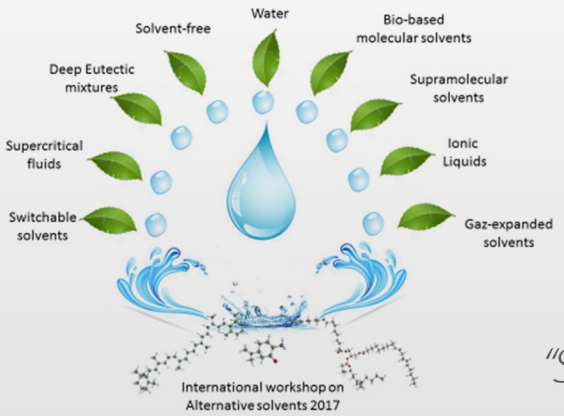
International Workshop on Alternative Solvents



WAS 2017

"Synthesis, Extraction, Purification and Formulation"

September, 28th - 29th 2017 Lyon

PROGRAM

UNIVERSITÉ DE LYON

Congrès Lyon 1

trimatec
Une technologie maîtrisée, un avenir préservé

UNIVERSITÉ D'AVIGNON ET DES PAYS DE VAUCLUSE

Eco Extraction

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SCIENCE & IMPACT

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IAR
LE PÔLE DE LA BIOÉCONOMIE

NATUREX

BASF
We create chemistry

Activation
Chemical Process Research & Catalysis

GATTEFOSSÉ

PREFACE

The **2017 Workshop on Alternative Solvents** aims at providing a complete overview of the current knowledge on alternative and green solvents used at laboratory and industrial scale for extraction, purification, formulation, and synthesis of natural product. A special emphasis will be dedicated to innovative and original methods and procedures, alternative solvents and safer products.

The workshop will gather professionals from industry, researchers and lecturers from academia engaged in natural product chemistry, and graduate students.

Plenary lectures given by internationally renowned experts in green solvents as well as contributions by industrial involved in the synthesis or use of green alternatives to conventional solvents will pave the 1.5 days of the symposium. A poster session will also offer the possibility to present your latest developments.

ORGANIZING COMMITTEE

Bruno ANDRIOLETTI, Université Claude Bernard Lyon 1
Farid CHEMAT, Université d'Avignon
Claudine COLIN, Pôle Trimatec
Ludivine JEAN-GERARD, Université Claude Bernard Lyon 1
Laurent STAVAUX, Pôle Trimatec
Anne-Sylvie TIXIER-FABIANO, Université d'Avignon

CONGRESS VENUE

The **2017 Workshop on Alternative Solvents** will take place at the Université de Lyon.

The entrance is at 92 rue Pasteur 69007 LYON.

Registration Desk

It is located in the Entrance Hall of the Building. You will collect your delegate badge and conference documentation at the registration desk and then check in. Please note that meeting and cocktail are accessible only with your delegate badge.

Warning: Vigipirate project

Please bring an ID card , it may be requested at the conference venue by security services.

Information on site

During the conference , participants should refer to reception desk for any changes in the program or need for information.

Working language

The working language of the conference is English. No interpretation in any other languages is provided.

Certificate of attendance

A certificate of attendance will be delivered to all registered participants.

Insurance

The organizers do not accept responsibility for individual medical, revel or personal insurance. Participants are strongly advised to take their own insurance policies.

Public Transportation (TCL) pass

In your delegate badge you will find two transportation pass valid for one day.

Do not forget to validate your ticket for each travel all day on the TCL network.

If you loose one, we will not be able to give you another one.

ACCESS

From Lyon Part-Dieu station:

Take the tramway line T1 (direction Debourg), stop at « Quai Claude Bernard » , then walk for 1mn

or

Take metro line B (direction Gare d'Oullins), stop at « Jean Macé », then walk for 5mn.

From Lyon Perrache station:

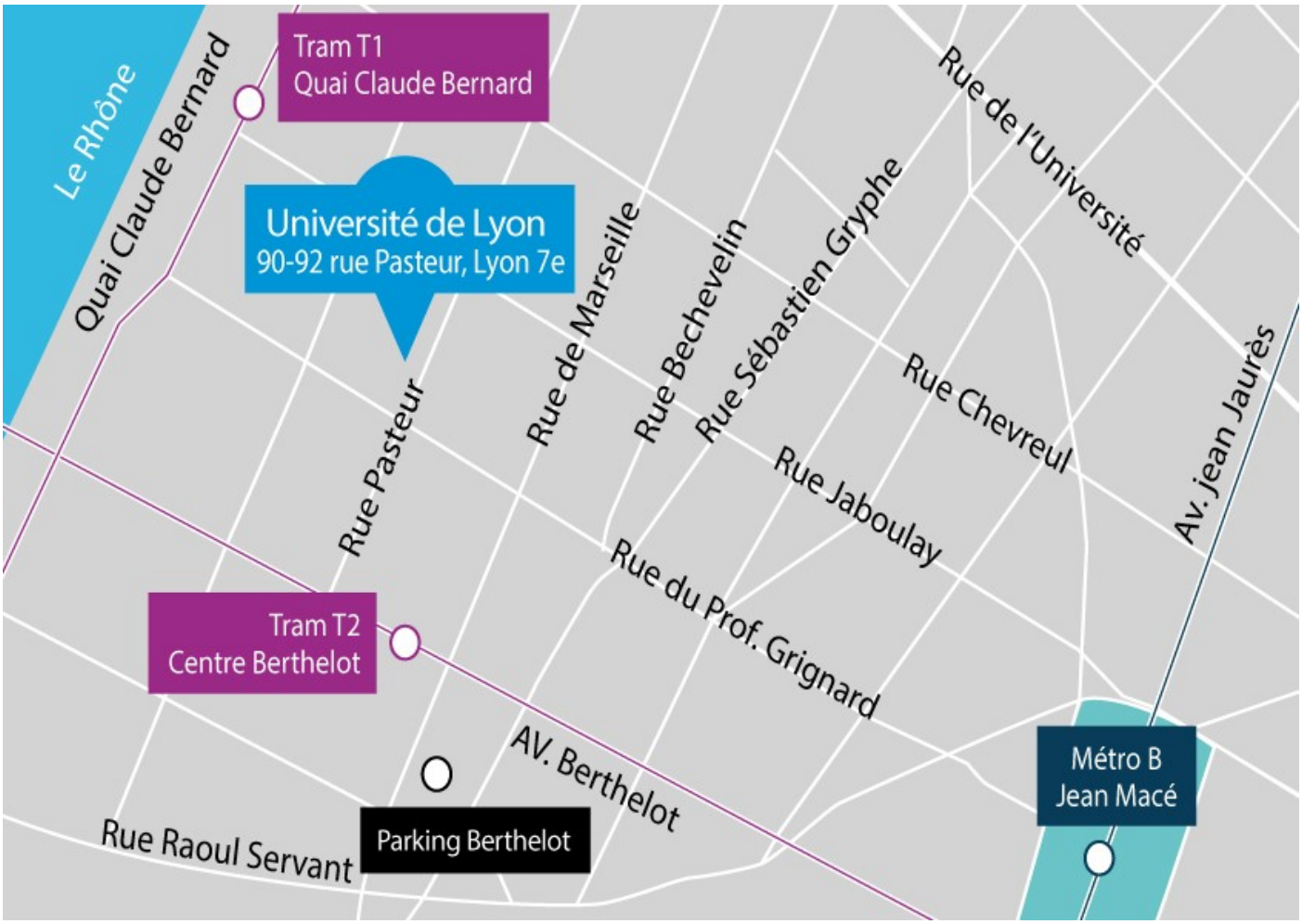
Take the tramway line T1 (direction IUT-Feyssine), stop at « Quai Claude Bernard » , then walk 1mn

or

Take the tramway line T2 (direction Saint-Priest Bel Air), stop at « Centre Berthelot », then walk1mn.

From Lyon Saint-Exupéry airport:

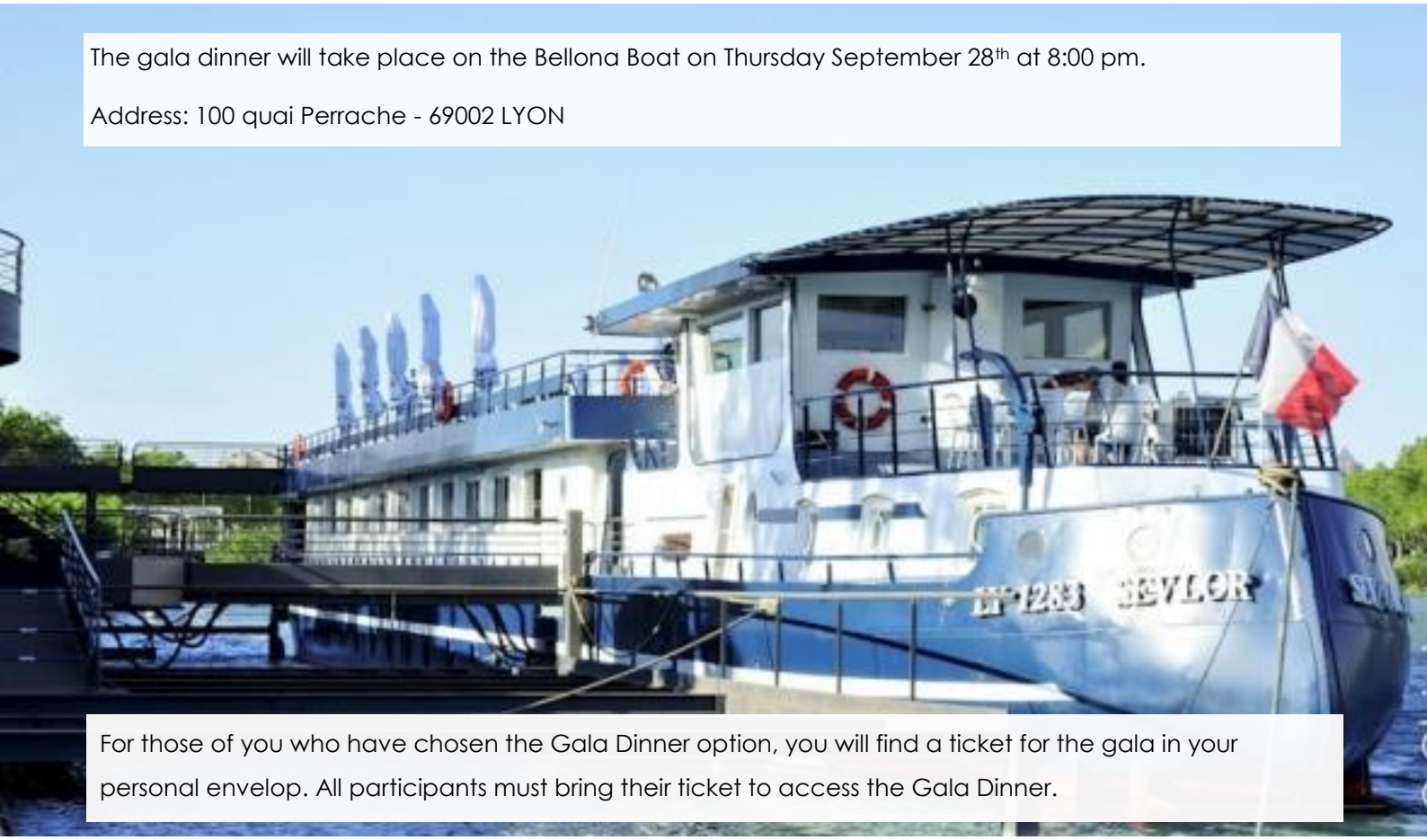
Join the Part-Dieu station via the RhonExpress.



