WELCOME

Dear Colleagues,

Formula VIII conferences, as previous Formula conferences, aims at advancing our knowledge, sharing ideas and working together in the field of product formulation. This is a very wide field, highly multidisciplinary, with much interest from both academia and industry, considering that advances produce a great impact in daily life. Formula VIII conference will cover all aspects in Formulation Sciences and Technologies, from the most fundamental and theoretical to the most applied aspects. The headline of the conference "Formulate your innovation. Innovate your formulation" intends to stress that scientific discoveries and technical innovation are the driving forces to offer breaking new products to the market, satisfying continuously evolving customer needs.

The first Formula Conferences were created and organized by the French Chemical Society (SCF). Later, Formula Conferences expanded and become larger events, thanks to the incorporation of various European Societies, namely the British Formulation Group of the Royal Society of Chemistry (FSTG/RSC), the German Society of Chemical Engineering and Biotechnology (DECHEMA, Germany), Scandinavia Chemical Societies (SP Chemistry) and the Spanish Group of Colloids and Interfaces of the Royal Societies of Chemistry and Physics (GECI/RSEQ-RSEF). Moreover, several companies (AKZO-NOBEL, BASF, BAYER and EVONIK also joined the organization, ensuring a truly and deep dialogue between Industry and Academia.

The Formula VIII Conference is being celebrated in Bercelona, 4-7th July 2016, following the past conference in Mulhouse (France) in 2013. Conference talks, together with poster sessions, will cover all fields in formulation science and technology and will provide cutting edge new aspects.

The main institutions that support Formula VIII are the Catalan Institute of Advanced Chemistry of Catalonia (IQAC-CSIC), the University of Barcelona and the Spanish Committee of Detergency, Surfactants and Related Products (CED).

Two other events are integrated in the organization and programme of Formula VIII: the 46th Symposium of the CED, and Nanoformulation 2016. Members of the organizing committees of these events are integrated in the committees of Formula VIII in order to achieve a most powerful event.

All participants will be welcome, wishing that their contributions and helpful discussions will greatly enrich the conference. Please take a look at his website, and consider the submission of an abstract and the registration to the event. We are very pleased to welcome you to Barcelona.

Jordi Esquena
Chairman of Formula VIII

WELCOME

The Comité Español de la Detergencia, Tensioactivos y Afines (CED), was founded the 1957.

It is an independent entity constituted by National associations and enterprises related to the detergency, cosmetics, and detergent raw material industry.

One of its objectives is to organize an annual meeting done since 1970, we are proud it is the oldest held annually and uninterrupted in Europe.

We are happy to collaborate with the prestigious Formula and Nanoformulation for our 46th Congress that symbiosis for the 2016 that will give us a new impulse for future meetings.

We welcome all the participants and invite you to visit Barcelona, Catalunya and Spain and to take your time to relax and enjoy it with all your senses!

Olga Sanahuja
President of CED

Nanotechnology provides fascinating new solutions for formulation problems. But also creates new challenges, which do not show up at the macro- or micro-scale. The NanoFormulation-session will provide actual insights into this still new and growing field with application examples from physics, chemistry, chemical engineering and pharmaceutical technology.

The NanoFormulation conference series started as part of the international events under an EU funded program called InForm (Integrating Nanomaterials in Formulations). InForm was an EU coordination action funded by FP7 involving 17 world-leading institutions which brought together formulation scientists from Europe, USA and Asia-Pacific involved in the formulation of nanomaterials. Starting as a yearly event, and now as a biannual event, NanoFormulation conferences have been held in different locations in Europe and Asia: 2010, in Stockholm; 2011 in Singapore; 2012 in Barcelona; and 2014 in Manchester. The NanoFormulation conference series has created a multidisciplinary community, building bridges between scientists developing novel nanostructured materials and formulators aiming to create new products in a variety of areas, from healthcare to energy.

The organizing institutions are bringing NanoFormulation2016 as part of Formula VIII, which which takes place in Barcelona between the 4-7th July 2016. We are delighted to invite formulators and scientists developing novel nanostructured materials to participate in this meeting and strengthen our community.

Flor Siperstein
Coordinator of Nanoformulation 2016

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Carlos Rodríguez, (coeditor), INL

Monday 4th July 2016

12:00 - 14:00 **Delivery of Documentation**

Room 1

14:00 - 15:00 **TANDEM TALK**

- **Melt emulsification as formulation platform: research and application aspects**
  Frank, Kerstin /Abramov, Serghei. Basf (Germany) /Karlsruhe Institute of Technology (Germany)

Room 1. DESIGN AND ENGINEERING OF FORMULATIONS. RELATIONSHIP BETWEEN STRUCTURE AND PERFORMANCE (1)

15:00 - 15:20 **Inventing a new category of formulation: a mouldable putty that turns into rubber**
Jerlhagen, Asa, FormFormForm Ltd (United Kingdom)

15:20 - 15:40 **Particle Formulation by a Spheronization Process: Experiments and DEM Study**
Weis, Dominik, University of Kaiserslautern (Germany)

15:40 - 16:00 **Emulsifiers for MWF: balancing performance, labeling and economics**
Hedoire, Claude, Solvay (France)

16:00 - 16:20 **Investigation of chemically modified inulin as encapsulation material for pharmaceutical substances by spray-drying**
Walz, Michael, University of Stuttgart (Germany)

Room 2. FUNDAMENTAL SCIENCE, PHYSICO-CHEMICAL PRINCIPLES AND MECHANISMS IN FORMULATION (1)

15:00 - 15:20 **The Impact of Depletion-Attraction on the Nucleation and Growth of Colloidal Crystals**
Patti, Alessandro, University of Manchester (United Kingdom)

15:20 - 15:40 **Development of Pectin Microparticles for Chlorhexidine Delivery: Physico-Chemical Studies and Formulation**
Lascol, Manon, University of Lyon 1 (France)

15:40 - 16:00 **Prediction of the Equivalent Alkane Carbon Number (EACN) of Polar Oils with COSMO-RS σ;-Moments: Application to the Aqueous Solubilisation of Fragrances.**
Illous, Estelle, University of Lille 1, UCCS (France)

16:00 - 16:20 **Practical Implementation of HLD-NAC Theory**
Gutiérrez, Alejandro, VLCI (Spain)

16:20 - 17:00 **COFFEE BREAK**

Room 1. DESIGN AND ENGINEERING OF FORMULATIONS. RELATIONSHIP BETWEEN STRUCTURE AND PERFORMANCE (2)

17:00 - 17:20	**Smart Alginate Microfibers** Chaurasia, Ankur, King's College London (United Kingdom)
17:20 - 17:40	**How to Relate Lipstick Sensory Properties to its Ingredients? The Importance of Understanding these Relationships to Formulate more Efficiently** Abidh, Sarah, Chanel Parfums Beauté (France)
17:40 - 18:00	**Emollients for Cosmetic Formulations: Towards Relationships between Chemicals, Physico-Chemical Properties, and Sensory Perceptions** Chao, Christina, Sorbonne Universities / Université de Technologie de Compiègne (France)

Room 2. FUNDAMENTAL SCIENCE, PHYSICO-CHEMICAL PRINCIPLES AND MECHANISMS IN FORMULATION (2)

17:00 - 17:20	**Synthesis and Characterization of Polyacrylamide / Poly(Acrylic Acid) Interpenetrating Polymer Network Nanoparticles** Rabelero Martín, University of Guadalajara (Mexico)
17:20 - 17:40	**Microgel Particles in Non-Aqueous Colloid-Polymer Mixtures** Van Duijneveldt, Jeroen University of Bristol (United Kingdom)
17:40 - 18:00	**Wetting and Bio-Fouling of Porous Coatings Impregnated with Oil** Horozov Tommy, University of Hull (United Kingdom)

18:00 - 19:30 **WELCOME CEREMONY AND RECEPTION**

Tuesday 5th July 2016

Room 1

09:00 -10:00 **PLENARY LECTURE 1**
Virtual Reality of Chemical Processes: Dream or reality?
Li, Jinghai Chinese Academy of Sciences (China)

Room 1. DESIGN AND ENGINEERING OF FORMULATIONS. RELATIONSHIP BETWEEN STRUCTURE AND PERFORMANCE (3)

10:00 - 10:30 **INVITED LECTURE**
Formulation of a W/O emulsion encapsulating polysaccharides to improve the efficiency of vegetable spraying
Clausse, Danièle, Unversité de Technologie de Compiègne (France)

10:30 - 10:50 **Formulation of Stimuli-Responsive Emulsions Using Citrus Pectin as a Natural Hydrocolloid Emulsifier**
Schmidt, Ulrike, S. Karlsruhe Institute of Technology (Germany)

10:50 - 11:10 **Cosmetic Formulation Promoting Skin Permeation based on Novel Bicontinuous Alpha-Gel Structure with Amphiphilic Tranexamic Acid Derivative**
Miyamoto, Masayoshi, KK Chanel Research and Technology Development Laboratory (Japan)

Room 2. NANOFORMULATION: INTEGRATING NANOMATERIALS IN FORMULATION AND FORMULATING AT THE NANOSCALE (1)

10:00 - 10:30 **INVITED LECTURE**
Progress in Structuring Novel Liquid Nano Vehicles for Enhanced Bioavailability and Functionality of Bioactives
Garti, Nissim, Hebrew University of Jerusalem (Israel)

10:30 - 10:50 **Formulation of Niosomes and Bicelles by Nonionic Double-Tailed Surfactants**
Aramaki, Kenji, Yokohama National University (Japan)

10:50 - 11:10 **Synthesis of PolyureaNanocapsules by Interfacial Step Polymerization using Cosurfactant-Free Microemulsions as Templates**
Achour, Walid, University Claude Bernard Lyon (France)

11:10 - 11:40 **COFFEE BREAK**

Room 1. DESIGN AND ENGINEERING OF FORMULATIONS. RELATIONSHIP BETWEEN STRUCTURE AND PERFORMANCE (4)

11:40 - 12:00 **Formulation of Artificial Finger Print**
Hasome, Ayano, Fujitsu Laboratories Ltd (Japan)

12:00 - 12:20 **Oligomeric Alkylglycoside Surfactants - New Power-Tools in the Formulation Toolbox**
Ulvenlund, Stefan, Enza Biotech Ab (Sweden)

12:20 - 12:40 **Stabilization of High Molecular Weight Silicone Emulsions**
Marchal, Frederic, Bluestar Silicones (France)

12:40 - 13:00 **Comparative Emulsifying Properties of Osa-Modified Starch: Granular Form vs. Dissolved State**
Matos, Maria, University of Oviedo (Spain)

Room 2. NANOFORMULATION: INTEGRATING NANOMATERIALS IN FORMULATION AND FORMULATING AT THE NANOSCALE (2)

11:40 - 12:00 **Photonic Materials Prepared Through the Entrapment of Quantum Dots into Silica**
Shchipunov, Yury, Institute of Chemistry, Russian Academy of Sciences (Russia)

12:00 - 12:20 **Magnetic Solid Foams from Highly Concentrated Emulsions**
Rodriguez-Abreu, Carlos, INL (Portugal)

12:20 - 12:40 **Micro-Mesostructured Silica from Ionic/Nonionic Surfactants Mixture**
Blin, Jean, Luc University of Lorraine (France)

12:40 - 13:00 **Formulating Polymeric Superhydrophobic Coatings based on Functionalized SiO2 Nanocomposites**
Sánchez, Margarita, Centro De Investigacion En Materiales Avanzados, Unidad Monterrey (Mexico)

13:00 - 14:00 **LUNCH**

Room 1. DESIGN AND ENGINEERING OF FORMULATIONS. RELATIONSHIP BETWEEN STRUCTURE AND PERFORMANCE (5)

14: 00 - 14:20 **Formulation of Emulsions stabilized with Biodegradable PLGA Nanoparticles for Pharmaceutical and Cosmetic Applications**
Albert, Claire Institut Galien Paris-Sud, University Paris-Saclay (France)

14:20 - 14:40 **Development of a Novel Generation of Softeners with Frangances Encapsulated in Quatsomes/Particle**
Bernal, Cristobal, Carinsa (Spain)

14:40 - 15:00 **Formation of Functional Pharmaceutical Nanoparticles using Membrane Dispersion Cell Combined with Solvent Displacement Method**
Othman, Rahimah, Loughborough University (United Kingdom)

15:00 - 15:20 **Encapsulation of Ferrous Sulphate in Niosomes for Yogurt Fortification**
Gutierrez, Gemma University of Oviedo (Spain)

15:20 - 15:40 **New Sophorolipids - Naturally Derived High Performing Biosurfactants**
Fender, Michael, Evonik (Germany)

15:40 - 16:00 **Formulation of Industrial Enzyme - Current and Future Grand Challenges**
Andersen, Kim, Bruno Novozymes A/S (Denmark)

Room 2. FUNDAMENTAL SCIENCE, PHYSICO-CHEMICAL PRINCIPLES AND MECHANISMS IN FORMULATION (3)

14: 00 - 14:20 **Steady-State Droplet Size in Pickering Emulsions**
Van Duijneveldt, Jeroen, University of Bristol (United Kingdom)

14:20 - 14:40	**Hierarchical Self-Assembly in Tranexamic Acid Cetyl Ester Hydrochloride System** Yamashita, Yuji, Chiba Institute of Science (Japan)
14:40 - 15:00	**Dynamic and Rheological Behaviour of a Polymer Melt Loaded with Polydisperse Nanoparticles** Burgos, José Javier, University of Manchester (United Kingdom)
15:00 - 15:20	**QSAR Study on Diverse Compounds for Effects on Thermal Stability of a Monoclonal Antibody** Oyetayo, Olubukayo-Opeyemi, Institute of Applied Biotechnology, Biberach University of Applied Sciences (Germany)
15:20 - 15:40	**PIT-Slope Method: a Simple Tool to Quantify the Amphiphilicity of Surfactants and determine the Structure-Interfacial Properties Relationship.** Ontiveros, Jesus F., Ecole National Supérieure de Chimie, Lille (France)
15:40 - 16:00	**Detailed Investigation of Concentrated Micro- and Nanodispersions by X-Ray Concentration Profiling** Lerche, Dietmar, Lum (Germany)
16:00 - 17:00	**POSTER SESSION + COFFEE BREAK** Free Afternoon

Wednesday 6th July 2016

Room 1

09:00 - 10:00 **PLENARY LECTURE 2**
Probing the interfacial properties of Janus particles at liquid interfaces
Hidalgo-Álvarez, Roque, University of Granada (Spain)

Room 1. APPLICATIONS AND CUSTOMER NEEDS (1)

10:00 - 10:30 **INVITED LECTURE**
Microbial product development – A formulation point of view
Wessman, Per, SP Sveriges Tekniska Forskningsinstitut, Borås (Sweden)

10:30 - 10:50 **Organic-inorganic patchy particles as a versatile platform for foam and emulsion stabilization**
Velikov, Krassimir, Unilever R&D Vlaardingen (The Netherlands)

10:50 -11:10 **NANOCYTES® - Core-shell particles for the particle-based formulation of active pharmaceutical ingredients**
Gruber-Traub, Carmen, Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB (Germany)

Room 2. NANOFORMULATION: INTEGRATING NANOMATERIALS IN FORMULATION AND FORMULATING AT THE NANOSCALE (3)

10:00 - 10:30 **INVITED LECTURE**
Responsible Management of Nanotechnology
Schmid, Dagoberto, BASF Española S.L. (Spain)

10:30 - 10:50 **Formulation Strategies for the Production of Pharmaceutical Powders out of Precipitated API Nanoparticles**
Melzig, Sebastian, Technische Universität Braunschweig (Germany)

10:50 -11:10 **Formulation of Polymer Composites as Functional Coatings based on Functionalized NP's for Use on Solar Panels**
Licea Jiménez, Liliana, Centro de Investigación dn Materiales Avanzados (Mexico)

11:10 - 11:40 **COFFEE BREAK**

Room 1. APPLICATIONS AND CUSTOMER NEEDS (2)

11:40 - 12:00 **Study of Emulsifiable Concentrates using Green Solvents**
Oliveira, Adriano, Oxiteno S/A Industria e Comercio (Brazil)

12:00 - 12:20 **Protein Evaluation in Food Formulations by Passive Microrheology**
Ramsch, Roland, Formulaction (France)

12:20 - 12:40 **Preparation of Stable Emulsions to Chlorpheniramine Recovery from Aqueous Solutions**
Razo, Teresa Alejandra, University of Guanajuato (Mexico)

12:40 - 13:00 **A Multiple Emulsion Approach to Deliver 1-MCP for pre-Harvest Applications**
Ghosh, Tirthankar, Agrofresh Inc. (United States)

13:00 - 13:20 **Predicting the Interfacial Tension of Multicomponent Liquid-Liquid Systems with COSMO-RS**
Reinisch, Jens, COSMOlogic Germany)

Room 2. NANOFORMULATION: INTEGRATING NANOMATERIALS IN FORMULATION AND FORMULATING AT THE NANOSCALE (4)

11:40 - 12:00 **Deep-Sea Inspired Process for Bottom-Up Production of Nanoemulsions**
Deguchi, Shigeru, Japan Agency for Marine-Earth Science and Technology (Japan)

12:00 - 12:20 **Polymeric Nano-Emulsions and Nanoparticles: Influence of Polymer Concentration on Size, Stability, Drug Encapsulation and Release**
Homs, Maria, IQAC-CSIC (Spain)

12:20 - 12:40 **Formulation Strategies for the Preparation of Nanoemulsions containing Sensitive Carotenoids**
Mira, Isabel, SP Technical Research Institute (Sweden)

12:40 - 13:00 **Sub-Micron Patterning of Polymer Brushes arising from the Inkjet Printing of Polyelectrolyte Macroinitiators**
Yeates, Stephen, University of Manchester (United Kingdom)

13:00 - 13:20 **Engineering New Hybrid Nanoparticles for Formulation of New Materials**
Celine, Hubert, Centre de Recherche Paul Pascal (France)

13:00 - 14:00 **LUNCH**

Room 1

14:00 - 15:00 **SUCCESS STORY**
Soft Matter and Colloids for the conservation of Cultural Heritage
Baglioni, Piero, University of Florence (Italy)

Room 1. APPLICATIONS AND CUSTOMER NEEDS (3)

15:00 - 15:20 **Aqueous Solubilisation of Fragrances in Volatile Solvo-Surfactant-Based Microemulsions**
Nardello-Rataj, Véronique, University of Lille (France)

15:20 - 15:40 **Fragrances with Double Functionality. Novel Perfume Composition for the Prevention and Control of Diseases and Biofilms**
Bernal, Cristóbal, Carinsa (Spain)

15:40 - 16:00 **Understanding the Role of Chelants in a Formulation**
Giles, Matthew, R Innospec Ltd (United Kingdom)

Room 2. CHARACTERISATION, PROPERTIES AND PERFORMANCES (1)

15:00 - 15:20 **Dispersibility of aqueous nanosized metal oxide as function of dispersion intensity and characterization of degree of flocculation**
Lerche, Dietmar, LUM (Germany)

15:20 - 15:40 **Design of Agro-based Coatings: from innovative raw materials to optimal performances, the critical input of property characterization**
Collinet, Marion, IFMAS (France)

15:40 - 16:00 **Determination of particle surface properties for liquids election regarding pigment formulation**
Süß, Sebastian, Friedrich-Alexander-Universität Erlangen, Nürnberg (Germany)

16:00 - 17:00 **POSTER SESSION + COFFEE BREAK**

Room 1. DESIGN AND ENGINEERING OF FORMULATIONS. RELATIONSHIP BETWEEN STRUCTURE AND PERFORMANCE (6)

17:00 - 17:20 **Concentrated Oil-In-Water Emulsions Stabilized by Amphiphilic Polymers**
Durand, Alain, University of Lorraine (France)

17:20 - 17:40 **Pickering Emulsions based on Clays: Fundamental Investigations and Potential Applications**
Pitarch, Jesus, Clariant (Germany)

17:40 - 18:00 **Stimuli-Responsive Capsules based on Pickering Emulsion**
Baillot, Marion, University of Bordeaux / Crpp (France)

18:00 - 18:20 **High Internal Phase Emulsion Stabilized by Whey Protein Isolate-Low-Methoxy Pectin Complexes**
Wijaya, Wahyu, Ghent University (Belgium)

18:20 - 18:40 **Formulation of Organic Crystals in Stirred Media Mills**
Konnerth, Christoph, Institute of ParticleTechnology (Germany)

18:40 - 19:00 **High-Throughput Development of Micro-Capsule Containing Formulations**
Paul, Johan, Flamac (Belgium)

Room 2. CHARACTERISATION, PROPERTIES AND PERFORMANCES (2)

17:00 - 17:20 **Fast Temperature Screening for Viscosity Determination of Thermoresponsive Polymers with Innovative Microfluidic Device**
Fleury, Mathias, Formulaction (France)

17:20 - 17:40 **Anisotropy in Liquid Crystalline Phases as Detected by Natural Levels of D2O: An NMR Method to Characterise Gel Phases**
Mendoza, Cesar, Unilever (United Kingdom)

17:40 - 18:00 **Nanoformulation: Water-In-Diesel Fuel Preparation (using High-Energy Emulsification Method), Stability and Physical Properties**
Mane Harishchadra, Swapnil, Institute of Chemical Technology (India)

18:00 - 18:20 **Novel Photocatalyst - Composite Membrane Filter for Treatment of Pharmaceutical Residues and other Organic Pollutants in Waste Water**
Persson, Karin, SP Technical Institute (Sweden)

18:20 - 18:40 **Determination of Density of Emulsion Droplets and inner Dispersed Phase Fraction of W/O/W Double Emulsions**
Lerche, Dietmar, Dr. Lerche KG (Germany)

18:40 - 19:00 **Green Synthesis os Silver Nanoparticles in Microemulsion Media**
Rivera Rangel, Rubén Dario, University of Guanajuato (Mexico)

20:30 **CONFERENCE DINNER**

Thursday 7th July 2016

Room 1

09:00 - 10:00 **PLENARY LECTURE 3**
Formulation of taylor-made liquid solutions with a special focus on green and sustainable chemistry
Kunz, Werner, University of Regensburg (Germany)

Room 1. DESIGN AND ENGINEERING OF FORMULATIONS. RELATIONSHIP BETWEEN STRUCTURE AND PERFORMANCE (7)

10:00 - 10:30 **About microemulsion-based gels, reversible adhesives and structured emulsions, 30 years re-search and industrial applications of block copolymers**
Quellet, Christian, Leugos (Switzerland)

10:30 - 10:50 **Optimum Formulation for Maximum Encapsulation in Multiple Emulsions**
Jahanzad, Fatemeh London South Bank University (United Kingdom)

10:50 - 11:10 **Formulation of industrial relevant enzymes**
Baier, Grit, Basf (Germany)

Room 2. FORMULATIONS FOR BIOMEDICAL NEEDS (1)

10:00 - 10:30 **INVITED LECTURE**
Interactions of nanomedicines with blood proteins and cells: modulation by nanoparticle surface design
Vauthier, Christine, University of Paris Sud, CNRS (France)

10:30 - 10:50 **Immuno-modulatory PPH dendrimer: from systemic to topical delivery?**
Turrin, Cédric-Olivier, Laboratoire de Chimie de Coordination du CNRS (France)

10:50 - 11:10 **Embracing the Circular Economy with Enzyme Technology**
Bartolini, Tony, Novozymes (Denmark)

11:10 - 11:40 **COFFEE BREAK**

Room 1. DESIGN AND ENGINEERING OF FORMULATIONS. RELATIONSHIP BETWEEN STRUCTURE AND PERFORMANCE (8)

11:40 - 12:00 **Formulation of Ceramic Foams: a New Class of Amphiphiles**
Celani, Andrea, University of Birmingham (United Kingdom)

12:00 - 12:20 **Enhancement of a Green Emulsion Stability by Tuning Its Formulation and Processing**
Santos García, Jenifer, University of Sevilla (Spain)

12:20 - 12.40 **Encapsulation by Supercritical Fluid and Pressurised Gas Processing**
Rose, Paul, Callaghan Innovation (New Zealand)

12:40 - 13:00 **Glucamide as a Bio-Based Sugar Surfactants for Home Care**
Schinle, Florian, Clariant (Germany)

13:00 - 13:20 **Benefits of Particular Silicones for Protecting Hair Fibers against Heat Damage**
Sabrina, Marchioretto, Dow Corning (Belgium)

Room 2. FORMULATIONS FOR BIOMEDICAL NEEDS (2)

11:40 - 12:00 **Amorphization of Crystalline Pharmaceutical Active Ingredients via Formulation Technologies**
Yee , Lim, Tau Institute of Chemical and Engineering Sciences (Singapore)

12:00 - 12:20 **Antimicrobial Soft Contact Lenses using Formulated Peptides**
Salvagni, Emiliano, IQAC-CSIC (Spain)

12:20 - 12.40 **Hyaluronic Acid Gels containing Liposomes for the Sustained Delivery of a Corticoid to the inner Ear: Formulation, Characterization and Evaluation**
Agnely , Florence, Institut Galien Paris-Sud (France)

12:40 - 13:00 **Stability of Immobilised β-Galactosidase on Meso-Macroporous Silica Support**
Fontainhas Prazeres, Sofia, University of Alcalá (Spain)

13:00 - 13:20 **Encapsulation of L. Rhamnosus GG (LGG) in Alginate-Silicate**
Haffner, Fernanda, Nano Group, SRSMC-CNRS University of Lorraine (France)

Room 1

13:20 -13:40 **CONFERENCE ENDING**

13:40 **LUNCH**

PLENARY LECTURES

Virtual Reality of Chemical Processes: *Dream or reality?*

Jinghai Li
Institute of Process Engineering, Chinese Academy of Sciences, Beijing 100190, China
Email: jhli@ipe.ac.cn

Facing global challenges, we are also expecting new S&T revolution and new paradigm of scientific research at the waves of big data, cloud computing and virtual reality. It is now natural for chemical engineers to think: what will be the next breakthrough in the field, with which the current trial and error R&D mode can be upgraded into a more quantitative mode to enable our capability in coping with global challenges?

We believe that there are two aspects of possible progresses crucial to give rise to a revolutionary changes in chemical engineering: one is physical understanding of mesoscale phenomena at different levels of processes; another is computational capability with sufficient predictability and scalability. Combining these two progresses, the long dream of chemical engineers to realize real-time simulation of chemical processes, that is, virtual reality, could become a real practice in chemical engineering. This was just a dream 10 years ago, but now would be probably a reality if sufficient efforts could be made along with this direction according to our 3-decade research on the relevant topics.

This perspective reviews the relevant progresses on these two aspects at Institute of Process Engineering, Chinese Academy of Sciences. It is indicated that there are huge potentials in integrating mesoscale understanding and computational capability to realize virtual reality in chemical engineering. Understanding mesoscale phenomena will gives rise not only to good predictability in physical modeling, but also to complete optimization of efficiency of computation, vice versa, computation will be an important tool in understanding mesoscale complexity which is likely not feasible for most of measurement technologies due to the limitation of resolution in both time and space. A demonstration version of virtual reality of gas-solid two-phase systems, based on this mesoscale strategy, will be presented. Challenges in next step of development will be identified. As long as virtual reality becomes a real practice, the capability of chemical engineering will be totally revolutionized! However, traditional thinking mode is not sufficient to lead to this change, and transdisciplinarity is the only path to reach this goal!

Probing the interfacial properties of janus particles at liquid interfaces

Miguel Ángel Fernández-Rodríguez, Miguel Ángel Rodríguez-Valverde, Miguel Ángel Cabrerizo-Vilchez and Roque Hidalgo-Álvarez*
University of Granada, Department of Applied Physics, Campus Fuentenueva, E-18071, Granada, Spain
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Janus Particles (JPs), named after the double-faced Roman god, are anisotropic colloids with two spatial domains of different physicochemical properties. Herein, we present a comprehensive review about the interfacial properties of Janus particles at liquid interfaces. The purpose of this work is to present the most relevant theoretical and experimental results obtained so far on the surface activity of amphiphilic JPs at fluid interfaces. The surface activity of JPs at liquid interfaces can be experimentally determined using two different methods: the classical Langmuir balance or the pendant drop tensiometry. The second method requires much less amount of sample than the first one, but it has also some experimental limitations. In all cases collected here the JPs exhibited a higher surface or interfacial activity than the corresponding homogeneous particles. This reveals the significant advantage of JPs for the stabilization of emulsions and foams. [1]

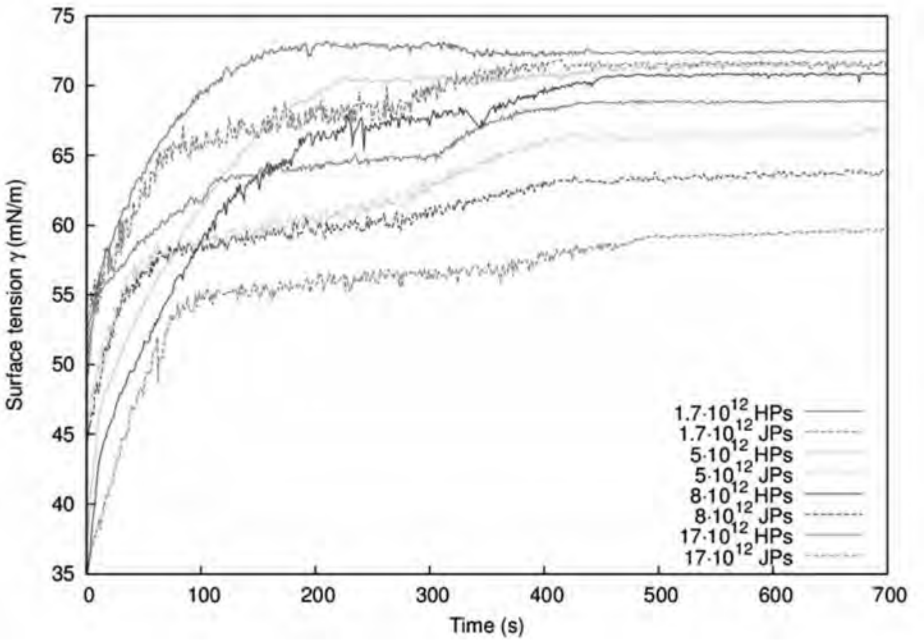

Figure legend. Surface tension evolution over time after depositions of gold HPs and JPs at the surface of an initial 5 μl MilliQ water pendant drop and subsequent growing at a 0.08 μl/s rate up to 20 μl. Each line corresponds to different depositions with different number of HPs or JPs. After the solvent evaporation, the surface tension remained stable.

References

[1] Miguel Angel Fernandez-Rodríguez, Miguel Angel Rodríguez-Valverde, Miguel Angel Cabrerizo-Vilchez and Roque Hidalgo-Alvarez, Advances in Colloid and Interface Science in press 2016.

Formulation of taylor-made liquid solutions with a special focus on green and sustainable chemistry

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Herein, we present several examples of formulations or ingredients for formulations that we developed over the last years and that are ready to use or even already commercialized. The first example [1] is a combination of a cheap vitamin (choline), used as counterion with commercial alkylsulfates or even with soaps. The advantage is a significant lowering of the solubilisation temperature so that even long-chain surfactants are water-soluble at room temperature. The second example concerns the combination of soaps with ribaudioside A (the Stevia sweetening molecule) that allows stable soap solutions to be formed even at neutral pH [2].

The combination of soap and stevia can give aqueous solutions at neutral pH.

Further examples are the formulation of a tea concentrate based on the corresponding essential oil extracted from fresh leaves, the formulation of a "drinkable" anti-graffiti spray and preliminary formulations of green but economically competitive biofuels.

We will also show the scientific strategy behind these formulations. To this purpose we begin with the discussion of classical and also new types of green solvents, such as drinkable Ionic Liquids and Deep Eutectic Solvents and their usefulness for modern formulation. Then we will discuss how to avoid surfactants whenever possible by taking profit of the Ouzo and pre-Ouzo effect [3,4], and finally, we come back to the utilization of surfactants and show that there can be a renaissance of soaps, a surfactant class that was unfortunately widely neglected in scientific research since the upcoming of sulfate- and sulfonate based surfactants.

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TANDEM TALK

Melt emulsification as formulation platform: Research and application aspects

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Wax dispersions are applied in many formulations, e.g. in paints and lacquers, printing inks, floor, furniture and automobile polish, paper coatings, foods, cosmetics, pharmaceutical formulations, etc. Such dispersions set application properties like scratch, rub and dirt resistance, water repellency, moisture and grease barrier, gloss, surface smoothness or a tailor-made release of actives. This requires customized product properties, especially spherical and individual particles as well as a precise adjustment of the particle size distribution. This can be realized in melt emulsification processes. Here, the future disperse phase is melted and dispersed into fine droplets. The size of the droplets is defined by the product and process conditions during emulsification. After emulsification, the droplets are cooled down and ideally individual solid particles of spherical shape are formed. Though there has been lot of progress in the field of melt emulsification within the last years, there are still a lot of open questions, especially in understanding of the basic mechanisms of wax hardening and the role of emulsifiers and process conditions in this step.

Within this contribution we will give insights in research and application issues of melt emulsification processes.

Research focuses on the cool down step, in which crystallization and hardening of emulsion droplets take place. Variances in morphology due to coalescence, aggregation, or flocculation and additional nucleation in the continuous phase are caused by material and process parameters such as o-phase solubility, emulsifier type and concentration, shear stress or super cooling during the liquid-solid-transition. Non-invasive optical and rheological analytical methods have been developed that allow investigating the crystallization of single droplets and their collectives. Different solidification mechanisms can thus be identified, their kinetics quantified and relevant parameters of influence determined. This allows us to improve the fundamental understanding of droplet crystallization in emulsions.

In the application part of this contribution we will present aspects of the development of a pilot-scale melt emulsification process for the production of automotive clear coat formulations. Formulation and process optimization aspects will be demonstrated with regard to the demanded rheological, optical and application technology properties.

SUCCESS STORY

Soft Matter and Colloids for the conservation of Cultural Heritage

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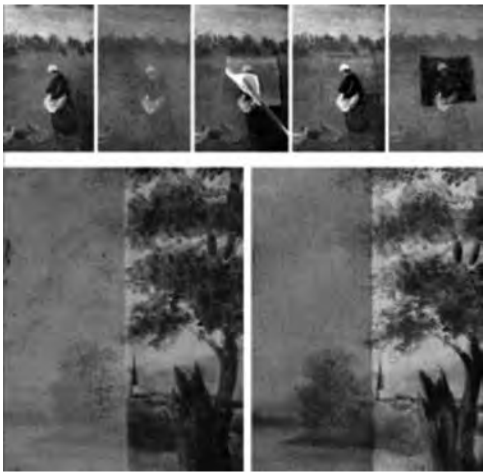

Works of art and artifacts that constitute our cultural heritage are subject to deterioration. Their surfaces interacting with the environment are the most prone to aging and decay; accordingly, soiling is a prime factor in the degradation of surfaces, chemical and mechanical degradation are often associated to soiling and lead to the disfigurement of a piece of art. The effects of these processes are usually strongly amplified in the presence of protective coatings (mainly acrylic and vinyl polymers), applied in previous restoration treatments. We pioneered the synthesis and the application of several advanced systems for the consolidation and the cleaning of works of art, as hydroxides nanoparticles, microemulsions and chemical/physical gels. All these systems constitute a new platform for Conservation of Cultural Heritage and are characterized by scale lengths below 100 nm in one or more dimensions. Soft matter and Colloids played a major role in the development of new palette of materials for the conservation: microemulsions, physical and chemical gels, magnetic gels, and microemulsion confined in responsive gels are the most important systems developed so far. In this talk examples from self assembled systems for the cleaning or the removal of coatings from pictorial surfaces will be highlighted. Micellar solutions and microemulsions constitute very efficient systems for the removal of acrylic, vinyl and alkyd polymers or grime/soil. These systems (as well as neat solvents used in "traditional" conservation) can be confined into chemical and physical gels having proper nano-domains for the upload or the delivery of compounds from/to the work of art. With the help of chemical gels, fine control of the cleaning procedure can be obtained even for challenging cleanings as water sensitive works of art, where the cleaning can be achieved by using water confined into gels, leaving no residues on the works of art. As an example, I'll report on a recently restored masterpieces as Pollock (in cooperation with Peggy Guggenheim Foundation), Beato Angelico (Pisa), etc..

