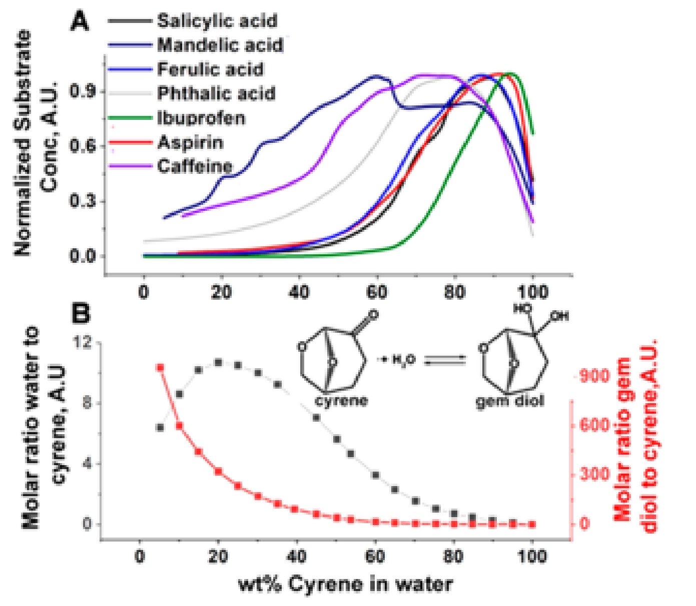
[†]Department of Chemical and Biological Engineering, University of Wisconsin-Madison, 1415 Engineering Drive, Madison, Wisconsin 53706, United States

[‡]Faculty of Science, Debye Institute for Nanomaterials Science, Utrecht University, Universiteitsweg 99, CG Utrecht 3584, The Netherlands

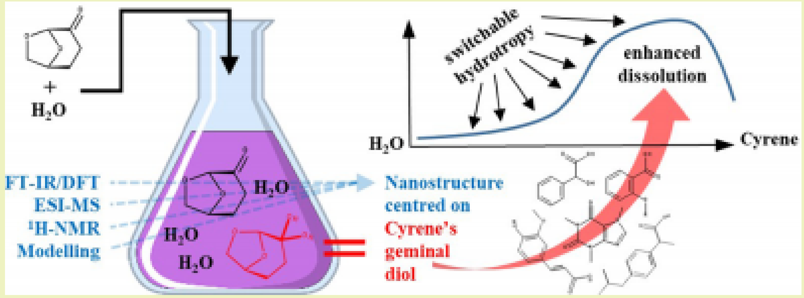
[§]Green Chemistry Centre of Excellence, Department of Chemistry, and [∥]Department of Chemistry, University of York, York YO10 5DD, United Kingdom

[⊥]Materials Chemistry Research Center, Department of Chemistry and Center of Excellence for Innovation in Chemistry, Faculty of Science, Khon Kaen University, Khon Kaen 40002, Thailand

[#]Department of Chemistry, University of Wisconsin-Madison, 1101 University Avenue, Madison, Wisconsin 53706, United States



ABSTRACT: The addition of water to dihydrolevoglucosenone (Cyrene) creates a solvent mixture with highly unusual properties and the ability to specifically and efficiently solubilize a wide range of organic compounds, notably, aspirin, ibuprofen, salicylic acid, ferulic acid, caffeine, and mandelic acid. The observed solubility enhancement (up to 100-fold) can be explained only by the existence of microenvironments mainly centered on Cyrene's geminal diol. Surprisingly, the latter acts as a reversible hydrotrope and regulates the polarity of the created complex mixture. The possibility to tune the polarity of the solvent mixture through the addition of water, and the subsequent generation of variable amounts of Cyrene's geminal diol, creates a continuum of green solvents with controllable solubilization properties. The effective presence of microheterogenieties in the Cyrene/water mixture was adequately proven by (1) Fourier transform infrared/density functional theory showing Cyrene dimerization, (2) electrospray mass-spectrometry demonstrating the existence of dimers of Cyrene's geminal diol, and (3) the variable presence of single or multiple tetramethylsilane peaks in the ^{1}H NMR spectra of a range of Cyrene/water mixtures. The Cyrene−water solvent mixture is importantly not mutagenic, barely ecotoxic, bioderived, and endowed with tunable hydrophilic/hydrophobic properties.



KEYWORDS: *Solvents, Nanostructure, Hydrotrope, Biobased, Switchable, Sustainable*

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AQUEOUS PERFUMES

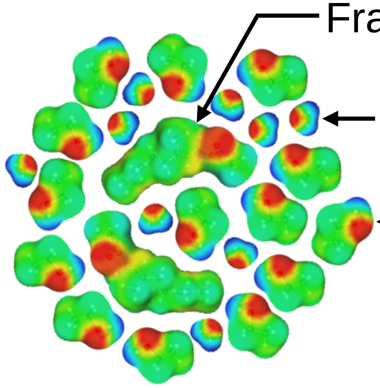
CISCO2 COLLOIDS CATALYSIS OXIDATION · HT SMART FORMU · centralelille ENSCL · SATT NORD · institut Chevreul · Université de Lille · CNRS

Fragrance solubilization in alcohol

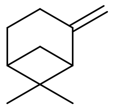
○ Perfumes = complex mixtures of fragrances dissolved into alcohols

Fragrance classification:

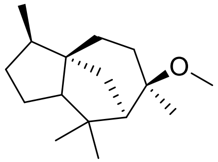
- ✓ *Perfume* ≈ 15 – 40 wt.%
- ✓ *Eau de Parfum* ≈ 10 – 20 wt.%
- ✓ *Eau de Toilette* ≈ 5 – 15 wt.%
- ✓ *Eau de Cologne* ≈ 3 – 8 wt.%
- ✓ *Aftershave* ≈ 1 – 3 wt.%



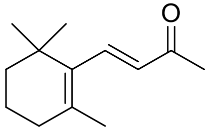
(Almost) no structuration !



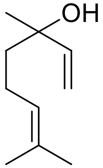
β-Pinene



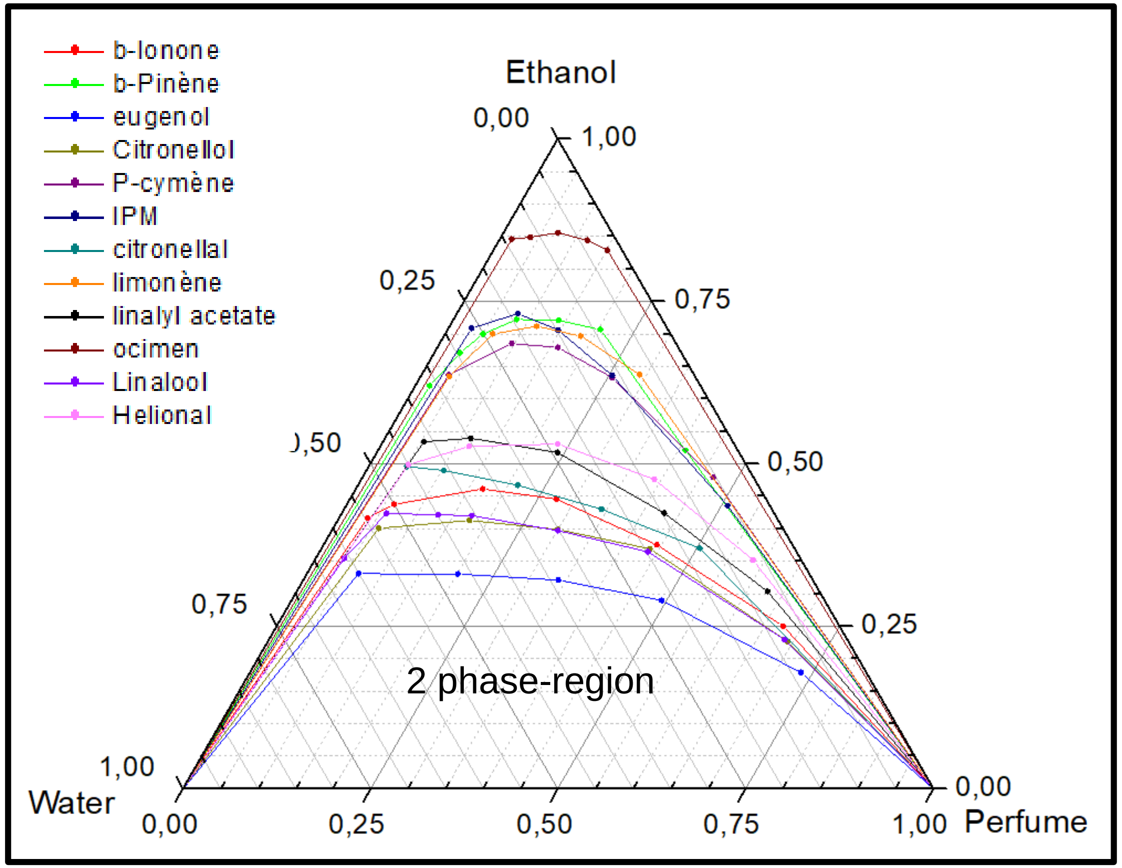
Methyl cedryl ether



β-Ionone



Linalool



Nano-droplet formation in fragrance tinctures. Kunz et al. Flavour Fragr. J. 2013, 28, 294–299

Why a need for ethanol-free systems?