GALA DINNER

The gala dinner will take place on the Bellona Boat on Thursday September 28th at 8:00 pm.

Address: 100 quai Perrache - 69002 LYON



For those of you who have chosen the Gala Dinner option, you will find a ticket for the gala in your personal envelop. All participants must bring their ticket to access the Gala Dinner.

To go to the Bellona boat from the Congress venue:

Take tramway line **T1** (direction 'Debourg') and stop at 'Musée des Confluences'.

Then cross the street to get to the boat.

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Scientific program

Thursday, September 28th

Session 1: Chairman Prof. B. Andrioletti (UCBL)

13:45 – 14:30: Prof. W. KUNZ (Univ. Regensburg, Germany)
"From Classical Green Solvents to Green Ionic Liquids and Deep Eutectic Solvents"
14:30 – 15:00: J. VANDEPUTTE (Pôle IAR)
"General overview on solvent issues"
15:00 – 15:30: A. CROIZIER et G. PITHON (Chimex, France)
"DEEP, Chimex approach for cosmetic extracts"
15:30 – 16:00: Dr. I. RODRIGUES (ENSIACET, Toulouse, France)
"Design of new solvents based on phase equilibrium sinergism of mixtures"

Session 2: Chairman Prof. F. Chemat (UAPV)

16:00 – 16:30: Prof. J. VERCAUTEREN (IBMM, Montpellier, France)
"Natural Deep Eutectic (NADE): the new solvents for a better understanding of life (of "bio"-chemistry)?"
16:30 – 17:00: V. ANDRE-FREI (BASF)
"Water, the main alternative solvent for Green Extraction of natural products"
17:00 – 17:30: A. MANDEAU (Pierre Fabre Research Institute, Toulouse, France)
"An innovative green extraction process for the development of native plant extracts"
17:30 – 18:15: Prof. G. CRAVOTTO (Univ. Torino, Torino, Italy)
"New routes for green solvent toward industrial applications"
18:15 – 18:30: S. MALANDAIN (Protex, France)
"Example of alternative solvents for the synthesis of polymeric paint additives"
18:30 – 18:45: A. VALLAGEAS (Celsius)
"Liquefied Gas as alternative solvents for vegetable extraction under pressure"
18:45 – 19:00: J. MONBRUN (Activation)
"Green solvents: from design to continuous flow synthesis"

20:00: Dinner

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Friday, September 29th

Session 3: Chairwoman Dr. L. JEAN-GERARD (UCBL)

9:30 – 10:00: Dr. T. ZEMB (ICSM-Marcoule)
Hydrotropes and solutes "inside-outside" exchange: a driving force towards enhanced hydro-alcoholic extraction ?
10:00 – 10:30: Prof. F. CHEMAT (UAPV, France)
Alternative Solvents for Green Extraction, Purification and Synthesis. Challenges and Opportunities
10:30 – 11:00: Dr. C. DOUCET (Total Special Fluids)
"BIOLIFE, Laying the foundation of a new chemistry of renewable fluids"

Session 4: Chairwoman Dr. Anne-Sylvie TIXIER FABIANO (UAPV)

11:00 – 11:30: B. CAPRIN (Gatefossé)
"NaDES ability for natural molecules dissolution"
11:30 – 12:00: Dr. F. JEROME (IC2MP, Poitiers, France)
"Catalysis in biphasic conditions: the Fisher glycosylation of carbohydrates with fatty alcohols as a case in point"
12:00 – 12:45: Prof. Y. H. CHOI & Prof. R. VERPOORTE (Leiden, Univ., The Netherlands)
"Potential and Limitations of Natural Deep Eutectic Solvents as a New Media for Natural Products Research"
12:45 – 13:00: N. PATOUILLARD (Pennakem)
"EcoXtract M for ecoextraction process using a bio-based solvent."
13:00 – 13:15: C. GUIZARD (IFS)
"Advanced subcritical water based technologies for extraction processes and biomass conversion"
13:15 – 13:30: N. ESSAYEM (IRCELyon)
"SC organic solvents coupled to heterogeneous catalysis: a unique tool for the selective liquefaction of wood components into chemicals"

Lunch

Round Table 1 Animation Prof. F. Chemat/Naturex
"Solvents for extraction"
Round Table 2 Animation: Prof. B. Andrioletti/Dr. Vivien Henryon (Activation)
"Solvent synthesis-Bottlenecks"
Round Table 3 Animation: Dr. Anne-Sylvie Tixier-Fabiano/Clarisse Doucet (Total Fluides SAS)
Solvent issues in formulation

Concluding remarks (Prof. F. Chemat; Prof. B. Andrioletti).

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Conferences – List of abstracts and CVs

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From Classical Green Solvents to Green Ionic Liquids and Deep Eutectic Solvents

Werner KUNZ*

University of Regensburg, *Regensburg, Germany*

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In this overview, I try to give an introduction and my personal view of "green" solvents. Biodegradability is probably the most important criterion, followed by low toxicity and many other criteria such as flammability, vapour pressure etc.

I will show a series of biogenic solvents, but also some petrol-based ones that can be considered as green.

Particular classes of solvents are Ionic Liquids and Deep Eutectic Solvents. Whereas in the past, they were praised as green in general, today's consideration is much more critical. I will try to critically discuss pros and cons of such systems for applications, in which the greenness of solutions is important.

Finally, I will say some words about spontaneous structuring in solvent mixtures and solutions that can be achieved without environmentally questionable surfactants.

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Werner KUNZ, University of Regensburg, Germany

Education

- 1972-1980: Gymnasium (High School) in Neustadt an der Waldnaab, Bavaria.
- 1980: University-entrance diploma (Abitur) 1.0 with the best average mark of all high school graduates in Bavaria in 1980.
- 1980-1985: Study of Chemistry at the University of Regensburg (diploma with highest possible grade: 1.0).
- 1985-1988: PhD at this university working on *Vapour Pressure Measurements and Statistical-Mechanical Theories for the Determination of Thermodynamic and Structural Properties of Electrolytes in Acetonitrile and Methanol* (supervisor: Prof. Dr. J. Barthel).

Scientific Career

- 1988-1992: Postdoctoral fellow in France with Prof. Pierre Turq at the Université Pierre et Marie Curie in Paris and at the Laboratoire Léon Brillouin, CEA, Saclay.
- 1992: French "Habilitation à diriger de recherches" working on the *determination of the structure and dynamics of solutions, especially with the help of neutron scattering experiments*. Reviewer inter alia: Pierre-Gilles de Gennes.
- 1992: Research fellow at the CEA, Saclay, France and assistant professor.
- 1993-1997: Professor at the Université de Technologie de Compiègne (UTC), France. In 1993 youngest professor of technical chemistry in France.
- 1995-1996: Interim Dean of research of the faculty of chemical engineering at UTC.
- 1997-now: Full professor and head of the Institute of Physical and Theoretical Chemistry at Regensburg University.
- 2008-2009: Dean of the Faculty of Chemistry and Pharmacy.
- 2012-now: Head of the Carl-von-Carlowitz Centre of Sustainable Chemistry at Regensburg University.

Selected Activities

- 1999: Founder of the Associate Institute of Technical and Applied Chemistry at Regensburg University (SKH Company).
- 2004: Founder and Coordinator of the European Master program "Complex Condensed Materials and Soft Matter" (COSOM-EMASCO) together with institutes at the universities of Versailles and Florence, Lille (ENSCL) and Montpellier (ENSCM).
- 1998-2006: Co-Editor of the *Journal of Molecular Liquids*.
- Numerous collaborations with industry (l'Oréal, BASF, Kao Chemicals, Procter & Gamble, etc.) and research institutions (CEA, Max-Planck Society). Consultant of two of the leading European chemical companies.
- Member of the scientific advisory boards of several start-up companies.

- Member of the scientific advisory board of TRIMATEC innovative cluster (south of France).

Distinctions and Awards

- Rhodia-Prize 2012 of the European Colloid and Interface Society.
- Gay-Lussac-Humboldt Prize 2014 of the French Academy of Sciences.
- Corresponding member of the European Academy of Science and Arts (Paris, London).
- Grants and fellowships from the State of Bavaria, the Studienstiftung des Deutschen Volkes, the Fonds der chemischen Industrie (Germany), NATO, the European Union, Elf Aquitaine.
- Several guest professorships (in Belgium, Australia, France) and numerous invited and plenary lectures

Description of Prof. Kunz' research group

Since 1997 Prof. Kunz is holder of the chair of physical and theoretical chemistry ("Solution Chemistry") at Regensburg University. In his lab two other professors (Prof. H. Motschmann and Prof. D. Horinek) and three assistant professors (Dr. R. Buchner, Dr. R. Müller and Dr. R. Neueder) have permanent positions. Currently more than 20 PhD students, and more than 10 undergraduate (master) students are working in the labs of the chair. From 1997-2004 Prof. Kunz was mostly involved in applied science performing numerous projects with industrial partners and running his own company (SKH GmbH). In 2004 he came back to more fundamental research, which is reflected by the increasing number of research papers and citations since then. Prof. Kunz and his group are interested in the characterization, conception and practical application of complex nano-structured liquids and their interfaces, with a special emphasize in Green Chemistry. The six currently employed professors at the chair have complementary research interests, but all in the field of solution chemistry. Together, they currently are considered as the world's leading group in this field.

Publication activities

At present, Prof. Kunz has more than 250 peer-reviewed publications in the field of complex liquids, especially salt effects, colloids, surfactants, and solvent effects, further to several patents, book chapters, book editions etc. Kunz' h-index is 41, his papers are currently cited more than 6900 times.