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INVITED LECTURES

Formulation of a w/o emulsion encapsulating polysaccharides to improve the efficiency of vegetable spraying

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The treatment of vegetables by spray is rendered difficult due essentially to the drift of the sprayed product and 80 % of the product can be lost. This has a consequence not only for the cost of the process but also for the environment. To solve this problem it has been proposed to reduce the drift by introducing polysaccharides in the product to be sprayed. Due to the poor solubility of the polysaccharides, this cannot be achieved by introducing them directly in the field conditions in the tank containing water plus plant protection products. To contribute to the resolution of this problem a European project VEGEPHY, labellised EUREKA and by the regional competitiveness cluster Industries & Agro-Ressources has been set up under the leadership of the industrial company CCL: Comptoir Commercial des Lubrifiants, Le Meux, France (Head: P.Paillisson, Scientific expert: J. Parmentier).

From preliminary studies the natures and the amount of polysaccharides requested to be in the final product have been determined. Guar gum is the one that has been selected. In this context the formulation of an emulsion W/O containing the polysaccharides trapped in the water droplets has been obtained [1]. This formulation has been made in the laboratory using high speed rotator to dissolve the products and by introducing glycerol that is known to enhance the solubility. For environmental problems the oil used to formulate the emulsion is a vegetable one. From various tests, the surfactant PGPR (PolyGlycerol PolyRicinoleate) was selected [2]. The relative amounts of water + guar, oil, surfactant PGPR were determined from studies about the stability of the emulsions obtained. The required stability was determined to be in accordance with the commercialization of the emulsion. Normalized tests have been retained (normal aging, accelerated aging and freezing – melting cycles of the emulsions [3]). To test the stability the classical tests have been used such as the bottle test, microscopy and a more sophisticated one based on the correlation between the freezing temperatures of the water droplets of the emulsion submitted to a regular cooling and the sizes of the droplets. The freezing is shown through the energy released during freezing which is registered by a calorimeter. It is found that the lower is the freezing temperature, the smaller are the droplets and the higher is the stability of the emulsion. Doing so the parameters leading to an emulsion containing the required amount of polysaccharide with a maximum of product obtained by making a high concentrated W/O emulsion have been set up. It has been checked by performing rheology tests that the emulsion obtained shows also a moderate viscosity to be dispersed in the water of the tank. Another point is to check that the trapped polysaccharides are released rapidly enough. To do so another surfactant has been used and conductivity test have shown fast release kinetic.

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IL 02

Progress in structuring novel liquid nano vehicles for enhanced bioavailability and functionality of bioactives

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In our modern life style human nutrition is often not well balanced and as a result the body is lacking vitamins, minerals and other minor ingredients that are essential for better health and prevention (or even cure?) of diseases. In recent years intake of food supplements (termed also nutraceuticals) is becoming common practice of all ages. The nutraceuticals market (22 10^9 UDS) includes various plant extracts that are exhibiting (but not always) some nutritional and health benefits.

Many of those supplements have low water-solubility and low bioavailability. Our studies in the last decade are aimed to develop novel liquid vehicles fully dilutable in water, that can solubilize large quantities of the nutraceuticals (high loading capacity).The novel vehicles are based on nano-sized molecular architectures of emulsifiers and other food-grade ingredients that form structures-like modified microemulsions, structured solutions, lyotropic liquid crystals, sponge phases, biopolymer amphiphilic gels, oleogels, etc.

In this presentation we will demonstrate progress that was made in determination of the prerequisites for constructing the mesophases. New nano vehicles formed in our lab, such as QL and sponge (L3) mesophases will be characterized. Compositions, type and nature of the interfaces and cores, their structural characteristic, phase transitions and loading mechanism, along with 'on-demand' discharge or release of the nutraceuticals, will be discussed.

Microbial product development – a formulation point of view

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Beneficial microorganisms have found use in a wide range of applications. For instance as probiotics to improve human or animal health by modifying gut microbiota, as biofertilisers or biocontrol agents which can help reduce our dependence on chemical fertilisers and pesticides in agriculture. The role of formulation is to make sure that cells are delivered fit-for-purpose to the various targets and can successfully compete with the existing microbiota in the gut or in soil, kill target insect pests, produce plant growth stimulating hormones or excrete substances supressing pathogens in soil. Product stability and commercial viability of the product is often a significant task with microbes as the active ingredient.

Many of the interesting candidate organisms are non-spore forming organisms, which present specific difficulties. For example, the delicate gram negative bacterial cell is generally sensitive to environmental stresses including desiccation, temperature and UV light. The commercial demands on a microbial product are despite this not more lenient as features such as long shelf life, easy to administer and cost effective production have to be fulfilled, aside maintained efficacy.

In microbial product development, formulation design is often a compromise between formulation processes, providing cells with optimal conditions to maximise shelf life, and the functionality of the product and the cells will inevitably be exposed to various environmental stresses.

Most production processes include drying in order to inactive the cells. Probiotics tend to be produced as dry powders which can then be further processed into different consumer goods. Seed treatments, i.e. inoculating seeds with beneficial microbes, include drying steps for ease of product handling and maintained seed vigour. The dried microbial cell is often susceptible to moisture and oxygen which needs to be addressed during product development. Encapsulation techniques have been developed to mitigate stresses related to process and delivery. Other formulation approaches include creating microenvironments characterized by high moisture content, the cells are metabolically active but likely in a dormant state.

In parallel to formulation development biomass production should be addressed. The microbial biomass (i.e. the active ingredient) often constitutes the major cost of a microbial product and it is important to optimise growth conditions to maximise yield and media. But the focus on yield often leads to overlooking the environmental fitness of resulting cells. Development of fermentation protocols aimed at improving both the inherent stability of cells in formulations and their performance in the field through manipulation of physiology and metabolic states of cells should go hand in hand with formulation development.

IL 04

Responsible Management of Nanomaterials

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Small Dimensions – Big Challenges: BASFs Approach to the Responsible Management of Nanomaterials.

Clean drinking water, high-performance insulation materials or scratch-resistant coatings: Nanotechnology contributes to sustainable solutions for more quality of life and to develop a careful handling of resources such as water and energy. BASF uses nanotechnology to develop new products and improve existing ones. Nanotechnology is a cross-sectional technology. It is used in many sectors, such as health, electronics, construction and automotive to develop innovative nanomaterials with new performance features.

The constant improvement in analytical capabilities is providing ever more detailed insights into the world of the tiniest structures, contributing to our growing understanding of the effects that nanostructure has on material properties. Because of their small size, nanomaterials often have new optical, magnetic, mechanical, chemical and biological properties. Consequently, they can be used to develop innovative products with new functionalities and special properties.

Parallel to the development of new nanomaterials BASF conducts extensive safety research and therefore BASF is constantly expanding its knowledge of nanomaterial safety. Over the past years, BASF has conducted more than 230 toxicological and eco-toxicological studies and participated in around 30 different projects related to the safety of nanomaterials. The results were published in more than 70 scientific articles. These can also be found on the website of BASF. One important finding is that toxicity is determined not by the size of the particles, but by the intrinsic properties of the substance.

In 2015, BASF published a concept for the integrated testing and potential grouping of nanomaterials together with the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC). BASF is currently discussing this concept with the European Chemicals Agency (ECHA), the OECD and national authorities and further developed it in various research projects, so it can be used for regulation of nanomaterials.

As the first and so far the only company BASF established the Dialogue Forum Nano in 2008. BASF employees meet regularly with representatives of environmental and consumer organizations, trade unions, academic institutions, churches and other companies to discuss current political and social developments and issues.

More information about nanotechnology are available under: www.nanotechnology.basf.com

Interactions of nanomedicines with blood proteins and cells: modulation by nanoparticle surface design

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Polymer based nanotechnologies are parts of the arsenal of nanosize scale objects applied as nanomedicines. Their use has found potential advantages to improve therapeutic efficacy of drugs with a narrow therapeutic window window or of drugs suffering from a low bioavailability. The nanoparticle have the potential to modify the absorption, distribution, metabolism and excretion profile of a drug in a way that optimizes its therapeutic efficacy. However, the success of the method is pending to the design of the nanomedicine and is greatly associated with surface properties of the carrier that gouvern its in vivo fate. The presentation will focus on the influence of discrete modulation of surface properties of polymer nanoparticles on interactions of the nanoparticles with blood proteins and cells. Consequences in terms of needs to achieve the characterization of nanomedicines will be discussed.

ORAL COMMUNICATIONS

Inventing a new category of formulation: A mouldable putty that turns into rubber

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Sugru is a multiple award winning consumer product that comes in the form of a hand-mouldable putty which cures to a tough rubber material when exposed to air. The material was envisaged by product designer Jane Ní Dhulchaointigh as an easy tool for the average consumer to mend and improve their belongings. The uncured material has texture similar to plasticine, is not sticky to hands but sticks to a variety of substrates and cures at room conditions via moisture-dependent vulcanisation reactions into a durable rubber. Being a design-driven invention, Sugru has led to the invention of a new category of formulation on which the company now bases their technology platform.

Sugru is a 1-part composite of chemically modified silicone polymer, additives and fillers. The silicone polymer carries a condensation cure system which allows the formation of crosslinks in the material when exposed to atmospheric moisture. Additives are utilised to control properties such as cure speed and adhesion to different types of substrates. Cured Sugru demonstrates adhesive behaviour to a wide range of materials such as aluminium, steel, ceramics, wood, some categories of polymer and rubber, and notably glass. The fillers in the formulation control the uncured texture such as plasticity and tackiness as well as modulus, strength and toughness of the cured material. Extending fillers bring the consistency from the viscous polymer base to a putty-like dough, and the tackiness is controlled by detackifying additives. The optimisation of these components control the properties of the uncured and cured material, as well as cure speed. When Sugru cures it is water resistant, tough, flexible and stable within a temperature range of -50 to 180^{o}C.

It is Sugru's mechanical and physical properties, of both the cured and uncured material, which are key to its global success. The characteristics of this patented formulation bestow its award winning user experience and has led to 9 million packs sold since its launch in 2006. To understand how material properties relate to user experience, scientists at Sugru have worked on various test methods to link the two. Cured material demonstrates a Young's modulus of 5-6MPa, 200-300% strain to failure and a Shore A hardness of 70. The texture of uncured material is characterised through Williams plasticity and various rheological techniques. These methods and many more are utilised to understand and quantify formulation challenges such as shelf life, adhesion and cure kinetics. Developing new routes to characterisation of these types of formulations are key to their design and optimisation. Sugru is seen by many as a wonder material and it is through understanding how various formulation routes impact user experience that this product has gained its well-deserved following.

ORAL COMMUNICATIONS
OC 02

Particle Formulation by a Spheronization Process: Experiments and DEM Study

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Granules with a high sphericity and a narow size distribution which can be produced by a combined extrusion and spheronization process are highly interesting for pharmaceutical applications [1]. The rounding of the cylindrical extrudates in the spheronization process is influenced by a variety of overlapping formation mechanisms. An important factor affecting those mechanisms is the particle dynamics in the spheronizer, which consist of a rotating disk having a structured surface, so-called friction plate, and a steady cylindrical wall (Fig. 1).

In this contribution, the particle dynamics in the spheronizer was studied by simulation with the Discrete Element Method (DEM). The distributions of particle velocities and collision velocities were simulated and analyzed in representative poloidal cut planes (Fig. 1). Besides the particle kinematics and the mixing behavior, the collision characteristic was in the focus. Therefore, the time averaged distributions of the collision rate and collision forces were obtained for interparticle collisions and collisions with the wall and the friction plate.

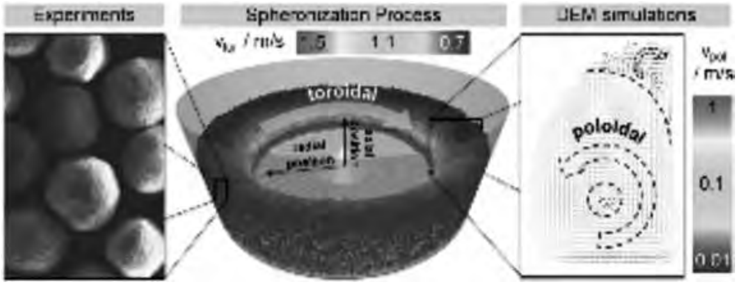

Figure 1: Spheronized MCC-lactose pellets (left), particle torus inside of the spheronizer colored by toroidal velocities (middle), simulated time averaged poloidal velocity field (right)

In addition to the DEM simulations of the process the spheronization experiments with extruded MCC-lactose pellets were performed. The deformation and breakage behaviour of produced wet pellets was studied by uniaxial compression tests. Based on the force-displacement curves the material parameters like stiffness, compressive strength, breakage probability and mass-related breakage energy distribution were derived. The energy dissipation was described by a coefficient of restitution which was obtained by cyclic compression and impact tests captured by high speed cameras. To predict the plastic deformation and breakage of pellets during spheronization the stress distribution in the spheronizer obtained by DEM was compared with mechanical behaviour of pellets measured by compression and impact experiments.

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Emulsifiers for MWF: balancing performance, labeling and economics.

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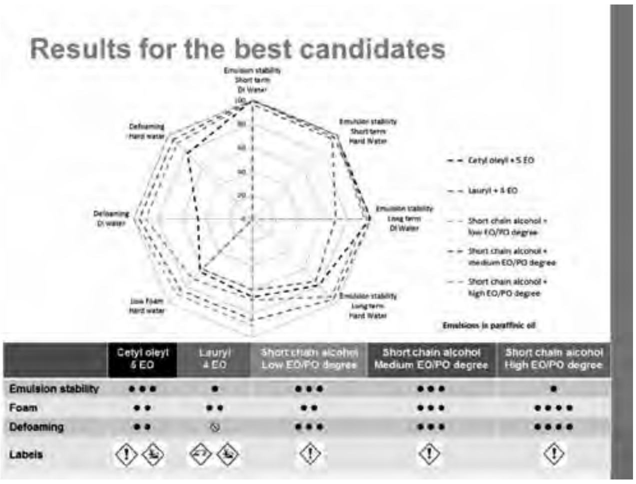
1 Introduction

Metalworking fluid formulators and emulsifier suppliers are facing numerous challenges with regard to performance demands, regulatory issues and commercial pressures.

Today's new generation of high-speed machine tools require much improved foam control. Additives and especially emulsifiers used for metalworking fluids for these newer machines must provide ultra-low foam and enhanced defoaming.

The worldwide strong regulatory context, with Globally Harmonized System (GHS) for substances and mixtures, but also specific local requirements like European Biocidal Product Regulation, triggers more stringent classification and labeling for some emulsifiers. Solvay wishes to develop emulsifiers with lower eco-toxicity milder labeling.


Results for the best candidates

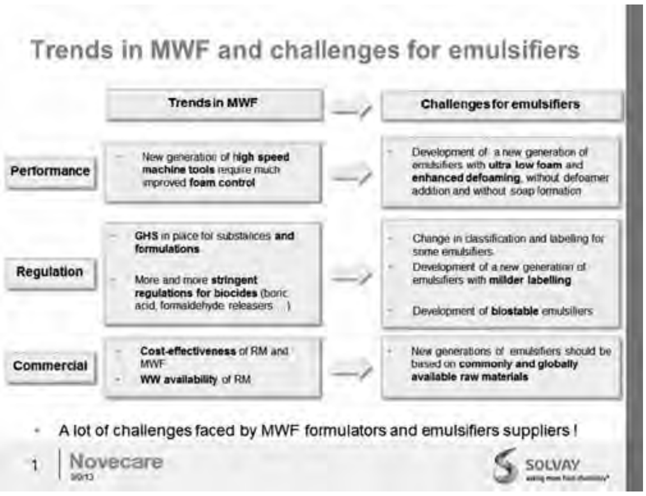
	Cetyl oleyl 5 EO	Lauryl 4 EO	Short chain alcohol Low EO/PO degree	Short chain alcohol Medium EO/PO degree	Short chain alcohol High EO/PO degree
Emulsion stability	●●●	●	●●●	●●●	●
Foam	●●	●●	●●	●●●	●●●●
Defoaming	●●	⊘	●●●	●●●	●●●●
Labels	⚠ 🐟	◇ 🐟	⚠	⚠	⚠

Thirdly, some raw materials are not available globally, and end users are demanding more cost-effective fluids. As a result, new generations of emulsifiers should be based on commonly and globally available raw materials, as well as economically efficient..

2. Summary

Solvay researchers took a number of steps to optimize the performance of alkoxylated fatty alcohol feedstocks. The first was propylene oxide insertion into alcohol ethoxylates. This provides similar performance to cetyl oleyl alcohol ethoxylates in terms of emulsion stability, and enhanced performance in terms of foam control and defoaming. The result is a new generation of emulsifiers with ultra-low foam and enhanced defoaming.

The next step was to optimize performance by fine-tuning the degree of ethoxylation and propylene oxide insertion to lower the eco-toxicity and avoid the dead fish label. The result is the development of new nonionic emulsifiers that optimize performance and economics, and allow milder labeling.


Trends in MWF and challenges for emulsifiers

	Trends in MWF	Challenges for emulsifiers
Performance	- New generation of **high speed machine tools** require much improved **foam control**	- Development of a new generation of emulsifiers with **ultra low foam** and **enhanced defoaming**, without defoamer addition and without soap formation
Regulation	- **GHS** in place for substances **and formulations** - More and more **stringent regulations for biocides** (boric acid, formaldehyde releasers …)	- Change in classification and labeling for some emulsifiers - Development of a new generation of emulsifiers with **milder labelling** - Development of **biostable** emulsifiers
Commercial	- **Cost-effectiveness** of RM and MWF - **WW availability** of RM	- New generations of emulsifiers should be based on **commonly and globally available raw materials**

- A lot of challenges faced by MWF formulators and emulsifiers suppliers !

Investigation of chemically modified inulin as encapsulation material for pharmaceutical substances by spray-drying

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The release of non-degradable polymeric particles into our environment has drawn the attention of the public. However, not only particles are damaging the ecological system, but also pharmaceuticals substances and their products of degradation can possibly harm our environment. Therefore, new methods of drug applications and formulations are needed to lower the required concentrations. Beside the continuous release of the drug, the particles should be degradable to prevent the described accumulations. [1]

Herein, we investigate the usage of carbohydrate based polymers from renewable resources as encapsulation material for the spray-drying technology. Inulin is used as a fructan from the chicory root, which already has several biomedical applications, e.g. drug-delivery for colon targeted substances and adjuvants for vaccines. [2] In order to adjust specific properties for the capsules, inulin is therefore chemically modified. In this work we investigate the influence of different functional groups on the release behavior of low molecular substances. The formulations are processed by spray-drying and analyzed via scanning electron microscopy and light scattering methods. The figure 1 below shows particles from native inulin and two derivatives, acetylated and propionylated inulin with encapsulated dexpanthenol. The particles showed a spherical structure with a size range from 0.7 µm to 5 µm. The release of dexpanthenol was determined in phosphate buffer solution by high performance liquid chromatography and discussed in respect to the chemical modification of inulin. Further studies on the release behavior of other substances (hydrophobic vs. hydrophilic and solid vs. liquid) regarding the chemical modification had been conducted.

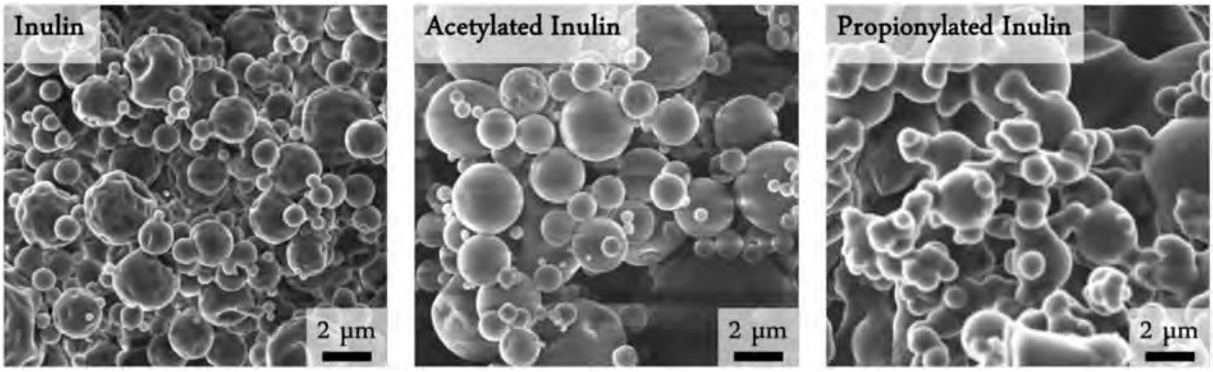

Figure 1: SEM images of spray-dried inulin and modified inulin particles containing 1 % dexpanthenol.

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The impact of depletion-attraction on the nucleation and growth of colloidal crystals

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We model the isotropic-to-crystal transition in systems containing hard rod-like particles and non-adsorbing polymer, which induces an effective attraction between the rods. According to the supersaturation and the polymer fugacity, we find nucleation and growth (NG) or spinodal decomposition (SD). In the NG regime, the crystals grow as single hexagonally-packed layers and the nucleation of other layers is hampered as the Gibbs free energy to form them is very high. In the SD regime, at low polymer fugacity, we observe independent clusters which at a given point coalesce to form a stable crystalline bulk phase, while at higher fugacity, smaller crystals coalesce to form long and thin filaments of crystalline layers with a non-uniform thickness. Eventually, these transient structures evolve into a thermodynamically stable bulk crystal phase.

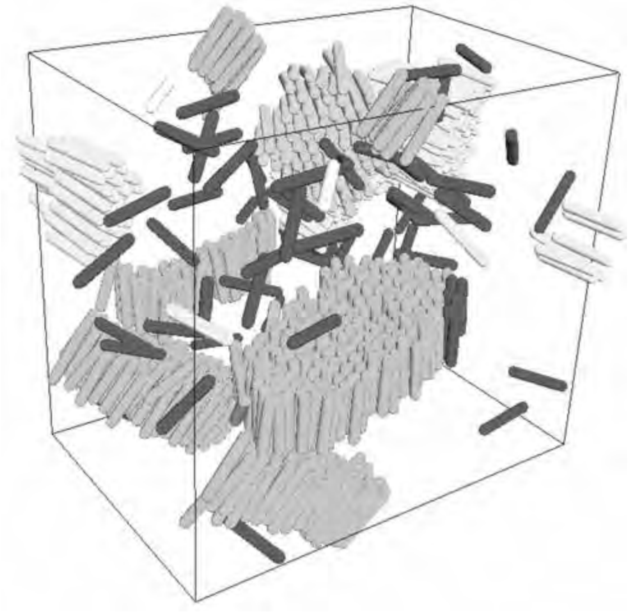

Fig. 1. Intermediate structures observed in the spinodal decomposition regime during the isotropic-to-crystal transformation.

OC 06

Development of pectin microparticles for chlorhexidine delivery: Physico-chemical studies and formulation

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Pectin is a natural anionic polysaccharide widely used as gelling or thickening agent in pharmaceutical field thanks to its biodegrability and biocompatibility. Pectin has the ability to form gel in the presence of divalent cations such as Ca^{2+}, Zn^{2+}, Mn^{2+}… This gelation results from a strong and specific ionic interaction between calcium divalent ions and galacturonate blocks and has been described by the well-known "egg box model" [1].

The aim of this study was the development of chlorhexidine (CX)-loaded pectinate mucoadhesive particles dedicated to the sustainable disinfecting of mouth sores or ulcers. Pectin-based drug delivery system was considered to promote buccal administration of the antiseptic substance CX. Indeed, due to the presence of saliva in association with swallowing and chewing, this type of drugs has a short retention time and thus a low therapeutic efficacy [2].

An emulsification/gelation method based on Ca^{2+}/pectin interactions and previously described by Pliscszak and al. [3] was thus envisaged. However, the first assays highlighted interactions between CX and the polymer leading to pectin gelation without the presence of Ca^{2+} dications. Hence, the aim of this study was to investigate the binding mechanism of CX with pectin through several physico-chemical studies performed in the dilute regime: relative viscosity, colloids size and potential zeta measurements, binding isotherm determined by ^{1}H NMR. The binding behaviour of Ca^{2+} and CX with pectin were investigated and compared. A similar binding process was observed for both divalent ions but a stronger binding was highlighted for CX due to additional intermolecular interactions. Several encapsulation assays were performed by prilling without presence of Ca^{2+} ions leading to the formation of pectin/CX beads characterized by satisfactory encapsulation efficiency and size distributions.

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Prediction of the equivalent alkane carbon number (EACN) of polar oils with cosmo-rs σ-moments : Application to the aqueous solubilisation of fragrances.

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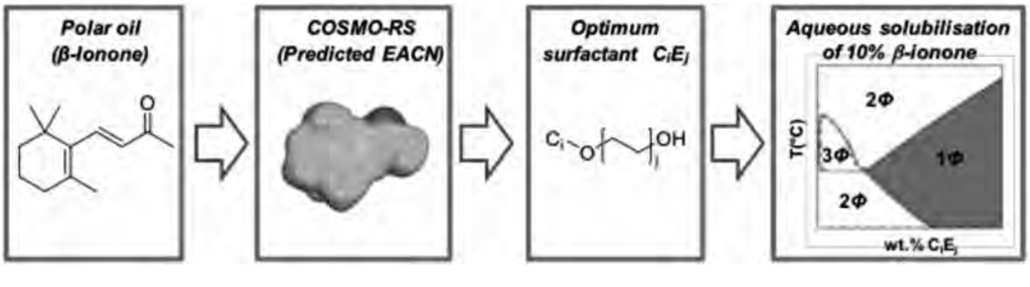
Aqueous surfactant solutions of polar oils such as fragrances are frequently found in end-use products such as liquid detergents, hard surface cleaners and shower gels. The solubilisation of these organic molecules in water requires the addition of appropriate amphiphiles, the efficiency of which depends strongly on the hydrophobicity of the oil. The **E**quivalent **A**lkane **C**arbon **N**umber (EACN) is a characteristic value expressing the hydrophobicity of an oil. It can be determined by comparing the"fish tail"temperature T* of Ethoxylated surfactant / Oil / Water systems where the oils are a homologous series of n-alkanes[1]. This unambiguous method for measuring the EACN has been applied to a large set of oils with various polarity.[2,3] However, this experimental approach is time consuming, especially when long tail surfactants are used since equilibration of the SOW systems might need days or weeks.

Recently a COSMO-RS model has been developed to predict the EACN value of a large set of hydrocarbon oils[3]. COSMO-RS is a theory, which combines quantum chemical calculations with statistical thermodynamics[4]. It is able to generate relevant physico-chemical descriptors of oils – the so-called sigma moments (M^i, i = [-2,…,6])-, which were then used in multilinear regression analysis to link the experimentally determined EACN values of oils to their molecular structures. Based on the surface area of the oil (M^0) and its overall polarity

(M^2), the model proved its relevancy in the prediction of the EACN values of alkenes, alkynes, terpenes or alkylbenzenes.

Within this work, the model is extended to polar oils, such as esters, ethers, ketones and nitriles etc. Thereby additionally to M^0 and M^2, a third relevant descriptor is identified, namely, the hydrogen bond acceptor capability (M^{-2}) of the oil. The latter descriptor is required for all compounds, which contain oxygen or nitrogen atoms, and thus a high local electron density due to their free electron pairs (red zone of the Van der Waals surface below).



The EACN value of a given oil is a key parameter to select the most effective surfactant able to dissolve the maximum amount of this oil with the minimum amount of surfactant. This approach is illustrated in the case of a typical polar oil used in perfumery, i.e. β-ionone. According to the EACN value of the oil predicted with the COSMO-RS model, an appropriate poly(ethylene) glycol monoalkylether (C^iE^j) has been chosen allowing the aqueous solubilisation of 10% of fragrance in water with only 10% of surfactant (blue zone of the phase diagram shown above).

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OC 08

Practical Implementation of HLD-NAC Theory

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In many industries we have to find the right surfactant for the job. We all know how hard this can be – so many surfactants to choose from and so little helpful information. A new approach has been proven to be much more useful in selecting the right surfactant(s) for (micro-) emulsions. It uses the theory, HLD-NAC, to make profound predictions about the type of emulsion (o/w, w/o) and how efficient the surfactant will be; $HLD = F(S)–k.EACN–\alpha(T\text{-}25) + Cc$ HLD-NAC takes into account the oil number (EACN), temperature, salinity (and co-solvent) based upon which a surfactant can be selected with the right parameter (Cc) to achieve the thermodynamic stable region (HLD = 0). From there, it is possible to develop your emulsion with the right basics, allowing for the most effective choice of surfactants.

A lot of cosmetic ingredients have HLD parameters, but can be difficult to determine. In addition, more and more bio based ingredients are coming into the market and it can be an extra challenge to measure their HLD parameters. This is especially the case for biobased surfactants as their structure is often complex, not so well defined and they usually have a co-solvent effect in addition to their surfactant role.

In this presentation, the determination of the parameters of bio based ingredients (1 oil and 2 surfactants) for personal care will be explained in a practical way. Based upon the parameter of the oil, the surfactants (combination) selection will be explained, and a proof of concept to prepare a micro-emulsion based upon HLD-NAC will be given.

Smart Alginate microfibers

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Biocompatible calcium-alginate microfibers are widely used in a variety of formats such as non-woven fiber pads and scaffolds, in pharmaceutical and biomedical applications like wound healing and tissue engineering [1]. The range of applications of alginate microfibers can be enhanced by encapsulating various aqueous as well as non-aqueous core materials in the fibers shell matrix, which are usually encapsulated in tubular and discrete segments respectively. The versatility of fibers with segmented non-aqueous encapsulates relies on their flexibility in tuning the oil-droplet geometry and location within fibers, which could be symmetric or asymmetric with respect to the fiber's central axis. In particular, fibers with asymmetrically-loaded encapsulates could provide a wide variety of surface morphologies, particularly in dried state. However, the current encapsulation techniques do not allow the asymmetric encapsulation of oil-droplets [2], whose encapsulate geometry is limited by the nature of the dispersed phase used, to be made. For example, a non-aqueous phase can only be loaded in discrete segments, while an aqueous phase is restricted to tubular encapsulation.

We introduce a unified and flexible microfluidic technique for fabrication of symmetric and asymmetric oil-loaded alginate microfibers with configurable encapsulate geometry. This technique was utilized to obtain a new class of smart responsive microfibers which can exhibit advanced functionalities like dehydration-triggered core-release at room temperature. The encapsulation geometry can be precisely tuned from continuous tubular to segmental geometries (Fig.1a). The impact of varying the encapsulate geometry was studied by comparing different fibers for their encapsulation volume, degree of waviness, and mechanical strength, all of which could strongly influence the selection criteria for specific applications. The fabrication technique could easily produce fibers with asymmetric encapsulates (Fig.1b-1e), which were exploited to obtain responsive fibers by tuning the fiber formulation and encapsulate geometry (Fig.1f). Additionally, the formulation of these fibers was tuned to obtain a hybrid fiber with reactive encapsulates, which could open the possibility to design fibers with self-repairing properties.

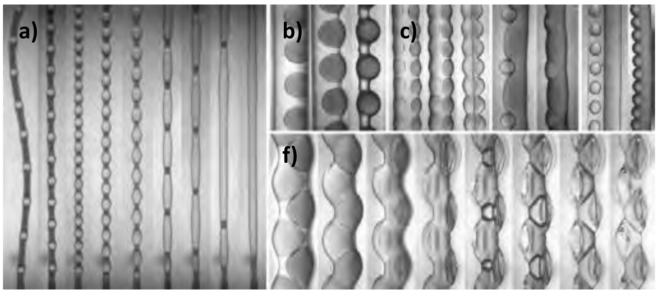

Fig.1. a) Oil-loaded alginate fibers with tunable encapsulate geometry. (b) – (e) A variety of fibers with asymmetric encapsulates are shown in hydrated and dehydrated state. f) Time-lapse images show a smart alginate fiber in action, where the contents from asymmetric encapsulates are released as the fiber dehydrates.

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How to relate lipstick sensory properties to its ingredients? The importance of understanding these relationships to formulate more efficiently

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Lipsticks have been used for thousands of years. From ancient Egypt to the first commercialized lipstick in 19th century France to nowadays, women have been wearing lipsticks made from crushed red rocks, beeswax and castoreum oil or synthetic materials. Every ingredient has its well-defined role in the lipstick formula and is related to specific sensory characteristics. But we never stop and try to understand how they are related. In this work, we decided to build on knowledge and understanding on the relationships between ingredients and sensory characteristics of lipsticks to formulate in an informed and sensory-driven way.

We built a design of experiments in which we varied 3 ingredients (two oils and a butter) for their supposed impact on key sensory attributes of lipsticks. To do this, we first created a simple but realistic formula which contains as few ingredients as possible. On this basis, we formulated 36 lipsticks and measured their sensory and physical characteristics. The sensory characteristics were measured by a trained jury of 17 women and the physical characteristics were measured using various techniques: DSC (Differential Scanning Calorimetery), pulsed-NMR (Nuclear Magnetic Resonance) as well as texturometery.

Multidimensional correlations between the percentages of ingredients, the sensory characteristics and texture measurements revealed that one of the oils (the fatty alcohol) has the strongest impact on the sensory and physical properties of the lipsticks while the butter-like ingredient has very limited impact. The higher the fatty alcohol content in the formula, the more slippery, melting, the oilier, softer and smoother the lipstick is and the less hard it is. DSC data uncovered an interaction that occurs between this specific oil and the wax used in the lipsticks. This interaction also affects the Solid Fat Content (SFC) of the lipsticks, as measured by the pulsed-NMR. These results lead us to hypothesize that the fatty alcohol acts as an inhibitor of the crystallization of the wax (and probably the butter) resulting in a change in its properties. This change creates a decrease of the wax hardness when the oil is present.

It seems reasonable to assume that this change in the wax properties is also responsible for some of the sensory properties mentioned above, such as the melting quality of lipsticks. While other characteristics, such as oiliness or softness, are probably related to the nature of this oil. Slipperiness seems to be associated with the viscosity of the mixtures of the two oils. Further experiments are underway to verify these interesting hypotheses.

With this understanding of the interaction between ingredients and its effect on the properties of lipsticks, we are not only able to associate ingredients with sensory characteristics but also to understand why these relationships exist. This should allow us to play with sensory characteristics and, for example, modify the slipperiness of the lipstick without changing its melting properties. This work opens opportunities for developing innovative textures in a more efficient way.

Emollients for cosmetic formulations: Towards relationships between chemicals, Physico-chemical properties, and sensory perceptions

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Emollient is a word usually used to describe a chemical compound in a formulation. In the cosmetic field, it refers more specifically to oils, and is associated with a sensory feel. As a definition, an emollient can be defined as a set of characteristics, felt or seen at a precise moment, that are directly linked to a sense of smoothness, elasticity and spreadability regarding skin feel, and to a sense of glossiness or matte degree for visual perception [1].

Emollients are widely used in cosmetic products because of their ability to form a homogeneous film onto the skin, which results in an improvement of water retention by the stratum corneum, and a skin softening sensation [2], [3].

Many emollients exist on the market and are generally characterized with sensory analysis. However, this type of characterization is time-consuming and requires an available and well-trained panel of assessors. In order to develop a fundamental knowledge base allowing the prediction of emolliency from physico-chemical properties and ideally chemical structures, we characterized a set of commercial emollients from various origins and compared them to each other by using multidimensional data analysis techniques.

For this purpose, thirteen emollients were selected, which include three fatty monoesters, three fatty diesters, one silicone, one fatty ether, three alkanes, and two mixtures of alkanes/fatty esters. Each compound was characterized with measurements of surface tension, viscosity, contact angle, density, percentage of weight loss after two hours, vapor pressure, spreadability, refractive index and boiling point at specific experimental conditions.

A sensory evaluation based on quantitative descriptive analysis was performed by two different panels: a professional one and an academic one specially trained for this study. The sensory attributes include: spontaneous spreading, spreading during application, penetration, and glossiness. The overall data are currently gathered and analyzed using multifactorial analysis and clustering techniques. Based on products mappings analysis, relationships between sensory and physico-chemical data will be established and the impact of chemicals (class/functional group) will be discussed. Further work and challenges will be the understanding of the complex interactions of multicomponents systems by studying the characteristics of emollients when included in model cosmetic systems. This should provide tools to ensure the formulation of cosmetic products based on scientific knowledge.