- European VOC legislation (Council Directive 1999/13/EC)
  → Replacing or, at least, reducing volatile organic compounds

- Practical concerns linked to EtOH:
  → Alcoholic odour
  → Drying action on skin & hair
  → Irritation
  → Generation of free-radical damages

⇨ Active research is being conducted by industry to offer new compositions for new markets driven by public health and environmental reasons ⇒ **WATER**

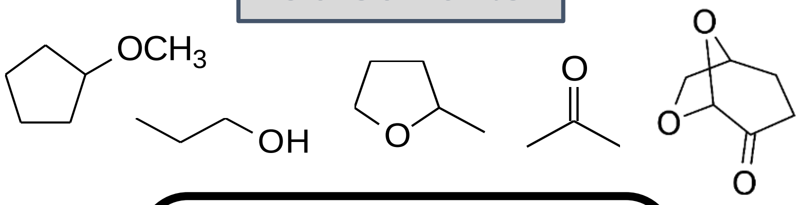
Unfavourable contact between surfaces of different polarity

Phase separation !

How to solubilize fragrance in water?

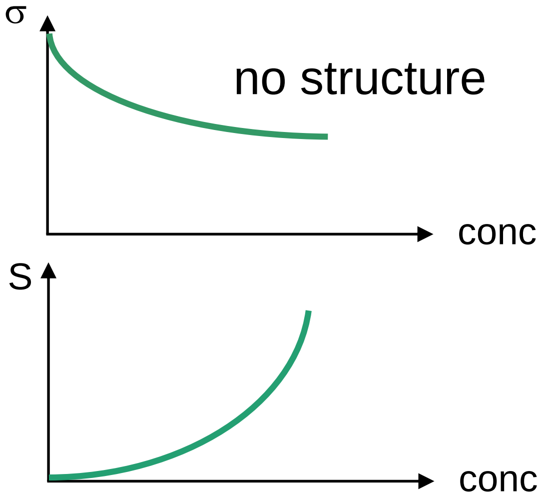
Molecular

Co-solvents



☺
- Very efficient
- Quite cheap

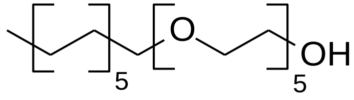
☹
- Biocompatibility
- Volatility (VOC)
- Odor



Micellar

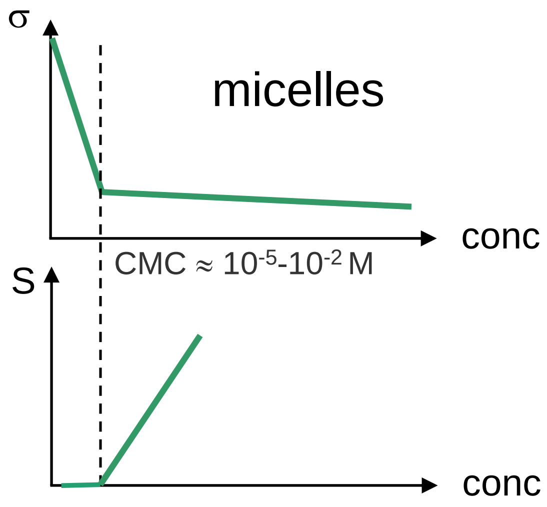
Surfactants

$C_{12}E_5$



☺
- Efficient
- No solvent

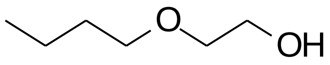
☹
- Residues
- Skin irritation
- LC formation



Hydrotropic

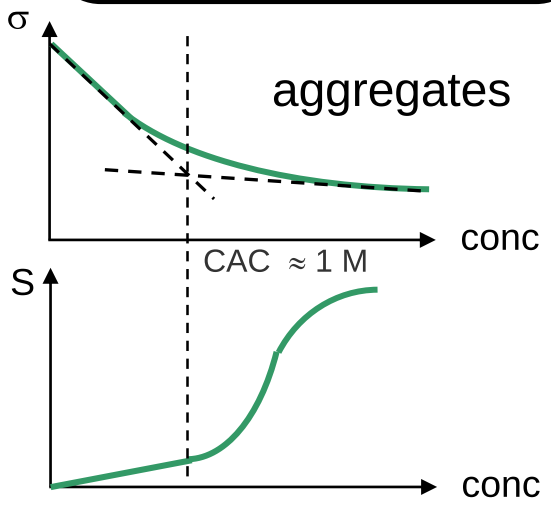
NI Hydrotropes

C_4E_1



☺
- Quite efficient
- Semi-volatile
- No LC formation

☹
- High CAC (cost, tox)



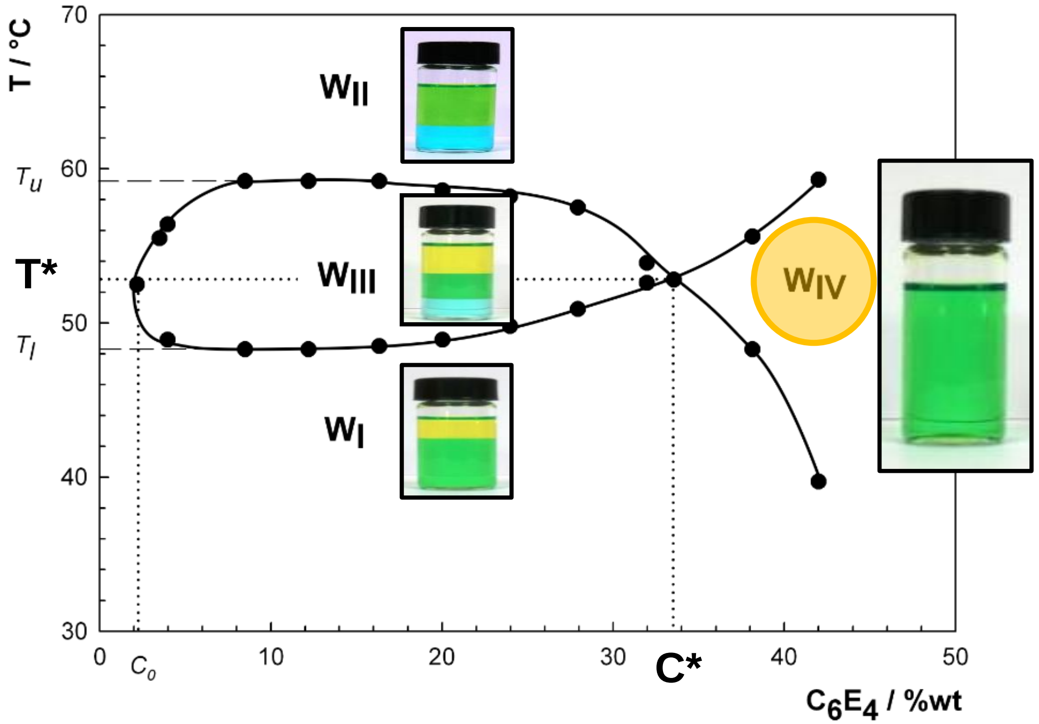
HYDROTROPE/FRAGRANCE/WATER MICROEMULSIONS

Water *Fragrance* *Microemulsion*

○ Main features of microemulsions:

- ✓ Submicronic dispersion
- ✓ Spontaneous formation
- ✓ Thermodynamically stable
- ✓ Clear solution
- ✓ $\phi_{droplets}$ = 10 – 50 nm
- ✓ Low viscosity
- ✓ Very low w/o γ_{int} (10^{-2} – 10^{-4} mN/m)

○ Types of microemulsions (Winsor systems)