General overview on solvent issues

Jacques VANDEPUTTE*

Pôle IAR

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Jacques VANDEPUTTE

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DEEP, Chimex approach for cosmetic extracts

Arthur CROIZIER, Grégoire PITHON

Chimex*, France*

Deep is a continuous plant extraction technology based on a process intensification approach. Short extraction time and a high thermomechanical effect can lead to a different use of extraction solvent with new extraction results.

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Arthur CROIZIER, Grégoire PITHON

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Design of new solvents based on phase equilibrium synergism of mixtures

Dr. Ivonne RODRIGUES DONIS

ENSIACET, *Toulouse, France*

ivonne.rodriguezdonis@ensiacet.fr

The search for alternative solvents is a topic of major interest from both academic and industrial points of view. In some applications, especially those without appropriate safety precautions for producers as well as consumers, finding alternatives to harmful traditional solvents has become mandatory. Finding a substitution molecule, the usual 'trial and error' approach seems inefficient unless high throughput screening is used. Instead, reverse engineering approaches, like Computer Aided Molecular Design (CAMD) are fit to handle several properties and to propose molecular structures matching the target values of these properties. However, the exponential increasing of the number of properties (physicochemical, thermodynamic, transport, Environmental Health and Safety issues) to be accomplished by the new solvent, pure component solvents hardly match with all specifications. Hence, the problem of substituting a molecule may result in proposing a mixture thanks to the synergism between the components promoting a non-ideal behavior of the mixture with a probable formation of azeotropic mixtures. Falling the boiling point means saving in energy consumption as well as low melting point enlarges the operating range of the fluid. Our contribution relies on the use of CAMD method for designing a new green fluid for aircraft uses. Rather than undertaking a trial and error search through existing chemicals, we have proposed to run a systematic search that implements a computer aided molecule and mixture design approach based on reverse engineering via the computational tool IBSS (InBioSyn-Solv software). As a result, pure components did not improve the efficacy of the existing fluids (around) 50% while binary azeotropic mixtures enhanced the efficiency until 90%. Ternary azeotropic mixtures was the ideal new fluid according to the final application requirements. The methodology can be straightly extrapolated to design new green solvents for natural products extraction.

Dr. Ivonne RODRIGUES DONIS, ENSIACET *Toulouse, France*

Ivonne Rodriguez Donis is an associate professor at Ecole Nationale Supérieure des Ingénieurs en Arts Chimiques et Technologiques de Toulouse (ENSIACET-INPT) with the research activities attached to Laboratoire de Chimie Agro-Industrielle (LCA-INRA). Her research interests include the eco-conception of innovative processes based on thermodynamic analysis of multi-phases system passing through simulation + optimization and experiments validation from laboratory to industrial scale. Substitution of hazard solvents by green solvents by using reverse formulation engineering principles coupled to computer aided molecular design (CAMD) tools. Her research activities are in collaboration with pharmaceutical, biotechnology and fragrance industries in Cuba (QUIMEFA, CIGB, CIM), France (Robertet – Charabot, Solvay, Safran Hispano-Suiza) and Denmark (Lundbeck, Novo Nordisk). She has edited three books chapters and co-authored about 40 papers in international journals and conference proceedings.

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"Natural Deep Eutectic (NADE): the new solvents for a better understanding of life (of "bio"-chemistry)?"

Prof. Joseph VERCAUTEREN

IBMM, *Montpellier, France*

jvercauteren@univ-montp1.fr

NaDES, standing for "**Natural** Deep Eutectic Solvents", were just discovered at the beginning of this decade by R. Verpoorte *et Al.*, when doing in-depth analyses of plants metabolism, namely by high field NMR as one of the tools used for "metabolomics". This discovery allowed him to make a few very innovative assumptions! Certainly, the most important one, being that "*metabolites that occur in large amounts in cells may form a* ***third type of liquid****, one separate from* ***water*** *and* ***lipids***"! True revolution in of natural substances chemistry, *per se*, since they make it possible to better understand certain biological "phenomena", unexplainable until there, such as: "how the many compounds of intermediate polarity in high concentrations (that neither dissolve in the lipid nor the water phase), are biosynthesized and stored?" as well as "*how, the enzyme mediated reactions, in cell biosyntheses, function with substrates and products that are poorly soluble, or even, insoluble, in water (cellulose, amylose, lignins)?*" Indeed, they prove to be of a scientific range, which very largely exceeds the limits of this field, … not saying there, of imagination!

Based on our very first experiments, in this paper, we will try to shed light on some of the revolutionary questions and on the conceivable and realistic developments raising: 1) "**Are NaDES at the origin of a revolution in the concepts which we have of the life?**", or, 2) "**Could NaDES become a new class of "therapeutic agents", and help to pave the way to new therapeutic strategies?**"

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Prof. Joseph VERCAUTEREN, IBMM *Montpellier, France*

Scientific Cursus

- 1977: Pharmacist, Faculty of Pharmacy, Reims
- 1979: 1st PhD, *Alkaloids of two Apocynaceae* sp. (director: **Pr Jean LE MEN**, Reims)
- 1983: 2nd PhD, *Total synthesis of pseudovincadifformine-type and azepino-indole alkaloids* (directors **Pr Jean LÉVY** and **Dr Georges MASSIOT**)
- 1983-1984: Post-Doctoral stay, *Chiral total synthesis of thienamycin by π-allyl palladium complexes* (**Pr Barry M. TROST**, Chemistry Department, Madison, Wi, USA)

Academic Positions

- 1979-1988: Chargé de Recherche CNRS: **URA CNRS n°492** (Pr Jean LE MEN), University of Reims Champagne-Ardenne, Faculty of Pharmacy
- 1988-2002: Full Professor of Pharmacognosy: Study of the properties, total synthesis, structural analysis of **Polyphenols**, University of Bordeaux, Faculty of Pharmacy
- 2002-present: Professor of Pharmacognosy at the Faculty of Pharmacy, Department of SLB (Synthesis of Bioactive Lipids) IBMM - UMR CNRS n° 5247, University of Montpellier, ENSCM
  Research Program: Development of **scavengers** (anti-COS) of reactive Oxygen Species (OS) along with reactive Carbonyl Species (CS = sugars and lipids oxidation metabolites). Structurally finely designed "Lipophenols" are able to target retinal tissue and to slow down the pace of cytotoxic A2E formation and the neurodegenerative subsequent events in AMD and juvenile (Stargardt's) diseases. This program includes the development of new formulations of the lead molecules in NADEs (Natural Deep Eutectic solvents) with promising results

Industry connexions

Important discoveries around lipophenols allowed us to develop polyphenolics anti-aging main applications in the cosmetic field (Caudalie®) and Polyphenols R&D

Scientific production (August 2016)

Inventor on Patents:	**34**
International Peer reviewed Publications and Invited Lectures:	**214**
Book Chapters, Oral Communications and Posters:	**236**
National Invited Lectures:	**61**
Supervisor of PhD Theses and DEA/Masters:	**37**

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Water, the main alternative solvent for green extraction of natural products

Valérie ANDRÉ-FREI

BASF, *Lyon, France*

valerie.andre-frei@basf.com

Water is the most abundant molecule on Earth, covering 70% of the surface. Life processes on this planet are crucially dependent on the presence of water. It is often recognized that the use of water as a solvent has tremendous benefits as a green extraction solvent because water is not only inexpensive and environmentally benign; but it is also non-flammable, nontoxic, providing opportunities for clean processing and pollution prevention.

At a critical concentration, it is unavoidable that the large hydrophobic hydration shells start to overlap, leading to mutually destructive breakdown of these water arrangements. This H-bonding interactions results in a solvent-induced sticking together of hydrophobic surface areas of the two solutes, primarily driven by the gain in entropy that comes from the release of water molecules from the hydrophobic hydration shells into bulk water. Hydrophobic hydration shells are quite voluminous. Depending on the nature of the hydrophobic molecules, one can distinguish pairwise interactions, the formation of small aggregates ('moving units', for example in the case of hydrotropes) and the formation of larger aggregates (bulk hydrophobic interactions) as in the case of surfactant aggregates like micelles and vesicles. The ultimate state of aggregation will, of course, involve phase separation.

Using water as alternative solvent for synthesis, purification or extraction is a research area that has an impact in several fields of modern chemistry. The advantages of using water as alternative solvent for extraction includes: reduced environmental impact, selective extraction, use of simple equipment, no hazards, faster start-up, and simplification of process steps.

We will present a complete picture of current knowledge on using water as alternative solvent for natural product extraction. It provides the necessary theoretical background and some details about extraction using water, the technique, the mechanism, some applications, and environmental impacts.

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Valérie ANDRÉ-FREI, BASF, *Lyon, France*

Education

- 1990: Engineer: Institut National des Sciences Appliquées de Lyon, specialty Biochemistry.
- 1991: Master degree Lyon University: specialty Genetic Differentiation & Immunology.
- 1995: PhD in Human Biology Lyon University: specialty Tissue Engineering and Biomaterials.

Experience

BASF Beauty Creations/BASF Beauty Care Solutions France

- 1994-2009: Project Leader then Tissue Engineering and Efficiency Testing manager.
- 2009-2013: R&D Site Group Manager.
- Since 2013: R&D Scouting & Communication expert.

While designing new ingredients or concepts for BASF Beauty Care Solutions, I set up more than 20 national and international scientific collaborations and actively contributed to the development of new methodologies to support BBCS cosmetic applications.

I'm currently in charge of scientific communication, scouting and particularly of strategic innovation.

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An innovative green extraction process for the development of native plant extracts

Anne MANDEAU,[1] Valérie TEYSSEYRE,[1] Laurent SUBRA,[2] Vincent DOUAY,[2] Marie MORARD,[3] David LAMOLINAIRIE,[3] Jean-Marie AUTRET,[2] Bernard FABRE[1]

[1]Herbal Product Laboratory, Pierre Fabre Research Institute, *Toulouse, France*,
[2]Industrial Development Center, Pierre Fabre Research Institute, *Gaillac, France*,
[3]Bois-Valor Society, *St Juery, France*

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Today, life cycle assessment, environmental impact and sustainability drive innovation in the field of plant extraction. Some extraction process came back to the cutting edge like microwaves- or ultrasound-assisted extraction, SFE, and we are witnessing the rise of new renewable solvents. Examining the extraction process, it occurs that the steps of greatest impact are:

- plant cultivation

- plant preparation: drying, grinding

- use of organic solvents (production, evaporation, waste-management).

The new technologies cited above aim to reduce solvent consumption, targeting the last of these steps. But what about the first two steps?

Using fresh plants is the best way to counteract the environmental impact linked to drying and grinding. Usually, plant juice is obtained by pressing the freshly harvested plant. Another way is to perform a solvent extraction directly with fresh plant.