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OC 12

Synthesis and characterization of polyacrylamide / poly(acrylic acid) interpenetrating polymer network nanoparticles

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Hydrogels that respond to external stimuli such as changes in temperature, pH, electrical fields and osmotic pressure variations [1-6], are increasing scientific and industrial interest because their actual and future applications in controlled drug delivery, catalysis, as sensors and in chemical separation processes. In recent years, interpenetrating polymer networks (IPN) and semi-IPN have been developed because it is possible to obtain temperature- and pH-responsive hydrogels and nanogels by choosing adequately the polymers pair [7-9]. The synthesis by sequential inverse microemulsion polymerizations of interpenetrating polymer networks (IPN) of Polyacrylamide/Poly(acrylic acid) (PAM/PAA) nanogels as well as PAM/PAA random copolymers to compare their swelling behavior as a function of both temperature and pH, is reported here. Both types of nanogels were characterized by gravimetry to obtain conversion, by dynamic light scattering to determine particle size, by FTIR spectroscopy to confirm the IPN formation and by ζ-potential measurements. The equilibrium swelling behaviors of the IPN and random copolymer nanogels were studied by QLS as a function of temperature in the range of 25 to 50 °C and pH from 3 to 11. Results indicate that only the IPN nanogels exhibit a sharp swelling increase with temperature, associated to their Upper Critical Solution Temperature (UCST), driven by hydrogen bonding interactions, and with pH, driven by electrostatic repulsions of the carboxylic groups of PAA, especially at pH larger than the pK^a of the PAA. The size and morphology of the IPN nanogels, determined by field emission scanning electron microscopy, indicates that the IPN nanogels are spheroidal with swelling sizes similar to those determined by dynamic light scattering (DLS).

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Microgel particles in non-aqueous colloid – polymer mixtures

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Microgel particles are crosslinked polymer latex particles that can swell under suitable solvent conditions. The ability of such particles to change size in response to changes in solvency makes them of particular interest for smart materials. Nonetheless, the inherent softness of these cross linked particles is a common topic of contention. Microgel particles are often described as being compressible, penetrable or even as core shell particles, with a hard interior and a soft polymer-brush like shell. The particle softness depends on the cross link density and solvent quality of the system, however how soft the particles really are, and how this affects their ability to model hard spheres, is still unclear.

Poly(styrene) and divinylbenzene microgel particles have been synthesised and swollen in non-aqueous solvents, where the only known parameter to control the particle's swelling is the solvency. Binary mixtures of microgel plus non-adsorbing polymer have been compared to that of hard sphere particles plus non-adsorbing polymer, using differential interface contrast microscopy and rheology. Two types of colloidal hard spheres were used, both of which formed weak gels on the addition of a critical polymer concentration, however for the microgel particles a higher concentration of non-adsorbing polymer was required to induce aggregation and even then, clusters rather than space-filling gels were obtained.

Ternary mixtures of microgels, hard spheres and polymers produced gel like structures when the polymer exceeded a critical concentration. Replacing some of the hard spheres with microgel particles led to an increase in the polymer concentration needed to induce an elastic gel, giving evidence that the microgels are not quite acting as hard spheres and that there is some element of deformability within their structure. Both confocal microscopy and energy-dispersive X-ray spectroscopy show a homogeneous network of hard spheres and microgel particles, without evidence for segregation of the two types of particle.

OC 14

Wetting and bio-fouling of porous coatings Impregnated with oil

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Inspiration and guidance for achieving control over wetting of solids have been drawn from natural organisms. Extreme water repellency of the lotus leaf and the mechanism behind it is well studied and used for the fabrication of self-cleaning surfaces [1]. Recently, the slippery mechanism of the rim of Nepenthes pitcher plant was revealed and mimicked in the so called Slippery Liquid-Infused Porous Surfaces (SLIPS) [2].

Here, we have fabricated nano-porous coatings using commercially available hydrophobic fumed silica. The coatings have been impregnated with different amounts of a non-volatile oil and their wetting properties investigated. The adhesion of algae cells to those coatings have also been studied. We demonstrate that this approach allows us to gradually tune the wetting behaviour of coatings from a superhydrophobic state in the absence of oil, through various intermediate (sticky) wetting states, to slippery surfaces at high loading of oil. Superhydrophobic and slippery surfaces produced were found to possess low retention of water drops and good anti-biofouling characteristics towards algae cells. Adhesion of both water drops and algae cells were found to follow similar trends thus indicating that adequate control over water adhesion may serve as a useful step to prevent the adhesion of cells and other micro-organisms to solid surfaces in aquatic environment.

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Formulation of stimuli-responsive emulsions using citrus pectin as a natural hydrocolloid emulsifier

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Citrus pectin is a polysaccharide that was shown to have great potential as an emulsifier and emulsion stabilizer in emulsions that should have a "clean label", i.e. be all natural in ingredients. Its molecular structure is characterized by the presence of carboxyl groups which can be methylesterified to a certain degree (degree of esterification DE). The DE was found to significantly influence the colloidal and emulsifying properties of citrus pectin[1,2]. In solution, the non-esterified carboxyl groups of citrus pectin dissociate leaving a negative charge on the molecule. As a result, citrus pectin is sensitive to the presence of monovalent ions which might influence its applicability as a natural emulsifier.

We will show that particularly the emulsifying behavior of low DE citrus pectin (pectin with a higher number of carboxyl groups) can be influenced by monovalent ions. At high ionic strength, citrus pectin forms microgel particles which exhibit excellent emulsifying properties. Furthermore, citrus pectin stabilized emulsions are sensitive to variations of the ionic strength which allows for the triggered release of oil soluble bioactives upon ion addition. Coalescence of oil droplets could be visualized which eventually led to a complete demulsification of these emulsions. This stimulus responsive behavior is of great importance for the use of pectin in emulsions that undergo changes in ionic strength during the production process. Suitable product ranges include pharmaceutical, cosmetic or food applications.

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OC 16

Cosmetic Formulation Promoting Skin Permeation Based on Novel Bicontinuous Alpha-Gel Structure with Amphiphilic Tranexamic Acid Derivative.

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A promising cosmetic formulation to promote skin permeation has been developed using a novel alpha-gel containing amphiphilic tranexamic acid derivative. Tranexamic acid cetyl ester HCl (TXC) is known as an active ingredient which inhibits skin pigmentation. On the other hand, as the consequence of the strong inter-molecular interaction of TXC, its beta or gamma crystal can be formed in aqueous media, which should be unsuitable for various cosmetic formulations from the point of view of quality assurance. Therefore, we focused on the alpha-gel phase although common alpha-gels are generally not in equilibrium, and found out to form a unique and long stable bicontinuous alpha-gel (BAG) phase in TXC-water-oil-cetyl alcohol-batyl alcohol quaternary system. This BAG structure could disturb crystallinity of TXC and help oil droplet to be dispersed, that is, the stable oil in BAG (O/BAG) emulsion is formed regardless of the size and size-distribution of the dispersed oil droplet. It is pronounced that this O/BAG emulsion can provide extremely higher skin permeation efficacy of TXC than conventional O/W emulsion at the identical composition (Fig.1). In addition, O/BAG emulsion could provide the characteristic texture. These can be due to not only the lower crystallinity of TXC but also the phase transition from alpha-gel to liquid crystalline state at the skin surface temperature, ca. 32 °C. Our presentation will demonstrate formulation of the thermo-responsive O/BAG emulsion consisting of TXC and its unique functions acceptable for the industrial applications..

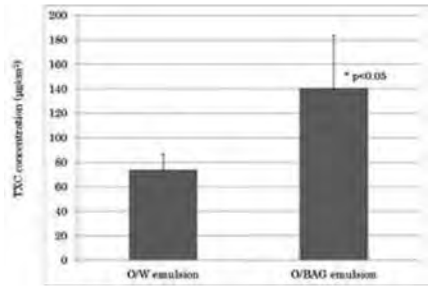

Fig. 1 TXC concentration in the dermis 48 hours after application of O/BAG or O/W emulsion at the identical composition

Formulation of niosomes and bicelles by nonionic double-tailed surfactants

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Nonionic vesicles, which are called niosomes or NSVs, have been the focus of attention as an alternative to phospholipid liposomes as drug carriers since niosomes have several advantages such as relatively lower cost, high purity, better chemical stability, possibilities of surface modification [1]. Apart from vesicles, smaller-sized bilayer particles are known as bicelles or bilayer disks. Because of smaller size of bicelles than vesicles, bicelles show greater transdermal drug delivery efficiency [2]. In this study, niosomes and bicelles were prepared based on the phase behavior of aqueous systems with the novel double-tailed nonionic amphiphiles, polyglyceryl dialkyl ethers [3].

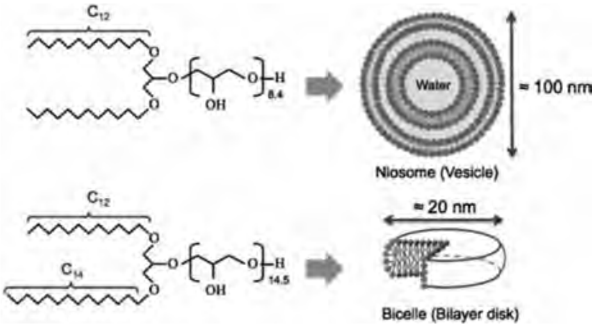

Figure 1 : Niosome and bicele formulation depending on the chain-length assymmetry of double tails of PDEs

The molecular structure of the polyglyceryl dialkyl ethers (PDEs) is the single head–double tail type (Fig. 1). We have prepared composition-temperature phase diagrams with several different PDEs having different polymerization degree in the polyglyceryl unit and different hydrophobic chain length. Most of the systems showed the lamellar phase throughout almost whole composition and temperature ranges, which is the similar phase behavior of aqueous systems of double-tailed amphiphiles such as phospholipids or dialkyl quarternary ammonium salts. In the dilute region of the system with the PDE with which two dodecyl chains, two phase equilibrium of the lamellar and excess water phases was observed. Niosomes were formulated in the dilute region by agitation such as vortex mixing or ultrasonication without preparing thin film beforehand. The niosome size was highly dependent on agitation power. By ultrasonication, small-sized niosomes (approx. 100 nm) were obtained. On the other hand, the bicelles was formulated in the system with the PDE with which dodecyl and tetradecyl chains, although the phase behavior was basically similar to the system with PDE having uniform alkyl chain length. Bicelle size as shown in Fig.1 was measured by TEM.

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Synthesis of polyurea nanocapsules by interfacial step polymerization using cosurfactant-free microemulsions as templates

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Since their discovery in 1943 by Hoar and Schulman, microemulsions have been much in the focus of interest by scientists in the field of colloid and polymer science. As thermodynamically stable systems consisting of water, oil, surfactant and sometimes a costabilizer, microemulsions form spontaneously without any energy input. Beside the simplicity of manufacture, microemulsion systems offer advantages like improved solubilization of hydrophobic drugs and large are-to-volume ratio for mass transfer. Despite numerous papers published annually to describe microemulsion-templated polymeric nanoparticle/nanocapsules synthesis, interfacial step polymerization has never been reported yet as being performed in microemulsion. In that context, we report here cosurfactant-free microemulsions as templates for the synthesis of polyurea nanocapsules. The ternary diagram of cyclohexane, water, and Triton X100 (TX-100) as non-ionic surfactant, was established to investigate the field of compositions inducing the formation of stable O/W microemulsions. Then the interfacial hydrolysis-addition of the isophorone diisocyanate (IPDI), a cyclic-aliphatic diisocyanate undergoing slow hydrolysis in water, added to the microemulsion, led to the formation of nanocapsules with a polyurea wall. The nanocapsules were analyzed by Dynamic Light Scattering and examined by Transmission Electron Microscopy. The size of the nanocapsules, comprise between 10 and 40 nm, appeared controlled by the amount of surfactant as well as the oil phase, but independent of IPDI concentration in the studied range. The chemical composition of the nanocapsules membrane was investigated by FTIR and MALDI-TOF mass spectrometry, whereas the kinetics of consumption of isocyanate groups during the polymerization reaction was followed by 13C NMR.

In conclusion, we demonstrated that interfacial step polymerisation of IPDI monomer in a cyclohexane/water and TX-100 cosurfactant-free microemulsion led to the formation of well-defined polyurea nanocapsules whose diameter, comprise between 10 and 40 nm, can be targeted by the amount of surfactant as well as cyclohexane.

Formulation of artificial finger print

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1. Introduction

Ubiquitous terminal such as smartphone is convenient to use outside, but also has a problem that their displays and bodies are contaminated with fingerprints during operation and carry. This issue gives users hard to see the screen and uncomfortable. And so, we are developing easy-removable finger print coating materials. In the development, we need to evaluate those in quantitative way. Whereas, in conventional evaluation method, they use human fingerprints as a measure, but this way doesn't work because human fingerprints' components change depending on age, sex, season, diet, and so on. We report here the formulation of artificial finger print which shows the similar adhesive property and wiping property to human finger print.

2. Experiment

(1) Mixture of oleic acid and other various oils are stirred at room temperature.
(2) Determine the viscosity and the angle to glasses of the prepared solution.
(3) The prepared solution was screen printed on glass, to create an artificial finger print.
(4) Wipe the artificial fingerprint by the automatic waiping device, and count the number of times wiped off.

3. Results and Discussion

We have found the formulation of the solution which shows the similar adhesive property and wiping property to human finger print when oleic acid (OA) was mixed with di-pentaerythrithyl tri-polyhydroxystearate (DP) and di-isostearylmalate (DM) (see figure). To print the artificial finger print solution, high viscosity and high angle of contact to glasses are needed. When DT is added to OA, the viscosity of solution was decreased considerably. And we demonstrated this phenomenon is caused by the formation of hydrogen bond between the carbonyl group of OA and the hydroxy group of DP. On the other hand, DM has an effect to decrease the angle of contact to glasses of DM-OA solution, thogh the viscosity of the solution was almost kept (see table).

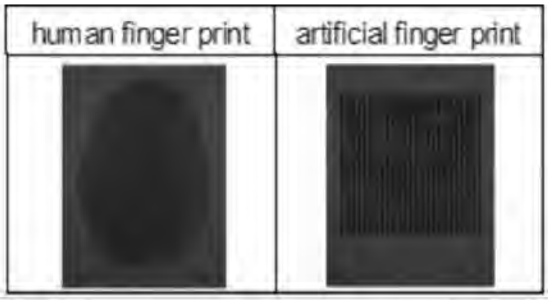
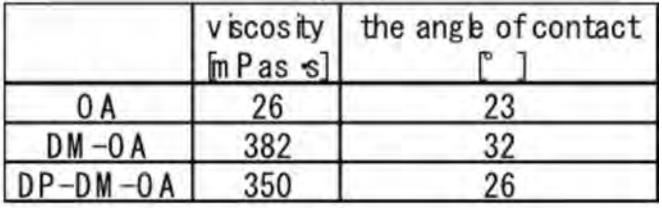


Table.

Figure.



	viscosity [mPas·s]	the angle of contact [°]
OA	26	23
DM-OA	382	32
DP-DM-OA	350	26

OC 20

Oligomeric alkylglycoside surfactants – new power-tools in the formulation toolbox

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Alkylglycoside surfactants have a number of beneficial characteristics, including excellent biocompatibility and high physical and chemical stability. They are therefore important ingredients in manifold formulated products, ranging from cosmetics to industrial detergents. Alkylglycosides used in commercial formulations are normally referred to as "alkylpolyglucosides", or "APGs" for short. However, this term is a misnomer in the sense that the hydrophilic head-groups in these surfactants are by no means polymeric. Rather, APGs consist of a mixture of species, in which the head-groups comprise merely one to three repeating hexose units. This constraint severely inhibits the full exploitation of alkylglycoside functionality, and many attempts to increase the head-group size have therefore been performed over the years. However, synthesis of alkylglycosides with longer head-groups by conventional means has proved prohibitively difficult, for reasons of physical incompatibility of the starting materials (glucose and fatty alcohols).

In collaboration with scientists at Lund University, Enza Biotech AB has recently developed enzymatic methods that allow for synthesis of alkylglycosides with longer (oligomeric) head-groups, thus circumventing the limitations of conventional synthesis. These surfactants are referred to using the trade name OLMAG™. The methods applied in the production of the OLMAG™ range of surfactants are readily scalable and possible to apply using renewable starting materials. So far, Enza Biotech has successfully synthesised alkylglycosides comprising head-groups with degrees of polymerisation ranging from 4 to 20, and with alkyl chain lengths from C12 to C18.

The present talk will describe the principles of the enzymatic synthesis of oligomeric alkylglycosides, as well as the aqueous self-aggregation and adsorption properties of OLMAG™ alkylglycosides with long alkyl chains (≥C16). Self-aggregation has been studied by dynamic light scattering and neutron diffraction, whereas the adsorption properties at hydrophobic model surfaces were studied by means of ellipsometry. The implications of the self-aggregation and adsorption of OLMAG™ surfactants on their use as wetting agents, dispersants and emulsifiers will be discussed.

Stabilization of high molecular weight silicone emulsions

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High molecular weight silicones are useful in several application fields, such as coatings, lubricants, textile and leather treatment or personal care.[1] In addition to the usual benefits of silicones (lubrication, hydrophobicity, touch), the high molecular weights offer the further advantage of substantivity, therefore durability.

The main problem associated with the incorporation of high molecular weight silicones into formulations lies in the difficulty to emulsify properly such viscous polymers. Specific emulsifying systems must be designed [2] and yet, average particle size will always be higher than with standard silicones, i.e. the emulsion will be more subject to destabilization.

We will discuss cases of high molecular weight silicone emulsification, and the stability issues encountered – how potential instabilities can be detected and how to avoid them. We will also illustrate the benefit of using such silicone emulsions in various applications.

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ORAL COMMUNICATIONS

OC 22

Comparative emulsifying properties of OSA-modified starch: granular form vs dissolved state

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BACKGROUND: The feasibility of using OSA-modified starch isolated from Quinoa in the dissolved state as sole emulsifier was investigated. The emulsifying ability of OSA-modified and native starch in the granular form, in the dissolved state and a combination of both was compared. This study aims to understand mixed systems of particles and dissolved starch with respect to what species dominates at the interface and how stability is affected by addition of one of the species to already formed emulsions.

RESULTS: It was possible to create emulsions with OSA-modified starch isolated from Quinoa as sole emulsifier. Similar droplet sizes were obtained with emulsions prepared at 7% (w/w) oil content using OSA-modified starch in the granular form or molecularly dissolved but large differences were observed regarding stability. Pickering emulsions kept their droplet size constant remaining stable against destabilization phenomena, while emulsions formulated with OSA-modified starch dissolved exhibited clear coalescence. All emulsions stabilized combining OSA-modified starch in granular form and in solution showed larger mean droplet sizes with no significant differences with respect to the order of addition. These emulsions were unstable due to coalescence regarding presence of free oil. Similar results were obtained when emulsions were prepared by combining OSA-modified granules with native starch in solution.

CONCLUSIONS: The surface coverage of starch granules was lower in presence of dissolved molecular starch what indicates that dissolved is more surface active than in the granular form. However, dissolved molecular starch led to unstable systems compared to Pickering emulsions which demonstrated to be extremely stable.

Photonic materials prepared THROUGH the entrapment of quantum dots into silica

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Silica is appropriate as a matrix for developing photonic materials because of its optical transparency and mechanical strength. Here it was used to entrap quantum dots. They were synthesized in aqueous solutions by exchange reactions to have CdS and ZnS and hydrothermal treatment in a case of carbon. Quantum dots of semiconductors needed the presence of mercaptosuccinic acid, glutathione or cysteine serving as stabilizing ligands. Carbon quantum dots were prepared without the stabilization because of functional groups on their surface. They all demonstrated bright luminescence. It was independent on the excitation wavelength for semiconductor quantum dots, whereas its change influenced the color of carbon samples.

The entrapment of quantum dots in silica matrix was made by the sol-gel technique. Syntheses were carried out in their aqueous solutions by adding a precursor. Completely compatible tetrakis(2-hydroxyethyl)orthosilica with ethylene glycol residues was used. Its advantage was in unrestricted water solubility and hydrolysis/condensation in neutral solutions. Therefore, processes were performed without the addition of an organic solvent and acid or alkali at ambient conditions that could influence the stability of quantum dots. Silica thus synthesized was optically transparent with bright luminescent.

It was found that the optical properties of hybrid materials changed under the laser lightening at $\lambda = 405$ nm. It concerned the optical absorbance coefficient and refractive index. Furthermore, red-shifting about 50 nm was observed for the emission maxima. When the lightening was ceased, the initial optical state was restored that evidenced of reversible nature of photonic effects.

Wide and small-angle X-ray scattering applied to study the influence of laser irradiation on the silica hybrids revealed structural changes in quantum dots. There was reversible restructuring of their crystalline lattice. A possible mechanism was suggested.

ORAL COMMUNICATIONS

OC 24

Magnetic solid foams from highly concentrated emulsion

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There is a growing interest on untralight (low density) solid composites that deliver required performance and show a minimalist use of materials while integrating multiple functionalities. The clasical approach to reduce density is to generate a porous matrix in which different embedded materials can be incorporated. Highly concentrated emulsions, also referred as high internal phase ratio emulsions (HIPEs) are emulsions in which the volume fraction of the disperse phase surpass that of the thickest regular packing of spherical droplets (i.e. 0.74). HIPEs are versatile systems that can serve as templates for macroporous solids or so-called solid foams; by judicious formulation of HIPEs, control over final total pore volume and pore size can be achieved.

Herein, we present a series of results on magnetic macroporous materials produced by incorporating magnetic nanoparticles into the continuous phase of water-in-oil (W/O) HIPEs. The nanoparticles are coated by an hydrophobic layer that facilitates their dispersion in a monomer continuous phase. After polymerization of monomers, a magnetic solid foam with low density is obtained. It is found that depending on the nature of the surface coating, nanoparticles either stay inside the pore walls or at the pore surface, which can be of interest for particular applications. The use of surfactants is not mandatory to produce stable foams: HIPEs can be also stabilized solely by the magnetic nanoparticles. The level of interconnection of pores can be modulated by the surfactant/nanoparticle ratio. Moreover, by changing the type of monomers and crosslinkers, rigid or flexible as well hydrophobic or hydrophilic materials can be obtained. Magnetic and mechanical properties of the obtained macroporous solids for targeted applications are discussed.

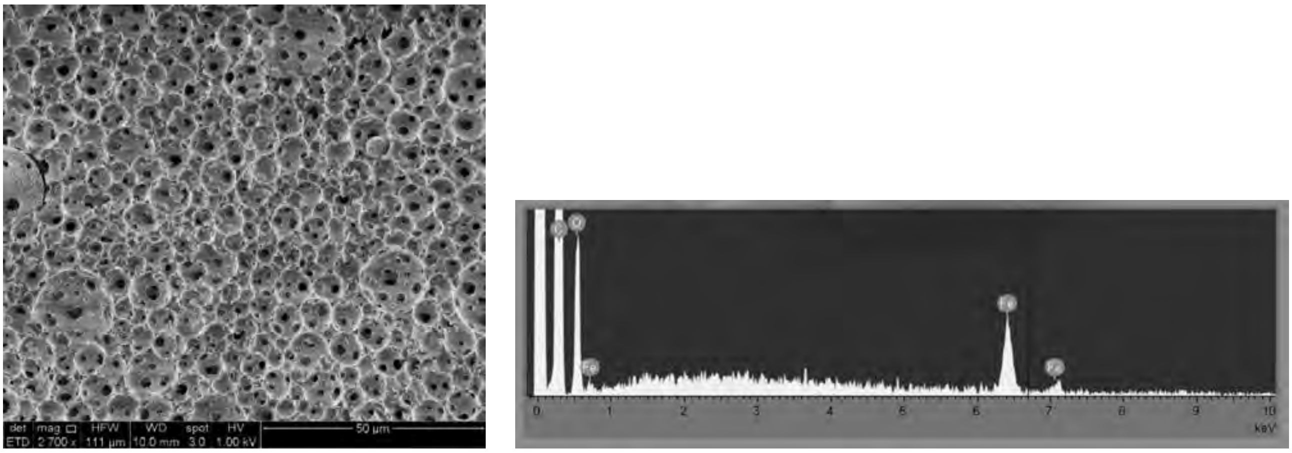

Figure 1: Scanning Electron Microscopy (SEM) image of a magnetic solid foam (left) and corresponding Energy-dispersive X-ray spectroscopy (EDS) analysis (right), confirming the presence of iron oxide in the composite.

Micro-mesostructured silica from ionic/nonionic surfactants mixture

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Recently, there has been a rapid growth in emerging research areas, such as nanotechnology, photonics and bioengineering [1]. However, these applications require materials with porosity at multiple length scales. For example a hierarchical combination of pores reduces transport limitations in catalysis [2]. One strategy to prepare dual mesoporous materials consists in using mixtures of templates [3-5]. Herein, micro-mesostructured silica materials have been prepared through both the cooperative self-assembly and liquid crystal templating mechanisms by using mixtures of polyoxyethylene fluoroalkylether [$C_8F_{17}C_2H_4(OC_2H_4)_9O$, labeled as $R^F_8(EO)_9$] and cationic quaternary ammonium [CTABr] surfactants as building blocks. The investigation of the $R^F_8(EO)_9$/CTABr/water phase diagram (Fig. 1A) shows that a micellar phase (L1) is formed. The SAXS diffusion spectra of the two surfactants micellar phases are different from that of micelles constituted of one component (Fig. 1B). This provides informations about the nature of the micelles, which are really mixed. A detailed investigation of the $R^F_8(EO)_9$/CTABr/water liquid crystals domain was also conducted, and results indicate the presence of a hexagonal mixed phase.

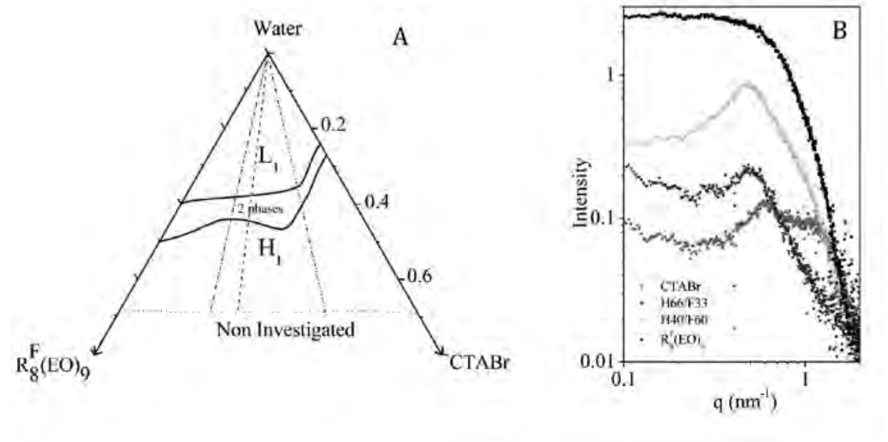

Figure 1 : $R^F_8(EO)_9$/CTABr/water phase diagram (A) and SAXS patterns of $R^F_8(EO)_9$/CTABr mixed micellar solutions (B)

Then, micro-mesoporous silica materials have been synthesized, using the surfactants mixture, and characterized by small angle X-ray scattering transmission electron microscopy and nitrogen adsorption-desorption analysis. The SAXS patterns show two hexagonal porous networks, showing the presence of the dual porosity.

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OC 26

Formulating polymeric superhydrophobic coatings based on functionalized sio$_2$ nanocomposites

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Functionalized SiO_2 nanoparticles (NPs) are highly versatile systems, which can be used for the development of tailor-made smart coatings. For example, proper functionalization and structuring of the NPs coatings may result in efficient self-cleaning films, resembling the lotus effect [1]. However, for exterior applications in which the system is exposed to the environment, such as in solar panels, excellent mechanical properties are also a requirement. This could be achieved by integrating such functionalized NPs into polymeric nanocomposites. In this investigation, SiO_2 NPs were synthesized by sol-gel method. Synthesis of spherical SiO_2 NPs of about 100 nm was followed by in-situ functionalization with various organosilane and fluorosilane molecules. The functionalized SiO_2 NPs were characterized by FTIR, XPS, AFM, and SEM; in particular, XPS and FTIR were consistent with successful functionalization. Dispersions of the functionalized SiO_2 NPs were used for the preparation of poly(acrylic acid) and polyurethane composite films by spin coating technique. Water contact angles up to 140º were obtained (Figure 1); water-droplet rolling up was achieved with composites based on SiO_2 NPs functionalized with PFOS (perfluorooctyl(trimethoxy)silane), in resemblance to the lotus effect. The optical and mechanical properties of the films were also evaluated. Finally, some aspects of the methodology for nanocomposite formulation were taken to higher scale by using a pilot-plant ultrasound probe. The obtained results demonstrate that this facile approach has a good potential for the development of self-cleaning smart coatings for exterior applications.

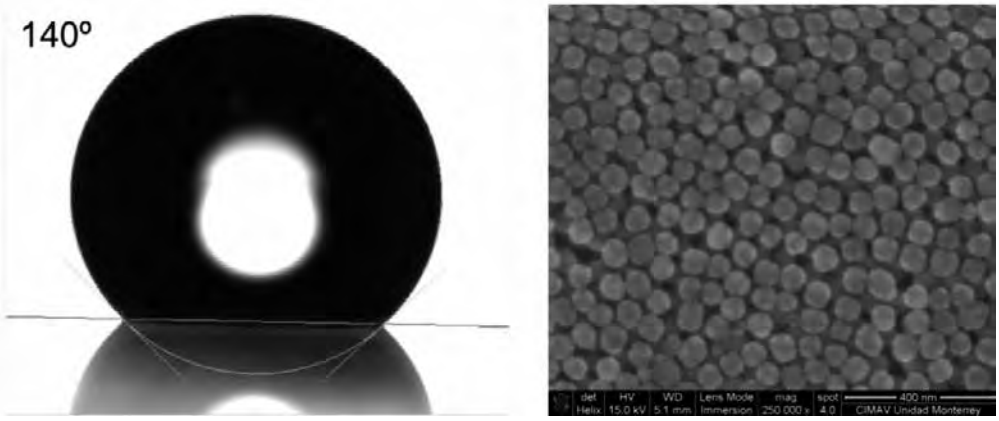

Figure 1. Water contact angle and SEM image of functionalized SiO_2 polymeric nanocomposite.

Acknowledgements: We are grateful to CONACYT-SENER, Fondo Sectorial de Sustentabilidad Energética (CEMIESOL P21).

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Formulation of emulsions stabilized with biodegradable plga nanoparticles for pharmaceutical and cosmetic applications

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The main objective of this study is to formulate, for therapeutic or cosmetic purposes, an emulsion stabilized by biodegradable and biocompatible nanoparticles. Indeed, our nanoparticles of poly (lactic-Co-glycolic) acid (PLGA) allow us to formulate long-term stable, biodegradable and biocompatible emulsions with the advantage of being potentially less toxic and irritant compared to emulsions stabilized with synthetic surfactants. Furthermore, it would be possible to co-encapsulated two active ingredients in the same formulation: a first one in the nanoparticles and a second one in the oil droplets. Co-encapsulation leads to an improvement of the observance of the patient and can lead to a synergistic effect between the two active pharmaceutical ingredients.

To clarify the mechanisms and the kinetics of stabilization with nanoparticles, a thorough physical chemistry study is performed. The interface between the oil and the aqueous phase is characterized using interfacial rheological measurements (drop tensiometer), using interfacial and surface tensions measurements (Wilhelmy blade, drop tensiometer) and also using nanoparticles adsorption measurements (balance of Langmuir), three-phase contact angle measurements (FreSca Cryo-SEM) or using imaging (confocal microscopy, freeze-fracture). A stability study of the emulsions is also performed (Bottle test, Turbiscan, laser particle-measurement instrument, optical microscopy) as well as a study of the contribution of the polymers stabilizing the nanoparticles on the emulsion stability.

A second part of the study consists in illustrating the feasibility of the co-encapsulation. For this end, we encapsulate cyclosporine in PLGA nanoparticles and calcitriol in the oil droplets (quantification with radiolabeled markers). Then we will determine the kinetics of release of the active ingredients from the emulsion (Franz cells, radiolabeling). We will also determine the cutaneous penetration of the nanoparticles of PLGA and the two active ingredients.

These Pickering emulsions using PLGA nanoparticles are very promising systems for the formulation of stable and bi-compartmentalized emulsions. This is why an application in dermatology is aimed for the treatment of skin diseases such as psoriasis or eczema, in collaboration with Dr. Laurence Michel of the UMR-S-976 "Immunology, dermatoly and oncology" (University Paris Diderot – Inserm) specialized on the dermatology.

OC 28

Development of a novel generation of softeners with fragances encapsulated in quatsomes/particles

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Nowadays fragrances are used in numerous applications, including personal care products (e.g., hair sprays, shampoos), home care products (e.g., fabric conditioners, fabric softeners, liquid laundry detergents), and food products. These fragrances are added to the products in order to enhance the consumer's enjoyment of the product. Thus more companies make efforts to improve the effectiveness of the fragrance materials for the final users, extending their life and improving their delivery in a control manner. In the case of detergent and fabric softeners industries, microencapsulation technology widely used by food and pharmaceuticals companies has been adapted by these industries to increase the persistence of fragrances on textiles.

Currently, different materials are used for fragrance encapsulation where polymers prepared from melamine–formaldehyde or urea–formaldehyde, and other aminoplastics are preferred. However, formaldehyde is a toxic chemical and probably should not be used in textiles that come in close contact with the body. Also the size of microcapsules prepared with polymers is often too large for textile applications, where particles with size below 20 μm are more easily incorporated into textiles during the final washing step [1]. Therefore materials used for encapsulation intended for wearable textiles should be nontoxic, biocompatible, biodegradable, low in cost, and should have the require size to be incorporated on textiles.

Here, we present a simple and easy to scale up one-step methodology to nanoformulate fragrances in small unilamellar vesicles (Quatsomes) using compressed fluids (CFs). The special characteristics of CFs between those of liquids and gases permit the straightforward production of materials with high structural homogeneity, which is very important for optimum performance of functional materials. In that context we have been using CO_2-expanded solvents for the preparation of molecular materials with controlled supra, nano and micro structure [2]. The resulting quatsomes were very stable, homogeneous and structurally well defined (Figure 1). This process can be easily transferred to large-scale operation with a high batch-to-batch consistency.

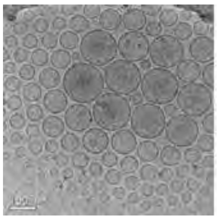

Figure 1. Cryo-TEM image of Quatsomes using compressed fluids (CO_2).

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Formation of functional pharmaceutical nanoparticles using membrane dispersion cell combined with solvent displacement method

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The purpose of this study was to develop a new solvent-displacement (nanoprecipitation) method [1] based on a micro-engineered membrane (10, 20 and 40 µm) with a regular array of uniform pores (spacing of 200 µm) to tailor the size of biodegradable and bioresorbable drug-loaded polymeric nanoparticles (NPs). Polycaprolactone (PCL) and acetone (Ace) were chosen in this study, where both have been proved by Food and Drug Administration (FDA) [2]. A natural macrocyclic lactone, rapamycin (RAPA) which is also known as a potent immunosuppressive agent [3] was used in the encapsulation experiment and drug release study. Nanoparticles were produced instantaneously by fast solvent switching once the organic phase was injected through the membrane pores into a stirred aqueous phase. The organic phase was made up of 0.3–0.6 %(w/w) PCL in Ace and the aqueous phase was consisted of 1 %(w/w) polyvinylalcohol (PVA) dissolved in Milli-Q water. The parameters that have been varied in the experiments were: (i) organic phase injection rate (2-5 ml/min), (ii) agitation speed of the stirrer (200-1300 rpm) and (iii) final volume ratio, V_{aq}/V_{or} (1.5–10.0). The experimental set-up is depicted in Fig. 1. The physical characterisations of formulated nanoparticles were determined by XRD, DSC and ATR-FTIR spectroscopy.