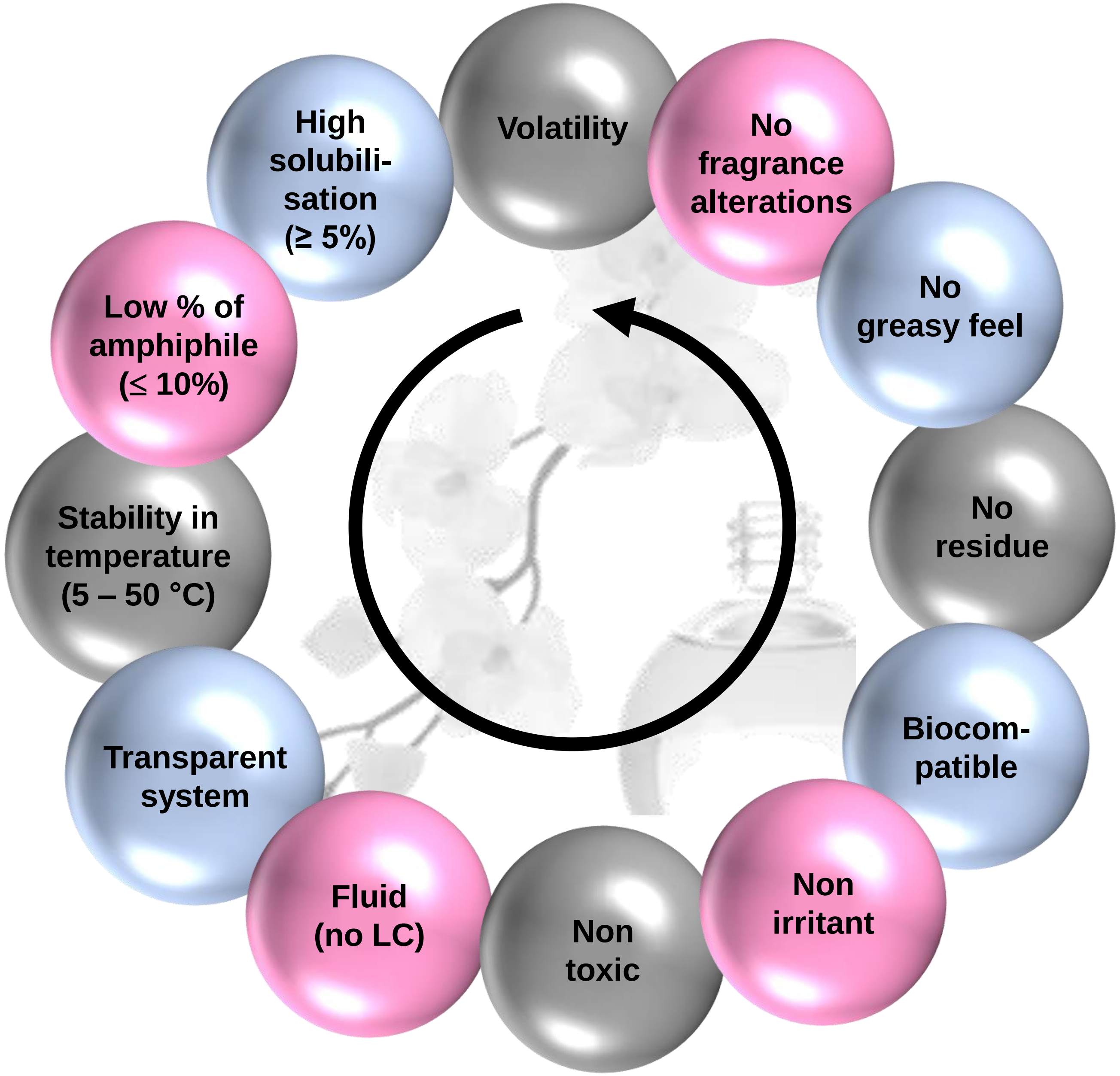


⇒ T* reflects the hydrophobicity of the oil

⇒ C* expresses the efficiency of the amphiphile

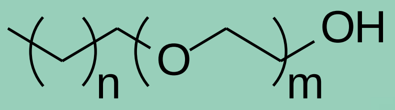
⇒ C* of hydrotropes >> C* of surfactants !

HYDROTROPE/FRAGRANCE/WATER MICROEMULSIONS



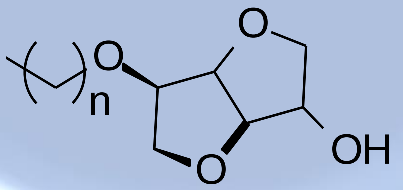
CHOICE OF HYDROTROPES

❶ Monoalkyl glycol ethers
C_nE_m



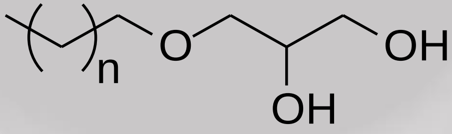
n = 4 to 6 m ≤ 4

❷ Monoalkyl isosorbide ethers
C_nIso



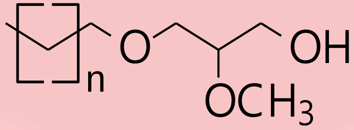
n = 3, 4, 5

❸ Monoalkyl glycerol ethers
C_nGly



n = 3, 4, 5

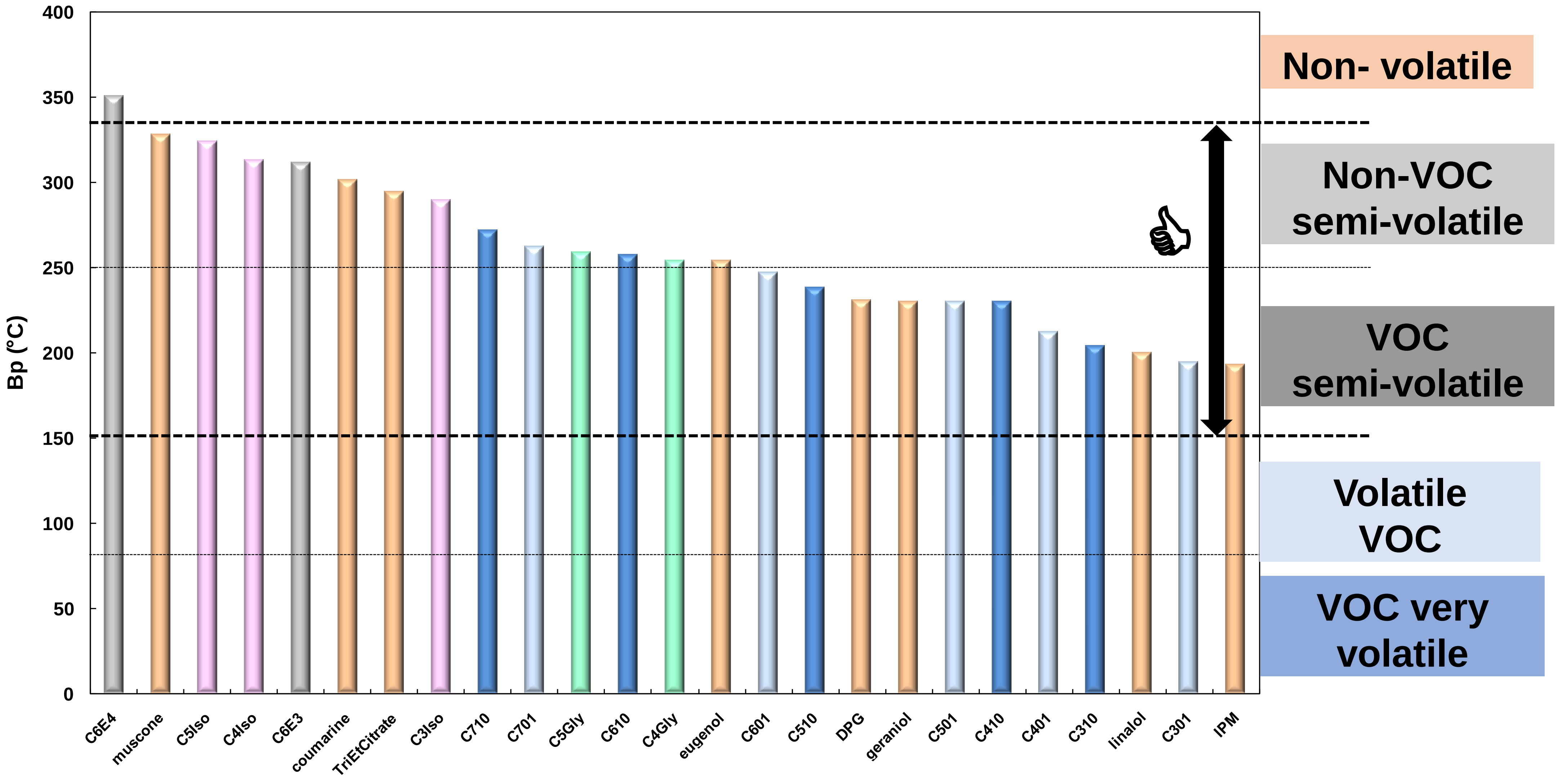
❹ Methylated monoalkyl glycol ethers
Cn01 & Cn10



n = 3 à 5

1) Solubilizing and Hydrotropic Properties of Isosorbide Monoalkyl and Dimethylethers. Durand et al. J. Surf. Deterg. 2009, 12, 371. 2) Volatile short-chain amphiphiles derived from isosorbide: esters vs. ethers. A. Lavergne et al. RSC Adv. 2013, 3, 5997. 3) Hydrotropic properties of alkyl & aryl glycerol monoethers. L. Moity et al. J. Phys. Chem. B. 2013, 117, 9262.