However, during the pressing process, the plant cell walls can restrain the access and recovery of some interesting compounds. Furthermore, it releases enzymes which could potentially modify and alter these compounds: hydrolases, oxidases, deglucosidases, etc.

Unless a cryo-extraction process followed by solvent extraction is employed, product alteration and compound recovery remain limiting factors to the handling of fresh plants.

We found out that the adaptation of a twin-screw extrusion technology, mainly used in food industries for plant juice expression, allows us to obtain an enriched extract, containing unadulterated compounds. Indeed, the combination of high pressure induced by the twin-screw rotation and rapid thermal treatment leads to complete destructuring of plant cell walls and an inhibition of enzyme activity, giving a juice with a higher yield and a higher active content. For example, in purple coneflower juice, the level of caffeic acids (caftaric and cichoric acids) obtained by this technology is 0.79 mg/g of plant wet weight, whereas it is 0 mg/g by simple juice expression (due to digestion by polyphenoloxidases[2]) and 0.12 mg/g of plant wet weight by water extraction at 100°C. Numerous plants are

traditionally used in their fresh form in order to preserve the compounds within and avoid the risk of denaturing occurring during the drying process.[1]

Continuing with our example, purple coneflower herb (Echinacea purpurea (L.) Moench.) expressed juice has a well-established use for the short-term prevention and treatment of common cold (EMEA/HMPC/104945/2006).

A comparative life-cycle analysis has been undertaken between this new extrusion process and a conventional aqueous extraction, showing important savings on carbon footprint, ozone formation, water resources, etc. Other examples will be given, demonstrating the interest of this green, natural technology using a thermomechanical process without solvents to obtain innovative plant extracts.

***Keywords**: Green extract, life cycle analysis, Plant juices, Purple coneflower, traditional medicine*

***References**:*

[1]Amarowicz, R., Carle, R., Dongowski, G., Durazzo, A., Galensa, R., Kammerer, D., Maiani, G., Piskula, M.K. Influence of postharvest processing and storage on the content of phenolic acids and flavonoids in foods. Mol. Nutr. Food Res., 2009, 53: S151-S183.

[2]Nüsslein, B., Kurzmann, M., Bauer, R., and Kreis, W., Enzymatic Degradation of Cichoric Acid in *Echinacea purpurea* Preparations J. Nat. Prod. 2000, 63: 1615-1618.

Anne MANDEAU, Pierre Fabre Research Institute, *Toulouse, France*

With a doctoral degree in Pharmacy from the Faculty of Pharmacy of Lyon (2001), Anne Mandeau also holds a Master Degree in the Biological Activity of Natural Substances, Molecular Identification and Cellular Communication (National Museum of Natural History, Paris, 2001) and a PhD in Natural Substances Chemistry (Pierre Fabre – CNRS Research Unit 2597, Natural Substances Research Centre, Toulouse).

She began her carrier as a researcher working on the pre-formulation of active ingredients in cosmetic products with Pierre Fabre's Physicochemical department (2005-2006).

In November 2006, she joined the Herbal Products Laboratory of Pierre Fabre's R&D Research Institute as a Project Manager. She is currently working on the proposal, research and development of new herbal enriched extracts (including analytical monograph and pre-industrial process) for cosmetic, nutraceutical and OTC applications. Specialized in Eco-extraction processes, she regularly participates in eco-extract workshops with Pôle PASS.

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New Routes For Green Solvents Toward Industrial Applications

Prof. Giancarlo CRAVOTTO

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The concepts behind green and sustainable chemistry are holistic in nature and aim to protect both the environment and human health from the risks posed by dangerous chemicals and solvents. As a means to further these endeavours, our group has investigated several applications of ionic liquids,[1] extractions with butane and fluoro-hydrocarbons as well as NADES (natural deep eutectic solvents) and GVL (γ-valerolactone) over the last decade. Solvent-free processes have also been successfully performed in ball mills[2] and microwave reactors.[3] These enabling technologies, together with cavitational reactors (ultrasound and hydrodynamic cavitation), have dramatically changed the way that green chemical processes are designed. We have recently focused our efforts on the use of GVL, a bio-based, dipolar and aprotic solvent that is commonly prepared via the hydrogenation of biomass derived levulinic acid. We have also reported the microwave-assisted, cascade production of GVL from lignocellulosic biomass which is particularly noteworthy for the fact that GVL is both the process solvent and product.[4] Example applications for this valuable, green alternative to polar solvents will be presented and, wherever possible, comparisons with classic organic solvents will be made.

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Prof. Giancarlo CRAVOTTO, University Torino, *Torino, Italy*

Current research interests

- Green chemistry
- Enabling technologies in organic synthesis (ultrasound, hydrodynamic cavitation, microwaves, ball milling, flow reactors, high shear mixers etc.)
- Heterogeneous catalysis
- Surface modification of carbon-based nanomaterials
- Biomass conversion
- Design of hybrid chemical reactors

Peer reviewed papers and Patents

~350 publications (Scopus H-index 43)

Academic career

- 1991-1992: Researcher, Techniche Universität Berlin
- 1992-2000: Technician then Researcher, University of Turin
- 2000-2006: Associate then Full Professor of Organic Chemistry, University of Turin
- 2007-present: Director of the Department of Drug Science and Technology.

Previous Experience

4-year experience R&D and production in the chemical and pharmaceutical industry (Chemat srl and Farmitalia-Carlo Erba Spa)

Main recent UE projects

"MAPSYN" – Highly efficient syntheses using alternative energy forms (FP7-NMP)

"ECOEXTRACTION" (UE – Alcotra)

"US4GREENCHEM" – H2020 BBI: Combined Ultrasonic and Enzyme treatment of Lignocellulosic Feedstock as a Substrate for Sugar Based Biotechnological Applications.

"COSMIC" – H2020 European Training Network for Continuous Sonication and Microwave Reactors.

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Example of alternative solvents for the synthesis of polymeric paint additives

Simon MALANDAIN

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Synthron is a subsidiary of the Protex International group, family owned company founded in 1932. Originally Protex International was exclusively producing chemical auxiliaries for the textile industry. Since then, the group has evolved as an international and multi-markets chemical producer with its headquarter based in Levallois, France.

Synthron is producing chemical additives for the formulation industry with the main producing site and R&D center in Château-Renault, France. Formulation additives are used in many different applications like: paint and coating, detergents, lubricants, construction materials, adhesives, composites, paper and agriculture. These additives are polymers or substances dispersed or solubilized in solvent or aqueous media for the liquid formulations.

End-users are looking for formulated products with the least toxicity for their final markets thus the need for Synthron to develop additives with environment friendly media. The presentation will deal with recent examples of two additives with new solvents, explaining the drivers for change of the composition of the additive and showing the various steps from the lab development to the validation at the customer.

With these two examples, the Protex International group wants to share its expertise about fulfilling the expectations of the market with the help of alternative solvents.

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Simon MALANDAIN, Protex, *Levallois, France*

Professional Experiences

- 1997-1998: Dow France, Paris, Sales Representative Dow Polyethylene
- 1998-1999: Dow Europe, Zurich, Switzerland. Technical support engineer Dow Polyethylene
- 1999-2003: Dow France, Paris – Account Manager Dow Polyethylene
- 2003-2006: Dow France, Lyon – Six Sigma Black Belt Project Leader for the European Sales and Marketing organization of Dow Plastics
- 2006-2012: Dow France, Erstein – Sales Manager for France/Benelux business in Polyurethane systems (*Subsidiary of The Dow Chemical Company revenue $60 Billions /year*)
- 2012-2015: Synthron subsidiary of Protex International, Levallois – Business Manager Europe for Specialty Chemistry Additives
- 2015-Current: Protex International, Levallois – **Technical Partnership and External Growth Director** (Family owned independent chemical producer, 600 people ; € 200 Millions/year)
  Identification of external competences, management of technical partnership projects Scouting for new acquisitions

Education

- 1991-1995: Ecole Nationale Supérieure de Chimie de Paris, France
- 2003-2004: Six Sigma Black Belt certification, Dow Academy, Atlanta, Georgia, USA
- 2005-2009: DeVos MBA Executive part-time, University of Northwood, Midland, Michigan, USA
- 2016: Certificate of Collaborative Innovation, Conservatoire National des Arts et Métiers (CNAM), Paris, France

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Liquefied Gas as alternative solvents for vegetable extraction under pressure

A. VALLAGEAS

Celsius
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Alain Vallageas presents the liquefied gas used for solid-liquid vegetable extraction: n-butane, Tetrafluroethane, HFO and dimethylether.

These solvent are chemically inert and some are designed for vegetable extraction in food industry according to European Directive.

The NECTACEL process developed and patented by CELSIUS is described and compared to other process'. The main advantages are due to isobaric and isothermal process in all the phases of maceration, solvent evaporation and solvent condensation for reuse.

Process is performed at room temperature which is an advantage for thermosensible molecules. Pressure is less than 10 barg and is able to be scaled up to industrial size without any limit of capacity. No pump or compressor is used except a final vacuum pump for complete desorption of solvent before matrix change for a complete solvent reuse.

Due to these characteristics NECTACEL industrial units are very competitive both in investment and in operation.

CELSIUS manufactured NECTACEL pilots of useful capacities 1, 200 and 500 litres which are available for demonstration, tests and parameter's optimization at Plateforme d'Eco-Extraction de Valréas.

CELSIUS has engaged Vincent Rapinel for a doctorate cursus in laboratory GREEN of Avignon with Professor Farid Chemat.

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A. VALLAGEAS, Celsius

Training

- Civil Engineer graduate from the Institut National Polytechnique de Grenoble (INPG – École Nationale Supérieure d'Électrochimie et d'Électrométallurgie)
- 5 Certificates of Advanced Studies in chemistry and metallurgy (University Joseph Fourier – Grenoble)
- Graduate of the Institut d'Administration des Entreprises (IAE-Lyon)
- Graduate of the Institut de Contrôle de Gestion (ICG-Lyon)

Experience

42 years of experience in the design, negotiation and implementation of contracts in all areas of the profession of **industrial equipment**: manufacture of machines, process installation, engineering, construction management and project management for heavy and light industries, environmental, food, chemical, pharmaceutical and cosmetics industries. Expertise in chemical engineering, food process engineering, thermodynamics, aerodynamics, metallurgy, mineral chemistry, automation.

CELSIUS SARL www.celsius-process.com

Founder in 2006, Chairman and Chief Executive of CELSIUS sarl. CELSIUS is a design and manufacturing company of process equipment for chemical industry, fine chemicals, pharmaceuticals and cosmetics. Two strategic business areas:

- Energy modules to manage the temperature of synthesis reactors. CELSIUS is a leader in its niche
- Starting-up business: Complete units for extraction of natural molecules patented by CELSIUS

Chief Executive of CELSIUS CHINA manufacturing Energy modules for Chinese market under the license of CELSIUS.