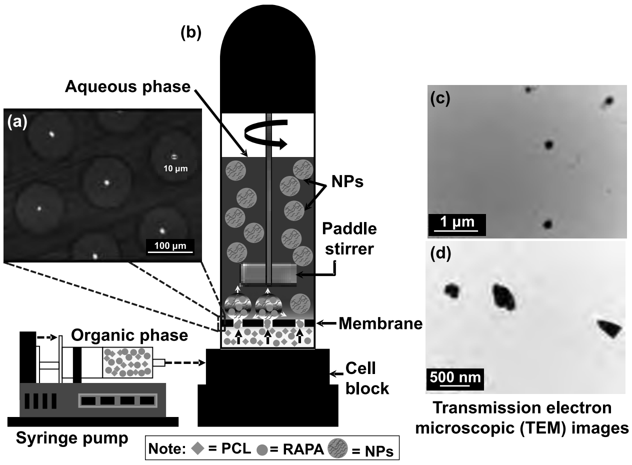

Figure 1 – (a) A photomicrograph of 10 µm nickel micro-engineered membrane. (b) Schematic diagram of the experimental setup used in this work. (c) TEM image of RAPA-PCL encapsulated nanoparticles. (d) TEM image of RAPA-without PCL NPs host.

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OC 30

Encapsulation of ferrous sulphate in niosomes for yogurt fortification

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Iron deficiency, with or without iron-deficiency anemia, affects all populations of the world irrespective of race, culture, or ethnic background. Iron deficiency can result from inadequate iron intake, decreased iron absorption, increased iron demand, and increased iron loss. Children, teenagers, and women of childbearing age are especially prone to develop iron-deficiency anemia.

Iron-enriched functional foods could play an important role in the prevention of iron deficiency, when the contribution of dietary iron is insufficient, especially at high-risk groups.

It has been proved that encapsulation of iron helps to reduce organoleptic problems of iron-fortified foods, to protect iron from oxidation caused by external agents enhancing its bioavailability and intestinal absorption, and to control its consequent delivery.

The aim of this work was to formulate and produce niosomes containing ferrous sulphate, citric acid and ascorbic acid, which were able to be incorporated into a fortified yogurt without compromising its taste, appearance, and stability.

Several formulations were tested to prepare iron-entrapped niosomes with high stability and encapsulation efficiency. A modified ethanol injection method was selected as niosomes preparation method. The effect of operating parameters on mean size and polydispersity of niosomes was evaluated.

The best formulations were selected for subsequent preparation of iron-fortified yogurts. The textural properties of these yogurts were analysed and compared to a regular yogurt prepared as control.

Results demonstrated that these iron-entrapped niosomes are suitable fortificants for these dairy products.

New sophorolipids – naturally derived high performing biosurfactants

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REWOFERM® SL 446 is a biosurfactant which belongs to the group of Sophorolipid sugar surfactants. It is made by a fermentation process with a natural, non-GMO yeast using European sourced sugar and oil feedstock. Especially no palm oil or derivatives thereof are applied for the production. Due to its environmentally benign production process REWOFERM® SL 446 has a low Carbon Footprint and a renewable carbon Index (RCI) of 100% stating it as a truly sustainable surfactant.

REWOFERM® SL 446 exhibits an excellent toxicological and eco toxicological profile and is completely biodegradable. It is of course compliant with European Ecolabel requirements. Moreover it also behaves as a super-mild surfactant to the skin, verified by an L/D value higher than 1000 in the RBC test. The replacement of chemically made and/or petro chemically based surfactants by REWOFERM® SL 446 boosts the efficacy of cleaning formulations, e.g. partial replacement of Betaine in Hand Dish Wash liquid yields a better foaming and a superior grease removal efficacy. In liquid laundry detergents an improved stain removal efficacy can also be achieved.

Thus REWOFERM® SL 446 makes it is possible to increase both the performance and the ecological footprint of your cleaning formulations.

OC 32

Formulation of Industrial Enzyme – current and future grand challenges

Dr. Ole Simonsen; Dr. Poul Bach & M.Sc. Kim Bruno Andersen
Speaker: Kim Bruno Andersen

Novozymes A/S has a more than 60 year track record within formulation of enzyme products for industrial applications. Formulation of industrial enzymes involve challenges ranging from the very cost competitive applications were every cent spend of formulation counts (e.g. in textile processing or bioethanol production) to "high tech" applications where the formulation is delivering a part of the total product performance, e.g. products for animal feed or products for house hold care applications.

The diversity in customer applications are reflected by the formulation technologies applied at Novozymes, and yet most of our products are formulated within a relatively narrow range of formulation chemicals and can roughly be divided into liquid and solid product formats.

In this presentation a broad introduction to the formulation technologies behind the Novozymes products will be given. Examples are given of how customer needs have been met with formulation development. Finally two major challenges within industrial enzyme formulation that still need to be solved are presented.

Steady-state droplet size in pickering emulsions

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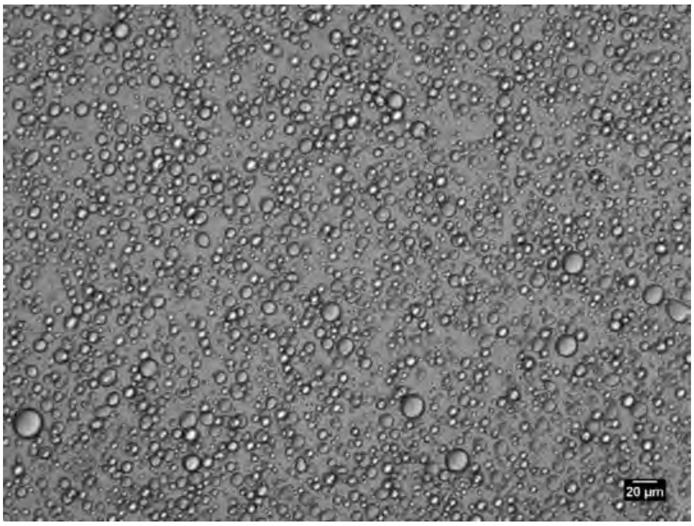
Presenting author: Dr Jeroen S van Duijneveldt



Clay platelets have the potential to be very effective Pickering emulsion stabilisers due to their large surface area. By optimising the surface chemistry using surfactants, well-stabilised emulsions were indeed obtained, but the final droplet sizes were an order of magnitude larger than theoretically possible [1].

We report new data [2] on emulsions of hexadecane in water, stabilised by montmorillonite platelets, as a function of both clay and oil concentrations. Emulsions were prepared using high shear mixing (UltraTurrax). Whilst the stability of such particle stabilised emulsions arises from the large adsorption energy of the particles at the oil-water interface (of order 10^5 *kT*), we argue that the results indicate platelets reach a steady-state between adsorption and desorption during the mixing process. A kinetic model is constructed that reproduces experimental observations well, and allows us to make predictions of optimal conditions for Pickering emulsion formulation.

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OC 34

Hierarchical Self-Assembly in Tranexamic Acid Cetyl Ester Hydrochloride System

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Tranexamic acid cetyl ester hydrochloride (TXC), which is synthesized by chemically modifying the tranexamic acid with the hydrophobic C16-chain, is utilized as an active ingredient in cosmetics. The chemical structure results in the higher hydrophobicity than water-soluble tranexamic acid which help percutaneous absorption through stratum corneum. Although TXC was designed for the sake of the transdermal permeability to enhance bioavailability, we are interested in its structure as cationic amphiphile. Therefore, our present study focused on the amphiphilic nature of TXC and the phase behaviour in its aqueous systems.

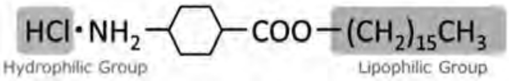

Figure 1. Chemical structure of tranexamic acid cetyl ester hydrochloride (TXC).

Binary mixtures at different compositions showed a variety of self-assembling structures. Increasing TXC concentration induced phase transition from the micellar solution to the lamellar liquid crystal via the hexagonal liquid crystal. Comparing with the general cationic surfactant systems, the TXC system showed highly organized orientation of LC, the higher Krafft temperature, and the lower critical micellar concentration due to its strong inter-molecular interaction between cyclohexyl groups which is a rigid six-membered ring conformation in the molecule. SAXS, DSC, and POM measurements demonstrated the specific molecular packing of TXC below and above the Krafft temperature. In our presentation, we will introduce an interesting self-assembly structure by TXC with cyclohexyl hydrophobe in the center of the molecule as a new generation amphiphile. In addition, the unique chemical structure and interaction enabled to construct a novel hierarchical structure; bicontinuous network with lamellae channel.

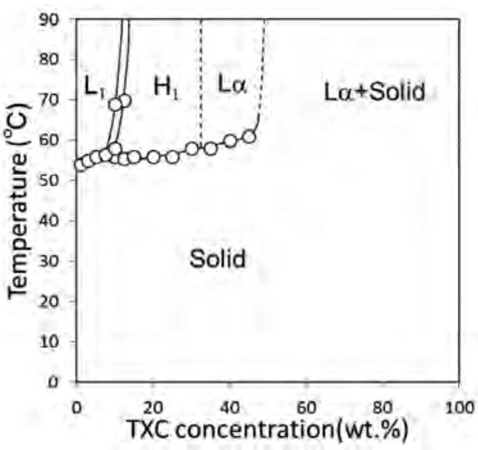

Figure 2. Phase diagram in water/TXC binary system.

Dynamic and rheological behaviour of a polymer melt loaded with polydisperse nanoparticles

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Polymer nanocomposites (PNCs) are hybrid materials incorporating organic or inorganic nanoparticles (NPs) with at least one dimension in the submicron scale. The size and shape of NPs affect the conformation and dynamics of polymer chains in the proximity of those NPs. In particular, the interfacial area might be dramatically altered by the NP/polymer interactions, the degree of distribution of NPs and their geometrical characteristics. Accordingly, macroscopic properties such as shear viscosity are affected as a consequence of the change in the dynamics and conformation of polymer chains. In this work, by performing computer simulations, we investigate the effect of size polydispersity of spherical NPs on the dynamics of unentangled chains in polymer melts. The effect of NP/polymer size ratios and NP's polydispersity index on the macroscopic response of the polymer nanocomposite is discussed. More specifically, we analyse the structural and rheological properties of a PNC containing polydisperse NPs and compare them with those observed in a pure polymer melt.

Keywords:

Nanoparticles, Nanocomposites, Polymer, Polydispersity, Molecular Dynamics

OC 36

Title: QSAR Study on Diverse Compounds for Effects on Thermal Stability of a Monoclonal Antibody

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Abstract:

The thermal melting curve of a protein provides information on its conformational stability and could provide cues on its aggregation behavior. Naturally-occurring osmolytes have been shown to improve the thermal stability of most proteins, they are therefore commonly employed as additives in therapeutic protein formulation. We attempted to probe and summarize molecular mechanisms for thermal stabilization of a monoclonal antibody (mAb) by developing quantitative structure-activity relationships using a rationally-selected library of 120 osmolyte-like compounds.Thermal stabilization potencies were experimentally determined by thermal shift assays based on differential scanning fluorimetry. The cross-validated QSAR model was developed by partial least squares regression using descriptors generated from Molecular Operating Environment software. Careful evaluation of the results with the use of variable importance in projection parameter (VIP) guided the selection of the most relevant descriptors influencing mAb thermal stability. For the mAb studied and at pH 7, the thermal stabilization effects of tested compounds correlated positively with their fractional polar surface area.

PIT-slope method: A simple tool to quantify the amphiphilicity of surfactants and determine the structure-interfacial properties relationship

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The Phase Inversion Temperature[1] of a reference $C_{10}E_4$/n-Octane/Water system exhibits a quasi-linear variation versus the mole fraction/mass concentration of a second surfactant S_2 added in the mixture. The corresponding slope is given as $dPIT/dx_2$ (°C). This variation is proposed as a classification tool to quantify the Hydrophilic-Lipophilic Balance (HLB) of commercial surfactants[2] and also for a wide range of well-defined non-ionic and ionic surfactants[3]. The comparison of various surfactants having the same dodecyl chain tail allows to rank the polar head hydrophilicity as showed in Figure 1.

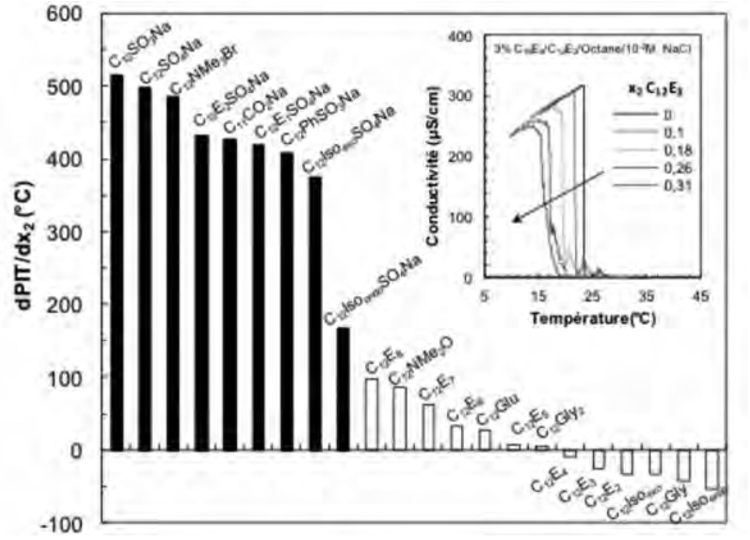

Fig. 1 $dPIT/dx_2$ for well-defined dodecyl surfactants with different polar heads

The influence on the surfactant hydrophilicity of other structural parameters, i.e. hydrophobic chain length, unsaturation, replacement of Na+ by K+ counterion, and isomerism is also investigated. Finally, the method is successfully used to predict the optimal formulation of a bio-based surfactant, the 1-O-dodecyldiglycerol, when performing an oil scan at 25°C. The potential determination of the Preferred Alkane Carbon Number (PACN) for non-ionic surfactants from the dPIT/dx parameter is established.

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OC 38

Detailed investigation of concentrated micro- and nanodispersions by X-ray concentration profiling

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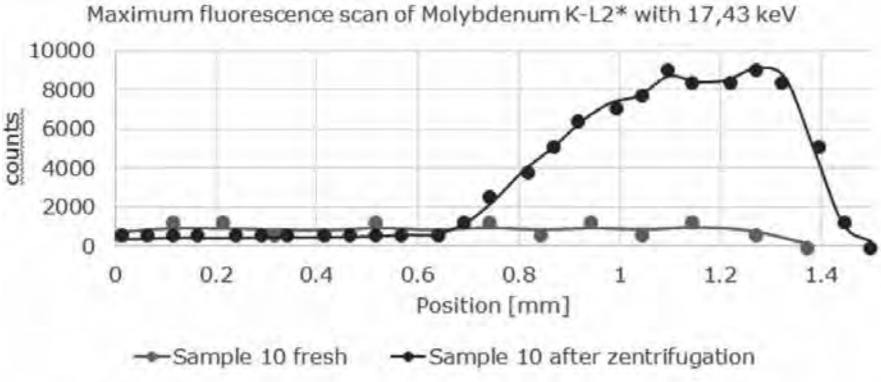
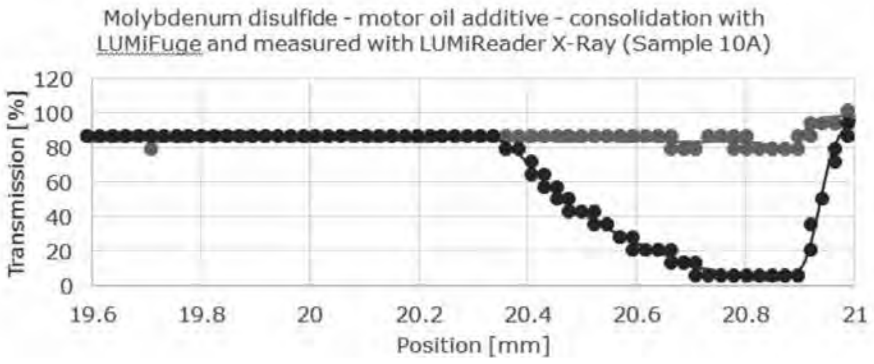
Characterization of dispersions, e.g. regarding separation phenomena (stability) and homogeneity is problematic for concentrated nontransparent dispersions but also transparent nanodispersions. This applies even more in case of complex mixtures, when dispersed phase is a mixture of two or more materials. In particular it is difficult to define position of interfaces and separation levels, and to quantify local differences in solids concentrations within dispersions and sediments. To overcome these difficulties a new analytical instrument–the LUMiReader X-Ray–has been developed. The working principle is based on measurement of space and time resolved x-ray transmission profiles over the entire sample height. In contrast to optical measurements x-ray transmits very highly concentrated dispersions, powders and composite materials. Recorded x-ray intensities depend only on mass concentration of particles and do not depend on particle size and shape. The new approach can be easily applied to detect inhomogeneities e.g. in mortars and creams or after dispersing particles in liquids or polymers. On the other hand kinetics of separation phenomena at earth gravity as well as in combination with analytical centrifugation can be analyzed and local sediment packing studied. Segregation results for dispersions made of mixtures of different materials (different x-ray absorption properties), like dispersions in paper industry, lubricants and colour cosmetics, will be also presented. In case of segregation in lubricants enrichment of solids at bottom was verified by complementary measurement of x-ray fluorescence as shown below.





Organic-inorganic patchy particles as a versatile platform for foam and emulsion stabilization

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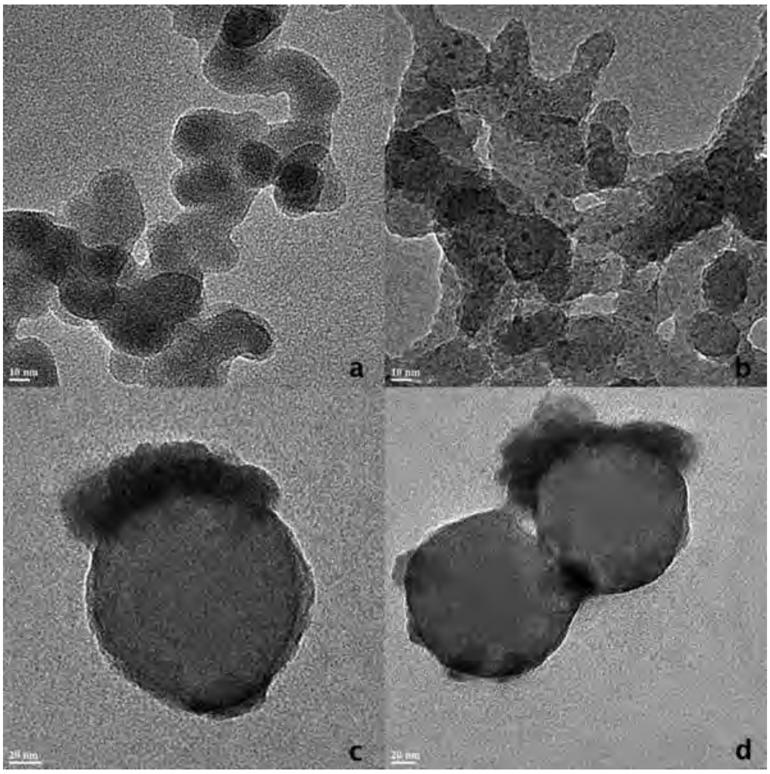
We present a new class of environmentally friendly organic-inorganic patchy particles for stabilization of fluid-in-fluid dispersions. Using solvent-based heterogeneous precipitation, we decorate silica particles with discrete domains of water insoluble plant protein (zein). By varying the extent of protein loading on the silica surface, we tune the particle interfacial potential. We observe an optimum foam stabilization, which is attributed to protein specific orientation creating surface anisotropy. The effect of surface coverage on foam stability is in line with the predicted pH dependent interfacial potential of the patchy particles in water. In emulsions, the extent of the protein loading on spherical silica particles causes a progressive bridging of oil droplets together into a close-packing configuration. The emulsion droplet size decreases with increasing in surface coverage, while phase inversion is triggered at low oil volume fraction. Protein-based organic-inorganic surface heterogeneous particles represent a new versatile platform for foam and emulsion stabilization.



TEM images of: (a) Fumed silica fractal structure, and (b) fumed silica particles with zein. Scale bar 10 nm. (c) and (d) Colloidal silica particles (100 nm) with zein patches. Scale bar 20 nm.

ORAL COMMUNICATIONS

OC 40

NANOCYTES®–Core-shell particles for the particle-based formulation of active pharmaceutical ingredients

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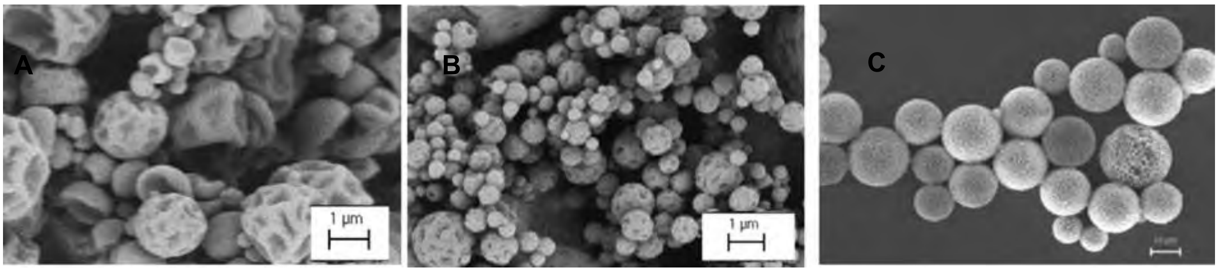
The formulation and application of active pharmaceutical ingredients (APIs), especially of therapeutic petides and proteins, is often still a challenge. For example the oral application of therapeutic peptides is hindered due to the proteolytic gastritic degradation and the poor adsorption mechanism out of the gut lumen. Due to the molecular weight biopharmaceuticals are often oral not applicable and have to be administered parenteral.

API-loaded core-shell particles for enhanced oral applications or for the intransal delivery of APIs are prepared at the Fraunhofer IGB by means of different technological approaches (e.g. direct spray-drying, emulsion technologies, solvent evaporation technology) and analysed in terms of size, morphology and physico-chemical characteristics.[1] Spray drying is one method that is used for an effective encapsulation of biomolecules like insulin or interferon in inulin or chitosan without the loss of the bioactivity of the encapsulated protein.[2] For the one-step preparation of core-shell particles by spray drying a three-component nozzle has been successfully integrated into the process. The core-shell structure is independent of the external or internal supply of the spray solutions. The phase added with a higher volume flow forms the shell of the particles.[2]



Scanning electron microscopic (SEM) images of different particles. (A) insulin-loaded Inulin particles, (B) insulin-loaded Chitosan particles, both prepared by an spray drying process and (C) PEG-PLGA particles prepared by emulsion technologies.

The biopolymer Chitosan is used as mucoadhesive particle material or as mucoadhesive coating. Chitosan can like other cationic molecules interact with the mucus surface. Chitosan and its derivatives possess permeation enhancing activity. We have demonstrated that chitosan hydrochloride (Chitosan-HCl) induced the opening of the tight junctions of Caco-2 cells.

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[3] K. Köberle, Master Thesis, University Stuttgart 2014.

Formulation strategies for the production of pharmaceutical powders out of precipitated api nanoparticles

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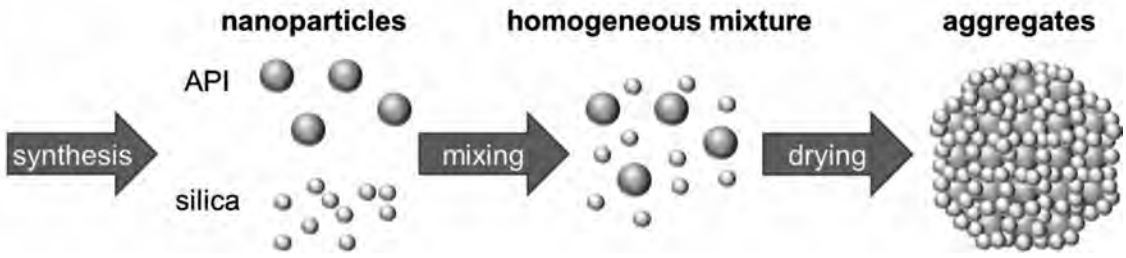
The pharmaceutical industry develops a great number of poorly water-soluble APIs (active pharmaceutical ingredients) which tend to show low bioavailability. Consequently, the establishment of suitable galenic methods, which increase bioavailability of these APIs, has become an important issue. A promising procedure to reach this goal is by converting crystalline APIs to their amorphous state via embedding them into mesoporous silica particles [1]. Furthermore, production of API nanoparticles and encasing them with sugars, polymers and other materials by maintaining the nanoparticular state of APIs is also a possible method to increase bioavailability [2].

The present work is focused on reaching this goal considering both aspects. In order to do so, the production of API loaded aggregates with defined properties (e.g. dissolution behavior and API loading) is aimed. For that purpose, amorphous API nanoparticles are co-spray-dried along with different kinds of materials such as silica nanoparticles or lactose. API nanoparticles are produced via antisolvent precipitation and silica nanoparticles via Stöber process. Besides, it is possible to adjust their particle size (API: 100-250 nm; silica 50-500 nm) so that the influence on the final product can be investigated. After particle synthesis, API nanosuspensions and excipients (dispersed or dissolved) are mixed at certain ratios and converted into powder via spray drying. At this point, several formulation (e.g. mass fraction) and process parameters (e.g. drying temperature and nozzle size) are under study in order to assess their influence on product properties and improve process performance. The figure below shows a schematic process chain to produce defined aggregates via co-spray-drying.



Schematic process chain with intermediate and final products

Afterwards, aggregates are analyzed by means of dissolution tests to compare different loading procedures regarding drug release. Furthermore, DSC (differential scanning calorimetry) and XRD (X-ray diffraction) measurements are used to prove the solid state (amorphous, crystalline) of APIs. Additionally, SEM (scanning electron microscopy) images enable to characterize the morphology of the aggregates.

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OC 42

Formulation of polymer composites as functional coatings based on functionalized np's for use on solar panels

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Interest in self-cleaning surfaces has grown rapidly in recent years due to their unique characteristics. Self-cleaning coatings have gain importance and have been commercially attractive and available in the building industry currently, since it can save significant maintenance cost. It's application has expands widely due to its impact, for example, when solar panels are exposed to environmental conditions a decrease in efficiency is observed; therefore, the use of self-cleaning coatings to reduce dirt accumulation is required. However, for applications such as self-cleaning on solar panels, high optical transparency is additionally required, as well as wear resistance.

In this work, the formulation of coatings from commercial nanoparticles systems based on TiO_2-SiO_2, CeO_2-Al_2O_3 that are functionalised with different coupling agents is presented. Preparation of polymer nanocomposites was performed by solution mixing in acrylic acid that acted as polymer matrix. This solution was spin-coated onto a glass substrates. Water contact angle was analysed by drop shape analysis (sessile drop), the obtained results allow us to observe mainly an hydrophilic behaviour and hydrophobic in some other cases depending on the nature of the nanoparticles and functionalization agent. The morphologies of the coatings were observed by SEM and atom force microscopy (AFM).

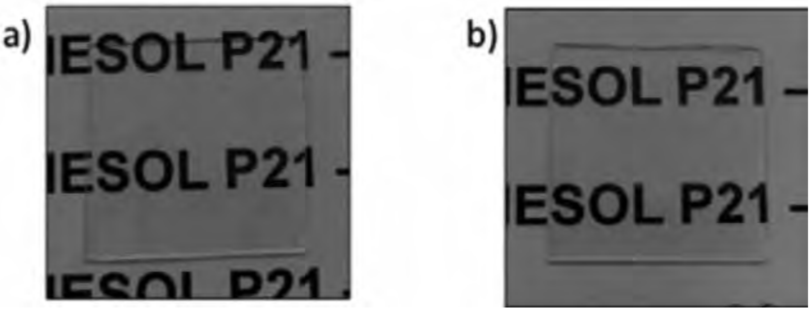

Figure 1. a) Dispersion of CeO_2-Al_2O_3/AF1/Acrylic and b) TiO_2-SiO_2/AF2/Acrylic and its deposition on glass substrate.

Acknowledgements

We are grateful to CONACYT-SENER, Fondo Sectorial de Sustentabilidad Energética (CEMIESOL P21)

Study of emulsifiable concentrates using green solvents

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The global tendency for sustainable products with superior performance is one of the main challenges of new formulations. In this way, to find solvents with environmental and toxicological advantages, when compared to typical solvents used for agrochemicals formulations, is a subject of great interest for many formulators.

The main class of solvents used in Emulsifiable Concentrated (EC) formulations are aromatic hydrocarbons which are very effective to solubilize several active ingredients (AI), but some concerns about their toxicological and environmental profile have been motivating the search for more friendly options. In general aromatic solvents have different levels of toxicity, as some of them are considered carcinogenic, teratogenic or mutagenic. Besides that, they are not from renewable sources.

The main objective of this work is to evaluate the use of alternative green solvents and their mixtures in typical EC formulations. The selection of solvents was done based on their features as green solvents in accordance to the principles of green chemistry and potential of good performance.

In this work, the first key factor evaluated was the solvency power that was determined from Hansen parameters of solubility by computer simulation.

As the following step the solubility was confirmed in the lab and the main challenge was to get a new formulation as an emulsifiable system. In order to keep the proposal of sustainability, emulsifiers with better biodegradability and derived from renewable sources were considered to stabilize this system.

The EC formulation developed according to this approach behaved as a very stable system with differentiated toxicological profile. Besides that, raw materials of renewable sources were incorporated, promoting a better carbon footprint for these new alternatives overcoming all the phys-chem requirements for this formulation.

In conclusion, from this study EC formulation were successfully re-formulated using the proposed green solvents, resulting in more sustainable alternatives than typical formulations based on hydrocarbons solvents.

OC 44

Protein evaluation in food formulations by passive microrheology

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This work presents studies on food formulations with protein addition using passive microrheology. Passive microrheology studies the mobility and displacement of micron sized particles which results from Brownian motion [1]. The motion of particles induces local deformations of the sample, which are directly related to its viscoelastic properties.

Our technique is based on Multi Speckle Diffusing Wave Spectroscopy (MS-DWS), which consists of Dynamic Light Scattering (DLS) extended to an opaque media. With a patented algorithm, the backscattered interfering light can be analysed in terms of Mean Square Displacement (MSD), which is directly related to the viscoelastic properties of a sample. Moreover, the optical method allows to study especially weak gels without any applied shear, which avoids perturbation of the sample.

Nowadays, proteins are widely used in food preparations in order to increase the nutritional value of foods. However, proteins behave particularly in combination with fats, (bio-)polymers and other proteins. Phase separation or synergistic effects are the consequence. This work shows how passive microrheology can be used to evaluate the influence of a protein preparation in comparison to a reference product. Viscoelastic properties and gel points [2,3] of the samples are determined, which helps the formulator to have an acceptable new, but nutritionally valuable food preparation.

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Preparation of stable emulsions to chlorpheniramine recovery from aqueous solutions

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The emulsion liquid membranes (ELMs) are essentially double emulsions of the type water/oil/water (w/o/w) or oil/water/oil (o/w/o) [1]. A double emulsion is formed by one emulsion of two immiscible phases. Depending of the double emulsion kind, one phase can be organic or aqueous and it is composed by hydrophilic or hydrophobic diluents, a superficially active agent (surfactant) and a carrier. The other phase, which can be aqueous or organic, has favorable conditions that allow breaking the carrier-target species complex and achieving the stripping. ELMs are a versatile and useful alternative for the recovery of different compound contained in wastewaters. Pharmaceuticals are within these compounds. They recently have provoked an environmental concern because of its growing detection in wastewater [2]. These substances are found in water at concentrations very low (ng.L^{-1} or mg.L^{-1}), however, they represent a serious problem due to their bioaccumulation may occur and provoking different adverse effects, unknown or not, on organism and the environment . Chlorpheniramine (CPM), a first-generation antihistamine, was identified qualitatively in wastewater treatment plants in cities, for example New York; in addition, being the most prescribed drug, it must be considered with highest priority for further studies because of its frequent release to environment [5, 6].

In this study a methodology for CPM recovery from aqueous solutions by emulsion liquid membranes (w/o/w) was developed. The organic phase was composed by the diluents Parleam 4, the surfactant Abil EM 90® at different concentrations (0.25 – 5% w/V) and the carrier soy lecithin (SL) at different concentrations (0.001 – 5% w/V), too. The inner aqueous phase (stripping phase) was composed of HCl (0.025 – 0.2 mol.L^{-1}) and the external aqueous phase by chlorpheniramine dissolved in sodium bicarbonate solution at pH 6.

In order to obtain a stable and efficient emulsion, several parameters were evaluated like surfactant and carrier concentrations, nature of stripping phase and volumetric fraction. On the other hand, extraction and stripping kinetics were studied, as well as, the droplet size distribution in order to observe the emulsion homogeneity.

The results show that emulsions prepared with Parleam 4 + soy lecithin at 3% w/V + Abil EM 90® at 5% w/V as organic phase and HCl 0.1 mol.L^{-1} as the inner aqueous phase presented the highest extraction and recovery yields (100% and 75%, respectively) with a transfer time of 10 min. So, an efficient system of emulsion liquid membranes with uniform droplet size distributions (2.4 μm of average diameter) was developed to the simultaneous extraction and recovery of CPM from aqueous solutions.

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OC 46

A multiple emulsion approach to deliver 1-MCP for pre-harvest applications

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Abstract. 1-methylcyclopropene (1-MCP; SmartFresh®; AgroFresh, Philadelphia, PA) is used widely in the apple industry to control postharvest ripening and quality loss of apples in storage. With the success of postharvest 1-MCP, interest has grown in the potential for the development of a sprayable form of 1-MCP for preharvest application in the orchard and in how such an approach might produce benefits to fruit quality maintenance after delayed harvest and after storage. Since 1-MCP is a gas, it has been challenging to develop formulations that can be applied using orchard sprayers. This talk will discuss novel approaches to address this challenge.

Predicting the interfacial tension of multicomponent liquid-liquid systems with COSMO-RS

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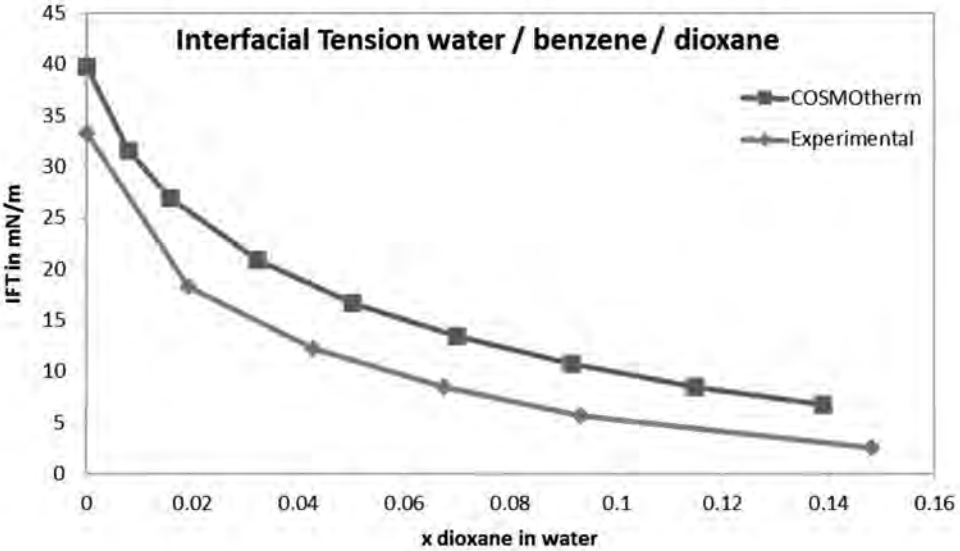
The quantum chemistry based COSMO-RS method meanwhile has been widely recognized as an efficient approach to the qualitative and quantitative understanding and prediction of the interactions and phase behavior of bulk liquid systems. In this contribution we demonstrate how the COSMO-RS concept can be extended for the prediction of the interfacial tension. Though various correlations or methods exist to predict the interfacial tension in water-organic systems, no general liquid-liquid method with a full temperature and concentration dependence had been available. The presented method uses predicted liquid phase chemical potentials and can thus be used for all liquid compositions accessible by COSMO-RS, including multiple compounds mixtures and organic-organic interfaces. It provides a sound picture of the relevant interactions of the molecules at the interface. Several examples application will be presented.