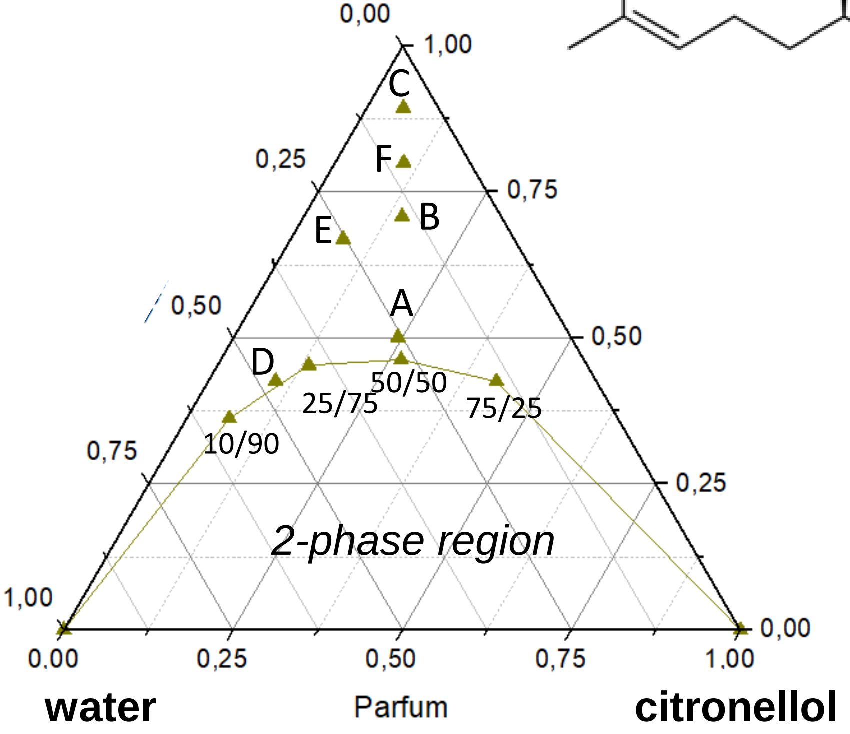
Volatility of Hydrotropes

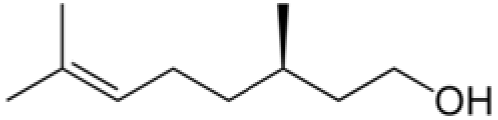


C_6E_4 > C_5Iso > C_4Iso > C_6E_3 > C_3Iso > C710 > C701 > C_5Gly > C_4Gly - C610 > C601 > C510 > C501 > C410 > C401