Previous experience

- 1976-1981: Project Manager in ETABLISSEMENTS NEU
- 1981-1984: Technical and CAPEX Manager in COOPAGRI LANDERNEAU
- 1985-1990: Technical Manager in GANGLOFF
- 1991-1993: Technical Manager in F-TEC
- 1995-2000: Project Manager in HTC
- 2000-2005: Chief Executive of VALLET PHARMA

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Green solvents: from design to continuous flow synthesis

Jérôme MONBRUN

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In 2014, Activation started a partnership on a 3-year collaborative project named SOragO aiming at *developing new biosourced solvents* and resins for coil coating. The objective of this consortium was to develop paint systems with the highest possible amount of bio-sourced carbon.

To this end, Activation has developed an *In Silico* multi factors decision support tool named *"Acti'solv"*. During this project, automated continuous flow reactors have been designed to produce these solvents at multi kg/day scale.

Dr. Monbrun will present these recent achievements and associated innovative technologies.

Jérôme MONBRUN, Activation, *Lyon, France*

Jérôme Monbrun received his PhD in Organic Chemistry (2004) from the National Graduate School of Chemistry and Chemical Engineering of Montpellier (ENSCM) where he developed asymmetric synthesis of new organophosphorus compounds, allowing new perspectives on unexplored phosphinosugar chemistry (phostines). He worked as a chemical development engineer at SanofiAventis (oligosaccharide chemistry) before joining Activation in 2006 as R&D scientist. His interest and expertise on chemical development was strengthened through multiple R&D projects followed by technical transfers to industrial partners. Closely involved in kg-lab creation and scale-up tools setup, he is now in charge of global Activation's R&D since 2012.

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Hydrotropes and solutes "inside-outside" exchange: a driving force towards enhanced hydro-alcoholic extraction?

Dr. T. ZEMB

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Dr. T. ZEMB, ICSM, *Marcoule, France*

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Alternative Solvents for Green Extraction, Purification and Synthesis. Challenges and Opportunities.

Prof. Farid CHEMAT

GREEN Extraction team, UMR408, INRA, Université d'Avignon, *Avignon, France*

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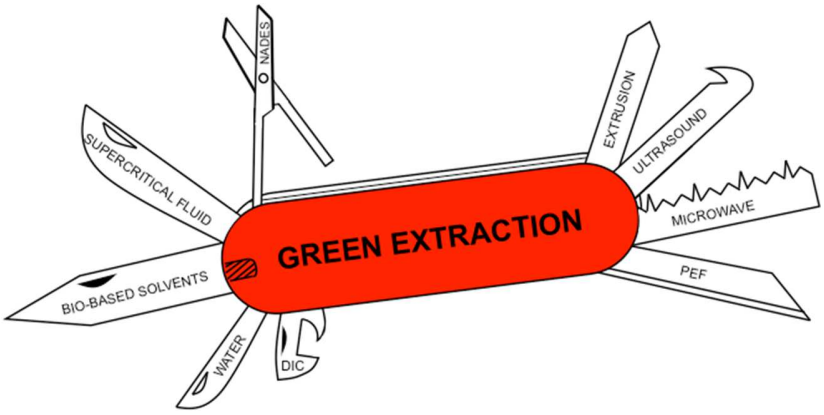

A general definition of green chemistry is the invention, design and application of chemical products and processes to reduce or to eliminate the use and generation of hazardous substances. In relation of green extraction of natural products, this definition can be modified as follows: "*Green Extraction is based on the discovery and design of extraction processes which will reduce energy consumption, allows use of alternative solvents and renewable natural products, and ensure a safe and high quality extract/product*". The listing of the "six principles of Green Extraction of Natural Products" should be viewed for industry and scientists as a direction to establish an innovative and green label, charter and standard, and as a reflection to innovate not only in process but in all aspects of solid-liquid extraction. The principles have been identified and described not as rules but more as innovative examples to follow discovered by scientist and successfully applied by industry.

Chemat F., Strube J. "Green Extraction of Natural Products. Theory and practice". Wiley-VCH, Weinheim, 11 chapitres, 384 pages. 2015. 978-3-527-33653-1

Prof. Farid CHEMAT, Université d'Avignon, *Avignon, France*

Farid CHEMAT is a full Professor of Chemistry at Avignon University, Director of GREEN Extraction Team (innovative techniques, alternative solvents, and original procedures for green extraction of natural products), and scientific coordinator of "Plateforme Eco-Extraction du Végétal" dealing with dissemination of research and education on green extraction technologies. He received his PhD degree (1994) in process engineering from the Institut National Polytechnique of Toulouse-France. After periods of postdoctoral research work with Prolabo-Merck, Rhone-Poulenc and Unilever (1995-1997), he spent two years (1997-1999) as senior researcher at University of Wageningen-The Netherlands. In 1999, he moved to the University of La Réunion-France DOM as assistant professor and since 2006 holds the position of Professor of Food Chemistry at the University of Avignon-France. His research activity is documented by more than 200 scientific peer-reviewed papers, and about the same number of conferences and communications to scientific and industrial meetings, 10 books, 40 book chapters and 10 patents. His main research interests have focused on innovative and sustainable extraction and processing techniques (especially microwave, ultrasound and green solvents) for food, pharmaceutical, bio-energy and cosmetic applications.

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BIOLIFE, Laying the foundation of a new chemistry of renewable fluids

Dr. Clarisse DOUCET

Total Special Fluids

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A breakthrough in the B-to-B chemical industry, BioLife is the first biodegradable and 100% renewable isoalkane fluid combining outstanding performances and high purity. BioLife products have enabled the development of innovative solutions for many applications such as cosmetics, inks, paintings, lubricants etc. thanks to an unique process and solid industrial partnerships.

Dr. Clarisse DOUCET, Total Special Fluids

Graduated with a PhD in chemistry and chemist engineer from ESCOM (Ecole Supérieure de Chimie Organique et Minérale).

Joined TOTAL group in 2001, at the research center of Solaize (Lyon) as Research engineer on the development of fuel additives.

Then, moved to a position within TOTAL Marketing France, HSEQ Direction as quality engineer in charge of the follow up of the quality of petroleum products (Diesel, gasoline, jet fuel) for the French market.

After a couple of years, joined TOTAL Fluides as technical coordinator for the special fluids products and project manager for the development of biosourced products.

Since 2016, change position as Prospective Research and Innovation manager in the strategy research and communication division, of TOTAL Fluides in charge of the coordination of the R&D within the special fluids.

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NaDES ability for natural molecules dissolution

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Natural deep eutectic solvents (NaDES) have attracted a great deal of attention in recent times as promising green media for extracting secondary metabolites from plants and for dissolving water insoluble compounds. Many biological properties are ascribed to resveratrol, a naturally occurring stilbenoids, such as antioxidant activity. However the formulation of this secondary metabolite is difficult due to its low solubility in polar solvents. The aim of this study was to identify a hydrophilic NaDES that could dissolve, stabilize and maintain the antioxidant activity of resveratrol. 25 solvents NaDES and conventional were compared in a dissolution study of resveratrol and piceid (resveratrol glycoside). Solubility was measured through RP-HPLC-UV analysis. It was shown that the maximal solubility reached for some NaDES was equal or higher than that of the best conventional solvents. NaDES solution containing 5 and 15% of resveratrol were then tested for stability and analysed through RP-HPLC-UV chromatography and DPPH assay. It was shown that the chemical and radical scavenging activity stabilities were interesting for NaDES solution in comparison with conventional solvent solutions. Furthermore, the formulation study of a NaDES solution enriched with resveratrol in emulsion was evaluated. This work leads to a demonstration that stable "oil in NaDES" emulsion is feasible. Finally, because the chemical rules of plant extraction are not entirely depending on dissolution and solvation features of a solvent, an extraction study of resveratrol and piceid from root of Polygonum cuspidatum was performed in order to compare the extractive performance of NaDES versus best conventional solvents. Interesting stilbenoids yield and radical scavenging activity of a NaDES extract was highlighted.

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Benoît CAPRIN, Gatefossé, *Saint-Priest, France*

Research engineer in plant extraction, GATTEFOSSE, Saint-Priest, FRANCE Benoit CAPRIN is working on Gattefossé Research and Development department since 2009. His first experiences concern industrial scale-up and development of extraction process (bio-based ethanol and supercritical CO_2). Nowadays, his main researches are related to the development of NaDES suitable for the cosmetic industry. He graduated as process engineer at the chemical engineer school in Clermont-Ferrand. The development and the application of his research has always been directed to natural products and green chemistry applied to the cosmetic market.

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Catalysis in biphasic conditions: the Fisher glycosylation of carbohydrates with fatty alcohols as a case in point

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Dr. François JEROME, IC2MP, *Poitiers, France*

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Potential and Limitations of Natural Deep Eutectic Solvents as a New Media for Natural Products Research

Prof. Young Hae CHOI & Prof. R. VERPOORTE

Leiden University, *Leiden, The Netherlands*

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Prof. Young Hae CHOI, Leiden University, *Leiden, The Netherlands*

Professional Career

- 2014-Present: **Associate Professor**, Institute of Biology, Leiden University, Leiden, The Netherlands
- 2009-2014: **Assistant Professor**, Institute of Biology, Leiden University, Leiden, The Netherlands and Section Process Equipment, Delft University of Technology (TU Delft), Delft, The Netherlands
- 2008-2009: **Researcher**, Section Process Equipment, Delft University of Technology (TU Delft), Delft, The Netherlands
- 2003-2008: **Senior Researcher**, Division of Pharmacognosy, Section Metabolomics, Institute of Biology, Leiden University, Leiden, The Netherlands
- 2002-2003: **Postdoctoral Fellow**, Division of Pharmacognosy, Section Metabolomics, Institute of Biology, Leiden University, Leiden, The Netherlands
- 2000-2002: **R&D Manager**, GreenTek 21, Seoul Korea
- 2000-2002: **Postdoctoral Fellow**, College of Pharmacy, Seoul National University, Seoul, Korea

Educational Background

- 1994- 2000: **PhD**, College of Pharmacy, Seoul National University, Seoul, Korea (PhD Thesis: "*Supercritical Fluid Extraction of Nitrogen Containing Bioactive Natural Products*", thesis advisor: Prof. Jinwoong Kim)
- 1992-1994: **Master of Pharmacy**, College of Pharmacy, Seoul National University, Seoul, Korea (M. S. Thesis: "*Studies on the Constituents of Lepisorus ussuriensis*", thesis advisor: Prof. Jinwoong Kim)
- 1988-1992: **B.S. of Pharmacy**, College of Pharmacy, Seoul National University, Seoul, Korea

Scientific Activities

- Author/co-author of 200 scientific peer-reviewed papers and 11 book chapters.
- 4 patent applications
- More than 150 Conference abstracts and proceedings
- Guest Editor of the Special Issue of Phytochemical Analysis (Metabolomics in Natural Products, January/February, 2010)
- Guest Editor of the Special Issue of Phytochemical Analysis (Pre-analytical methods in metabolomics: sample preparation and extraction, July/August 2014)
- Associate Editor of Phytochemical Analysis (Wiley, 2010-2014)
- Editorial Board of Phytochemistry (Elsevier, 2016-Present)

Prof. Robert VERPOORTE, Leiden University, *Leiden, The Netherlands*

He holds a Pharmacists degree (1972) and a PhD (1976) from Leiden. He was lecturer at Leiden University 1976-1987, and since 1987 professor and head of the department of Pharmacognosy. He was guest professor in London (UK), Uppsala (Sweden), Amiens (France) and Reims (France). From 1992-1998 he was Vice-Chairman and Chairman of the committee of the Phytochemical Society of Europe (PSE). Since May 2011 he is professor Emeritus at Leiden University.