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Deep-Sea Inspired Process for Bottom-up Production of Nanoemulsions

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MAGIQ (Monodisperse nAnodroplet Generation In Quenched hydrothermal solution) is a novel bottom-up process for making nanoemulsions [1]. It was inspired by extreme environments around deep-sea hydrothermal vent (Figure 1), where vent water is sometimes in the supercritical state (T_c = 374 ºC, P_c = 22.1 MPa). At such high temperature and high pressure, water becomes freely miscible with various oils [2]. In MAGIQ, emulsification was performed by cooling homogeneous solutions of oil in supercritical water (SCW), and oil droplets were formed in a bottom-up manner by self-assembly of oil molecules (Figure 2). The process is completely different from conventional processes for making emulsions, where energy is applied to oil/water mixtures to repeatedly disrupt large droplets to finer ones.

A flow-type instrument was developed to perform MAGIQ. The instrument allowed to apply fast and deep temperature-quench, ~200 ºC/sec, to homogeneous solutions of oil in SCW so that the oil phase-separated rapidly to generate nano-sized droplets. In tests using dodecane and a nonionic surfactant, Brij 97, emulsions containing nano-sized and monodisperse dodecane droplets with average diameter of 61 nm were obtained in just 10 seconds.

Mechanisms of droplet formation are completely different between conventional top-down processes and bottom-up MAGIQ. Recent experimental results show that dynamic surface tension of surfactants plays a critical role in determining size of droplets that are formed by MAGIQ. More specifically, surfactants that quickly adsorb to the oil/water interface tend to give smaller droplets. The results will be discussed in terms of the droplet formation mechanism in MAGIQ.

Figure 1. Photograph showing a hydrothermal activity in the Urashima hydrothermal field at the Southern Mariana Trough at the depth of 2935 m. The highest recorded temperature of the vent water was 270 ºC.

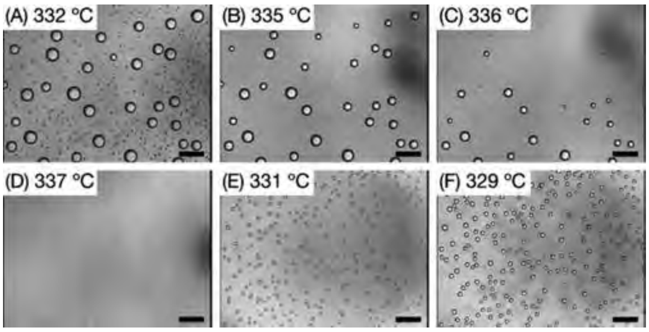

Figure 2. **A**–**D**) *In situ* optical microscopy images of droplets of dodecane in water taken at a constant pressure of 25 MPa. Images were taken while heating the mixture at 11.6 ºC/min. **E** and **F**) Formation of dodecane droplets upon cooling from (D) at 4.5 ºC/min. Scale bars represent 50 µm.

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Polymeric nano-emulsions and nanoparticles: influence of polymer concentration on size, stability, drug encapsulation and release

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Nano-emulsions are dispersions of two immiscible liquids (e.g. water and oil) stabilized by an interfacial surfactant film, with droplet size in the nanometric scale, generally between 20-200 nm. Due to their small droplet size, nano-emulsions are transparent or translucent and possess stability against sedimentation or creaming [1,2]. Nano-emulsions can be used as template to prepare polymeric nanoparticles using preformed polymers, e.g. poly (lactic-co-glycolic acid (PLGA), dissolved in an organic solvent as dispersed phase followed by solvent evaporation [3-5]. The aim of this work was to study the influence of polymer concentration on droplet size, stability drug encapsulation and release of the template nano-emulsions and the resulting nanoparticles. Polymeric (PLGA) nano-emulsions were prepared by the Phase Inversion Composition (PIC) method at constant temperature by stepwise addition of water to surfactant/PLGA in ethyl acetate mixtures. Phase diagram determinations of water/nonionic surfactant/(PLGA in Ethylacetate) system showed that the region of nano-emulsion formation increases with the polymer content and that phase inversion takes place during the emulsification process. Polymeric nanoparticles were prepared from polymeric nano-emulsions by solvent (ethyl acetate) evaporation. Nano-emulsion droplet size and nanoparticle size, assessed by DLS and electron microscopy increase with the polymer content and kept constant during the experimental time of 7 days. Moreover, no destabilization process was observed by light transmittance/backscattering. A model drug, Dexamethasone, encapsulated in the polymeric nanoparticles, did not modify particle size. No effect of polymer concentration was observed in the encapsulation efficiency (above 88%). In vitro drug release tests showed that the higher the polymer content the lower the release rate (i.e. the higher the drug entrapment), favouring the controlled drug release. This study reports a promising system to obtain polymeric nanoparticles by nano-emulsion templating.

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OC 50

Formulation strategies for the preparation of nanoemulsions containing sensitive carotenoids

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Among the many advantages offered by nanoemulsions in pharma and nutraceutical applications are their long-term colloidal stability, improved dermal and mucosal transport of actives, improved oral bioavailability and greater aesthetic appeal and skin feel. A common way of preparing nanoemulsions with drops in the nanometre size range is by means of high-energy methods such as high-pressure homogenization and ultrasonic emulsification. Less common are the milder, low-energy methods such as spontaneous emulsification and phase inversion. These methods, often involving low temperatures and low shear, are mainly dependent on the tuning of the intrinsic physicochemical properties of the emulsion components and the preparation protocol to yield nanosized emulsion droplets. In the context of pharma and nutraceutical applications, production of nanoemulsions using mild processing conditions results appealing as it might bring advantages when dealing with sensitive drug molecules or actives prone to degradation and oxidation such as e.g. carotenoid mixtures and single carotenoids.

The work presented here deals with the evaluation of different emulsification approaches for the production of nanoemulsions intended for delivery of the two carotenoids lutein and zeaxanthin. Evidence from epidemiological and intervention studies suggests that these two carotenoids are associated with a reduced incidence of the two common eye diseases: age related macular degeneration (AMD) and cataracts [1-3]. In this study, high-pressure microfluidisation as well as low energy emulsification methods, including spontaneous emulsification and phase inversion, were thus tested for the production of prototype nanoemulsion formulations for topical and/or oral delivery of lutein and zaexanthin. The physical stability of the emulsions as well as the chemical stability of the carotenoids through the emulsification process was followed. Based on these results, the advantages and limitations of the different emulsification approaches are identified and discussed.

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Sub-Micron Patterning of Polymer Brushes arising from the Inkjet Printing of Polyelectrolyte Macroinitiators

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Thin films formed of polymer chains densely end-grafted to a surface are known as ***polymer brushes***. The vast range of chemistries and interesting fundamental properties of polymer brushes has led to emerging applications in diverse fields such as biomedicine, microelectronics, photovoltaics and sensing. Patterned polymer brushes are finding application in areas such as directing cell growth, "gecko-mimetic" switchable adhesion, etch resists and photonic based sensors, however no universal and accessible technique capable for the rapid iteration of high resolution patterns (below 1 μm) over large areas currently exists.

Here we report the high-resolution deposition of polyelectrolyte macroinitiators using electrohydrodynamic printing and subsequent polymer brush growth using SI-ARGET-ATRP. We go on to demonstrate for the first time a controlled ***sub-micron*** patterning phenomena through a fundamental understanding of formulation interactions through the drying process. It has been found that through the addition of either a appropriately like charged polyelectrolyte homopolymer or through careful control of ionic strength that deposition of macroinitiator in micron scale structures can be directed and defined at the sub-micron scale. As a result patterning of polymer brushes down to ca. 200 nm is reported. We present a possible mechanistic model and consider how this maybe applied to other polyelectrolyte-based systems as a general method for ***sub-micron*** patterning.

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Engineering new hybrid nanoparticles for formulation of new materials

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In this communication, we report on a new route to synthesize new hybrid particles with a controlled number of dimples as well as on their potential use for the formulation of new colloidal suspensions with unusual morphology and optical properties. These new hybrid particles were derived from colloidal molecules [1] made of a central silica core surrounded by a precise number n of polystyrene satellite nodules [2,3]. We succeeded in promoting the growth of the silica core of these colloidal molecules. While growing, the silica surface conforms to the shape of the PS nodules. After functionalization of the inter-nodule surface area and dissolution of the polystyrene nodules, homogeneous batches of silica particles with dimples can be produced in large quantities [4,5]. The morphology of the silica particles was evidenced by TEM characterization (see Figure) as well as the regioselective functionalization. These particles offer the unique capability of formulating new colloidal suspensions by controlling the solvent quality to drive their self-assembly. Suitable for many applications such as sensing, metamaterials, photonics, etc.

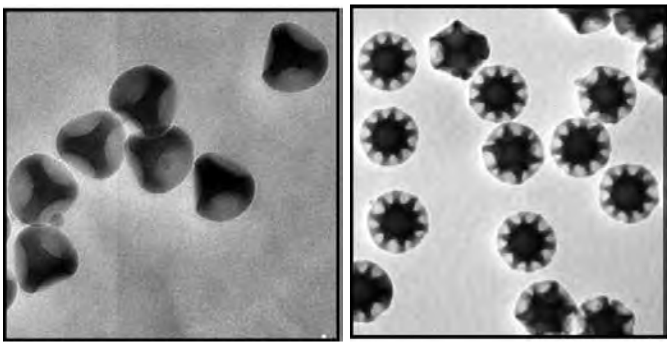

Fig. TEM image of silica particles with four (left) and twelve (right) patches defined here as dimples [4].

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Aqueous solubilisation of fragrances in volatile solvo-surfactant-based microemulsions

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Fragrances are present in numerous day-life products, either as actives in fine perfumery or as additives in personal and home care products. In fine perfumery, the complex mixtures of fragrance molecules are generally solubilised in aqueous ethanol while in formulated products, their solubilisation is ensured by surfactants and hydrotropes. One challenge for perfumers today is to replace ethanol by water. Indeed, the European Union imposes to reduce the emission of VOCs and ethanol falls under this regulation. Although it has barely a negative effect on the environment, effects on the human health have been observed. Furthermore, ethanol is known to cause irritations and skin drying. The application of a perfume directly on the skin can thus be harmful for the skin, resulting in redness and itching.

There is thus an increasing demand for water-based fragrance formulations. One way to overcome the fragrance/water incompatibility is to use solubilising systems based on surfactants like LRI which is a synergistic non-ionic surfactant mixture. However, such systems are not entirely satisfactory due to residues they can leave on the skin and clothes and to tacky feel they can provide. On the other hand, solvo-surfactants which can be defined as volatile hydrotropes can avoid such disadvantages but the amounts required to solubilise fragrances hinder their use for such an application.

In this context, we have developed water-rich microemulsions systems for the solubilisation of fragrances and essential oils. The technology is based on the synergy between solvo-surfactants and surfactants allowing a considerable reduction of amounts required for the solubilisation of fragrances. 10% of a fragrance can be solubilised in 80% water using 9% of solvo-surfactant and less than 1% of surfactant while the solubilisation would require about 40% of solvo-surfactant or 10-15% of surfactant alone. The solvo-surfactants are short chain (C_3–C_5) glycol ethers (C_iE_j) or glycerol ethers (C_nGly) as biobased alternatives. Furthermore, their combination with ionic surfactants can guarantee the stability of the systems from 5 to 45 °C. Such a mixture leads to a microemulsion system which is transparent and presents the same viscosity as water.

In this presentation, the solvo-surfactant/water and solvo-surfactant/ fragrance/water systems phase diagrams and the influence of ionic surfactants will be addressed in order to draw some rules for the elaboration of such nanodispersed systems that bring a response to the question “how solubilise a perfume in water?”.

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OC 54

Fragrances with double functionality. Novel perfume composition for the prevention and control of diseases and biofilms.

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Nowadays we are living in a constantly changing society. Consumers demand for new products and are aware of their health and the environment. In the food field, a lot of functional products have been launched. This means, that apart from its main function that is nourishing, there are additional properties such as to control health and prevent diseases.

Under this motto, we consider that there are many R+D projects that can be done in the fragrances field. A long time ago, Egyptians, Greeks and Romans used fragrant substances not only for beauty, but care. Back in the seventeenth century, Culpeper published a work which listed all the effects of medicinal plants that were known at that time. It demonstrated that plants have enjoyed a firm place in pharmaceuticals and cosmetics for centuries as a result of their beneficial and therapeutic effect.

Modern fragrance compositions are typically blends of natural and synthetic raw materials. Depending on the product where the fragrance will be applied, some interesting properties can be added using the most convenient ingredients. We are not only talking about essential oils, we also refer to ingredients obtained by biotechnological processes (microbial fermentation and enzymatic synthesis).

While most consumers believe that our home is a safe space, we cannot forget that many of the most common infections in developed countries originate in the home environment by producing episodes of gastrointestinal, respiratory or even eye infections. In spite of this, there is a great tendency to use shorter cycles and lower temperatures in automatic washing and the elimination of most harmful environmental bleaching systems.

Biofilms are the source of persistent hygienic problems in industrial and domestic areas. Conventional disinfectants, which are often toxic and carcinogenic, may contribute to inefficient biofilm control and to the dissemination of resistance. Consequently, there is a necessity to develop new sustainable strategies for biofilm prevention.

Within this line of research, Carinsa wants to develop a range of perfumes with dual functionality. We must ensure a pleasant perfume as main function that also provides a sanitizing activity with antibiofilm and antimicrobial activity for the efficient disinfection and bad odor removal, which will be formulated in cleaning products.

Another area of interest is the control of tropical diseases infected by mosquito bites. It is known that certain essential oils have mosquito repellent activity, so after formulating these products and encapsulating them, in order to enhance their activity, clinical studies will be done to ensure efficacy of these fragrances against mosquitoes.

Understanding the Role of Chelants in a Formulation

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The word chelation is derived from Greek, chēlē, meaning "claw" and chelating agents, or chelants as they are also known, are molecules which form complexes with metal ions (figure 1). They are a key ingredient in many diverse products and the formulator needs to understand how they work to get the best out of them. Chelants can carry out a number of different roles, these included softening the water, removing deposits, as stabilizers, and transporting metals to name but a few. It can therefore be very difficult to choose the right chelant or to change from one chelant to another.

This presentation will guide you through the complex world of chelating agents and to understand how they will perform in your formulation. The application area can also introduce regulatory requirements for some chelating agents. It will cover what a chelant stability constant means in terms of chemical speciation and how these can be used to calculate the selectivity of a chelant for a particular metal.[1]

The chemistry of laundry powders[2] and metal surface cleaning[3] will be used as examples of how it can be difficult to select the correct chelating agent. The examples will highlight the chemistry of mixed metal systems, issues associated with hard water systems and the fact that the selectivity of a chelant can have a dramatic effect on a formulations performance. The synergistic use of blends will also be discussed.

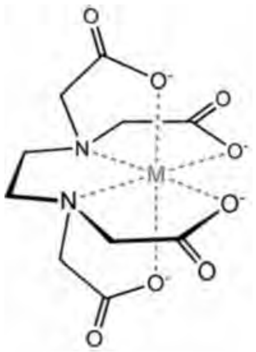

Figure 1. The hexadentate complex formed by EDTA

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Dispersibility of aqueous nanosized metal oxide as function of dispersion intensity and characterization of degree of flocculation

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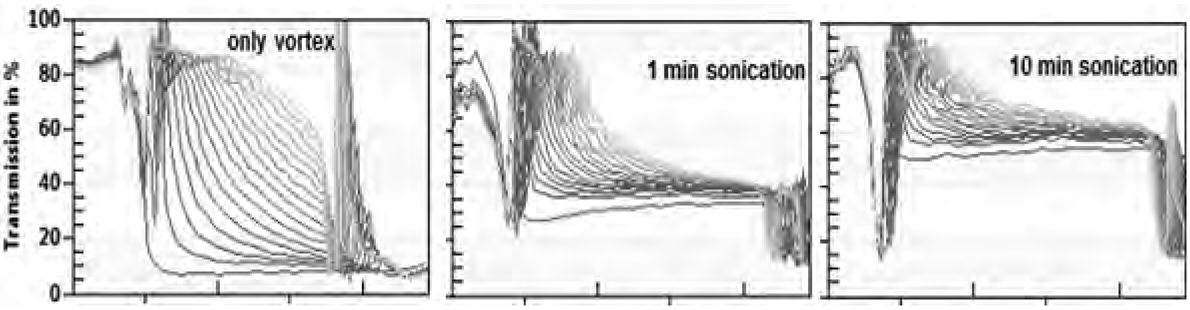
To make an economic use of raw materials in suspension based formulations one has to obtain a high degree of dispersion. This is related also to practical aspects like achieving high hiding power at lower pigment concentration and of outstanding material properties in composites. Dispersibility and the resulting quality of dispersion is determined by several factors including structure/quality of the raw materials and dispersion media, dispersion process and additives. A classical example is the dispersion of fumed metal oxide powders, which are composed of agglomerates and strong aggregates of nanosized primary particles.

Mostly there is a clear correlation between degree of dispersion and separation velocity of product in gravity and enhanced gravity fields. Especially in case of submicron particles there is a strong dependence of extinction coefficient on particle size, i.e. the degree of dispersion obtained. Even more the turbidity ratio (ratio of extinction measured at 2 wavelength) is very sensitive to changes in particle size distribution in case of process of dispersion as well due agglomeration.

STEP-Technology (Measurement of Space and Time resolved Extinction profiles) allows for a detailed in-situ visualization of separation processes with information on separation velocity (distribution), packing density in the sediment and residual turbidity but also for determination of initial optical dispersion properties and of the turbidity ratio. This allows for fast evaluation of dispersibility and agglomeration alike.

The investigations were carried out on nanosized alumina. In a first step the degree of dispersion as function of dispersing intensity was characterized. This was followed by an investigation on the effect of electrolyte and pH on dispersion state of suspensions of nanoparticles.



Evolution of transmission profiles for 10 % Aeroxide Alu C dispersions as function of dispersing intensity. Centrifugation at RCA 2300, 20°C (left vortex mixer only, followed by increasing dispersing intensity – different duration of high intensity sonication). First profiles red, last profiles after 2550 s green, interval between profiles 150 s).

Design of Agro-based Coatings: from innovative raw materials to optimal performances, the critical input of property characterization

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IFMAS (**Institut Français des Matériaux Agro-Sourcés / *French Institute of Agro-Based Materials***) is a key player in research and development of innovative materials from renewable resources. Our teams work at all stages of the bio-based material industry: from renewable feedstocks to end-products, including plastics, solvents and surfactants. With its own research center, divided in 6 laboratories (***Synthesis, Polymerization, Plastic processing, Analysis, Structural characterization and Formulation***), IFMAS has the required know-how and capabilities for a precise evaluation of the properties of its new products.

Developing innovative products based on renewable resources requires to match or even to exceed performances of the petro-based products that are aimed to be substituted. Each step of the development process is thus followed by a precise evaluation of the physico-chemical properties and the performances of the intermediate and final products. Design and synthesis of new raw materials are generally ended by:

- an assessment of chemical nature and purity of the molecules,
- checking the reactivity (e.g. thermal- or photo- polymerization kinetics, oxidability, reactivity in cross-linking…) and/or the stability of the products,
- an evaluation of their compatibility (e.g. miscibility, mixture stability, presence/absence of reaction…) with the other components expected in the final product.

In the case of coating development, during the processing and formulation steps, several conventional methods of coating characterization (Persoz hardness, scratch test, BK drying time recorder test…) are useful to check the performances of a final product. But, due to an increase in the technology degree involved in the field, new methods of analysis have to be elaborated, based on the combination of appropriate techniques. For example, improvement of the drying process in the case of alkyd paints requires to investigate both the reactivity towards oxidation of the components and the global drying mechanism of the whole alkyd paint. To achieve this goal, adequate characterization methods have been developed to understand and optimize the oxidative process [1]. Another common puzzling issue in the field of coating is the study and improvement of the coating-substrate adhesion, which is critical and can have important impacts on global performances (e.g. anti-corrosion properties, impact resistance, washability…). Understanding the driving forces of adhesion mechanism for a specific coating/substrate couple generally requires to characterize the interface, which can be achieved by combining appropriate surface analysis techniques [2].

Several examples of the strong link between properties and performances will be discussed, with a specific focus on the development of appropriate characterization methods needed for a proper evaluation of them.

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ORAL COMMUNICATIONS

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Determination of particle surface properties for liquid selection regarding pigment formulation

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Solubility parameters are widely used in various industrial fields, e.g. polymer solutions and formulation, especially to understand and adjust the dispersibility of dyes and pigments. An appropriate approach is the concept of Hansen Solubility Parameters (HSP). HSP are based on the Hildebrand-Parameter, which describes the cohesive energy density of a molecule related to its energy of vaporization. To account for different interactions by HSP, the HP is subdivided into disperse, polar and H-bond contribution.

Herein, a standard procedure using analytical centrifugation (AC) was developed to measure HSP of the pigment carbon black (CB). AC is a powerful method to characterize in situ the stability of a dispersed system. The dispersion is prepared by applying ultra-sonication to the suspension. If for a defined set of solvents with known HSP experimentally relative sedimentation velocities are determined, HSP of CB can be evaluated via HSPiP-software and surface properties of CB are accessible. We established a standard operation procedure (SOP), by developing a reproducible method for an objective evaluation of measured AC profiles and appropriate ranking of CB in different liquids. By performing similar measurements at both affiliations (LFG and LUM), we showed the high accuracy, reproducibility and strength of our method. Thus, a suitable continuous phase (dispersion media) for pigments can be determined according to the particular needs of the application. To analyze the sensitivity of our approach, we investigated two different types of CB (Printex L and Printex U, Evonik Industries AG), which are produced by different synthesis routes. In line with our expectations, the obtained HSP are in the same range but slightly differ from each other. This is attributed to small but measurable differences of the two materials due to the varying synthesis procedure.

In the second part, we investigated the influence of the applied energy input during redispersion on the obtained HSP. Dispersion may lead to bond cleavage thus altering the surface chemistry of the dispersed particles. Moreover, the applied energy may induce mechanochemical acitivation, e.g. by grafting solvent or stabilizer molecules to the particle surface. To investigate this in detail, we varied the intensity of the applied energy input as well as the time of exposure and analyzed the resulting HSP. The experiments show a clear dependence of HSP on sonication time and intensity. With increasing dispersion energy, the H-bond contribution to HSP decreased significantly.

In conclusion, our work shows how surface properties are accessible by standardized routines in high resolution. Due to AC, experiments become independent from the experimenter's skills or subjective evaluations. This knowledge can be used to tune the interactions of pigments and particles for the later application in dyes or for all sort of other formulation of particulate systems.

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Concentrated oil-in-water emulsions stabilized by amphiphilic polymers

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Highly concentrated emulsions are dispersions with a volume fraction of dispersed phase larger than the critical volume fraction of 0.74, which corresponds to the most compact arrangement of uniform and hard spheres [1, 2]. Emulsions containing up to 99 % v/v of disperse phase may be prepared following convenient procedures.

In the last years there has been an increasing tendency to substitute molecular surfactants by chemically modified biopolymers to formulate suspensions of nanoparticles or emulsions [3]. Such polymeric stabilizers possess various advantages as compared to molecular surfactants like their strong adsorption at interfaces, their ability to form thick and viscoelastic adsorbed layers which provide efficient barriers against coalescence.

Dextran is a nonionic bacterial polysaccharide which exhibit a lot of reactive hydroxyl groups (3 groups in each repeat unit). Hydroxyl groups were used for covalent attachment of aliphatic or aromatic hydrocarbon chains along polysaccharide backbone through the formation of ether links. Hydrophobically modified dextrans were shown to exhibit surface active properties and to act as efficient emulsion stabilizers. When a limited amount of hydrocarbon groups were attached (less than 25 % of repeat units carrying one hydrophobic tail on average), oil-in water emulsions were prepared with submicronic or micronic droplets depending on the emulsification procedure [4-8].

In the present study, hydrophobically modified dextrans were used for the first time as stabilizers for preparing highly concentrated oil-in-water emulsions using a semi batch process with volume fraction of dispersed phase going from 0.8 up to 0.95. Various formulation parameters were varied (the volume fraction of dispersed phase, the concentration and the extent of hydrophobic modification of dextran, and the nature of the dispersed oil phase). Highly concentrated oil-in-water emulsions were characterized by determining their droplet size distribution and their rheological behavior. Adsorption of hydrophobically modified dextrans at oil/water interface was characterized in terms of kinetics of decrease of interfacial tension and dilational rheology. Results with amphiphilic polysaccharides were compared to those obtained with commercial amphiphilic block copolymers (Tween 80 and Pluronics).

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Pickering emulsions based on clays: fundamental investigations and potential applications

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Surfactant-free emulsions stabilized only by particles that are adsorbed at the oil-water interface have attracted in the last years the attention of academia and industry in view of their high performance features such as high-stability and enhanced protection of actives [1]. The use of this novel type of formulation concept paves the way for the development of products with new properties, to overcome drawbacks deriving from the use of surfactants (i.e. migration, irritation) [2] or even enhance their performance [3]. Though several different types of materials have been shown to act effectively as solid emulsion stabilizers, there is still room for enlarging the Pickering formulation space and exploring potential applications.

In this work we present the results of our investigations regarding the ability of seven types of natural clays, with different surface polarities and cation exchange capacities, to stabilize oil-in-water emulsions. The effect of clay concentration, salt, pH and dispersed oil phase on the emulsion properties will be discussed and the performance of the clays illustrated in comparison to the synthetic clay Laponite. Furthermore, replacement of surfactants by natural clays in cosmetic formulations will be discussed with special emphasis on the rheological properties of the corresponding emulsions.

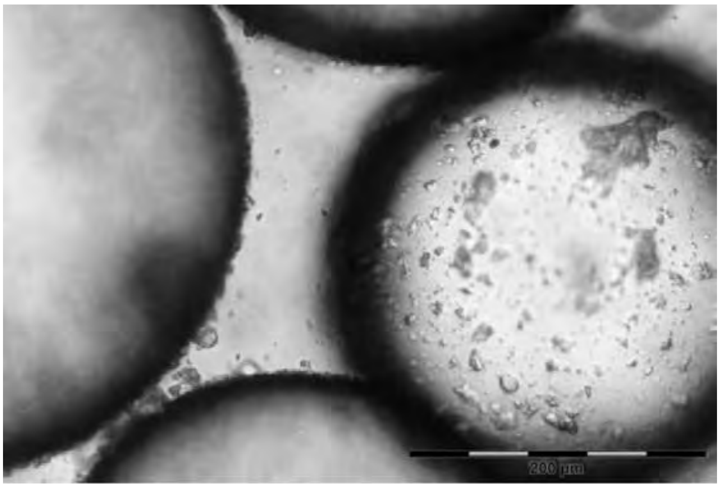

Figure 1. Microscope image of clay-stabilized oil-in-water emulsion.

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Stimuli-responsive capsules based on pickering emulsion

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Microencapsulation is used to protect actives in cosmetics, paints and pesticides useful for our daily life. The diversity of applications and the variety of encapsulated products offer large industrial prospects. Thus, encapsulate ion is an extremely dynamic area of research, showing multidisciplinary and tremendous competition.

We propose a synthesis path that combines emulsions science and sol-gel chemistry, where Pickering emulsions and the associated limited coalescence allow generation of monodisperse drops. In a second step, to obtain capsules, a shell is synthesized around the droplets. Indeed, the sol-gel method allows the formation of a rigid and brittle shell at the oil/water interface by hydrolysis and condensation of a silica precursor, the tetraethyl-orthosilane (TEOS) [1,2,3].

Taking the benefit of this process, we synthesized capsules constituted of a dodecane core and siliceous shell. Varying the amount of silica particles and TEOS, it is possible to obtain a range of capsules. This type of approach offers an interesting route to provoke the release by a mechanical threshold pressure [4].

After one step polycondensation synthetic path, we reached limited shell thickness from 43 to 115 nm with a resistance against the application of an external pressure from 0.5 to 6 MPa [5]. When addressing a sequential mineralization route, we were able to reach both better shell homogeneity, higher values of shell thickness and better resistance to breaking under pressure (See Fig.).

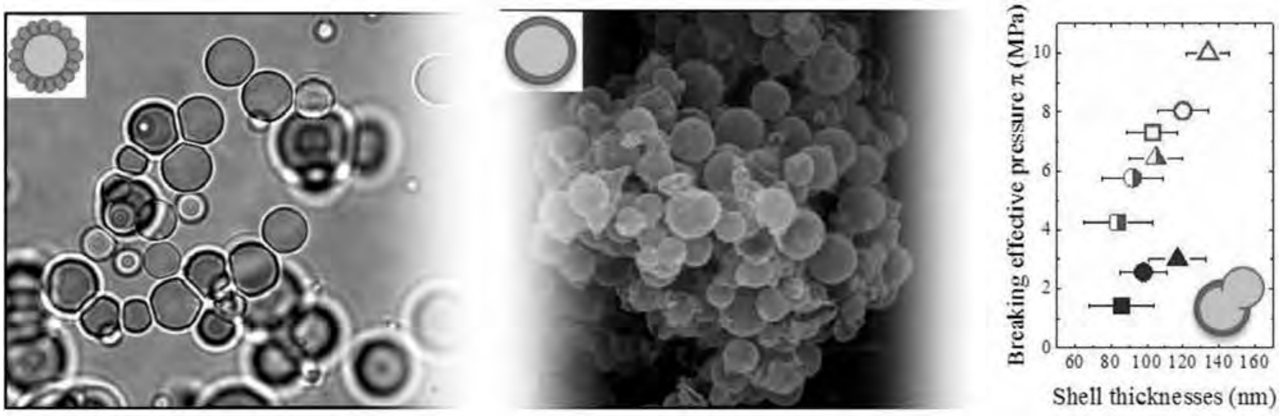

Figure. Representation of the process from Pickering emulsion formulation to the capsule breaking

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High internal phase emulsion stabilized by whey protein isolate-low-methoxy pectin complexes

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This work describes a formulation of surfactant-free high internal phase emulsion (HIPE) stabilized by whey protein isolate-low-methoxy pectin complexes. This HIPE has several advantages compared to HIPE stabilized by whey protein isolate, including close packing of particles at the oil-water interface, improved the emulsion stability, and improved structural-rheological properties. The particle size of the biopolymer complexes, oil droplet size and microstructure of the emulsions were evaluated. Moreover, rheology measurements (small-amplitude oscillatory shear rheometry and flow behavior study) were conducted to gain more insights into the properties of these new HIPE formulation. This formulation of high internal phase emulsion can be a viable strategy for structuring liquid oils into semi-solid fats without the use of saturated or trans-fats.

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Formulation of organic crystals in stirred media mills

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The demand of organic submicron particles in the pharmaceutical industry increased tremendously in the last decades. The fact that a high number of new drug candidates exhibit a poor aqueous solubility, which is associated with a poor oral bioavailability, formulation technologies such as particle size reduction techniques became more important for product engineering of drug particles to overcome problematic bioavailability issues. The reduction of particle size down to the nanometer range leads to an enhanced dissolution rate of the solid resulting in a higher oral bioavailability of active pharmaceutical ingredients (API) [1,2].

Structurally different crystalline organic model compounds were wet ground in a batch stirred media mill. Besides the commonly investigated key parameters stress energy (SE) and stress number (SN), the influence of process temperature on different product properties has been studied in detail. It could be shown that besides SE and SN the applied process temperature is a key parameter during processing of organic crystals. A positive effect of lowering the process temperature with respect to final particle sizes could be observed. It was found that the limiting product particle size is rather determined by the temperature-dependent solid–liquid equilibrium (dissolution and precipitation phenomena) than by fracture mechanisms [3].

Moreover, the influence of formulation paramteres such as type and concentration of applied polymeric stabilizers on the production of organic nanoparticles has been investigated. A relationship between limiting product particle size, polymer affinity and solubilization capacity has been observed. Thus, the smallest product particles were obtained applying excipients with a high affinity as well as small solubilization capacities, supporting the hypothesis that final product particles are rather determined by the (temperature- and excipient-dependent) solid-liquid equilibrium than by pure mechanical fracture [4].

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OC 64

High-throughput development of micro-capsule containing formulations

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During recent years an increased interest has grown in the development and of application of micro-capsule containing formulations. Microencapsulation is a smart manner of improving the performance of formulated products. By using this technology, an active of interest can be isolated and kept unmodified for extended periods of time and be released (or not) upon a change of the surrounding environmental conditions to target specific needs.

Nowadays, microcapsules can not only be found in pharma products but in a huge variety of products and applications ranging from agricultural products as well as consumer products, like food, house and personal care products.

An important technique for microencapsulation involves emulsification and in situ polymerization processes. However, the development of new synthesis chemistries as well as optimizing the final formulated products is very often performed via a trial-and-error approach. This often results in a time consuming and error-prone process.

Therefore, Flamac has developed unique high-throughput platforms for accelerating the synthesis and testing of micro-capsules up to the formulation and testing of capsule containing formula. Firstly, a high-throughput platform has been developed for the accelerated synthesis and testing of micro-capsules. This allows us to select the right micro-capsules with targeted particle size distribution, mechanical strength, release properties, etc. Secondly, the formulation matrix can be optimized using a high-throughput formulation platform, aiming to develop a stable micro-capsule containing formula.

This presentation will highlight the successful use of these unique state-of-the-art technologies in areas such as personal care products and coatings. Besides new encapsulation and formulation chemistries also data regarding the added value of high-throughput methodologies compared to the traditional way of experimentation will be presented.

Figure 1: Picture of high-throughput formulation platform.

Fast temperature screening for viscosity determination of thermoresponsive polymers with innovative microfluidic device

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Viscosity is an essential physical property when studying polymers behavior. However rheological studies remain a challenging task for many laboratories as traditional techniques are time consuming and do not allow to measure samples in desired conditions. We propose a new instrument: FLUIDICAM to measure viscosity as a function of shear rate and temperature in a single experiment set-up. Using a small sample volume, the technology allows flow viscosity measurements of liquid products from water-like inks to thick formulations, under a wide range of shear rates (including high values up to 10^5 s^{-1}).

During the measurement a sample and a viscosity standard are pushed together through a microfluidic chip (Y-junction) at controlled flow rates. Images of the resulting laminar co-flow are acquired with digital camera and the position of the interface is measured. The position is related to the viscosity and the ratio of flow rates between the sample and the reference allowing to determine the viscosity.

In this work, bio triblock copolymers (Poloxamers–(PEO)x(PPO)y(PEO)x) and PNIPAm (Poly(***N***-isopropylacrylamide) were studied. They are well known for their reversible phase transitions (sol-gel) under specific thermal conditions and thus they are good candidates for innovative drug delivery systems, microgels, biosensors… We have used solutions at various concentrations to measure the viscosity in function of the flow rate between 5 and 80°C in less than an hour (5min per temperature step). This work will demonstrate the influence of the polymer concentration on sample behavior and viscosity demonstrating the capabilities of FLUIDICAM to conduct fast temperature screening measurements and sharp viscosity measurements.

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Anisotropy in liquid crystalline phases as detected by natural levels of D2O: an NMR method to characterise gel phases.

Mendoza, C., Cooke, M, Hughes, E., Apperley, D., Tiddy, G.J.T.

For many years proton (^{1}H) NMR has been employed to examine the structure of soft solid formulations. Deuterium NMR has been used extensively to investigate ordering and anisotropic motion in solids, but the low natural abundance of ^{2}H has prevented applications to formulations because of the need to add D_2O to the product – an expensive procedure. There are distinct advantages to the employment of ^{2}H NMR because ^{2}H possesses a nuclear quadrupole which splits the NMR signal into multiple lines. This splitting is modulated by molecular motion, in particular rotations of bonds and molecules. It has been used previously to investigate anisotropic liquid crystals, especially liquid crystal systems whose properties are dependent on the water concentration. In many commercial food and cosmetic systems or in biological samples, the anisotropic phase may produce only weak quadrupolar splittings and these may be drowned out by the NMR signal arising from the isotropic components present. To overcome this problem a double quantum deuterium NMR experiment may be performed that essentially picks out components of the water signal that are in an anisotropic environment. Water arising from isotropic environments within the complex sample does not produce a double quantum signal. During the NMR experiment there maybe exchange of water between isotropic and anisotropic environments. These exchange dynamics can further modulate the signal, reducing the final double quantum signal observed. Therefore, quantitative analysis of the double quantum signal in terms of the amount and extent of different anisotropic phases present in the sample is complex.