SELF-AGGREGATION OF THE HYDROTROPES

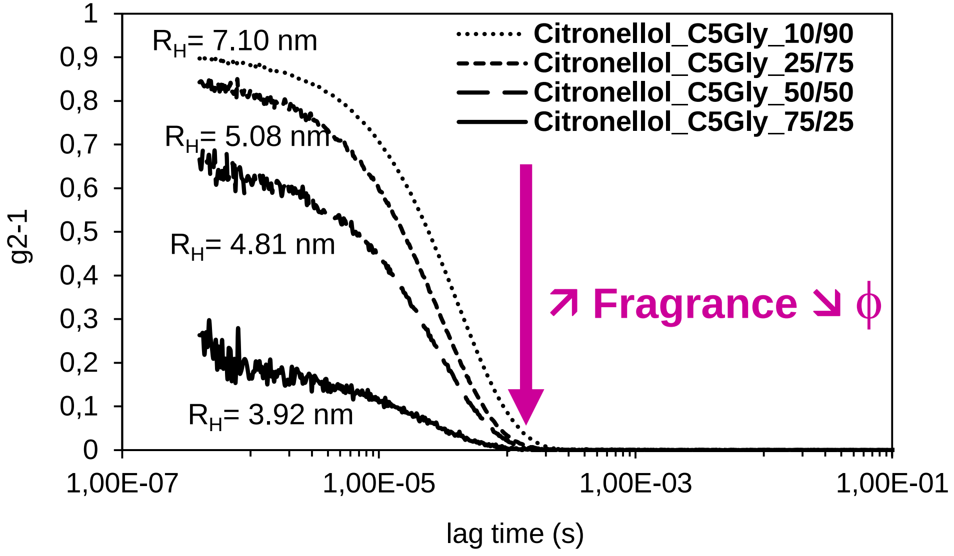
C_5Gly/Citronellol/water



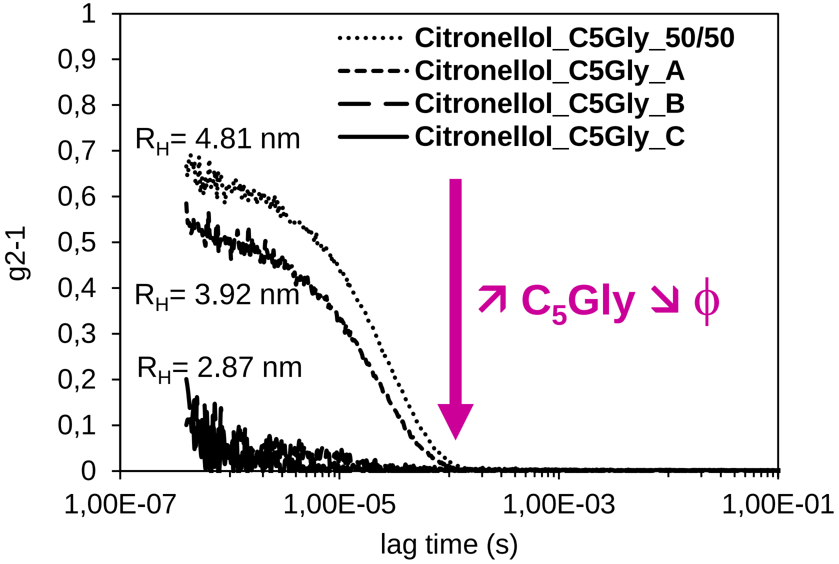


Structuration
in the one-phase region

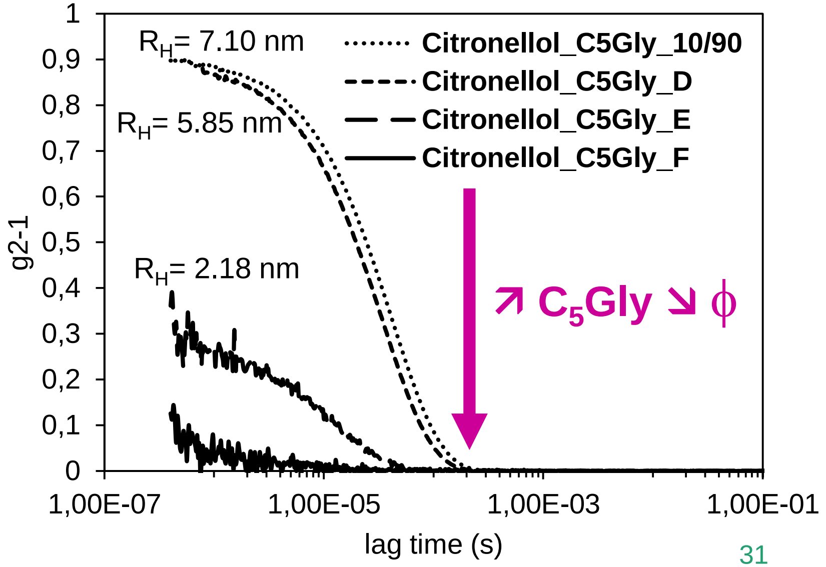
At the limit of demixion



Water/Citronellol = 50/50



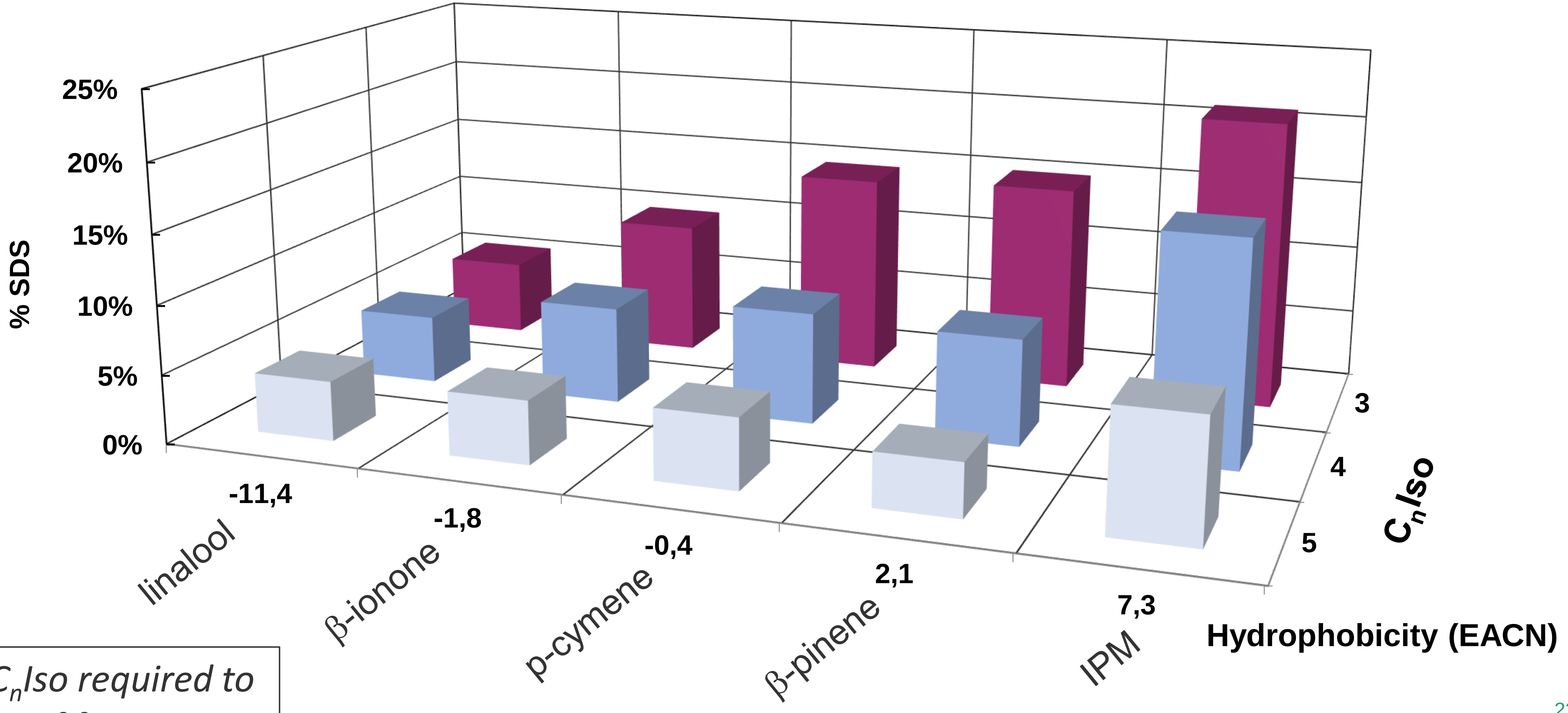
10% Citronellol



Synergy between hydrotropes and surfactants

- **Hydrotrope + Anionic surfactant = Synergy ⇒ ↘ of the hydrotrope and surfactant amounts**

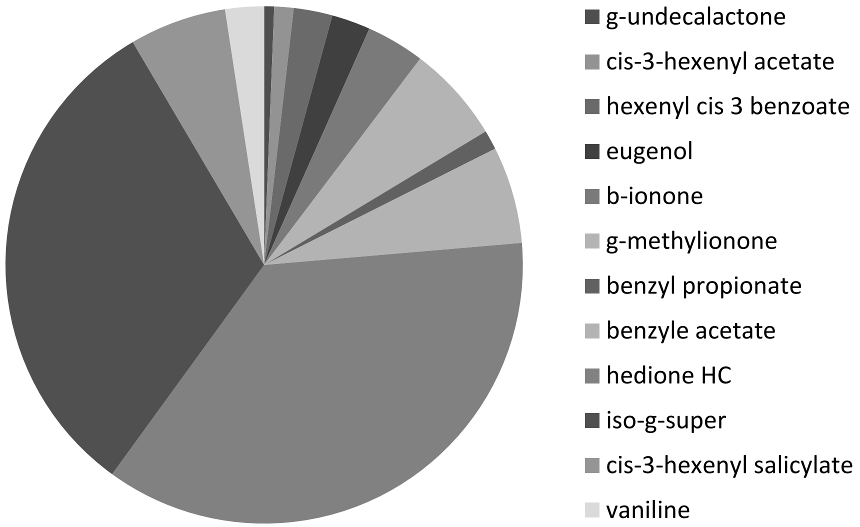
% SDS required to solubilize 10% of fragrance with 10% of C_nIso

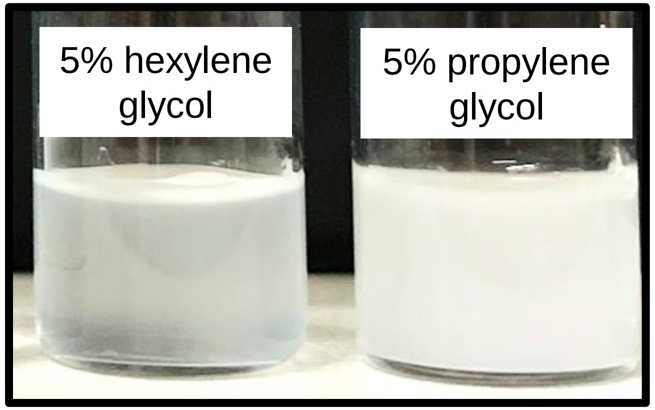


***Note:** 40% of C_nIso required to solubilize 10% of fragrance*

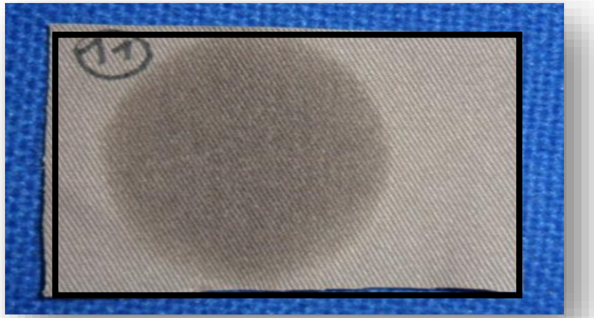
FORMULATION OF WATER-BASED FRAGANCE SYSTEMS

Reformulated perfume (P)





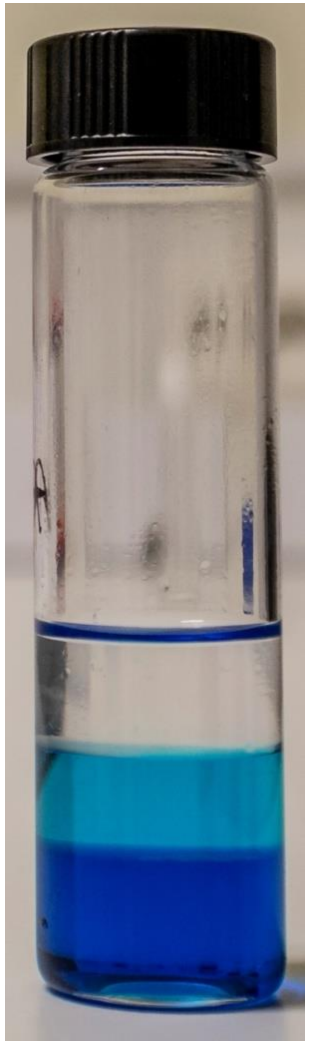
Clear and fluid water-based fragrance microemulsion stable from 5 to 50 °C



Perfumes in the form of aqueous microemulsions. O. Boucenna Verdier, V. Rataj-nardello, Jean-marie Aubry, G.Douyere, C. Mainguy WO2018220147A1

Formulation of water-based fragance systems

- **Nonionic hydrotropes** derived from ethylene glycol, glycerol and isosorbide
- **Strong synergy** when combined with surfactants
- Decrease of the amount of hydrotrope by a **factor up to 5**
- Formulation of **green, transparent, fluid, volatile and stable fragrance-in-water microemulsions** containing high amounts of fragrances
- Possibility of mono-, bi- and triphasic systems (Winsor)
- Very promising systems for various domains where aqueous solubilization of hydrophobic compounds is desired (e.g. window cleaners)



Groupe Chimie Durable – 28 Septembre 2021

Société Chimique de France
Le réseau des chimistes

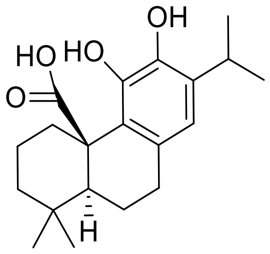
HYDROTROPIC EXTRACTION

CISCO2 COLLOIDS CATALYSIS OXIDATION · HT SMART FORMU · centralelille ENSCL · SATT NORD · institut Chevreul · Université de Lille · cnrs