He is author/co-author of 725+ scientific papers, 4 books and 6 patent applications and is Editor (1996-2002) and Editor-in-chief of Journal of Ethnopharmacology (IF 3.055)(2003-2016) and Phytochemistry Reviews (IF 2.686) (since 2001) and Executive Editor Biotechnology Letters (IF 1.639)(since 2006). He supervised 65 PhD-theses, and 150+ MSc theses.

He received an Honorary Doctorate University of Amiens, France (2004) and of the University of Uppsala, Sweden (2012). In 2007 he received the PSE Medal. He is a honorary professor at the Hong Kong Baptist University since 2015. In 2015 he was awarded the Gusi Peace Prize in Manila, The Philippines. In 2017 he was awarded the Egon Stahl golden medal for his lifetime scientific achievement by the Society of Medicinal and Natural Products Research.

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Eco-extraction process using a bio-based solvent EcoXtract® M

Norbert PATOUILLARD

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Pennakem LLC has practiced renewable chemistry for more than 60 years by utilizing the waste biomass from the corn and sugar cane industries. Pennakem's **Solvent** product line is targeted at a range of applications including chemical processing, agro-chemical formulations, surface treatment (paint stripping or metal degreasing) and natural product extraction. This last segment of market is covered by its **EcoXtract® M** product.

More recently Pennakem expertise in catalysis allows developing a new bio-based solvent having also some interesting properties in such field. This product derived from our furan chemistry is the 1,2- pentanediol traded as **Pentiol Green+ ™** which is finding many interesting properties in the ecoextraction applications.

Thanks to its specific physical chemical properties our **EcoXtract® M** has the required characteristics (boiling point, polarity, safety properties) to replace petrochemical derived solvents commonly employed for extraction of natural products. The first studies done by external labs have shown great promises in use of **EcoXtract® M** for extraction of lipophilic substrates such as oils and butters. High extraction yields were found comparable to other common solvent systems using hexane, cyclohexane, dichloromethane, ethyl acetate.

Pentiol Green+ ™ belongs to the alkane diol family, and has such is formulated with other similar chemical structures to find application in inks or cleaning systems. Its unique properties are making it a valuable ingredient in cosmetic industry, as a substituent of conventional systems based on many hazardous undesired petrochemicals. Recently, interesting solvent properties were demonstrated for hydrophilic ingredients extraction fitting the eco-extraction approach for the cosmetic segment.

This solvent range contributes to reduce the carbon footprint of processes and formulations where they are employed. **EcoXtract® M** and **Pentiol Green+ ™** will help to reduce the environmental impact of chemical processing and make the world better for the next generation.

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Norbert PATOUILLARD, Pennakem

Graduated in chemistry from University of Marseille Provence I dedicated myself on sales and marketing in the mid-90s holding my first position at former **DEGUSSA** now known as **EVONIK**. I spent 12 years+ in that international group having various responsibilities in sales organizations. My experience and language skills ultimately brought me to work in various industrial segments and in multicultural environments for company achievements. Last position at Evonik was as Europe and South America Sales and Marketing manager for scCO2 extraction. After some resilience in the petrochemical based industry I moved to the renewable world by joining **PENNAKEM**, part of **MINAFIN** French group, in the end of 2011; to promote strongly green chemistry and especially focusing on furfural derivatives. I hold now a sales and marketing position for Continental Europe and South America to make renewable chemistry come true in various fields of application. Member of IAR cluster and ACDV organization PENNAKEM, through Norbert, is now well represented on the old continent to make C5 derived sugar chemistry well known to the industry and subject to developments, sustainable for the future of our industry and our world.

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Advanced subcritical water based technologies for extraction processes and biomass conversion

Dr. Christian GUIZARD, Karine Seaudeau, Stéphane Sarrade

IFS, *Alixan, France*

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Subcritical water behaves very differently not only from water at room temperature but in some aspects also from supercritical water. Actually as the temperature of water rises between 100 and 374 °C and the pressure is increased high enough to maintain the liquid state, there is a marked and systematic decrease in permittivity, an increase in the diffusion rate and a decrease in the viscosity and surface tension. In consequence, moderately polar and non-polar molecules are extracted most efficiently due to a less polar medium induced by elevated temperature. So, subcritical water extraction (SWE) has proved to be a new and powerful technique for the extraction of active compounds from different biomass materials with low process cost, mild operating conditions, short process times, and environmental sustainability. Moreover, the relatively high density combined with the high dissociation constant of subcritical water, favors ionic reactions. Examples are dehydration of carbohydrates and alcohols and aldol splitting. Consequently, there has been a strong interest in using subcritical water as a solvent and reaction medium for biomass conversion. Several examples of application are provided showing the potential of subcritical water.

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Dr. Christian GUIZARD, IFS, *Alixan, France*

Christian Guizard was awarded an Engineer Doctorate degree (Institut National Polytechnique de Grenoble) in 1976 and a Doctorat d'Etat degree (Université Joseph Fourier de Grenoble) in 1981 in the field of Polymers Science. He holds a permanent position at CNRS (France) in 1976 working consecutively on physics of polymers and sol-gel chemistry of hybrid and inorganic materials. He was appointed Directeur de Recherche at CNRS in 1992 and worked at the European Membrane Institute (Montpellier) in the field of membranes science including hybrid and inorganic membranes. From 2004-2012 he moved to the Company Saint-Gobain CREE as head of a research laboratory devoted to developing advanced ceramics. Author of more than 280 publications and 25 patents in the field of materials science, he is currently the scientific director of IFS (Innovation Fluides Supercritiques), Alixan, France.

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SC organic solvents coupled to heterogeneous catalysis: a unique tool for the selective liquefaction of wood components into chemicals

Eternot, M.; Rataboul F.; Dr. Nadine ESSAYEM

IRCELyon, *Villeurbanne, France*

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At the end of the seventies, the application of sub-and supercritical fluids in the treatment of lignocellulosic biomass (LCB) appeared in the literature. Supercritical fluids offer a lot of possibilities from extractions of "extractives" up to the lignocellulosic biomass liquefaction into bio-oils. In this field, it is now well documented that the presence of a catalyst leads to the formation of bio-oils of higher energy value.

We did pioneering works in this area: we have shown the ability of SC MeOH-Water mixture[1] or SC butene[2] to liquefy LCB in minimal time producing few light products in catalyst free conditions whereas upon acid catalysts addition, ethyl or sec-butyl levulinates were obtained in 20 wt% yield.

A step further towards the direct selective conversion of LCB into chemicals relies most likely in the control of the selectivity at two levels:

1) The selective fractionation of one LCB component (cellulose/hemicellulose/lignin) keeping the others un-attacked by choosing the adequate solvent and conditions.

2) The selection of efficient heterogeneous catalysts to assist the LCB component fractionation/liquefaction into high value added chemicals.

This approach is still in its infancy with very recent publications in conventional solvents, alcohols,[3,4] water.[5,6]

The objective of this talk is to present the potential of SC organic fluids assisted by heterogeneous catalysis to go further, towards the development of a strategy of catalytic fractionation of LCB into chemicals.

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"BYPROVAL: Cloud Point Extraction, an Innovative Solution for Carotenoids Extraction"

Subcritical water extraction of phenolic compounds from *Arbutus unedo* leaves, flowers and fruits

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Since the eco-extraction concept created in 2012, several innovative, consumer-friendly and more respectful of the environment processes were developed [1]. Among them, subcritical water extraction (SWE) – still not widespread in companies- looks like a promising step for sustainable chemistry [2]. In this work, the chemical composition of different parts of *Arbutus unedo*: leaves, flowers and fruits were studied. Indeed, *A. unedo* species which are very common in Corsica and Atlantic coastlines could find applications in cosmetics.

To achieve this, the separate organs of *A. unedo* were submitted to a subcritical water extraction (SWE) after an optimization stage of the extraction parameters. Metabolomic profiling of the natural products was performed by targeted analytical approaches using hyphenated techniques combining liquid chromatography and mass spectrometry (LC-MS/MS) in MRM mode. Antioxidant and anti-browning properties were evaluated with spectrophotometric tests such as ORAC, DPPH and tyrosinase inhibition.

The present study showed the selectivity of the SWE process for several secondary metabolites belonging to phenolic compounds family. SWE was more efficient to extract arbutin, quercitrin, myricitrin, epicatechine, gallic and p-coumaric acid than conventional hydro-alcoholic maceration. Finally, leaves and flowers extracts showed the highest biological activities.

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Enzymes for increasing color extraction from botanicals

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Introduction:

Plant cell walls are made up of a fibrous network. Small molecules, such as anthocyanins and carotenoids can become trapped in this matrix during extraction. This results in valuable color compounds being discarded in the pomace rather than captured in the juice. Enzymes can be used to degrade cell wall components and release trapped compounds, thus increasing color yield. This study looked at increasing color yield from carrots and blueberries.

Method:

Carrots were milled with an equal part water. Pectinase was dosed at 200 mL per ton carrots. The mixture was held at 50°C for 1 hour and then decanted. β-carotene content was determined by AOAC Method 2005.07. Juice yield (%) was calculated based on weight.

Blueberries were pureed with an equal part water. Pectinase was dosed at 500 mL per ton blueberries. The mixture was held at 50°C for 2 hours and then decanted. Color intensity was determined by measuring absorbance at 510 nm. Juice yield (%) was calculated based on weight.