In this study we have used deuterium NMR to investigate the stability of a number of samples of gel phases, where the sample composition has been systematically changed. Gel phases are notorious for exhibiting slow changes in properties with storage time, particularly the viscosity. The aim of the study was to see if the experiment could follow the shelf-life of the materials in terms of the presence of an anisotropic phase and its development during the course of storage. Pilot plant samples of gel phases were dosed with added D_2O, and ^{2}H spectra taken over a period of months, along with parallel X-ray and rheology measurements. The results give an insight into the changes in anisotropic phases responsible for the changes in product properties. During the course of the investigation we recorded spectra of samples with no added D_2O. Not only were the normal single quantum spectra readily observed, but we were able to obtain double quantum spectra. This technique should be applicable to a wide range of soft solid products, giving information on product structure not available by other methods.

Nanoformulation: Water-in-diesel fuel- Preparation (Using High-Energy Emulsification Method), stability and physical properties.

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The aim of this research is to develop alternative fuel system with reduced exhaust emissions, reduced cost, increased transportability (due to increased flash point), and increased efficiency of diesel engine. The proposed alternative fuel system in this paper is "water in diesel nanoemulsion". The effect of surfactant concentration and HLB value on stability of emulsion is studied by preparing the emulsions with varying composition of fuel blends within HLB range of 1.8-10.6. The main focus of this study is to enhance the stability, transparency by selecting optimum proportion of emulsifier, water and fuel constituents. Emulsion stability is further enhanced by using suitable co-surfactants with proper concentration. Fuel properties (such as density, viscosity, flash point, pour point, stability) of the selected blends was examined and compared to those of conventional diesel. In comparison with diesel, increases in viscosity, density, and flash point is observed. Most important thing to be noted is that, our nanoemulsion system is found to stable for more than 180 days with mean droplet diameter 106.7 nm and polydispersity index is 0.195.

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OC 68

Novel Photocatalyst-Composite Membrane Filter for Treatment of Pharmaceutical Residues and Other Organic Pollutants in Waste Water

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Background Toxic organics, pharmaceuticals and antibiotics are currently only partially or not at all removed from wastewater, as waste water treatment of today will only to low extent degraded those substances. Therefore those substances will be found in the effluent from the waste water treatment plants and this is seen as a possible threat to both human health and aquatic species.

Photocatalytic membranes are known as a potential application in water and wastewater treatment , which show great promise as novel methods to combat the challenge of toxic organics in waste water.

Membrane and filtration set-up

For this study a photocatalytic membrane has been prepared by integrating photocatalysts into the membrane structure, see Figure 1. The membranes were produced aiming for 100 micrometer thickness of the membrane, which was achieved, see Figure 2.

A dead-end membrane filtration set-up was constructed and used see Figure 3.

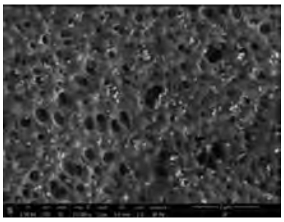

Figure 1 SEM image of the membrane showing the photocatalysts on the PVDF membrane.

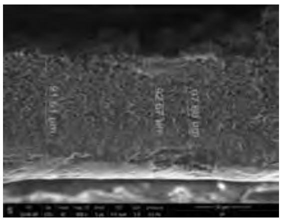

Figure 2 Membrane thickness shown in a cross section of the membrane.

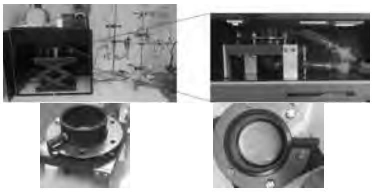

Figure 3 The dead-end membrane filtration set-up used, with a close up of the membrane when fitted into the holder.

Results

As seen in Figure 4, many of the investigated pharmaceuticals can be removed to high degree using fotocatalytic membrane filtration. While some of pharmaceuticals are removed to a large degree even without using UV light, (Citalopram, Setralin, Fluoxetine and Risperidone) others show high removal rate only when UV irradiation is used. This is expected due to the large variations in chemical structure between the different substances.

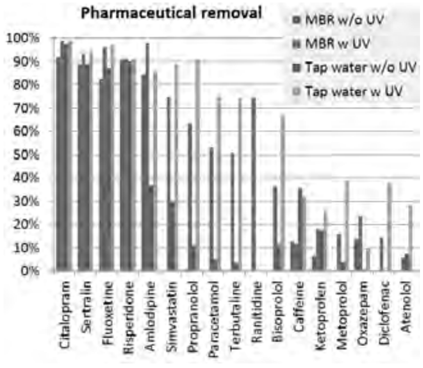

Figure 4 Removal of pharmaceuticals from spiked tap water, and MBR effluent, with and without irradiating the photocatalytic membrane during filtration. (w= with UV light irradiation w/o= without UV light irradiation.

Conclusion

Photocatalytic membrane filtration has shown great promise for degradation of pharmaceutical residue.

The final part of the project will:

a) analyze the reasons behind the differences observed between the three categories of pharmaceuticals: 1) removed with membrane, 2) degraded with membrane + UV irradiation, 3) not removed.

b) optimize the running conditions of the unit

Determination of density of emulsion droplets and inner dispersed phase fraction of W/O/W double emulsions

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Water in oil in water (W/O/W) double emulsions [1, 2] are multi disperse liquid systems in which droplets contain other droplets (Fig.1). They have been the subject of research and product development since several decades, because innovative product requirements (e.g. drug loading, delayed release, protection from degradation, product texture) may be realized by this technology. For the effective development and production of such complex emulsion systems measuring methods are needed which are suitable to characterize emulsion stability and applicable also under industrial conditions. The quantification of the inner dispersed phase fraction (DPF) plays a crucial role in adjusting and control of the product properties.

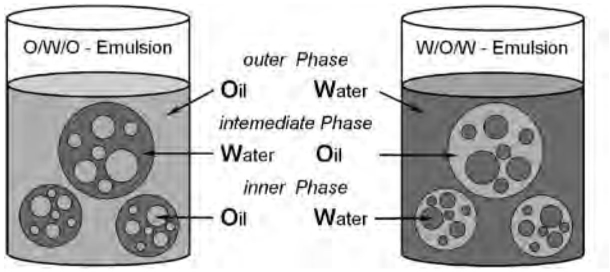

Fig. 1: Schematic drawing of double emulsions. The outer and the inner phase may be the same. However, they may differ by their chemical compositions. The inner phase forms the inner droplets and the intermediate phase, the outer droplets.

The DPF quantifies the mass ratio of the inner water phase *i* to the total mass of the emulsion: ϕi=mijmj=mimgesamt Changes in the DPF and thus the mass ratios therefore reflect a changed composition of the outer droplets and hence an altered integral droplet density. Using an innovative approach for direct and accelerated measurement of separation rate of dispersed droplets in emulsions by analytical photocentrifugation (LUMiSizer®, LUM GmbH, Germany) [3] a method was established to determine the density of the droplets. In this paper we describe a new approach to determine hydrodynamic density of emulsion droplets [4], which was recently also applied to determine particle densities in liquid environment based on experimentally measured separation rates and the Archimedean and Stokes Laws.

The method is described in detail and first results on droplet density of different single and multiple emulsions are presented and discussed (Fig.2).

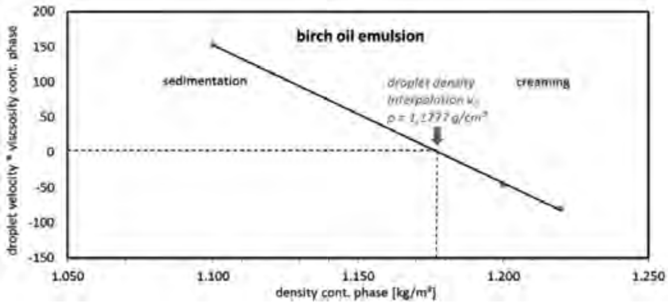

Fig. 2: Normalized droplet velocity as a function of the density of the continuous phase of a birch oil emulsion. Calculation of the droplet density by interpolation on the density of the continuous phase at the droplet zero velocity. Separation Analysis: LUMiSizer®, 7°C, 3000 rpm, 865 nm

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OC 70

Green synthesis of silver nanoparticles in microemulsion media

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The green synthesis of nanoparticles offers a new sustainable way in the obtention of metal nanoparticles. In this context, the use of microorganisms and plant extracts has been studied in the recent years, being the latter methods the best alternative due to the ease and efficacy in the reduction of metal ions by certain plant extracts because of the presence of a high content of antioxidants [1]. Consequently, no hazardous chemicals for environment and living organisms are involved. However, depending on the reaction media the polydispersity of sizes in the nanoparticles obtained vary and is one of the great disadvantages [2].

The synthesis of nanoparticles in microemulsions presents advantages for the control of size and shape [3]. Water-in-oil (W/O) and oil-in-water (O/W) microemulsions are used for production of metal nanoparticles and interestingly it has been reported that O/W microemulsions are advantageous in the obtention of stable colloids [4]. However, the systems used until now are mainly composed of organic solvents derived from petroleum which are non environmentally-friendly [5]. New studies replacing these petroleum-based oils with vegetable oils are emerging and giving new options in microemulsion formulation [6,7]. Vegetable oils are composed of mixtures of long-chains triglycerides and are a challenge for the formation of microemulsions. Only few reports on the formation of microemulsions using vegetable oils as oil component have been published and the microemulsion formation zone in the corresponding phase diagram is very small [8]. The study of microemulsions formation in systems with vegetable oils and plant extracts is important for the development of new and green reaction media for the production of metal nanoparticles in an ecofriendly way and using soft reaction conditions.

The objective of this work is to propose a new methology for production of silver nanoparticles in a green way using microemulsions without or with low-risk for the environment and living organisms. Thus, in the present research new microemulsion systems with castor oil, a nonionic surfactant and geranium leaf aqueous extract (as reducing component) were used as nanoreactors for the synthesis of silver nanoparticles. Microemulsion formation was determinated by mean of phase diagrams. The synthesis was carried out in both W/O and O/W microemulsions. The nanoparticles obtained in this green synthesis in microemulsion media were characterized by different techniques (UV-Vis, FT-IR, zeta potential, dynamic light scattering (DLS) and electron microscopies). The properties of the nanoparticles obtained have been related to those of the template microemulsions.

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About microemulsion-based gels, reversible adhesives and structured emulsions, 30 years research and industrial applications of block copolymers

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This talk is a journey through some of the multiple facets of block copolymers as functional polymers in formulation. It is also a retrospective of the author's academic and industrial research in this area over the last 30 years, exemplified by the discussion of three case studies and their implementation in day to day products.

The first part of the talk is dedicated to microemulsion-based gels, nanogels and transient networks, from their discovery in the 80's to the most recent advances as delivery systems and texturing agents in cosmetics. The second part is about the application of POE/POP block copolymers in emulsion polymerization and their impact on the adhesive profile of waterborne adhesives. The third part deals with PE/POE block copolymer-reinforced lamellar crystalline phases for the controlled release of small and volatile molecules, such as fragrances.

The structure-property relationships are discussed, emphasizing the importance of phase diagrams and macromolecular properties, such as block length, morphology and dynamics.

As a conclusion, we attempt to identify new perspectives for block copolymers in formulation, based on what is missing today and future requirements.

ORAL COMMUNICATIONS

OC 72

Optimum Formulation for Maximum Encapsulation in Multiple Emulsions

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Multiple emulsions or double emulsions have considerable potentials for breakthrough applications in cosmetic, food, agricultural, and pharmaceutical in which they can assist the sustained release and transport of active materials.[1] Multiple emulsions are usually produced by two-stage emulsification methods using at least two types of surfactants; one hydrophilic (with high hydrophilic-hydrophobic balance (HLB) and one hydrophobic (with low HLB).[2] Multiple emulsions usually have strong tendency for coalescence, flocculation and creaming. For these reasons, the emulsification process and formulation variables have to be rightly assigned in order to reconcile two opposing emulsion morphologies together into one single emulsion.[1] The stability of multiple emulsions has traditionally been studied during post preparation over a long time in terms of hours and days, if not months.

In this research, we aim to investigate the effects of different formulation and process variables on the encapsulation efficiency of multiple emulsions during their fabrication (i.e, short-term stability) which occurs within several minutes. We monitor encapsulation efficiency with time using a model for the internal droplet exit that also represents the time evolution of emulsion morphology. We show how instability of multiple emulsions during emulsification can be tracked and how that significantly affects the encapsulation efficiency. The results show that with increasing dispersed phase ratio of the primary emulsion the encapsulation efficiency decreases (Fig. 1a), while the encapsulation efficiency remains resilient to changes in dispersed phase ratio of the secondary emulsion. We systematically show that there is a range of agitation speeds for preparation of primary and secondary emulsions which gives a maximum encapsulation efficiency (Fig. 1b). We demonstrate how changes in surfactant concentration and phase ratio can easily be translated into the changes in the average emulsion HLB. This can have a significant impact on the properties (encapsulation efficiency, drop size, etc.) of the multiple emulsions beyond the intended change.

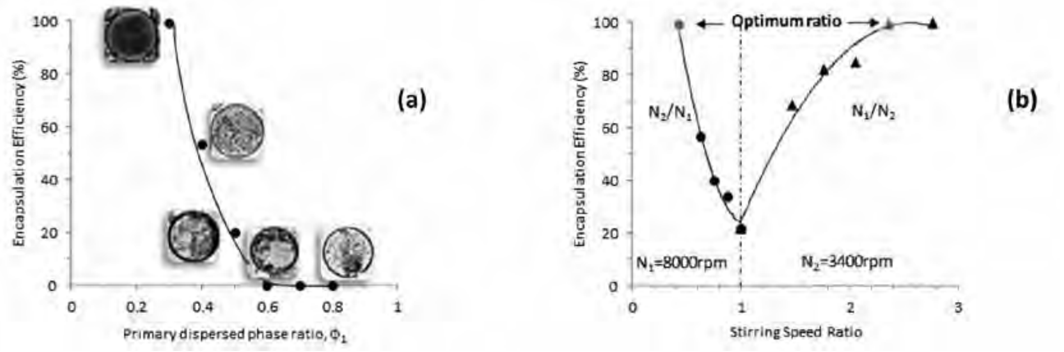

Fig. 1. Effect of (a) phase ratio of primary emulsion, and (b) ratio of primary (N_1) and secondary (N_2) emulsification stirring speed on encapsulation efficiency right after formation of the multiple emulsion.

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Formulation of industrial relevant enzymes

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Industrial enzymes are an attractive market with high annual growth. They are key performance enablers for food & feed applications and for detergent formulations in the laundry area. New methods and appropriate enzyme formulation approaches are of crucial importance to protect enzymes against environmental influences. In addition to the established phytases and proteases, BASF will focus in future on the formulation of different enzyme classes as well. Fundamental knowledge is necessary to formulate enzymes without any loss of enzyme activity which is directly connected to the performance and subsequently to the margin of the product.

We will present different strategies (e.g. polyelectrolyte complexes, coacervates, hydrogels, encapsulation processes) to formulate enzymes. These approaches enable the design of both liquid and solid formulations for stabilizing and delivering enzymes. The aim is to provide stabilization and activity in applications using enzymes with activities greater than average. Afterwards, the colloidal and physico-chemical stability was characterized in terms of size, size distribution, electro-kinetic potential, and morphology. The thermodynamic parameters of interactions in solution were analyzed by calorimetry. Enzyme shelf life was checked by specific enzyme test assays and showed promising results with regard to their potential in stabilizing enzymes.

OC 74

Immuno-modulatory PPH dendrimer: from systemic to topical delivery?

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We have shown that a series of phosphorus-containing dendrimers (PPH dendrimers) terminated with phosphonic acid functions provide ***ex-vivo*** an early activation and/or amplification of various immune cells subsets (monocytes,[1] NK cells[2]…). Dendrimers are highly branched macromolecules with a precise structural topology which offer unprecedented possibilities for accurate macromolecular engineering. In this respect, we have followed a wide-scope study to measure the influence of structural parameters of dendrimers on these biological studies, and a lead compound **G1-ABP** was identified.[3]

This compound is currently under preclinical evaluation for the treatment of Multiple Sclerosis (MS) and Rheumatoid Arthritis (RA) by systemic administration, and we have initiated preliminary studies to evaluate the potential of this compound for topical applications, for which formulation is a pivotal issue.

The presentation will focus on a brief presentation of the discovery of dendrimer **G1-ABP**, its *in-vivo* properties for the treatment MS[4] and RA[5] in murine models and its safety profile on murine models and non-human primates.[6] Recent results and issues regarding its formulation for topical purposes will also be discussed. Actually, Psoriasis exhibit common immune disorders with RA and MS (and common therapeutic strategies), and we have recently demonstrated the promising topical efficacy of **G1-ABP** *in vivo* in an Imiquimob-induced mouse model of psoriasis.

In order to improve the topical penetration of this dendrimer, we have prepared pre-formulation of ABP-like dendrimer candidates with skin penetration enhancers. The resulting catanionic surfactant associations are prone to form spontaneous vesicles[7] that can delay and control the dendrimer release[8]. Further experiment will be dedicated to the entrapment of these "dendrimer reservoirs" in biocompatible and tunable hydrogel matrixes.

Notes

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Embracing the Circular Economy with Enzyme Technology

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The circular economy is embraced by the entire detergent industry and Novozymes also support the topic by enabling our partners to become more circular and durable while delivering at the moment of truth. Consumers mind the end result and more and more seems to beyond cleaning – but also caring.

Novozymes see enzyme inclusion as a mean to become more circular and to improve both the sustainability profile of the detergents but certainly also the performance profile even at low temperature which levers the opportunity for claim building to make or keep brands competitive and relevant for the consumer.

In several European markets cold wash is being promoted. This combined with detergents containing high water content or high pH as well as tough storage conditions the new bio-technological solutions from Novozymes will enable a best in class enzyme performance by improving protein as well as starch soil removal. The solution will allow formulators to reduce or remove stabilization systems based on chemistry which could be of concern.

OC 76

Formulation of Ceramic Foams: a New Class of Amphiphiles

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Ceramic materials have a key role in catalysis due to their use as catalyst supports. Recently, there has been a significant growth in interest in their use as an alternative to traditional catalyst supports due to the increased macro-porosity of the foam leading to reduced transport resistance. Ceramic foams can be produced by different methods such as replica technique and direct foaming [1]. In the latter, air is directly introduced into a ceramic slurry leading to the formation of a stable wet foam. The structural properties of this foam (e.g. porosity, pore size distribution) are strongly affected by the initial formulation of the ceramic slurry [2]. In particular, the surface properties of the ceramic particles are modified by the addition of an amphiphile resulting in different foam structures depending on the degree of particle hydrophobisation.

In this work, a new class of amphiphiles is proposed and assessed that is more environmentally benign and present a wider operational window than those reported in the literature. The effects of the amphiphile concentration and structure on the foam properties were investigated. Water pick up experiments and image analysis of SEM images were used to determine the foam porosity and pore size distribution respectively.

Surface tension measurements were used to establish a hydrophobicity index for the different amphiphiles. A linear relationship between the hydrophobicity index and the maximum porosity obtainable was found. This strong correlation allows a priori selection of the most appropriate amphiphile depending on the desired foam properties opening up to the possibility of tailoring the structure of ceramic materials.

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Enhancement of a green emulsion stability by tuning its formulation and processing.

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There is an increasing interest in new eco-friendly solvents due to the need to replace some traditional organic solvents. N,N-dimethyldecanamide (AMD-10™/BASF) is considered a safe bio-solvent, according to the Environmental Protection Agency. However, emulsions only containing AMD-10™ in the dispersed phase show destabilization by Ostwald Ripening. In order to solve this problem, other green solvent can be added to the formulation. D-Limonene, a naturally occurring terpene, has recently received much interest due to its bactericide, antioxidant, chemo-preventative properties [1]. Emulsions were formulated with 30 wt% or 40 wt% dispersed phase (75 AMD-10™/25 D-Limonene mass ratio) and a polyoxyethylene glycerol ester surfactant (Levenol® C-201). The latter possesses an eco-label (DID list: 2133). The optimum ratio of solvents was previously determined by Santos et al [2]. The objective of the present research was to evaluate the influence on droplet size distribution (DSD), stability and rheology of these emulsions of a) homogenization rate (3000-8000 rpm) in a rotor stator device equipped with a fine emulsor screen and b) dispersed phase content. The laser diffraction technique revealed that an increase in homogenization rate yielded a decrease in droplet sizes. Emulsions exhibited shear thinning behavior, which fitted the Cross model. The zero shear viscosity increased with both the dispersed phase concentration and homogenization rate. It must be noted that a great jump in zero shear viscosity was observed from 5000 to 6000 rpm for 40 wt% emulsions, probably due to a flocculation process. Furthermore, 40 wt% emulsions processed above 5000 rpm exhibited viscoelastic properties and showed flocculation-induced coalescence with aging time, whereas creaming was the predominant destabilization process in 30 wt% emulsions.

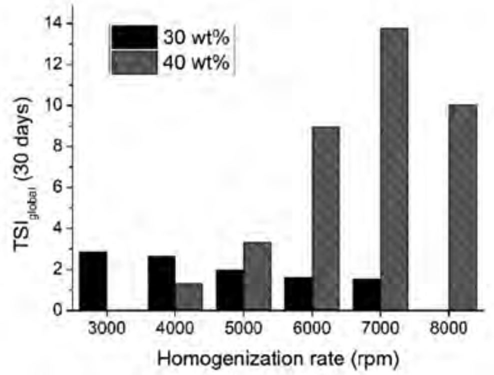

Figure 1. Turbiscan Estability Index (TSI) for all emulsions studied at 30 days of aging time.

The TSI was used to quantify all destabilization processes. It showed that the stability enhanced at higher homogenization rates in 30 wt% emulsions, conversely to 40 wt% emulsions. The most stable emulsion was achieved with 40 wt% dispersed phase using 4000 rpm. Interestingly, a more concentrated emulsion was achieved using less energy input.

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OC 78

Encapsulation by supercritical fluid and pressurised gas processing

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We present the use of compressed, liquefied gases (carbon dioxide, dimethyl ether or propane) as anti-solvents to precipitate natural products such as polyphenolics from solutions, including the enablement of microencapsulation, toward food or nutraceutical formulations.

The use of pressurised solvents in natural product processing is beneficial due to the ability to recycle the solvent within the system as an alternative to the use of large volumes of liquid solvents, and can offer novel advantage in terms of process and product control [1, 2]. Supercritical CO_2 is commonly used as a food grade solvent; similarly, dimethyl ether (DME) and propane are also suitable for food products; a key process benefit being the high volatility of the solvent employed. The theory and application of supercritical and near-critical fluids toward microencapsulation is discussed.

An example process is presented here whereby a fruit polyphenolic extract is microencapsulated with dairy proteins by precipitation from an aqueous solution using DME as an anti-solvent to yield a dry, uniform powder. The product is characterised by its protein and polyphenolic content and by analysis of its physical characteristics (see Figure 2 for SEM images of the powder products). This process offers benefit by directly producing a functional product in one step, without the use of organic solvent or further drying step, under mild temperature (40 – 60 ºC).

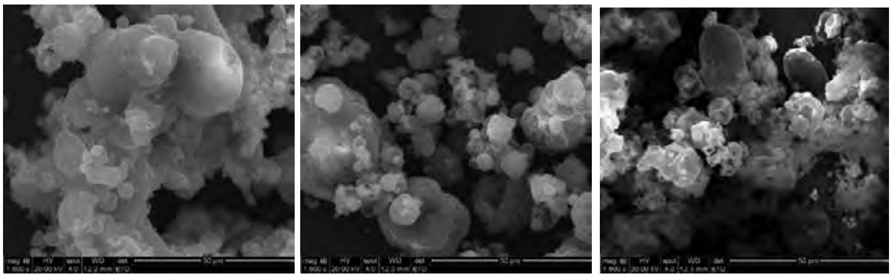

Figure 2. From left: Protein powder before treatment; protein-polyphenol particles from anti-solvent DME process; protein-polyphenol particles by spray drying.

The fruit polyphenols were found to bind to the tryptophan residues of whey proteins, with the process offering some selectivity toward binding of different phenolic classes.

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Glucamide as a bio-based sugar surfactants for home care

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The demand for renewable sources as an alternative to fossil origin of consumer goods is growing steadily. Nevertheless, the majority of used surfactants in cleaning products is still based on nonrenewable petroleum. On the other side an analysis of purchasing behavior in home care of the past 10 years shows that whilst the economic value of a product is the customer's top concern, the importance of ecological aspects is constantly increasing. Besides the quality evaluation, which is taken from the buying habits, the power of a protective label like the Nordic Swan and the EU Flower or more recently the "Blauer Engel" have increasingly gained importance in the decision making process.

The combination of corn-derived carbohydrates with renewable fatty acids results in bio-based sugar surfactants with a renewable carbon index of 94% or higher and no aquatox labelling. In addition to this, the so called "Glucamides (GlucoPure® Series) have an outstandingly small distribution to the critical dilution volume, which is of more and more importance with the increasing demand for ecolabels by the consumer market.

Besides the major eco criteria, performance is fundamental for sustainable products to reduce water and energy waste during the use. Standard application tests prove that Glucamides are high performers in various home care applications, providing the optimal combination of efficiency and eco friendliness.

OC 80

Benefits of Particular Silicones for Protecting Hair Fibers against Heat Damage

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Nowadays, consumers use more and more heat-styling devices, such as high temperature blow-dryers and straightening and curling irons, to obtain longer lasting or trendy hair styles. In paradox, repeated use of these devices considerably damages the hair fibers and leads to reduction in the hair's healthy appearance (1, 2, 3, 4). Polydimethylsiloxanes and their derivatives have been used for many years to smooth the cuticles and provide reduced friction to hair, facilitating hair manageability. Little information existed on the heat protection performances of silicones using test methods close to consumer habits. Additionally, comprehension of their action mechanism was still vague. This study explores the ability of particular silicones to considerably reduce fiber heat damage, without compromising hair styling.

Test protocols close to consumer habits were developed to reproducibly treat and heat damage different hair types such as slightly bleached Caucasian hair or Latino Curly hair. Tresses treated with different silicones were consistently exposed for 2 min into a calibrated oven from 130 up to 240°C and compared to untreated tresses and/or control formulation. Best performers were identified, such as:

- Bis-Hydroxy / Methoxy Amodimethicone
- Amodimethicone (and) Cetrimonium chloride (and) Trideceth-3 (and) Trideceth-15
- Bis-Diisopropanolamino-PG-propyl Dimethicone/Bis-Isobutyl PEG-14 Copolymer (and) Polysorbate 20 (and) Butyloctanol

Mechanical resistance of heat damaged hair fibers was evaluated using hand combing test to quantify the weight of broken fibers of wet tresses. Results show a significant reduction of broken hair when hair is treated with non-functional silicones. Results also demonstrate further protection with specific functional silicones, as well as improved styling. To understand the protection mechanisms of these silicones, a list of hypothetical factors was first dressed. Modelisation of these hypotheses helped to predict main factors contributing to silicone heat protection. Theory was finally validated in practice through a series of qualitative and quantitative tests. This study used IR camera for temperature analysis, optical microscope for cuticle integrity protection, stereomicroscope for hydrophobicity preservation and SEM EDS to understand how the silicones deposit on hair.

In conclusion, this study is based on a new method, close to typical consumer regimes, to evaluate heat protection of hair. It also includes potential mechanisms to understand how specific silicones can lead to heat protection benefits. Finally, it demonstrates that, by choosing the right silicone technology at the right addition level, heat protection can be optimized, helping to preserve the natural strength and volume of hair.

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Amorphization of crystalline pharmaceutical active ingredients via formulation technologies

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Biopharmaceutics Classification Scheme (BCS) Class II drugs are notorious for their low aqueous solubility, which hampers its bioavailability and delivery to the human body. There are various approaches to improve the dissolution of this class of drugs via formulation techniques have been reviewed in literature; some examples include micronisation/nanonization, amorphization, soluble complexes and use of lipid formulations. In this study, three different formulation technologies such as co-milling (COM), co-spray drying (SD) and supercritical anti-solvent (SAS) process were used to amorphize indomethacin (IDMC) with a water-soluble polymer excipient poly(vinylpyrrolidone) (PVP) to achieve dissolution rate enhancement. Formulations were conducted at IDMC to PVP ratios of 60:40, 50:50 and 20:80 for the three processing techniques. The untreated, COM, SD and SAS powders (before and after storage) were characterised using scanning electron microscopy (SEM, morphology), X-ray powder diffractometry (XPRD, crystallinity), USP dissolution tester, Fourier transformed infrared spectroscopy (FTIR) (IDMC-PVP molecular interactions) and thermogravimetric (TGA, composition). Accelerated physical stability stress tests were also conducted on COM, SD and SAS co-precipitates in open pans at 75% RH and 40 °C in order to evaluate their physical stability. SD and SAS co-precipitates with PVP contents more than 40 wt.% were X-ray amorphous form and remained stable after more than 4 months of storage at 75% RH and 40 °C. COM powders with PVP contents less than 50 wt.% re-crystallized after 7 days of storage at 75% RH and 40°C. Raman mapping measurements on COM, SD and SAS samples (IDMC:PVP=60:40) were performed using a Raman microscope and the collected data were further analyzed using the band-target entropy minimization (BTEM) algorithm in order to have a better understanding on the differences in physical stability of COM, SD and SAS co-precipitates.

OC 82

Antimicrobial soft contact lenses using formulated peptides

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This work presents novel formulated materials bearing antimicrobial peptides for contact lenses with the potential to minimise corneal infection risk. Although commercial contact lenses already show excellent performance, up to date they do not exhibit anti-bacterial properties. It is well known that one of the most common problem related to contact lenses is associated with the risk of eye microbial infection. This is a significant health issue given the large population of contact lenses wearers worldwide [1]. In this study, contact lenses (or associated materials) functionalised with antimicrobial peptides were developed; these materials offer the prospective of reducing microbial infection thus significantly improving quality of life and diminishing health care costs relative to such a risk. Our approach, based on chemical modification of commercial contact lenses, permits to achieve enhanced products without altering the bulk material features. Commercially available soft contact lenses are hydrogels made of copolymers mainly based on 2-hydroxyethyl methacrylate (HEMA) and polisiloxanes. These materials contain hydroxyl groups that provide a suitable platform for prompt functionalization, either through electrostatic and van der Waals interactions, or through covalent bonding (Figure 1A). Antimicrobial peptides (AMPs) are suitable candidates for this purpose, as they exhibit excellent antimicrobial activity and may present advantages against strains resistant to traditional antibiotics [2]. Antimicrobial peptides with a broad spectrum activity were immobilized in thehydrogels and their stability was evaluated. Full characterization was performed through different analytical techniques such as contact angle measurements, Raman spectroscopy and fluorescence studies (Figure 1B). All these aspects will be discussed within the frame of product development.

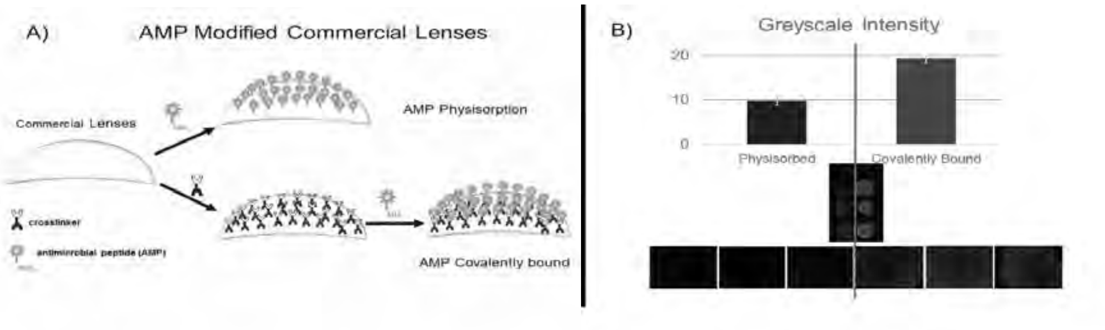

Figure 1. A) Schematic representation of AMP modified soft contact lenses. B) Fluorescence studies on the AMP modified contact lenses and relative greyscale intensity.

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Hyaluronic acid gels containing liposomes for the sustained delivery of a corticoid to the inner ear: Formulation, characterization and evaluation

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Nowadays, inner ear diseases are not adequately treated by systemic drug administration mainly because of the blood-perilymph barrier that reduces exchanges between plasma and inner ear fluids. Therefore, local drug delivery methods are currently developed to treat inner ear disorders more efficiently [1]. However, the inner ear remains one of the most challenging target organs for drug delivery. Transtympanic injection is a promising approach in otology. It involves the injection of the drug into the middle ear using a fine and long needle and relying on the diffusion of the drug through the round window membrane for access to the inner ear. However, this method requires a specifically developed pharmaceutical formulation in order to enhance its efficiency and reduce the number of injections. This work evaluates a new formulation based on the incorporation of liposomes within a hyaluronic acid (HA) gel as a sustained drug delivery system to the inner ear. Indeed, HA may allow a long residence time into the middle ear thanks to its mucoadhesive properties whereas liposomes could act as a reservoir for a sustained release of the drug. In this study, the physicochemical properties (phase behavior, rheological behavior, microstructure, and mobility of the liposomes) of such mixtures were thoroughly assessed for HA at different concentrations and for liposomes characterized by different surface properties (positively or negatively charged, neutral, with a corona of polyethylene glycol (PEG)). Above the polymer entanglement concentration, the viscosity and the elasticity of the HA solutions increased with the addition of liposomes, the highest effect being observed with PEGylated liposomes. Despite their high viscosity at rest, all formulations remained easily injectable in conditions used for transtympanic injection [2]. PEGylated liposomes also displayed the best mobility into HA both microscopically (single particle tracking measurements) and macroscopically. This result might be explained by the bicontinuous structure of this gel, as observed by atomic force microscopy. The most promising formulation for transtympanic injection was thus obtained with PEGylated liposomes and was used for the encapsulation of a corticoid, dexamethasone phosphate (DexP), into the vesicles. The safety of the liposomal gel was then evaluated ***in vivo*** in Guinea pig and biodistribution studies were performed. The administration of HA liposomal gel in the middle ear appeared to be a safe and efficient strategy to deliver corticoids to the inner ear in a sustained manner.

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OC 84

Stability of immobilised β-galactosidase on meso-macroporous silica support

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β-galactosidase (EC 3.2.1.23), most commonly known as lactase, plays an important role in human nutrition once it acts on the hydrolysis of lactose, the predominant sugar in milk. Lactase catalyzes the breakdown of lactose into glucose and galactose. An appropriate amount and a good activity of this enzyme are required in the small intestine in order to avoid the passage of the undigested lactose into the colon, and consequently the manifestation of lactose intolerance. In order to prevent the symptoms of this syndrome, appropriate lactase levels could be reinstated by the oral supply of the enzyme that should be protected against the extreme stomach conditions. A common strategy to increase the stability of enzymes consists of their immobilisation on a support material. Lactase has already been immobilised on several materials such as chitosan, cellulose and dioxide nanoparticles by physical or chemical interactions. [1] These studies have demonstrated the enhancement of enzyme's stability under different pH and temperature conditions, following the immobilisation process.

In this context, we are currently studying the stability of β-galactosidase after physical adsorption on a meso-macroporous silica support, material not used before for this purpose. This silica support has been synthesised through a dual templating mechanism combining solid lipid nanoparticles (SLN) and surfactant micelles. Recently, SLN have been proposed an adequate template for silica materials in order to be used as carriers for drugs delivery. [2][3]

The present study shows the results concerning lactase stability under different conditions, after immobilisation on the silica support. *Ortho*-nitrophenyl-β-galactoside (ONPG) has been used as substrate to estimate the enzyme activity. β-galactosidase hydrolyses the ONPG, resulting in the production of galactose and o-nitrophenol (ONP) that is measured by spectrophotometry at wavelength of 420 nm. The stability of free and immobilised lactase is being compared under different pH and temperature values. Moreover, some of our results are showing that the supported enzyme is still being active 6 months after immobilisation.

Acknowledgements

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Encapsulation of *L. rhamnosus* GG (LGG) in Alginate-Silicate hybrid beads

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One way to reestablish the microbiota equilibrium is to administrate functional food containing probiotic cells (***e.g.*** LGG). To insure protection of the living matter during food processing and gastrointestinal transit, encapsulation is oftentimes required [1]. Herein we propose the use of silica-based hybrid carriers as new delivery systems of probiotics. Silica matrix should offer a chemical resistance to the gastric acidic environment and to bile salts in the small intestines [2], which is superior to that shown by commonly used bioadhesive polymers, such as alginate.