Hydrotropic extraction of carnosic Acid

Objective

Extraction of CA from rosemary with maximum recovery



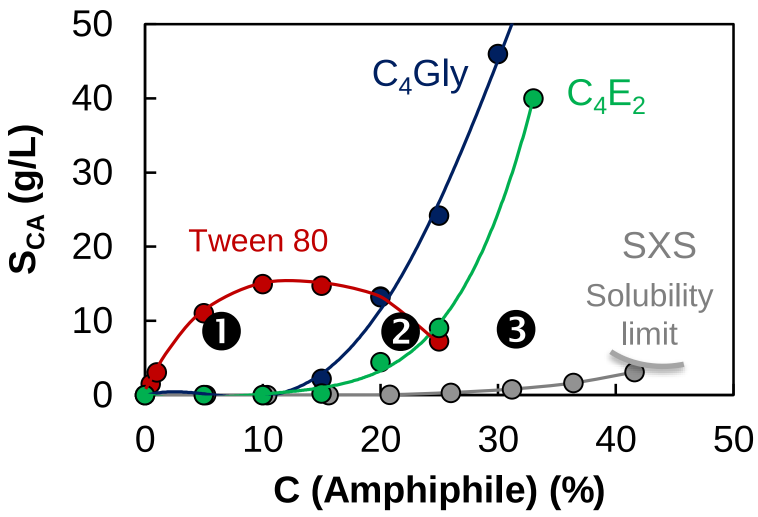
Rosemary leaves:
2.7 % CA

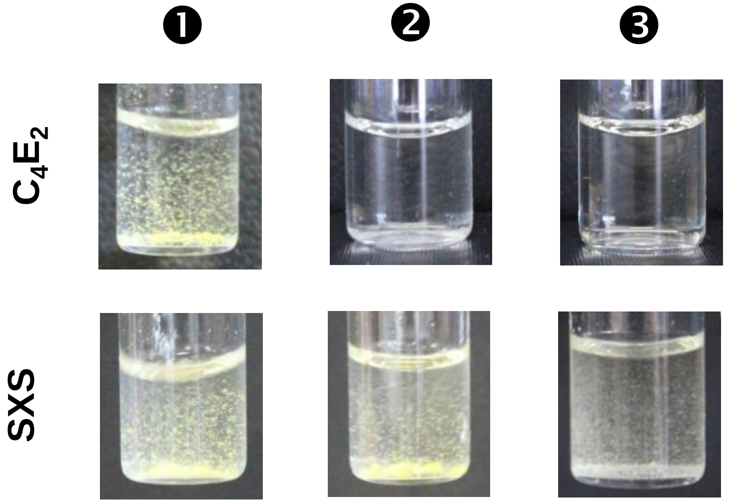
Common plant/solution ratio:
1 g / 10 mL

⇒ Solubility required: 2.7 g/L

Solubility curves of CA

Stirring 24h, 25 °C, pH 2





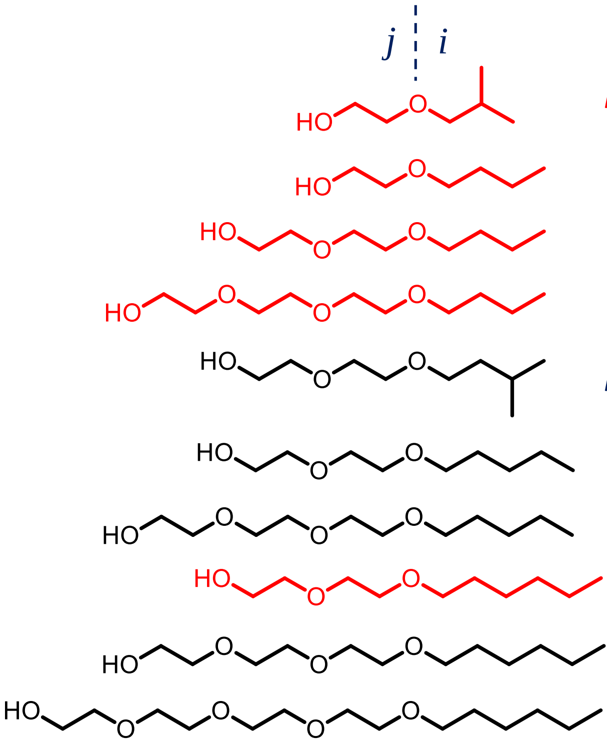
Solubilization = prerequisite for extraction

Mazaud, et al., *ACS Sustain. Chem. Eng.*, **2020**, 8, 15268–15277.

Investigated Hydrotropes

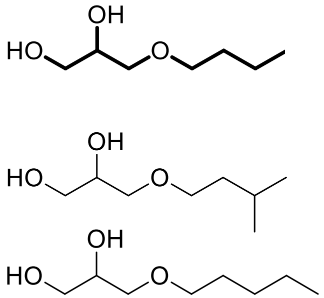
Nonionic hydrotropes

Alkyl polyethylene glycol ethers (C_iE_j)



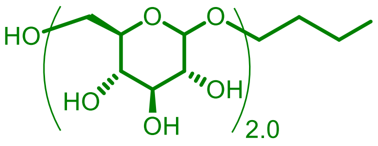
iC_4E_1
C_4E_1
C_4E_2
C_4E_3
iC_5E_2
C_5E_2
C_5E_3
C_6E_2
C_6E_3
C_6E_4

Monoalkyl glycerol ethers (C_iGly)

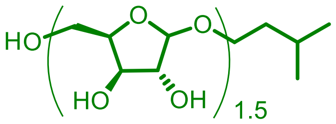


C_4Gly
iC_5Gly
C_5Gly

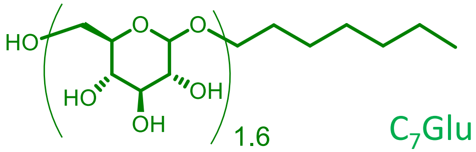
Alkyl polyglycosides (C_iGlyco)



C_4Glu



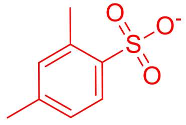
iC_5Xyl



C_7Glu

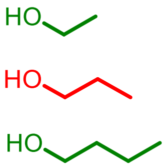
Other amphiphiles for comparison

Ionic hydrotrope



Sodium xylene sulfonate (SXS)

Alcohols



Ethanol
Propanol
Butanol

Surfactants

$C_{8/10}Glyco$
(C_8Glu, $C_{10}Glu$, C_8Xyl, $C_{10}Xyl$)
$C_{6,-2}Glu$

C_8E_3, C_8E_4,
$C_{10}E_4$, $C_{12}E_4$

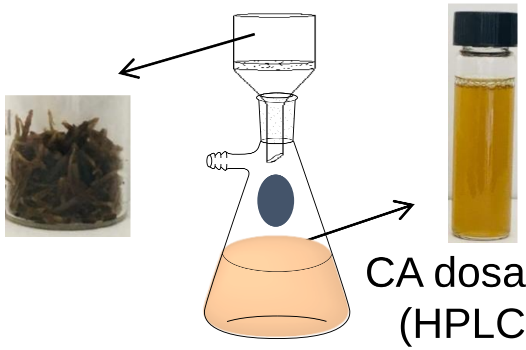
DIFFUSION THROUGH THE PLANT CELL BARRIERS

Rosemary (1 g)
Whole leaves

Hydrotrope (10 mL)
30 wt.%

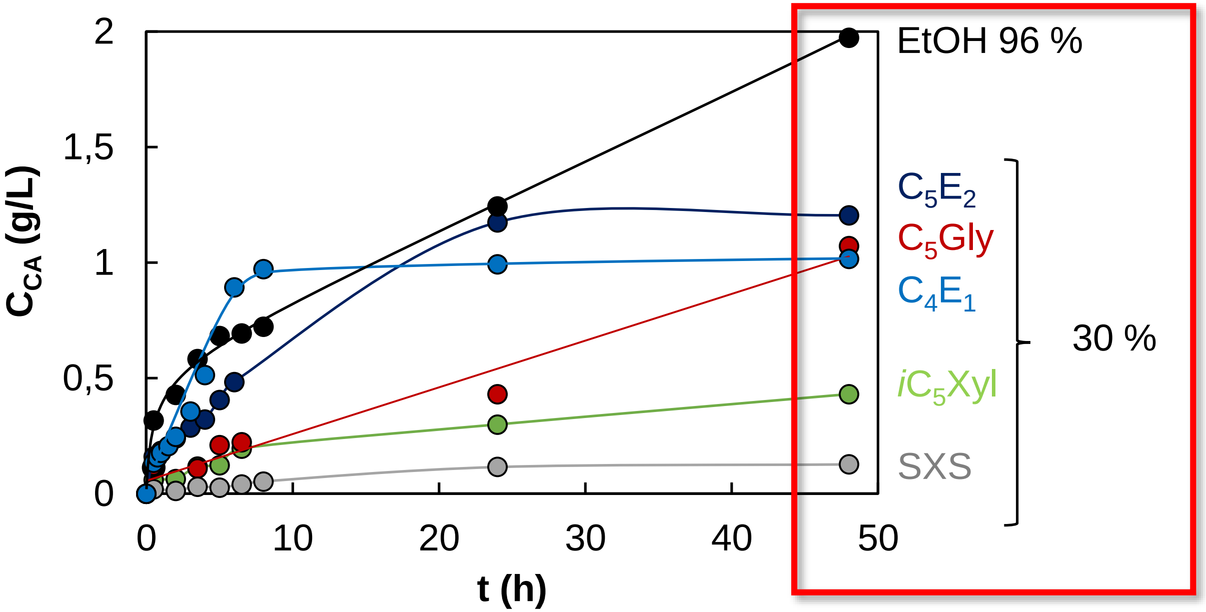
S/L extraction
Rotative stirring (48 h, 25 °C)