Results:

For carrot puree, β-carotene content of the pectinase treated sample was nearly double that of the control (18.9 compared to 9.5 mg/L). Juice yield was similar for control (70%) and pectinase treated (67%) carrot puree (table 1).

For blueberries, color intensity of the pectinase treated sample was higher than the control (8.8 compared to 6.5). Juice yield was similar for control (82%) and pectinase treated (84%) blueberry puree.

Conclusion:

Using enzymes to increase natural color yield can lead to lower overall production costs. This study demonstrated that pectinases can increase color extracted from carrots and blueberries. Similar increases in yield can be expected from other fruits and vegetables.

Table 1. β-carotene content and juice yield (%) of carrot and water (1:1) puree incubated at 50°C for 1 hour with and without pectinase.

	Control	**Pectinase treated**
β-carotene content (mg/L)	9.5	18.9
Juice yield (%)	70%	67%

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Liquefied gases as alternative solvents for extraction of natural products

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Nowadays, numbers of extraction processes of valuable lipophilic compounds from natural products are still performed using toxic organic solvents such as *n*-hexane, dichloromethane or methanol. Recently, new regulations about consumer's safety have incited producers of natural extracts to look for safer extraction solvents. As cleaner alternative to those solvents, we developed a new process using non-toxic lipophilic liquefied gases, such as n-butane, dimethyl ether or HFO-1234ze, used as liquid solvents with low boiling points and gentle vapor pressures. The possibility of performing both extraction and solvent vaporization steps in such gentle experimental conditions of temperature (< 40 °C) and pressure (<10 bar) make them potentially suitable for extraction of heat-sensitive or highly volatile compounds.

The industrial feasibility of this substitution process was assessed with experimental data (extraction yield, quality of the extract) obtained with various plant material but also taking into consideration the potential safety and environmental impacts of the extraction process.

Several experiments[1-2] have been performed in a 1-liter scale with several well-known plant material such as lavender, orange peels and caraway seeds (aromatic compounds), carrots (carotenoids), olive leaves (polyphenolic compounds) or rapeseeds (fats and oil). Even if the results were not positive for polyphenols (low extraction yields), the extraction of more lipophilic compounds (carotenoids, terpenes, triglycerides) showed promising results, with good yields and better extracts quality, compared with classical solvents. Regarding to the industrial feasibility, even if the use of flammable gases implies some specific safety precautions, liquefied gas extractions (LGE) generate lower environmental footprints (toxicity, waste generation, energy consumption etc.) than conventional processes. Therefore, the use of liquefied gases as extraction solvents offers new alternatives to classical toxic solvents, in particular for sensitive compounds.

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GREEN EXTRACTION USING MICROWAVE AND CENTRIFUGAL FORCE: EXTRACTION OF NATURAL PRODUCTS

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In many industrial processes, liquid/solid separation is achieved by a combination of mechanical and thermal (drying) processes, resulting in in a low final water (or solvent) content in the product. Thermal drying in a mechanical separation device offers a lot of advantages (lower investment, higher productivity...). Moreover, coupling mechanical and thermal effects may lead in some cases to synergic effects allowing an optimal use of energy. Thermal input by dielectric heating may be adapted to a centrifuge. Previous work (Xabier Apaolaza (2014)[1]) was performed to develop a centrifugation pilot allowing the implantation of microwaves in a rotating machine and will be used for the extraction of natural products.

First experiments have been conducted on lettuce for extraction of phenolic compounds. Extraction efficiency has been evaluated as a function of rotational speed and power of microwave. The results show the influence of superimposition of dielectric heating and centrifugal force on extraction.

This pilot will be multifunctional and adapted to different extraction methods, either by distillation for obtaining essential oils and flavors, gravity[2] for obtaining fluid extracts, or by food-sourced solvent such as vegetable oils to obtain extracts rich in bioactive compounds. Ultimately, the new MW/C process could be used for the extraction of high value-added molecules in the food industry, cosmetics, pharmaceuticals and food supplements. The proposal of a mechanical / thermal coupling in the field of green extraction appears to be a real innovation and could allow a high yield extraction of high valuable products.

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Catalytic process for dimethyl carbonate from methanol and urea in deep eutectic mixture

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Keywords: carbon dioxide valorization, dimethyl carbonate, methanol, urea, catalytic, deep eutectic mixtures

Reduction of greenhouse gas is one of the most important environmental challenge of the last fifty years and a major contribution to this challenge is the valorization of carbon dioxide in chemical industries [1]. Many efforts are made to develop alternative processes to petroleum-based processes and non-fossil methanol production includes the use of carbon dioxide. On the other hand, carbon dioxide is part of urea formation, a carbonyl donor used for the formation of the valuable dimethyl carbonate (DMC) from methanol. Recently, a process has been developed for the production of DMC from methanol and urea using deep eutectic mixtures [2]. DMC presents many applications fields [3] and its role as extracting agent was also studied [4].

In our process, the carbonyl donor urea [5] reacts with methanol in the presence of a catalytic mixture formed by the association of a promotor (zinc sulfate/zinc oxide) with a support (inorganic chloride salts of zinc, tin, or iron) and produces dimethyl carbonate and ammonia. This catalytic association forms a deep eutectic mixture with urea that present the advantage to keep methanol in the reaction solution selectively, while releasing ammonia [6]. The reaction occurs at 120 – 165 °C and atmospheric pressure. After reaction, a binary mixture of DMC and methanol is obtained and 35% yield of DMC (from initial urea) can be achieved after purification by fractioned distillation. This work proposes an efficient and green process of dimethyl carbonate production by the use of deep eutectic mixture formed by the reactants and no additive (auxiliary, solvent, or other) is needed. This process is combined with a successful application of dimethyl carbonate as extracting agent.

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Dimethylcarbonate as a new green solvent for fragrant extracts: extraction and recovery processes

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Keywords: dimethyl carbonate, extraction, distillation, fragrances

Dimethylcarbonate (DMC) is widely used as an organic synthesis reagent. Alkylcarbonates are also used as solvents in some applications like inks or paintings. DMC is now recognize as safe and a "green" solvent [1] and publications or patents propose its renewable sourcing, and safe production [2]. Our purpose was to use it on fragrant raw material, instead of using traditional solvent like hexane and derivatives. This is challenging as DMC boiling point is much higher and less volatile than hexane isomeres distillation fractions. Many plant organs (seeds, leaves, fruits) or exsudates (gum) were extracted with DMC and analysed [3].

Recovery process by using batch distillation of DMC from a mixture of six reference compounds found in essential oils and considered as volatile is investigated with the help of experiments and simulation with Prosim BatchColumn [4]. Thermodynamic properties are described with the Modified UNIFAC model accounting for non ideality in the mixture. Preliminary calculations have been used to determine the operating pressure, so as to avoid possible azeotropes between the mixture compounds and the solvent. The batch distillation process simulator is used to find the most suitable operating parameters: number of trays, reflux ratio and boiling rate. Lab and pilot scale experiments are used to validate the simulation results. Up to 95% of DMC can be recovered with a purity greater than 99%, with a loss of the most volatile essential oil model molecule limited to 12%. As a conclusion DMC is a very interesting solvent for fragrances and flavours, and could be registred as a food grade extraction solvent.

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International Workshop on Alternative Solvents
Sept 28-29, 2017; Lyon - France.

Self-assembly of a bio-based extractant in vegetable oils and its advantage in an oleo-eco-extraction process. A study presenting a combination of small angle X-ray scattering experiments and molecular dynamics simulations.

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Antioxidants used in cosmetic and food formulations are currently extracted from plants using maceration processes. Vegetable solids are usually immersed in a solvent such as hexane, acetone or dichloromethane in order to solubilize the targeted active molecules in the liquid phase. One of the drawbacks of these methods is to be harmful for the environment due to the use of synthetic solvents.In order to reduce the environmental footprint, a new type of process, namely "oleo-eco-extraction" (OEE), was developed and patented by OLEOS SAS. The OEE is based on the six principles of eco-responsible processes. [1][2] The use of natural green solvents, as vegetable oils or melted waxes, and micro-waves and ultrasounds technologies are the major evolutions towards making the OEE process an environmentally friendly process.

A possible way to improve the solvent-extraction of polyphenols - a family of antioxidants - from plants in a OEE process is to use molecules that spontaneously build nano-structures in oils. In this study we focus on the aggregation of polyglyceryl-3-diisostearate (PG3DS), a bio-based amphiphilic molecule, and the influence of water on the nano-structuration as well as on extraction properties.[3] The nano-structures of PG3DS aggregates in methyl esters (ME) – a model polar oil - were accessed by combining small and –wide angle X-ray scattering (SWAXS) experiments and molecular dynamics (MD) simulation. The combination of SWAXS with MD simulation has proved recently to be successful for the characterization of such small supramolecular assemblies in oil [4] and shows in that case an excellent agreement.[5]

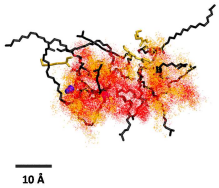

Figure 1. Snapshot of an observed aggregate of PG3DS in ME-C7 with an aggregation number of 8 where the PG3DS are represented through atomic cloud densities, that is, trajectories superposition of oxygen atoms from PG3DS (red) and C=O groups of ME-C7 (in orange), obtained by MD simulations

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The natural-based hydrocarbons mixture Cetiol® Ultimate as green solvent for extraction of lipophilic compounds.

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Key-words: green chemistry, alternative solvent, botanical extracts, lipophilic compounds

The principle of eco-extraction is based on the development of extraction processes that can reduce energy consumption, use preferably alternative solvents and renewable raw materials. In order to achieve these targets, there are two ways to proceed: working on the global process or focusing on each individual step. Thus, the research of green alternative solvents significantly increased the past twenty years.

The main challenge is to find new methods to obtain botanical extracts while keeping good yield in comparison with traditional organic solvents. For example, active ingredients have to be efficient, safe, biodegradable and easy to formulate.
Using functional ingredients as solvents appears like a promising way to develop new eco-extracts.

Cetiol® Ultimate (INCI name: Undecane (and) Tridecane)] is a very light and volatile emollient. It's a 100% renewable-based and volatile hydrocarbons mixture that is readily biodegradable and approved by Ecocert and Cosmos.

In this study, we evaluated the efficiency of Cetiol® Ultimate as new solvent for the extraction of specific targeted compounds such as carotenoids and lignans.
The results showed that the yields of phytochemical tracers with Cetiol® Ultimate extraction can reach and even overcome those obtained with hexane or ethanol 80%.
This results confirm the interest of Cetiol® Ultimate for the preparation of botanical extract and its uses in cosmetic compositions.