Alginate-silicate beads were obtained via emulsification or electrospraying with further coating. When using the emulsification technique, LGG-loaded hybrid beads were synthesized by silicalization of alginate with sodium silicate in a W/O emulsion containing exclusively food grade excipients. Resulting beads have sizes in accordance with the mouthfeel requirements of the food industry. In the case of the electrospraying technique, LGG is entrapped in alginate beads of higher sizes with respect to emulsification process. The cells lose only one log cycle after the electrospraying procedure, which is promising in the probiotics encapsulation field thus it uses mild temperatures and no shearing forces [3]. A thin silica shell is formed in a second step. The materials are characterized via ATR, SEM, OM, CLSM, NMR, TEM.

The study offers a proof of concept for the potential use of hybrid silica/biopolymer systems in oral delivery of probiotic bacteria.

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Antifungal and antibacterial pickering emulsions based on cyclodextrins

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Surfactants are usually used for the preparation of emulsions. However, potential drawbacks on the human body or on the environment can be observed for some of them (***e.g.*** skin irritation, hemolysis, protein denaturation, ***etc***.).[1] However, it is possible to use biocompatible emulsifiers such as native cyclodextrins (α-, β- and γ-CD). Indeed, the mixture of oil (paraffin oil or isopropyl myristate), water and native CDs results in the formation of Pickering emulsions.[2] The mechanism of emulsification was investigated by optical and transmission microscopies. The results prove that the oil/CD complexes precipitate and adsorb at the oil/water interface, and act as a solid emulsifier. Indeed, the precipitated complexes form a dense film at the oil/water interface. The multiple light scattering analysis proves that the dense interfacial film avoiding the coalescence of the dispersed phases. This kind of emulsions (biocompatibility, stability and surfactant free) can been used to obtain sustainable formulations of antifungal and antibacterial econazole (ECZ) nitrate (Figure 1).[3]

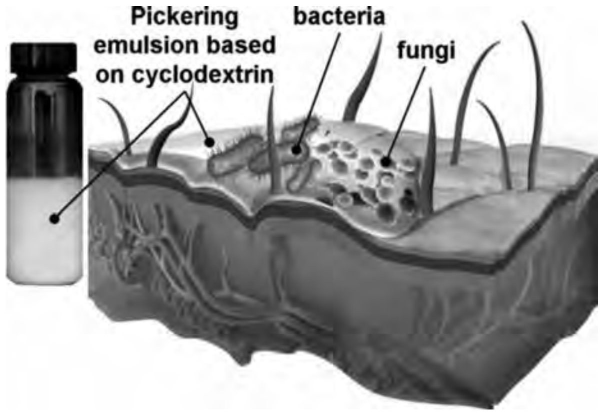

Figure 1. Concept for Antifungal and antibacterial Pickering emulsions based on cyclodextrins.

The properties of these Pickering emulsions can be adjust depending on the relative proportions of water, oil and CD. pH, texture and viscosities are influenced by the size of the CD. Though, all the formulated Pickering emulsions remain acceptable for topical applications. These emulsions are globally stable without the use of other stabilizers such as polymers, colloidal silica or charges. The antifungal and antibacterial test showed that these Pickering emulsions, charged with ECZ nitrate, are able to inhibit fungus and bacterial growth (***i.e***. ***C. albicans*** and ***S. aureus***). According to these results, it is anticipated that this Pickering emulsions based on CDs can be used for epidermal/dermal skin targeting. They offer the great advantage of avoiding the use of common petro-sourced surfactants and potentially toxic nanoparticles while keeping the same performances.

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Static Multiple Light Scattering to characterize emulsions in terms of stability and size

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Emulsions are widely used in the industry and stabilized with different process as polymers, proteins... to increase the stability. Depending on the nature and concentration of stabilizers, the stability and size of droplets will change, and the systems with form well dispersed droplets or networks like arrested gels.

In this work, Multiple Light Scattering device is used to monitor the behaviour of w/o emulsions stabilized with polymers or proteins. The heart of the optical scanning analyser is a detection head, which moves up and down along a flat-bottomed cylindrical glass cell (see figure). The detection head is composed of a pulsed near infrared light source (wavelenght = 880 nm) and two synchronous detectors. The transmission detector (at 180°) receives the light, which goes through the sample, while the backscattering detector (at 45°) receives the light scattered backward by the sample. The detection head scans the entire height of the sample, acquiring transmission and backscattering data every 40 µm.

We propose a description of the behaviour of o/w emulsions stabilized with different polysaccharides, we will show the advantages of using Multiple Light Scattering (MLS) to monitor their stability and propose a method to predict stability of these emulsions thanks to their size evolution in the first days after preparation. This work will show also protein efficiency in terms of surfactant on the droplet size and emulsion stability, we will compare pea protein and sodium caseinate.

Mitigation of microplastics impact caused by textile washing processes. MERMAIDS project

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European oceans are contaminated by marine litter, mainly by plastics. Microplastics are particularly worrying because water treatment plants do not take them into account in their management processes and they are deposited in waterways and sewage sludge.

The European Marine Strategy Framework Directive (2008/56/EC) establishes a framework in order for Member States to contribute to create a Good Environmental Status (GES) in the marine environment by 2020 through the monitoring of different indicators, among them microplastics.

Microplastic particles of synthetic clothes coming from laundry wastewater have been encountered in marine sediments, ecosystems and runoff and sewage waters. The ***"Accumulation of Microplastic on Shorelines Worldwide: Sources and sinks***" study states that "***the source of the microplastic fibres in the sewage treatment plants is most likely to be from washing machine wastewater as the mixture of fibres found in synthetic textiles is similar to the mixture of microplastic fibres found in beaches at disposal sites and in the wastewater of sewage treatment plants.".*** On average, more than 1900 fibres of microplastics can be released by a synthetic garment during one wash[1].

Microplastics concentrate Persistent Organic Pollutants via partitioning and they can be ingested by marine biota entering in the food web[2].

The main objective of MERMAIDS is to contribute to the mitigation of the impact caused by micro and/or nanoplastic particles resulting from laundry wastewater on European seas' ecosystems, by demonstrating and implementing innovative technologies and additives for laundry processes and textile finishing treatments. A reduction of at least 70% of the total amount of microplastic fibres that is currently discharged in laundry wastewater is sought by means of the improvements achieved.

Policy recommendations will be set in order to promote the widespread implementation of technologies which promote garments' microplastics retention in washing processes contributing to reach a GES by 2020. With the same aim in view, good practices guidelines on microplastic retaining for plastic fibres manufacturers, textile industry, detergent manufacturers and households will be elaborated.

Notes

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Supply Chain and Sustainability: Key Information Drivers and Management Techniques in your internal Supply Chain

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Supply chain complexity is quickly becoming a significant business pressure. In a survey of global executives, 44% claimed increasing supply chain complexity as their biggest business challenge. At the same time they are being pushed to innovate quickly, while mitigating risks imposed by the ever increasing regulatory and compliance landscape. There is a tremendous need to consolidate and communicate the right information to the right stakeholders at the right time so that products can get to market as quickly, and safely as possible.

How do businesses today attack this challenge? The solution partly lies in the combination of material search, R&D, procurement and regulatory information within your own company. This enables companies both large and small to analyze data and make decisions as well as communicate key business and regulatory drivers up and down the supply chain.

Platform solutions that consolidate various data sources such as — internal and third party test data, public sources, procurement data, and a powerful vendor data management system— exist today. The consolidation allows you to gather critical information from all of your suppliers, from raw material to tier-1, while protecting intellectual property rights. The end result allows you to leverage an infrastructure you thought was impossible and provide a decision-making dashboard for your entire organization.

Platforms like these can help you organize and provide business critical information to the right decision makers so you can bring innovations to market faster, while mitigating regulatory risk.

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For the past 5 years, Michael has been implementing solutions for the electronic exchange of information throughout the life sciences industry. He has extensive knowledge in information exchange using cloud technologies. Prior to UL, Michael spent 9 years in marketing and the sales and implementation of electronic security systems. He graduated from Rutgers University with a Bachelors of Education and Psychology.

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Use of environmentally-friendly chaotropic agents for textile printing

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In textile printing, chaotropic components are usually added to print paste formulations. The role of these agents is to promote the hydration of textile fabrics by disrupting the hydrogen bonding network between water molecules, and thus, weakening hydrophobic interactions. For such a purpose urea is commonly used in textile industry. The action of urea during the printing process is extremely complex [1]. However, the use of urea results in environmental problems due to high nitrogen content of effluents [2], which causes water eutrophication. For this reason, urea reduction or replacement by other environmentally-friendly products is one of the major challenges in the printing process. In the present work, we have studied an alternative chaotropic product to replace urea. An experimental design has been carried out to optimize various parameters such as viscosity of the print paste and the fabric color strength, and the corresponding contour graphic was obtained (Figure 1). Also, color fastness to water, perspiration and rubbing of printed fabric were evaluated. The results showed that a reduction of 76% of urea was achieved by using the alternative product. The viscosity of the print paste was 7,5 Pa.s. The printed fabric showed similar color strength to the fabric printed with the conventional method. Moreover, good fastness was obtained.

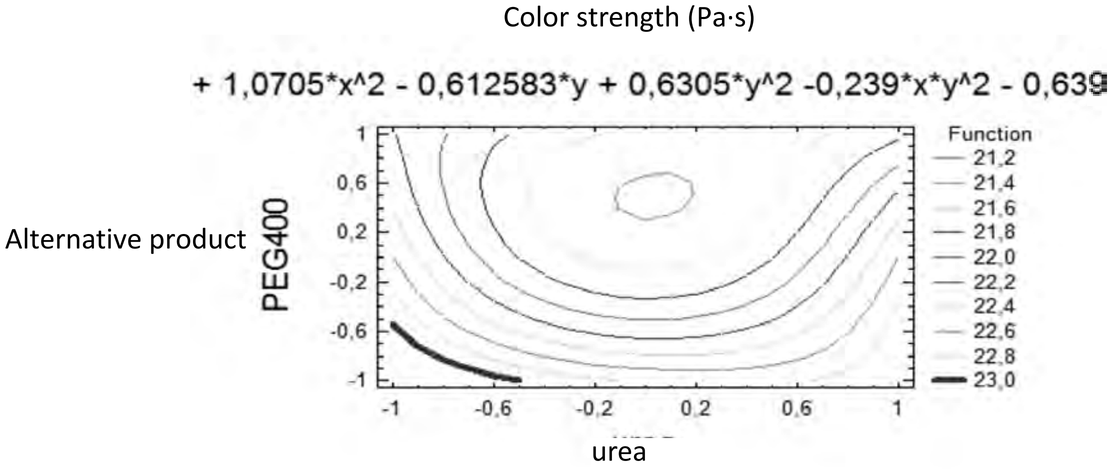

Figure 1: Color strength contour graphic of print paste.

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POSTERS

P 06

Delivering Gillette Shaving Benefits via Solid Formulation

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Shaving is no longer just about hair removal. Consumers also want to enjoy the shaving experience by receiving various benefits including but limited to lubrication and a cooling sensation. Our product delivers the benefit chemistry via a solid form, which introduces the additional consideration of maintaining good mechanical properties of the form during use. The technology behind our chemistry formulation is presented along with the link to current and future consumer shaving trends. Among the formula topics covered are formula design approach and ingredients descriptions.

Micellar extraction of iris rhizomes using green soap solutions

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Iris butter obtained from iris rhizomes is one of the most luxurious raw materials for perfume industry. The attractive violet-like fragrance is due to irones, i.e. terpenoids formed by oxidative degradation of iridals during rhizome aging. Conventional extraction methods are steam distillation and solvent extraction, which both exhibit drawbacks such as relatively long process duration with high energy consumption and the use of flammable and toxic solvents like hexane.

Therefore a simple, efficient and mild extraction method with natural, biocompatible and biodegradable soap solutions was developed to receive a product ready to formulate containing the fragrance compounds of iris rhizomes.

By using aqueous soap solutions, especially a myristate solution, an almost complete extraction of the desired irones was possible within a short time (30 min) and moderate temperatures (~ 40°C). This gentle method prevents the degradation and volatilization of the fragrances at high temperatures, which are disadvantages of conventional extraction methods. Furthermore, it has to be mentioned that various fatty acids, particularly myristic acid, are naturally occurring in the rhizomes. Thus, this extraction method uses an intrinsic plant substance as a highly efficient extraction medium and solubilizer.

After the removal of the rhizomes from the aqueous soap solution, myristic acid containing the desired nonpolar fragrance molecules was precipitated by neutralization and separated from the remaining aqueous phase. Excess myristic acid can be easily recovered by crystallization in cold ethanol in order to concentrate irones and other fragrance molecules. As myristic acid is already a frequent ingredient of formulations like cremes and lotions, the final product with its remaining fatty acid represents an ideal basic raw material for cosmetics.

The innovation of this micellar extraction method is the use of a green soap as an extraction medium and in the final product its corresponding fatty acid as a matrix for fragrance molecules for direct use in cosmetic formulations.

P 08

Analysis of fat properties thanks to microrheology

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The melting properties of fats in cosmetics (lipsticks, balms…) were studied thanks to microrheology. Passive microrheology studies the mobility and displacement of micron sized particles [1]: we used Multi Speckle Diffusing Wave Spectroscopy (MS-DWS) coupled with a temperature ramp in order to probe the particle displacement to analyze the viscoelastic properties of an opaque product.

Under heating or cooling conditions, particle movements can be related to the crystalline form of the fat: the rearrangements occurring during melting or during crystallization provide crucial data about the fat's polymorphic transitions.

Crystalline form and melting temperature of fats are important data for the elaboration of new products or for quality control of finished products. In the case of balms or lipsticks, the microrheology analysis during temperature ramp and cycling can identify the impact of formulation or process (crystallization, storage…) on melting properties, and so help to predict its stability against exudation.
In addition to the analyses of melting temperature of fat, the MS-DWS provides data on viscoelastic property changes.

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Mean size and dispersibility determination in real and concentrated liquid dispersions with Static-Multiple Light Scattering

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A technique based on Static Multiple Light Scattering is proposed to measure mean particles size in a large range of concentration between 0.0001 and 95%, for sizes between 10 nm and 100 µm by Turbiscan LAB technology. This technique has the advantage to measure in one click, without sample preparation or dilution, the mean particles size and so the dispersibility efficiency particularly for concentrated suspensions. Other optical techniques such as DLS or PTA can perform this measurement but only at a very high dilution which denatures the agglomerates and give an erroneous size of the native particles.

In this work we present different studies : mean size measurement of various products, dispersibility characterization of pigments, protein aggregation monitoring.

P 10

Investigation of slow structuring processes in formulations
Interaction of dissolved biomolecules and particles

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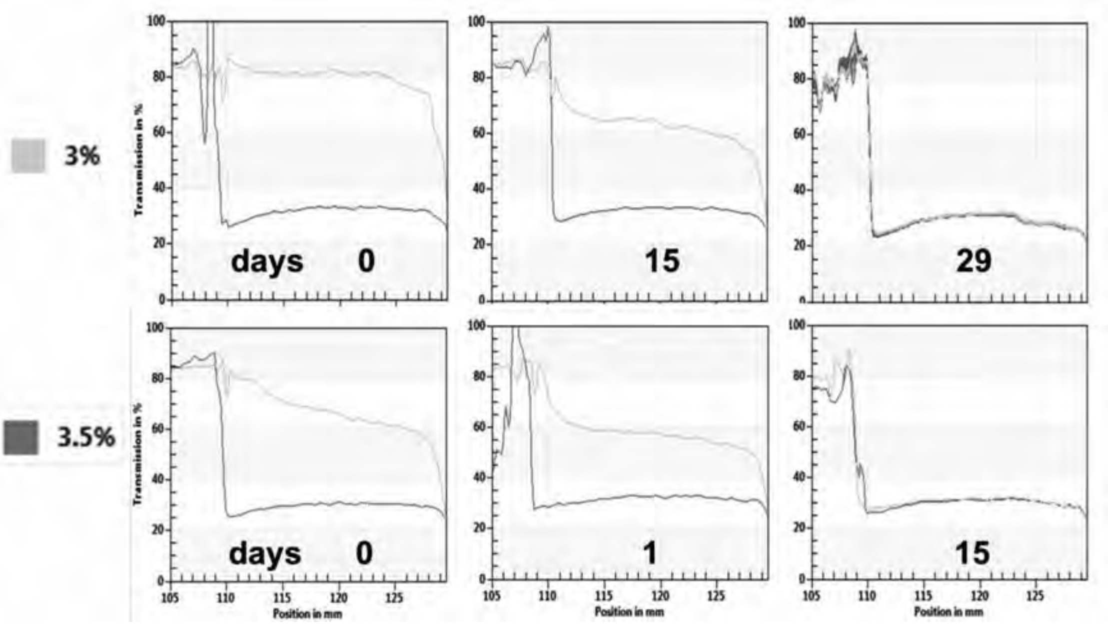
Dispersion based formulations often exhibit structuring processes after production and filling processes over time of storage until the final consumption. Consequently, state of dispersion and product quality changes. Exemplarily, biopolymers like pectins, frequently used in food industry to build texture and adjust the rheological behavior of liquid and semisolid products, undergo a continuous dynamic structuring process, on a slow scale though.

From an experimental point of view it is very difficult to investigate this process without breaking the structure during sampling for measurement.

To this end the potential of multisample analytical centrifugation with photometric detection (LUMiSizer) was evaluated. Model dispersions of monodisperse silica with varying pectin concentration were filled after preparation into cells and stored for aging different times before measuring separation behaviour in centrifugal field. This way the process of structure build up can be investigated quasi in-situ.

The model system allows further to trace apparent viscosity of pectin solutions in centrifugal field and study interaction between biopolymer and particles (flocculation).



Degree of tracer particle separation during centrifugal separation (128 min, RCF =2300) for pectin concentration of 3 and 3.5 % after indicated days of storage (red initial profiles, green last profiles).

Estimation of surface tensions using the COSMO-RS sigma-moments: application to emollient oils for cosmetics

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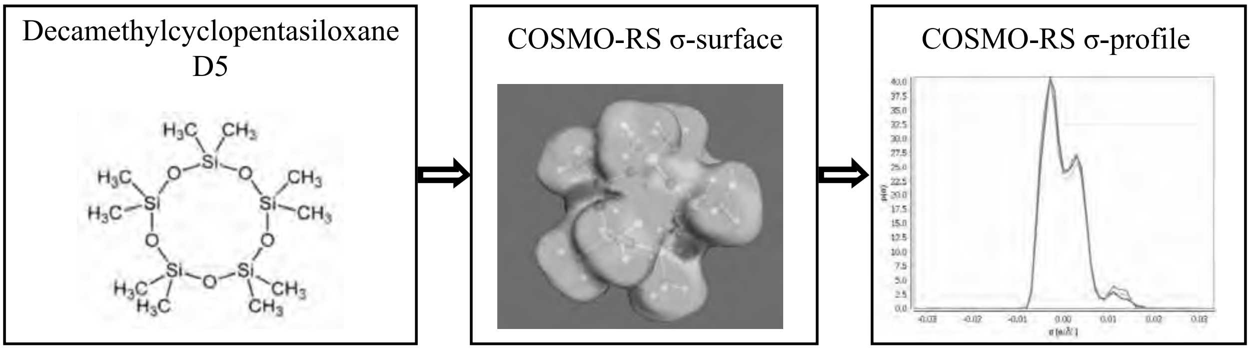
Emollience is a general term which highlight both cosmetic qualities and functional properties linked to measurable physico-chemical parameters. Indeed, emollient oils offer effective spreading on both skin and hair and present a pleasant touch feeling. Moreover, emollient oils are known to be film-forming, water-resistant and also for their blocking effect thanks to their volatility and their good permeability. Among the emollient oils available on the market, silicone oils for instance are included in the formulation of many personal care products, such as conditioning shampoo, lipsticks or skincare creams and bring to the products unique sensorial properties: non-sticky feeling, brightness, good spreading or even moisturizing and protective effect due to their blocking effect. All these remarkable cosmetic properties are the result of several physico-chemical properties such as vapor pressure, rheological behavior or interfacial and surface tension.

In this context, a study have been carried out to predict the surface tensions of a large set of emollient oils using the COSMO-RS method. COSMO-RS or Conductor-like Screening Model for Real Solvents, is a theory which combines both quantum chemistry calculations and statistical thermodynamics to predict a wide range of physico-chemical parameters of several molecules [1]. Physico-chemical descriptors, the so-called sigma-moments, are determined using the COSMOtherm software and are then used in a multilinear regression in order to rationalize and to predict the surface tensions of emollient oils.



Surface tensions have been measured to allow a comparison between experimental and predicted values and a validation of the theoretical model.

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Influence of the emollient structure on the properties of cosmetic emulsion containing lamellar liquid crystals

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Emulsifying agent is one of the most important raw materials in cosmetic industry. Its primary role consists in emulsion stabilization, by decreasing the surface tension between the oily and the aqueous phases. In addition, the surfactant molecule may form organized structures, so-called liquid crystals, due to its unique chemical properties. Lamellar liquid crystals are similar to the stratum corneum lipidic structure [1]; therefore, they have a great skin hydration potential [2].

The aim of this study was to understand the impact of the emollient properties (chemical structure, polarity, etc.) on the lamellar liquid crystal formation. For that purpose, 7 emollients differing by their polarity (from mineral oil toward cocoglycerides), all liquid at ambient temperature, were tested at level of 20% in the cosmetic emulsions containing 5% or 10% of emulsifier of alkyl polyglucoside/fatty alcohol (APG/FA) type, known for lamellar liquid crystals formation [3]. Each serie of tested emulsions (5% and 10% emulsifier level) only differed by the emollient, thus allowing to elucidate the surfactant-emollient interactions and the effects on the properties of the systems.

The microscopic observations under the polarized light revealed birefringent structures, called "onion rings", so evidencing lamellar liquid crystals presence in all emulsions. Otherwise, the quantity and the appearance of "onion rings" varied depending on the oil polarity and APG/FA concentration; this clearly demonstrates that the liquid crystals organization is highly influenced by these parameters. In order to investigate which type of lamellar phase (lamellar gel or lamellar liquid crystalline) is predominant in each sample, wide angle X-ray analysis was performed. It was shown that increasing oil polarity strongly affects the lamellar organization, by favoring the liquid crystalline phase formation.

Consequently, the type of liquid crystal organization underlies the product's unique physical properties. The decrease in the emulsion droplet size was related to the increase in the emollient polarity by means of granulometry. The behavior of the sample's structural network under stress/strain solicitations was analyzed through rheology tests. It was observed that the tanδ (the ratio between loss and storage modulus) has its maximal values for the emulsions containing nonpolar oils, which is in accordance with the X-ray and granulometry results. These data were completed with additional characterizations, namely texture and thermal analyses, in order to highlight the differences between emulsions.

All these physical data were completed with sensory evaluations, and the impact of the emollient on the hydration potential of the lamellar phases was also studied. In conclusion this project showed that the oil structure has a great impact on the physical and the sensory properties of the cosmetic emulsions containing liquid crystals.

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Comparative study of Acetaminophen Immediate release tablet by three continuous dry granulation techniques: Moisture assisted granulation technique, roller compaction and hot melt extrusion technique.

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To develop and improve the physical properties of solid oral dosage form during manufacture-Granulation technologies are widely used. Three granulation processing methods; Hot melt extrusion (HME), Dry granulation (Roller compaction) and Moisture assisted dry granulation (MADG) were assessed to develop a high dose immediate release tablet of acetaminophen drug compound. Hot melt granulation by extrusion assessed with three polymers. A massive enhancement in drug loading of 4:1 was achieved via melt processes using low molecular weight thermo-binders as PVP K30, HPC SSL and Maltodextrin. Different characterization techniques were used to enumerate poor physical property characteristic for drug including hygroscopicity, low solubility and bulk density, and poor powder flowability. Granules produced by melt processing contained less fines compared to MADG and dry granulation. A formulation and process for dry granulation by roller compaction was developed. Roll force, and roll gap parameters were evaluated. Particle size distributions of milled ribbons analysed by sieve analysis. As well as porosity of compacted ribbons was studied by mercury intrusion porosimetry. Higher density granules produced with roll force of 15 kN/cm and improved flow properties compared to the pre-blend and less fines content (<75 µm) was observed. Drug loading (API:excipient ratio) in roller compaction was 8:2. Developed IR formulation of acetaminophen using MADG method and characterised its granular and tableting properties. Acceptable content uniformity was obtained using each technology. The type of granulating process and polymer affected the granulation particle size distributions and bulk/tap densities. Both melt extrusion and moisture assisted dry granulation are viable granulation process choices for scale up to overcome the physical property limitations of Acetaminophen drug.

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P 14

Oil-in-water emulsion stabilization by droplets organogelation: application to drug delivery

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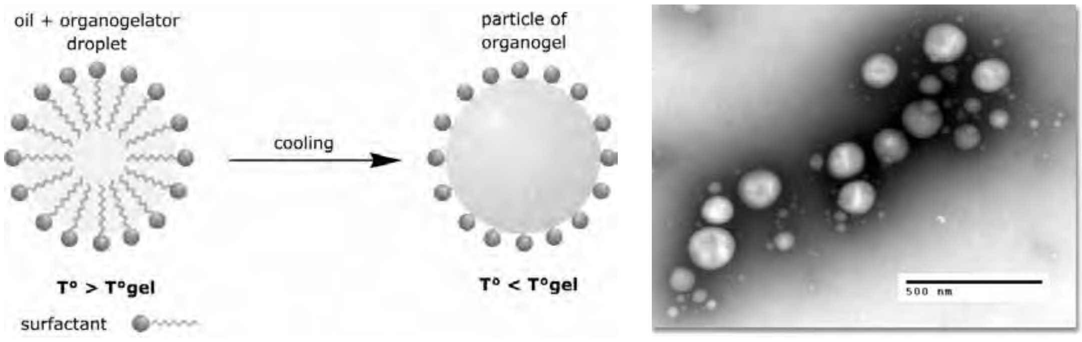
Emulsions that are formed by dispersing a water-immiscible liquid into an aqueous phase are termed oil-in-water (o/w) emulsions. Like all emulsions, they are thermodynamically unstable, and over time the droplets tend to coalesce to reform separate bulk oil and aqueous phases. To explain this instability different mechanisms are involved, like creaming, sedimentation, flocculation, coalescence and Ostwald ripening.

In order to prepare stable systems emulsifiers must be added; nevertheless they still remain instable over long period of storage. This instability is a real problem in pharmaceutical industry and particullary for drug delivery. Coalescence is an important factor that is very difficult to limit, and to reduce this phenomenon we can decrease droplet contact by reducing attraction, increase repulsion or resistance of membrane to rupture.

In this work we describe how to limit the coalescence by gelling the oil droplets and consequently to drastically increase the stability by forming nanoparticles of gelled oil. Organogels are soft materials, which result from the immobilization of an organic liquid or oil in a three dimensional network by a gelator. The organogels in this study were obtained from a vegetable oil and a low molecular mass organic gelator (LMOG). Water dispersion of gelled particles were obtained by hot emulsification (T > Tgel), with a stabilizing agent (surfactant or polymer), and cooling at room temperature (T < Tgel).



Scheme of droplet stabilization by gelation and TEM of organogel nanoparticles

The dispersion is very stable, and the gelled particles are able to encapsulate hydrophobic drugs for a controlled delivery.

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Investigation of Miscible Properties of Inorganic-Organic Hybrid Materials Depedinging on the Surface of Inorganic nanoparticles in Solvents and Polymer Resins

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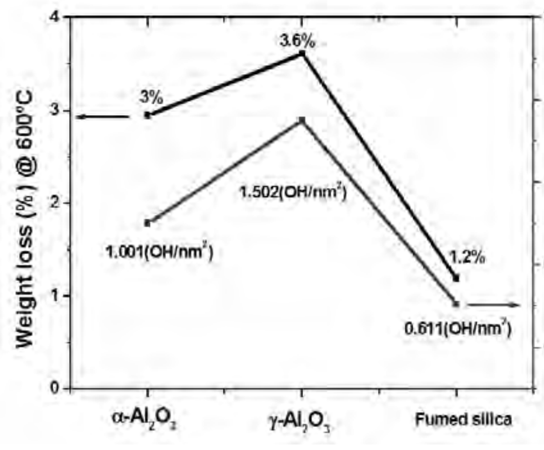
Organic-inorganic hybrid materials as functional smart coatings have been applying to cellular phone's cases, protective or optic films, high quality automotive clear coat, and so on [1-2]. Generally, inorganic oxides have excellent physical properties such as an abrasion resistance, a corrosion resistance, thermal stability, electrical insulation, and thermal conductivity. However, inorganic oxides have lower affinity and unstable dispersion stability in solvents and organic polymer matrix. In this presentation, the surface properties for three kinds of inorganic oxides such as α-Al_2O_3, γ-Al_2O_3 and fumed silica were characterized by acid-base titration to observe OH group number of inorganic oxides as displayed in Fig.1. Herein, these silane amounts modified onto the surface of Inorganic oxides were also correlated with OH number of inorganic oxides. The miscible properties of inorganic oxides modified by silane in solvent or polymer matrix were observed by particle size analyzer(PSA) and viscometer. In Fig.2, the dispersion stability of α-Al_2O_3 in N-methyl-2-pyrrolidone solvent was controlled according to the variation of silane amount. The silane % was calculated by the surface area of inorganic oxide and minimum covering area of silane. In addition, to improve the dispersion of inorganic particles in polyamideimde resin, a nano-dispersed sol was prepared by bead-milling process. Miscible properties of organic-inorganic hybrid material in the resin are depending on the OH number and preparation condition of inorganic oxide, the kind and amount of silane coupling agent. Moreover, it is very important to understand the surface characteristics of inorganic particle, in order to control the physical properties more precisely between inorganic oxide and solvent/polymer resin.



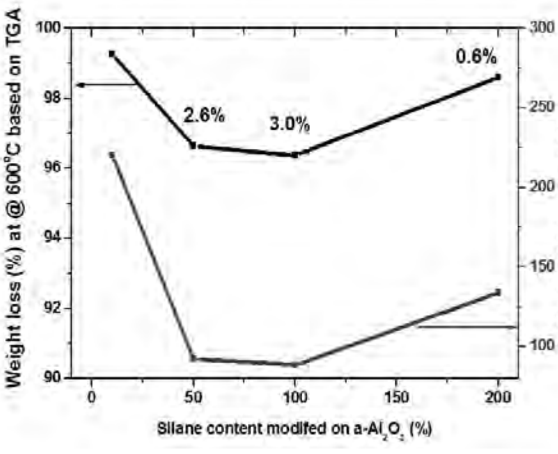


Fig. 1. Correlation between weight loss of modified silane Fig. 2. Correlation between average particle size and

and surface OH site density (Ds) of the inorganic materials. silane amount modified on α-Al_2O_3.

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P 16

Spray drying formulation of grape marc polyphenols with natural carriers: stability study and release profiles

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Valorization of winemaking by-products has attracted increasing attention over the last few years due to the growing interest on natural-based health-promoting products, together with 3R policies [1-3]. The most important of these by-products is grape marc, consisting of the grape seeds and skins obtained after pressing and which are rich in polyphenols with strong antioxidant properties. The extraction of these compounds from grape marc is a well-researched process [4], but a further formulation step is crucial to ensure their applicability. We have studied the formulation of a polyphenol enriched grape marc extract using natural carriers (maltodextrin, whey protein isolate and pea protein isolate) in different concentrations and a pilot scale spray-dryer. The products obtained have been characterized in terms of morphology (particle size) and composition (total phenolic and anthocyanin content, moisture, water activity and antioxidant activity). The minimum amount of carrier required for efficient drying (i.e. at least 50% drying yield) has been established (Figure 1). The effect of storage on the stability of the products has been studied by keeping them at constant temperature (25ºC) with and without the presence of natural light during 6 months. Finally, dissolution tests have been carried out in simulated gastric and intestinal fluids in order to study the dissolution rate of the polyphenols and the effect of the encapsulating material.

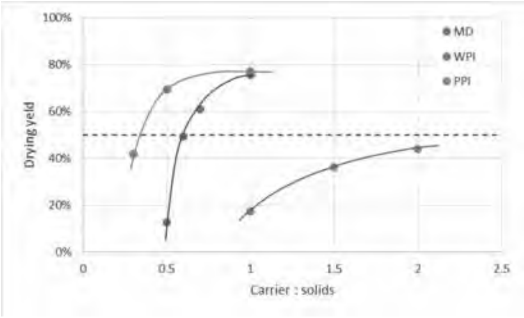

Figure 1. Effect of carrier type and concentration on powder recovery

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Acknowledgements:

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Physical characterisation of NIPAAM hydrogels of bevacizumab

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Therapeutic proteins are increasingly used to treat blinding diseases. Monthly to bimonthly intravitreal (IVT) injections of antibody derived proteins are often required [1] for the treatment of age related macular degeneration. Prolonging the ocular residence time of therapeutic proteins in the posterior cavity is important to reduce the frequency of IVT injections. Here we describe new injectable thermoresponsive N-isopropylacrylamide (NIPAAM) hydrogels that are prepared with different relative amounts of a hydrophilic cross-linker, poly (ethylene glycol diacrylate) (PEGDA-700 Da). Thermoresponsive hydrogels can be injectable at one temperature range and then made to collapse to form a solid implant at another, often higher, temperature such as 35-37˚C. This behavior is related to the hydrophilic-hydrophobic balance of the gel [2]. The type and percentage of cross-linker used can affect the hydrophilic-hydrophobic balance of the gels. In an effort to determine correlations, gels with different relative amounts of PEGDA were prepared and characterised regarding their injectability, volume phase transition temperature (VPTT) and swelling ratio (SR) at both ambient temperature and 37˚C. Each formulation was prepared by dissolving NIPAAM monomer (40 mg), ammonium persulfate (4 mg) and N,N,N',N-tetramethylethylenediamine (20 µl) as the initiator in distilled water (1 mL). Different amounts of PEGDA (4 µl, 8 µl, 12 µl and 15 µl) were used.

Gels made with 4 and 8 µl were injectable while 12 and 15 µl were non injectable. Gels with higher percentage of cross-linker became less responsive to temperature changes when injected. The SR at 37ºC of (4, 8, 12 and 15 µl) gels were (1.46, 3.2, 7.49 and 9.6) respectively. This will affect their ability to retain water after injection. The ability of the gels to retain water at 37ºC is increased by increasing the cross-linker percentage. Softer hydrogel implants will be formed. These implants will contain a larger amount of water, which is the driving force for the release of loaded proteins. This may have a potential effect on the release of the loaded protein. There was no significant difference in SR between 4 and 8 µl gels at 37ºC. Based on these results 8 µl was chosen for protein loading. The water used to prepare the gel was replaced with the bevacizumab solution from the pharmaceutical formulation (25 mg/mL in bevacizumab). The presence of the antibody during polymerisation had no significant difference on injectability, VPTT and SR at 37ºC of the gel. The use of a hydrophilic cross-linker (PEGDA) affects the behavior of the gels and their thermal responsiveness. Gels made with 8 µl cross-linker have the potential to be used as an injectable delivery system to control the release of bevacizumab in the posterior segment.

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A Novel Rheology Modifier for Flowable Formulations

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Flowable formulations require a rheology modifier to prevent sedimentation phenomena. Rheology modifiers produce a "three-dimensional" gel network in the continuous phase resulting in a non-Newtonian fluid which provides stability to the formulation. The rheology modifier must give high viscosity so the product does not separate during long term storage but still allow the product to be easily poured from the package.

The objective of this research was to evaluate a novel polymeric alkoxylate (PA) with carbendazin (500 g/L) for its effect as a rheology modifier on the formulation properties of viscosity, yield point, shear stress, shear thinning, stability and spray droplet contact angle. PA has been formulated with other surfactants and solvents as a ready-to-use liquid rheology modifier.

Formulations with four concentrations of PA formulated as a ready-to-use liquid (0.5, 1.0, 1.5, and 2.0% w/v), were evaluated and compared to formulations with four concentrations of a xantham gum (0.05, 0.1, 0.15, and 0.2% w/v). Formulations with PA performed comparably to xantham gum for viscosity.