Büchner filtration



CA dosage
(HPLC)

Kinetics of extraction



Kinetic (< 8h): C_4E_1 < EtOH < C_5E_2 < C_5Gly < iC_5Xyl < SXS

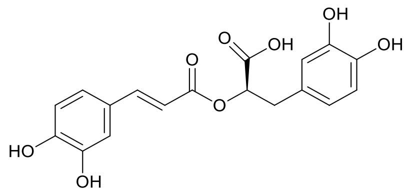
Efficiency (48 h): EtOH < C_5E_2 < C_5Gly < C_4E_1 < iC_5Xyl < SXS

SELECTIVE HYDROTROPIC EXTRACTION

Influence of the solute

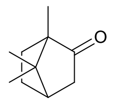
log *P* | **Solutes**

0.8



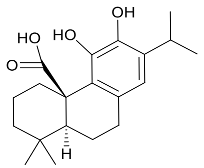
Rosmarinic acid (RA)

2.1



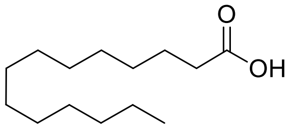
Camphor (C)

5.4



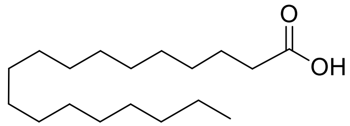
Carnosic acid (CA)

5.8



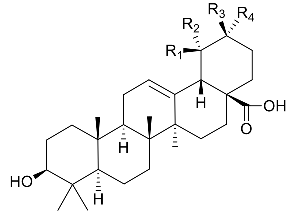
Myristic acid (MA)

7.8



Stearic acid (SA)

8.7



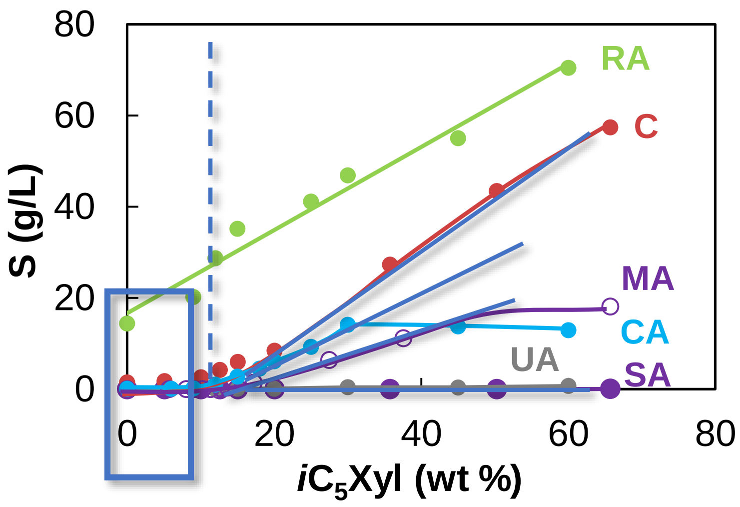
Ursolic acid (UA)

Solubility curves | ***iC$_5$Xyl***

Stirring 24h, 25 °C, pH 2
HPLC UV, ELSD or GC-FID analysis

Sigmoïdal ↗ with $C_{hydrotrope}$

Solubility ↘ when log *P* ↗
MHC ↗ when log *P* ↗



Solubility in water (g/L)

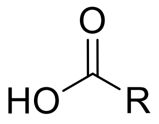
Minimum Hydrotropic Concentration (MHC)

Solubility enhancement coefficient

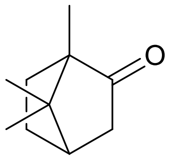
Selective Hydrotropic Extraction

Model molecules

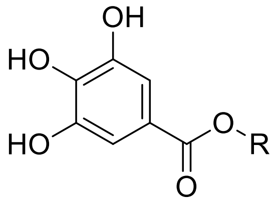
Fatty acids (C_iFA)



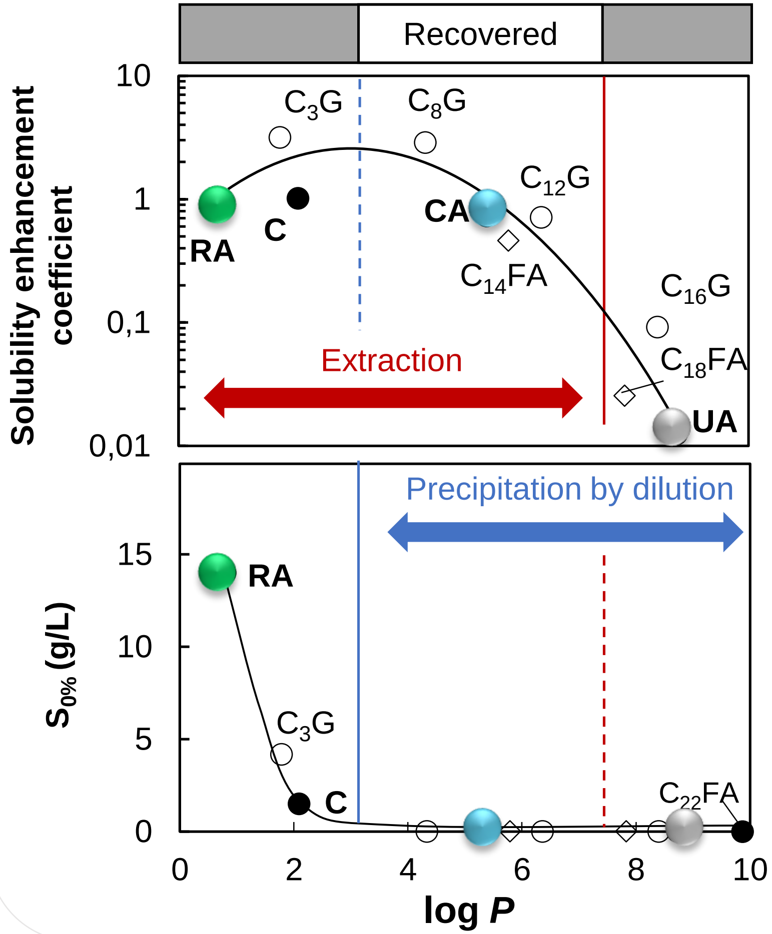
Camphor (C)

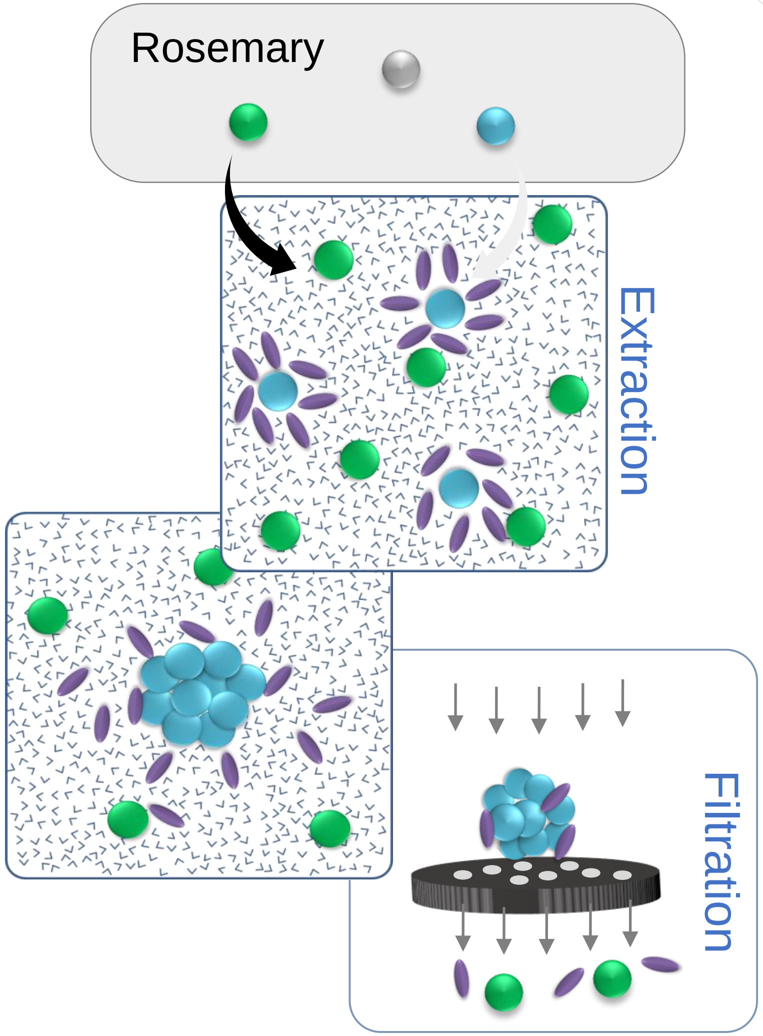


Alkyl gallates (C_iG)