How to modulate the extraction of Frankincense essential oil using water and microwaves

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Intrroduction

Boswellia species, also named olibanum or frankincense, is an oleo-gum-resin from which extracts and essential oils have been used medicinally as antiseptic agents and to cure cough and asthma[1]. The essential oil is extracted by the conventional method of steam distillation (SD). Despite its robustness, this method is time and energy consuming and does not allow chemical and sensorial modulation of the end product. In this study, we propose to evaluate an alternative method which is microwave assisted distillation (MAD). The productivity, energy consumption, power efficiency as well as the chemical profile of the conventional and alternative methods are compared.

Material and Method

Boswellia serrata oleo-gum-resin (S) samples were introduced in the extraction vessel of 1 L. Water (L) was added in the ratio of 5 to 1 (L to S). A straight adaptor connect the vessel to a double jacket Clevenger (Milestone, Italy). Conventional and microwave assisted distillation were carried out using a heating mantle (HORST 6145 Lindenfels type HME 2/1) and a microwave over (Milestone ETHOS X) respectively. The cooling system was a Smart H150-2100 chiller (Lab Tech; USA). The same glassware was used to compare both methods. Each extraction was repeated at least three times. The chemical analysis of essential oil was carried out in a GCMS-QP2010 Shimadzu and an apolar column ZB-5MS (30m x 0.25 mm x 0.25 μm).

Results and conclusion

The whole of the essential oil from oleo-gum-resin is extracted in 180 minutes with the conventional method. Two power densities were tested for MAD extraction (1 and 2 W/g $_{resin}$). No significant differences were observed in extraction kinetics at 1 W / g compared to the conventional method. However, a substantial reduction of the batch time to 48 minutes is confirmed when the specific power is doubled. The energy consumed by the new process is 2.7 times less than steam distillation (4 kW.h). It was also proved that MAD is more power efficient (22.15%) compared to SD (6.09%). GC/MS analysis revealed 53 compounds in the essential oil. We have observed substantial change in the chemical composition of the essential oil regardless of the microwave parameters. It appears that the essential oil obtained at 1W / g has a better antioxidant activity than that obtained by SD. In conclusion, MAD is an eco-friendly solution to be seriously considered for a frankincense essential oil commercial extraction.

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Green solvents: from design to continuous flow synthesis

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Activation is a privately-owned and independent company, specialized in the process research of innovative reaction conditions, mainly through catalysis. Since 2003, we innovate for the performance and the sustainability of industrial processes focusing on three axes: new reactions, technologies and renewable raw materials (biosourced).

In 2014, we started a partnership on a 3-year collaborative project named SOragO[1] aiming at *developing new biosourced solvents*[2] and resins for coil coating. The objective of this consortium is to develop paint systems with the highest possible amount of bio-sourced carbon in order to provide more sustainable and environmentally-friendly coating products.

In charge of the renewable solvent technical package, Activation set up and developed an *in silico*[3] *multifactors decision support tool "Acti'Solv"* based on the analysis of existing solvents and associated formulations. New solvent candidates and their suitable combinations can now be rapidly selected based on: viscosity, range of boiling points, chemical stability, HSE, production costs…

First samples were synthesized *via* batch processes. Then we turned to continuous processes developed to gain flexibility and productivity compared to the batch approach (lowering future CAPEX & OPEX for production). *A set of succinate based esters* was produced with different ranges of viscosities and boiling points *to substitute competitively current petrosourced dibasic ester*.

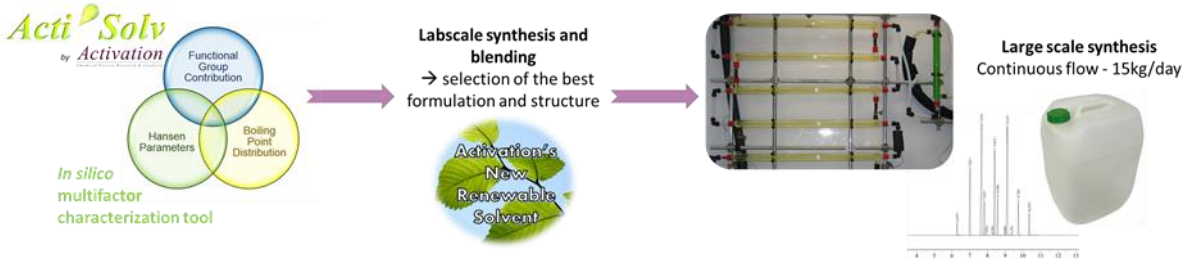

Figure 1. New solvent: from "in silico" decision support tool to flexible production at kg-scale

Our designed continuous flow systems, *offering an improved productivity over 15kg/day* of solvent, were successfully involved to deliver numerous kg scale samples for evaluation in formulations by our industrial partners. This flexible tool is ready for *on demand production of tunable samples of solvents*.

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Phenolic Compounds from Olive Pomace, Alpeorujo, Obtained with Deep Eutectic Solvents (DESs)

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Introduction. Deep Eutectic Solvents (DESs) are mixtures of natural substances produced in living organisms capable of solubilizing organic material such as phenolic compounds [1]. During the extraction of virgin olive oil, a single and contaminant by-product is generated named alpeorujo, which is rich in polyphenols, potent natural antioxidants with bioactive activities. The objective of this study was to determine the extractive capacity of two DESs for the obtention of phenols from alpeorujo of the Manzanilla cultivar.

Materials and Methods. Two DESs were prepared [2] using Choline Choride-glycerol (DES-1) and Choline Choride-Xylitol (DES-2) and compared with two methanol-water mixtures 80% v/v (M-1) and 50% v/v (M-2). The extraction was performed using a simple method, mixing 10 g of fresh alpeorujo and 10 g of solvent, stirred 1 h at 40 ºC and centrifuged, this step was repeated twice. The solvent phase was pooled and analyzed in HPLC-DAD and HPLC-ESI IT/TOF-MS.

Results and Conclusion. Figure 1 shows the sum of extracted polyphenols quantified individually by using each solvent. DESs were most extractive than conventional solvents M-1, M-2 and water. DES-2 extracted 44.6% more polyphenols than M-1, 70.5% than M-2 and 83% than water. DES-2 achieved 13.2% more phenols than DES-1. When analyzing individual phenols, we denoted that DESs, were able to extract mainly phenols of low polarity and bioactive molecules such as oleocanthal, oleacin, other derivatives of oleuropein and ligstroside and the phenylpropanoid verbascoside.

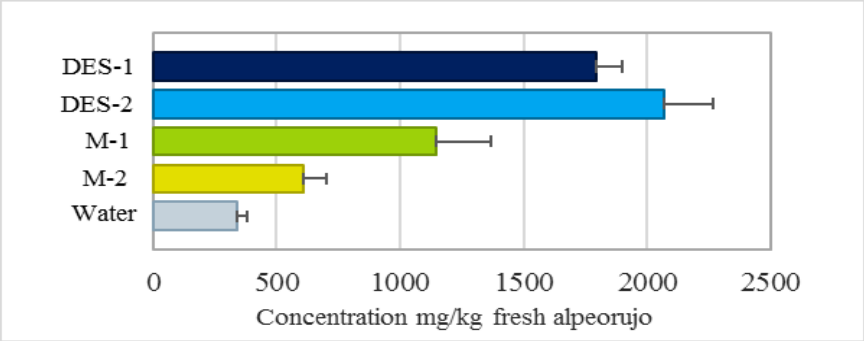

Figure1. Sum phenolic compounds extracted by the different solvents, DES-1, DES-2, M1, M2 and water.

In this work, 22 phenolic compounds have been extracted from fresh olive pomace by using DESs. We also demonstrated the highest efficiency of DESs to obtain polyphenols from alpeorujo when compared to conventional solvents.

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Evaluation of Solubility and Bioavailability of Quercetin by Means of Deep Eutectic Solvents (DESs)

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Deep Eutectic Solvents (DESs) are emerging solvents due to its versatility and extractive capacity. In this study eleven DESs were prepared using amino acids, sugars, alcohols and organic acids to evaluate their ability to dissolve the flavonol quercetin, a phenolic compound ubiquitously present in vegetables with a wide range of health benefits [1]. However, application of quercetin is limited due to its low solubility and consequently, poor bioavailability. We have compared the capacity of DESs to solubilize quercetin, with conventional solvents as dimethyl sulfoxide (DMSO) or ethanol. We found that DESs constituted by choline chloride-glycolic acid-oxalic acid and choline chloride-glycerol were most effective dissolving quercetin. We then hypothesized if the antioxidant properties of quercetin were still present when it was solubilized in DESs [2]. For this purpose, Caco-2 cells were treated with a dose of quercetin diluted in two different DESs and DMSO prior the addition of tert-Butyl hydroperoxide solution (THB), inducer of intracellular reactive oxygen species (ROS).

Upon detection of ROS by fluorescence microscopy on a fluorescent plate reader , we observed that the ability of quercetin to reduce ROS production did not differ when solubilized in DESs and DMSO.

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New Valorisation Pathway for Vegetable Waste by a Combination of Extraction and Biogas Production - Cloud Point Extraction, an Innovative Solution for Carotenoids Extraction

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Introduction

Fruit and vegetable waste management can be very costly for a business while they often contain valuable bioactive plant components that are of great interest to the food, pharmaceutical, and cosmetic industry. Simultaneously, the biogas sector in the long term will be more dependent on organic waste materials in order to operate sustainably. The BYPROVAL project completely fits the current trends in by-product valorization. The goal of the ongoing work is the development of a combination of valuable compounds extraction and biogas production as a new valorisation pathway for by-products of the fruit and vegetable industry. The development aims at the integration of extraction unit at a biogas plant, which implies technico-economical restrictions (low cost unit, no use of organic or flammable solvents). High-value targeted compounds are polyphenols (polar compounds) and carotenoids (non-polar compounds). In this publication, only non-polar compounds extraction using Cloud Point is presented [1-3].

Methods

Three food grade surfactants (Genapol X-080, Tween 80, nonionic biobased surfactant under development) were selected according to their HLB (12-13). Carotenoids, thermolabile compounds, from carrots and pea hulls, were extracted using the surfactant with the lowest Cloud Point Temperature.

Results/Conclusion

First results indicate that 66 % of β-carotene present in pea hulls were extracted using Cloud Point Extraction (CPE). In contrast, only 0.2% were extracted from carrots but lutein extraction was favoured in carrots (53% versus 20% in pea hulls). CPE success depends on the type and concentration of surfactants, concentration of the target compounds in the raw material, and matrix composition (competition risk). Optimisation could lead to higher extraction yield. CPE is a green attractive alternative technique for lipophilic compounds extraction.

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