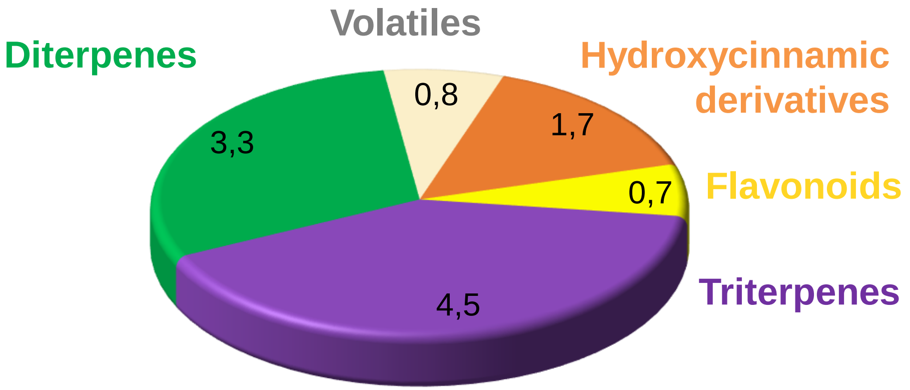
Selectivity of iC_5Xyl





Selective Hydrotropic Extraction

Composition of rosemary (g/100g)

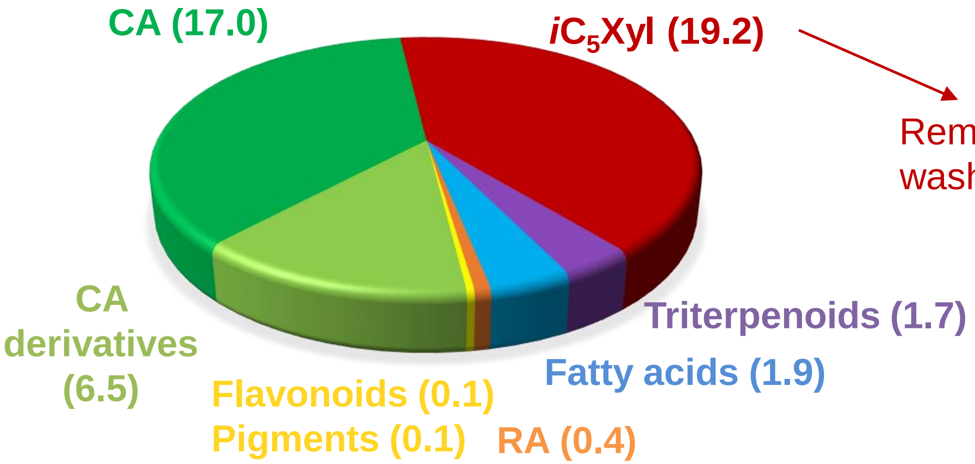


Tri and diterpenes: major compounds

Composition of a dry extract

Extraction
22.5 wt.% iC_5Xyl, pH 2
25 °C, 30 min, 250 rpm

Precipitation
stirring 30 min, 350 rpm,
resting 30 min



Removal in three washings (water)

CA and iC_5Xyl major compounds

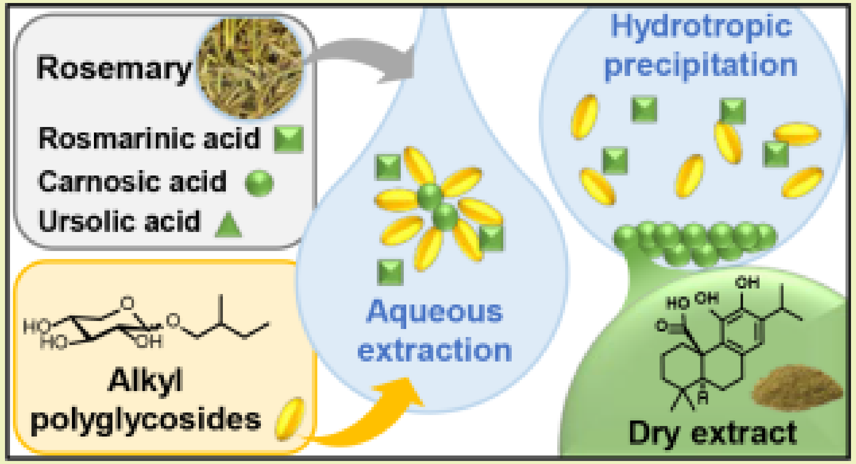
Di/triterpenes ratio in extract >> rosemary

Amyl Xyloside, a Selective Sugar-Based Hydrotrope for the Aqueous Extraction of Carnosic Acid from Rosemary

Agathe Mazaud, Raphaël Lebeuf, Christel Pierlot, Mickaël Laguerre, and Véronique Nardello-Rataj*

Cite This: https://doi.org/10.1021/acssuschemeng.0c09366

ABSTRACT: Rosemary (*Rosmarinus officinalis* L.) is a Mediterranean herb known for its high antioxidant power that has been widely attributed to carnosic acid (CA). Passive extractions of CA have been performed in water by using five commercially available short-chain alkyl polyglycosides (APG) with alkyl chain lengths ranging from 4 to 10 carbon atoms and polar heads composed of pentoses and/or glucoses. APGs are nontoxic amphiphiles with high biodegradability. Their solubilizing capacity for CA has been determined, highlighting heptyl glucoside (C_7Glu) as the most efficient one, followed by 2-ethylhexyl glucoside ($C_{6,-2}$Glu) and isoamyl xyloside (iC_5Xyl). However, iC_5Xyl exhibited the highest selectivity toward CA solubilization as compared to ursolic acid (UA), a potential coextracted compound of rosemary leaves. In addition, it was found to be the most efficient amphiphile to extract CA from both ground and whole rosemary leaves. To optimize the maceration process and the recovery of the extract, a full factorial design 2^4 was performed investigating iC_5Xyl concentration, temperature, stirring, and extraction time. A high concentration of hydrotrope was found to be the most important condition to optimize the maceration step, while the temperature particularly increases the yield, but in detriment of the CA content in the final dried extract.



KEYWORDS: *Green extraction, Rosemary, Carnosic acid, Hydrotrope, Xyloside, Antioxidant*

ACKNOWLEDGMENTS

UCCS

Université de Lille

institut Chevreul

SATT NORD

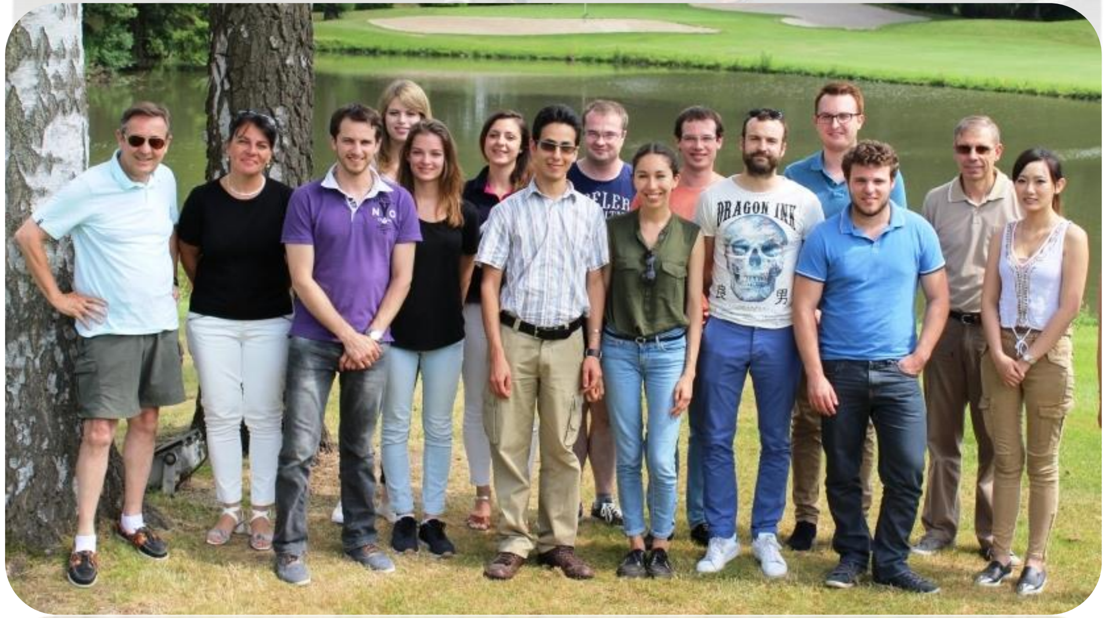
centralelille ENSCL

HT SMART FORMU

CISCO$_2$ COLLOIDS CATALYSIS OXIDATION

cnrs

NATUREX part of Givaudan



THANK YOU FOR YOUR ATTENTION !

Email: veronique.rataj-nardello@univ-lille.fr