PA provided desired behavior in shear stress and shear rate studies, and there was little variation in response due to changes in concentration. PA provided a higher yield point than xantham gum. Xantham gum provided stable formulations at all concentrations as measured by bleeding, settling and particle size distibution. PA provided acceptable formulation stability at concentrations of 1.5% (w/v) or greater. When diluted in water for field application, formulations containing PA had lower contact angles than xantham gum formulations which will result in improved wettability. PA is classified as a non-eye irritant and has a very good eco-toxicological profile.

Evaluation of the release of r-LIMONENE from Multilayer oil-in-water (O/W) emulsions submitted to heat treatment

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Abstract

The lipophilic volatile compounds, e.g. aromas, are of great importance in different industrial fields. However, high temperature used in some industrial processes can lead to the loss of these types of molecules. Accordingly, the use of multilayer emulsion as a system of encapsulation of aromas could be an alternative to improve the stability of emulsions (O/W) and thus reduce the loss of volatile aromas during industrial processing and subsequent storage. Therefore, the aim of this study was to evaluate the effect of the composition of multilayer emulsions on the release rate of limonene at different temperatures. The multilayer emulsions were prepared by the layer-by-layer technique, which entails the subsequent addition of polyelectrolyte solutions to a primary emulsion presenting an opposite charge and favoring the electrostatic binding. Protein isolate from a novel lupin variety (Alu***Prot***-CGNA) was used as an emulsifier for preparing a primary emulsion (E1) containing the model aroma (R-limonene). Then, E1 was mixed with a chitosan solution (cationic polysaccharide) to form a secondary emulsion (E2). After that, three anionic polysaccharides were used and tested to stabilize the tertiary emulsions: sodium alginate (E3A), apple pectin (E3P), and xanthan gum (E3X). Limonene released from multilayer emulsions (containing 2.5 ppm of limonene) was analyzed by using solid phase microextraction (SPME) at 25 and 65 °C over 1 hour and measured by FID-GC. Among the tertiary emulsions, limonene release at 65°C was lower in E3A than in E3P or E3X, resulting in limonene release rates of 36%, 56% and 79%, respectively, in comparison to the primary emulsion. On the other hand, at 25°C the release rate showed a similar pattern to 65°C, but with lower limonene release values. It should be noted that the retention of volatile compounds is closely related to the stability of the emulsion as established by other authors [1]. The present work provides interesting information about the retention of volatile compounds and the stability of multilayer emulsions with potential applications in food and cosmetic industries.

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Magnetic nanoparticles for cancer diagnosis and treatment: detailed characterization of their physico-chemical, magnetic and relaxivity properties

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According to the America Cancer Society (2016) nowadays cancer accounts for one in every seven deaths in the world [1]. In this context, there is an urgent need in going beyond the traditional techniques and investigating effective and affordable approaches for the early detection and treatment of cancer. In the last years, magnetic nanoparticles have received considerable attention due to their unique characteristics at the nanoscale, which make them suitable for biomedical applications. On one hand, magnetic nanoparticles are increasingly investigated as diagnosis probes by magnetic resonance imaging (MRI). Iron oxide magnetic nanoparticles (magnetite and maghemite) are the only magnetic materials FDA approved for use as contrast agents in humans [2], providing an efficient alternative that solves the toxicity issues shown by the traditional Gd chelates used in the clinic nowadays. By adjusting the magnetic core size, type of coating, coating thickness, surface chemistry, etc., the magnetic and relaxivity properties of these nanoparticles can be optimized [3,4]. On the other hand, by proper nanoparticle surface modification, the physical/chemical attachment of anti-cancer drugs can be favored [5], allowing for the preparation of a multifunctional drug carrier system able to image and (magnetically) induce a drug delivery at the tumor site.

In this work, we conducted the synthesis and detailed characterization of biocompatible coated iron oxide nanoparticles prepared by modified co-precipitation and hydrothermal methods, in which the coating agent (PEG, PAA) was added during the synthesis (in situ approach). As main results, the particle size of PEG-coated nanoparticles resulted to be two-fold larger than those coated with PAA, as evidenced by transmission electron microscopy (TEM). Both PEG and PAA polymeric coatings were confirmed by Fourier Transform Infrared Spectrometry (FTIR), whereas thermogravimetric analysis (TGA) revealed a much higher amount of organic matter for PAA-coated nanoparticles. Importantly, measurements of z-potential indicated that both coated nanoparticles were strongly and negatively charged. In terms of magnetic properties, both coated samples behaved as superparamagnetic at room temperature, whereas the saturation magnetization (Ms) for the larger PEG-coated nanoparticles was found to be as high as that of bulk magnetite. On the other hand, relaxivity and magnetic resonance imaging properties evidenced a clear enhanced T2-effect for the larger PEG-coated nanoparticles. Preliminary results on the influence of their final physico-chemical properties on the design of theranostic magnetic nanoplatforms aiming both at MRI-based imaging and at drug loading and delivery capabilities for cancer treatment will be discussed.

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Synthesis of environment friendly biosurfactants based on vegetable oils and characterization of interfacial properties for cosmetic and household products formulations

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Recently, Interest in biosurfactants has been steadily increasing due to their diversity, environment friendly nature such as nontoxicity and excellent biodegradability, possibility of large-scale production, selectivity, performance under extreme conditions, and potential applications in environmental protection. In this study, phospholipid biosurfactants were synthesized from renewable vegetable oils. The structure of the resulting products was elucidated by FT-IR, ^{1}H NMR, and ^{13}C NMR spectroscopies and environmental compatibility such as biodegradability and acute oral toxicity was evaluated. The interfacial properties of synthesized surfactants have been examined such as CMC, static and dynamic surface tensions, interfacial tension, wetting property, emulsion stability, viscosity, and foam property. The prescription test in shampoo formulation prepared with synthesized biosurfactants indicated better sensory feeling and excellent foaming ability compared with silicon. The patch test also indicated no irritation during 48 hours, indicating potential applicability in cosmetic and household products.

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Fragance dispensing formulation for sanitizing and odor control in high traffic areas

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In the industry of household and commercial/institutional products, and in particular regarding products for high traffic toilet areas, one of the most popular trends are quality products with high intensity, long-lasting air freshening effect. This is reflected in the variety of fragances, presentations, and advertising campaigns of products that offer a multipurpose approach for sanitizing, cleaning and odor control.

We have developed an improved version of a sanitizing dropping liquid product by modifying a microemulsion formulation in terms of the amount of surfactant and the incorporation of certain environmentally-friendly biodegradable solvents (alcohol and esters). The product has many advantages with respect to traditional air fresheners, since the dosing unit is automatic, the use of toxic solvents needed for aerosol products is avoided, and in addition to provide a nice smell to toilet areas, it also eliminates bacteria that cause diseases and bad smell. It also contributes to the cleanliness of the toilets thanks to the presence of detergents in the formula.

The strategy was based on reducing the amount of surfactant and replacing it by some environmentally-friendly solvents that may aid in the release of the fragrance [1,2]. Thus, the resulting product should be more attractive from the environmental, economic and fragrance performance point of view.

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Myricetin, rosmarinic and carnosic acids as superior natural antioxidant alternatives to α-tocopherol for the formulation of oils, cosmetics and fragrances

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Polyunsaturated fatty acids (PUFAs) are classified as essential fatty acids. Moreover, terpenes are the major components of fragrances. However, both of them are particularly sensitive to oxygen and are therefore subject to oxidative degradation initiated by heat, light, and trace metals. Therefore, the formulation of stable oils, cosmetics and fragrances against oxidation is a relevant challenge. Synthetic phenolic antioxidants, like butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), are widely used in order to protect PUFAs. Nevertheless, due to an increased safety concern for synthetic antioxidants from the consumer side and a strong push to replace them by natural alternatives, the objective is to find new natural phenolic antioxidants, with equal or greater efficiency. It is in this context that we studied new natural polyphenols and classical antioxidants in order to evaluate their antioxidant capacity using theoretical and experimental methods.

First of all, the 2,2-diphenyl-1-picrylhydrazyl ($DPPH^{\cdot}$) test is used to predict the antioxidant efficiency of phenols [1]. This experimentation is based on the kinetic rates of hydrogen transfer reaction from phenolic antioxidants to the stable radical. Furthermore, measurements of oxygen consumption during the autoxidation reactions of oils are carried out under oxygen pressure with a new device: the PetroOxy [2]. This test offers insight into induction period and oxidation rate in presence of antioxidants. Finally, the results obtained are compared to the thermodynamic data such as the Bond Dissociation Enthalpy (BDE) of phenolic bond (O-H) calculated by density functional theory calculation [3]. This DFT calculation permits to build a scale of reactivity in vacuum. Surprisingly, this work highlights really good correlations between the different parameters. In conclusion, myricetin, rosmarinic and carnosic acids are found to be superior natural antioxidant alternatives to α-tocopherol for the formulation of oils, cosmetics and fragrances.

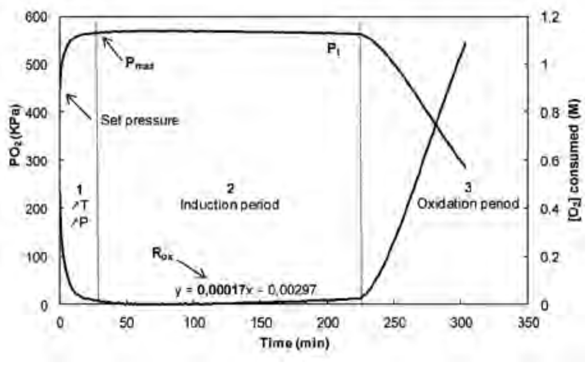

Figure: Monitoring of the oxygen pressure (primary axis) and the concentration of oxygen consumed (secondary axis) during the oxidation of oil in the presence of α-tocopherol

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Low temperature stability of sodium dodecyl sulfate systems

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The homecare and personal care markets are industries that require the use of surfactants throughout the formulation bases of products such as dish liquid, shampoos and creams. Due to the high global demand of such household products, there is a requirement for these formulations to demonstrate phase stability at a variety of climates. As such, the surfactant-based products must retain appearance and function at low temperatures and sub-zero climates when there can be a risk of surfactant crystallisation. Through this project, the aim is to provide an understanding of the behaviour of such surfactant mixtures at low temperatures. Sodium dodecyl sulfate (SDS) aqueous solution is the initial model system to begin to understand the phase transitional behaviour. SDS, present in many detergent formulations, is manufactured in situ from its respective alcohol 1-dodecanol [1]. From an industrial perspective, these detergent formulations often contain remnant 1-dodecanol, originating from the in situ production of the surfactant. Investigations into the effect of 1-dodecanol addition on SDS crystallisation from aqueous solutions were performed on the model system. Through differential scanning calorimetry (DSC) and optical microscopy studies, it is found that 1-dodecanol facilitates the crystallisation of aqueous SDS systems through a seeding mechanism in addition to enabling for stabilisation of the crystalline surfactant form until a higher temperature upon heating. Following this experimental study, the implication of any remnant 1-dodecanol on the low temperature stability of SDS based detergent products was predicted.

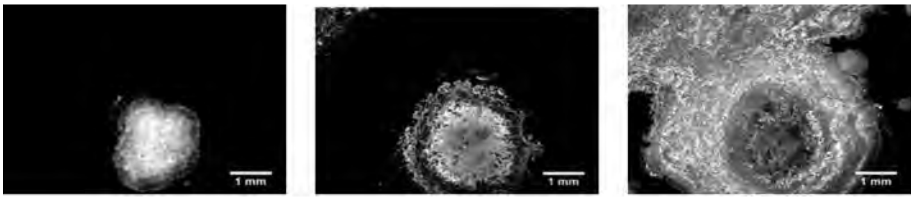

Figure I. 20 wt. % SDS solution with 5 wt. % dodecanol solution under optical microscopy displaying the seeding effect of a 1-dodecanal globule on SDS crystallisation

Alongside this investigation, the low temperature stability effect of the addition of the non-ionic surfactant, N, N-dimethyldodecylamine N-oxide (DDAO) to SDS solutions is considered since detergent formulations are typically mixed anionic – non-ionic surfactant systems. From DSC investigations it a is deduced that, on addition of DDAO, the crystallisation temperature of an aqueous SDS system can be lowered resulting in a linear correlation with the amount of DDAO, a phenomenon which is attributed to the formation of mixed micelles [2]. Further investigation from NMR and XRD studies provides information on the composition of the precipitate in these mixed systems and enables for the role of water in these mixtures to be inferred. Through broadening the understanding of such processes, the knowledge acquired can be applied to enable improvements to low temperature stability of such systems so as to increase efficiency, decrease costs and improve shelf life of the final product.

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Effect of isomeric form of surfactant on rheological properties of wormlike micellar solutions formulated with novel bio-based isosorbide surfactants

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Isosorbide surfactants having an isosorbide group as a building block is one of bio-based surfactants. There are some reports on significant aqueous phase behavior, foaming properties, Krafft temperatures and critical micellar concentrations [1, 2]. In this presentation, we report a wormlike micelle formation with a mixture of sodium dodecyl isosorbide (SDSS) and 2-***O***- or 5-***O***-dodecylisosorbide (EXO or ENDO, respectively). We studied viscosity behavior of the 3wt%NaCl aq./SDSS system with EXO or ENDO at constant surfactant concentration (5wt%). A maximum of viscosity was given at the same surfactant mixing composition for both systems but the maximum viscosity is higher in the ENDO system. This interesting result was caused by isomeric molecule structure of the cosurfactant. We have also studied dynamic rheological behavior. Oscillatory-shear (frequency sweep) measurements were performed on the viscoelastic samples formed around the viscosity maximum composition. Liquid-like behavior (***G'***<***G"***) was observed at low frequency region whereas solid-like behavior (***G'***>***G"***) was observed at high frequency region. Maxwell-type oscillatory rheological behavior of viscous micellar solutions can be related to the transient network formed by the entanglement of wormlike micelles. Maxwell equations were also fitted to the data, indicating wormlike micelle formation. The results obtained in this work will contribute to the formulation of liquid detergents or shampoo with reduced environmental impact.

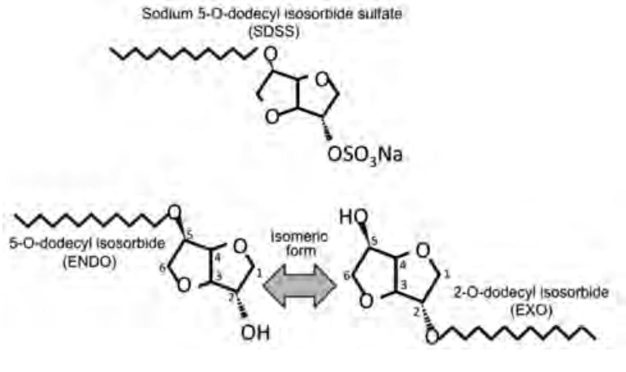

Figure 1 Structure of sodium dodecyl isosorbide (SDSS), 2-O- or 5-O-dodecylisosorbide (EXO or ENDO)

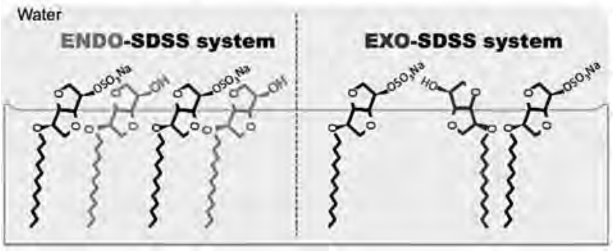

Figure 2 Proposed mechanism of molecular structure isomer effects

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Ab-initio approach as product design tool for controlled release of active ingredients from highly concentrated emulsion formulations.

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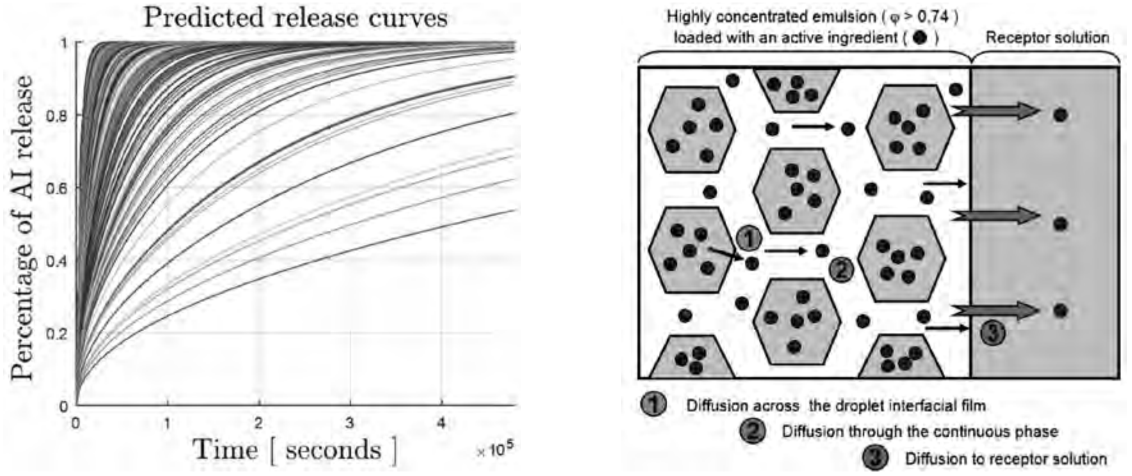
In recent years, increased attention has been focused on novel controlled release systems within pharmaceutical, food, and cosmetic industries. However, finding the formulation that gives a particular active ingredient (AI) the desired profile is still a major challenge for firms. Procedures to systematize the design of these typically complex products should also be developed, avoiding the usual experimental based trial-and-error approach that is known to be time consuming as well as error prone. From numerous materials providing interesting possibilities, emulsions have been all long identified as a complex system very flexible regarding composition, size distribution, phase equilibria, interface type, morphology and viscosity. For these reasons, highly concentrated emulsions have been chosen as a model system for the experimental validation of this research.

The main aim of this work is to quantify, through an ab-initio approach, mass transfer as a function of product composition (active ingredient, surfactant, dispersed/continuous phase...) and structural parameters (dispersed-phase volumetric fraction, droplet diameter or viscosity…).This goal requires relevant physicochemical models.

A particular attention has been focused on the assessment of the mass transfer occurring at the different interfaces of this multiphase system and appropriate thermodynamic modeling and descriptor tools (such as group-contribution methods to obtain reliable knowledge of phase equilibrium or Van der Waals volume calculation for molecules) have been developed to rank generated systems versus an optimal target function. Experimental results show that using this"ab-initio"approach it is possible to pertinently predict release kinetics from concentrated emulsions. This kind of modeling tools could be of very high interest in the domain of formulation by allowing fast and robust screening preliminary studies on a broad range of components as well as precise and rigorous prediction tools to optimize controlled release from an identified system.



(Left). Sketch of diffusion steps from highly concentrated emulsions considered on the ab-initio model.
(Right). Examples of some release curves predicted by the ab-initio model for different emulsion-based formulations.

Bionanocomposites formulated with cellulose nanofibrils

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Nanofibrillated cellulose or nanocellulose has aroused considerable interest owing to its unique mechanical and optical properties. It is considered as a very appropriate building block in various formulations for developing functional nanomaterials of diverse applications. Here cellulose nanofibrils were used itself to prepare aerogels further mineralized and they served also as a template to synthesize optically birefringent and chiral mesoporous silica.

Cellulosic nanofibrils were separated by combination of sulfuric acid hydrolysis of initial cotton and intense mechanical treatment. When a biocompatible precursor was admixed into aqueous solutions of dispersed nanocellulose to carry out the sol-gel processes in a neutral aqueous solution at ambient temperature, silica was obtained with embedded nanofibrils. It was templated by nanofibrillated cellulose which regulated material structure and properties. In particular, a birefringent silica found was a cast of a chiral nematic liquid crystal formed from the self-assembled nanofibrils. Template removal by the calcination resulted in a mesoporous material with high surface area

Another approach in the formulation of advanced nanocellulose materials is based on aerogels. They are prepared by freeze-drying aqueous solutions of nanofibrils. Aerogels had high porosity and low density varying between 0.02 – 0.1 g/cm^3. Coating of nanofibrils by silica was performed via the mineralization by green sol-gel chemistry with two novel biocompatible silica precursors. One of them contained a non-hydrolysable methyl group attached directly to the silicon atom. By regulating their ratio in the reaction mixture, it was possible to tune the hydrophilicity/hydrophobicity of nanofibrils. When morphology was additionally adjusted, it allowed fabricating superhydrophobic aerogels. They could work as an efficient absorbent for nonpolar organics including oil that is promising for removal of spills from a water surface.

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The formulation of a stable suspending vehicle

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Pharmaceutical specials are defined as extemporaneous non-sterile liquid preparations prepared under good manufacturing practice (GMP), by a licensed specials manufacturer [1]. They are commonly used as an alternative dosage form for those who cannot or are unable to swallow solid dosage forms, such as tablets. Therefore, specials have become increasingly popular in paediatric care and in the care of the elderly and vulnerable. Specials are prepared by dispersing the Active Pharmaceutical Ingredient (API) or a compounded tablet into an appropriate suspending vehicle producing an oral liquid dosage form. However, the stability of pharmaceutical specials is a major concern. Due to their poor stability and short shelf-life, specials are currently prepared as soon as an order is placed, or a prescription received. Therefore, it is desirable to produce a stable suspending vehicle which allows for specials to be prepared in advance, left on the shelf, and distributed or used when required.

In order to formulate a desirable suspending vehicle, an AR2000 cone and plate rheometer (TA Instruments) was used to determine the rheological behaviour of current commercial suspending vehicles. In addition, the ingredients of popular suspending vehicles, along with any potential health implications, were researched in order to ascertain the fundamental categories of ingredients, as well as the areas in which novel, alternative ingredients were required. From this initial research, a criterion for the novel formulation was obtained which includes a shear thinning fluid containing certain categories of ingredients with a defined viscosity range, similar to that of the commercial vehicles.

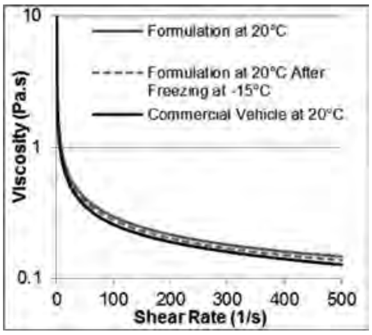

Figure 1: Viscosity of the Novel Vehicle and a Commercial Suspending Vehicle

During the formulation process, the same method was used each time, but the ingredients and proportion of ingredients varied. The rheological properties of all formulations were analysed and compared to that of the commercial vehicles. Two potential formulations were then selected and the effects of numerous process variables such as duration of mixing, temperature, mixing speed and the type of mixer used were investigated in order to obtain the optimal process parameters. A potentially novel suspending vehicle used as a base to carry APIs or ground tablets has been formulated. It exhibits shear thinning behaviour, and a desirable viscosity, similar to that of the commercial product (Figure 1), which helps ensure that particles are easily suspended. In addition, due to the careful selection of novel ingredients, initial studies suggest that the formulation undergoes no degradation once frozen, thus enhancing stability.

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Manufacturing polymeric capsules for encapsulation of liquid absorbents and liquid ion exchange media using glass capillary microfluidics and on-the-fly photopolymerisation

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In this study, we have developed a novel continuous process for the fabrication of monodispersed core/shell capsules of controllable size and shell thickness using microfluidic emulsification and "on-the-fly" in-situ photopolymerisation. The process allows for 100% encapsulation efficiency of the core material and can be used to encapsulate liquid ion exchange media inside an ion-permeable polymer shell. Conventional methods for fabrication of core/shell capsules such as internal phase separation, interfacial polymerization, complex coacervation and layer-by-layer deposition typically require multi-stage processing and do not allow precise control over the shell thickness and capsule size [1,2]. The process was tested by encapsulating an aqueous solution of K_2CO_3 of different concentrations and the capsules were used to capture CO_2 from the environment (Fig. 1).

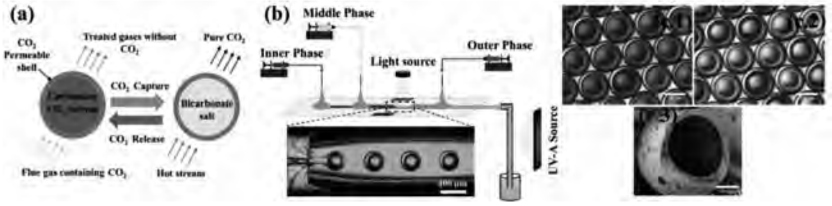

Figure 1. (a) conceptual schematic of CO_2 capture and release by the microcapsules; (b) Schematic view of the experimental set-up consisting of a glass capillary microfluidic device for generation of core/shell droplets and a UV-A source for on-the-fly in-situ photo-polymerisation of the shells; (c.1) The synthesised capsules with purple blue dye prior to CO_2 capture test, scale bar is 200 µm. (c.2) Microcapsules after CO_2 capture, 200 µm. (c.3) A FIB/SEM image of a microcapsule, 100 µm.

The shell phase was a UV-curable liquid silicon rubber (Semicosil→ 949) containing 0-2 wt% Dow Corning 749 Fluid added as a lipophilic stabilizer. The minimum UV light intensity and the minimum exposure time for a complete shell polymerization were 13.8 mW·cm^{-2} and 144 s, respectively. It was found that the drop generation process was stable for more than one hour. The capsule diameter and the shell thickness were precisely adjusted over the range of 200-400 and 20-30 µm, respectively by controlling the flow rate of the three fluid streams. Prior to CO_2 uptake, the capsule interiors were purple because the pH was above 11 (Fig. 1c.1). After exposure to CO_2, the core liquid turned to yellow (pH < 7.5, Fig. 1c.2), due to the chemical reaction: $K_2CO_3 + H_2O + CO_2 \rightarrow 2KHCO_3$. The capsule can be regenerated by heating, which causes the reaction to proceed in the opposite direction and a pure stream of CO2 is released: $2KHCO_3 \rightarrow CO_2 + K_2CO_3 + H_2O$. The capsules were thermally stable up to at least 180°C and they kept structural integrity during regeneration cycles.

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Production of spherical molecularly imprinted polymeric particles containing CO_2-PHILIC nanocavities

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In this study, we have developed novel spherical molecularly imprinted polymeric particles containing amine-decorated nanocavities for CO_2 capture, called CO_2-MIPs, using suspension polymerization (Fig. 1). The key parameters for high affinity of CO_2-MIPs towards CO_2 molecules are (a) tuned chemical architecture of the nanocavities, and (b) the presence of amine functional groups, which are covalently incorporated within the nanocavities. Previously, it was shown that CO_2-MIPs produced by bulk polymerization have a high CO_2 selectivity (separation factor up to 340) and stable capture capacity in the presence of moisture and impurities, such as SO_2, NO, and O_2 [1, 2]. However, the bulk polymerization includes crushing, grinding and sieving steps, which are time-consuming and wasteful, because only 30-40% of particles can be recovered. In addition, the produced particles have irregular shapes and sizes and can undergo mechanical attrition and break down to finer particles during the CO_2 capture process. Moreover, the bulk polymerization process is hardly scalable. On the other hand, suspension polymerization is an established method for industrial-scale production of polymeric particles in which each individual monomer drop acts as a tiny batch reactor, leading to an increase in the heat transfer and faster polymerization.

The size of the particles was 70-210 µm, depending on the agitation speed in the jacketed reactor. The nitrogen adsorption-desorption analysis showed Type IV isotherm, implying the uniform pore size distribution. The specific surface area and pore volume of the particles were up to 457 m^2/g and 0.92 cm^3/g respectively. The thermogravimetric analysis revealed that the particles were thermally stable up to 220°C. By comparing CO_2 breakthrough curves of imprinted polymer (CO_2-MIPs) and non-imprinted polymer (NIPs) particles, it was found that the presence of nanocavities resulted in a higher CO_2 capture capacity (Fig. 1c). In addition, increasing the NH_2 density on the surface particles caused higher CO_2 uptake.

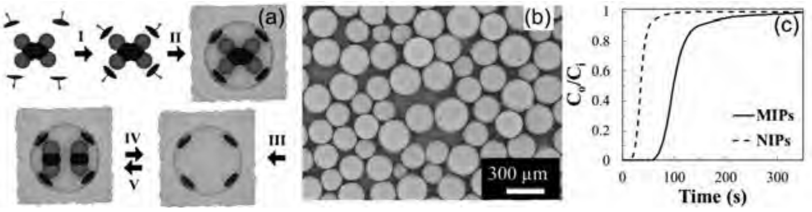

Figure 1. (a) A conceptual scheme of CO_2-MIPs synthetize process: (I) Monomer-template self-assembly, (II) Crosslinking of monomer-template complex, (III) Template removal, (IV) CO_2 capture, (V) CO_2 released; (b) SEM image of produced particles; (c) Comparison of CO_2 capture capacity of MIPs and NIPs. Acrylamide, oxalic acid, ethylene glycol dimethacrylate, and azobisisobutyronitrile were used as a functional monomer, template, crosslinker, and initiator respectively.

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Effects of ethoxylated fatty acid alkanolamide concentration and processing on D-LIMONENE emulsions

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Nowadays there is a growing social concern about issues such as environmental impact, health hazards and rational use of energy as well as of raw materials under the frame of the so-called sustainable development. This is influencing the formulation of emulsions in different fields (cosmetics, pharmacy, medicine, food, agrochemistry). This presentation is a contribution to the development of concentrated D-limonene/water emulsions. D-limonene is a terpenic biosolvent, which has interesting bactericide, antioxidant and therapeutic properties. In fact, the design of D-limonene emulsions is raising increasing interest (1-2). We report the effects of a) surfactant concentration, namely of an ethoxylated fatty acid alkanolamide, and b) the homogenization rate on the droplet size distribution (DSD) and physical stability of 30 wt% D-limonene/W emulsions prepared with a rotor-stator equipped with a toothed dispersing unit. In addition, the effect of pressure when using a Microfluidizer with a Y-type interaction chamber was also studied. The surface response methodology using a 3^2 factorial design with three replicates of the center point was used and the results obtained fitted a quadratic model. An increase in surfactant concentration (2–4) wt% and homogenization rate (2000-10000 rpm) shifted to the left the DSD, resulting in lower mean droplet sizes. Multiple light scattering demonstrated that creaming rate was clearly influenced by surfactant concentration and homogenization rate (fig. 1). The best physical stability was achieved avoiding depletion flocculation with 3.25 wt% surfactant and 10000 rpm.

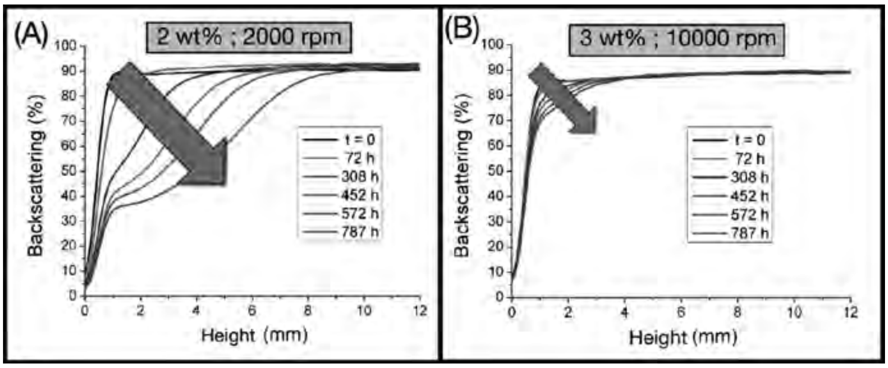

Figure 1. Changes in backscattering profiles as a function of the sample height with the storage time for the emulsions prepared (A) with 2 wt% at 2000 rpm and (B) 3 wt% at 10000 rpm. T= 20 °C.

Mean diameters decreased with the homogenization pressure of the Microfluidizer, but only the emulsion prepared using a rather high pressure, 25000 psi, exhibited lower mean diameter ($D_{3,2}$= 420 ± 10 nm) than the corresponding pre-emulsion ($D_{3,2}$= 570 ± 40 nm).

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Rheology, microstructural characterization and physical stability of w/α-pinene/w emulsions formulated with copolymers

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W/O/W emulsions are composed of oily droplets dispersed in an aqueous phase, which themselves contain aqueous droplets. They present many interesting possibilities of application in diverse fields such as chemistry, pharmacy, cosmetics, food and agrochemical industries. However, multiple emulsions are prone to undergo severe instability problems.

The aim of this work was to study the relation between the composition and the physical stability of W/α-pinene/W emulsions formulated with gellan gum as thickener. Specifically, we investigated the ratio of two copolymers with different HLB used as emulsifiers. The ability to decrease the interfacial tension and their high molecular weight make the use of amphiphilic copolymers interesting as emulsifiers [1]. Outer droplets of multiple emulsions are stabilised by the copolymer of high HLB (polyakylene oxide (EO-PO) block copolymer), while the inner droplets of multiple emulsions are stabilized by that of low HLB (poly (12-hydroxystearic acid) esterified with poly alkylene glycols).

Emulsions were prepared following a primary homogenisation step with a rotor-stator device followed by a secondary homogenisation with a high-pressure valve homogeniser. Subsequently these emulsions were mixed with a gellan gum dispersion. The resulting emulsions were characterized 1 and 15 days after preparation.

Confocal laser scanning microscopy (CLSM), laser diffraction, conductivity measurements and rheological tests were the characterization techniques used. Rheological measurements were conducted with a controlled-stress rheometer AR1000 (TA Instruments). A SPE CLSM was used to observe the microstructure of emulsions at a given height. Red Nile dye was used to stain the oil phase. Droplet size distribution measurements were performed by laser diffraction with a Malvern Mastersizer Hydro2000 MU.

All multiple emulsions showed viscoelastic properties with storage modulus above the loss modulus in the whole frequency range studied. In addition, they exhibited shear thinning flow behavior at 20ºC. A decrease in the high HLB copolymer/low HLB copolymer mass ratio (R) yielded a dramatic decrease of both moduli, greater volume mean diameters and a wider droplet size distribution. The emulsions formulated with both copolymers were stable when $2<R<5$ due to the fact that the high HLB copolymer was able to build hydrogen bonds with water of the continuous phase improving the steric interactions among oil droplets. However, destabilization by creaming was observed for $R<2$. In addition, when one of the copolymers was used alone, coalescence was the predominant destabilization mechanism.

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Predicting the interfacial tension of multicomponent liquid-liquid systems with COSMO-RS

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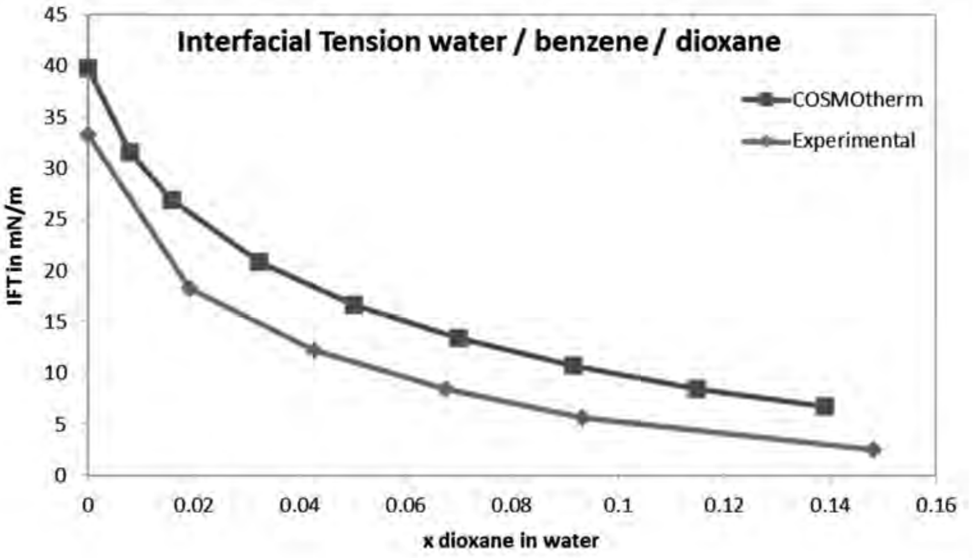
The quantum chemistry based COSMO-RS method meanwhile has been widely recognized as an efficient approach to the qualitative and quantitative understanding and prediction of the interactions and phase behavior of bulk liquid systems. In this contribution we demonstrate how the COSMO-RS concept can be extended for the prediction of the interfacial tension. Though various correlations or methods exist to predict the interfacial tension in water-organic systems, no general liquid-liquid method with a full temperature and concentration dependence had been available. The presented method uses predicted liquid phase chemical potentials and can thus be used for all liquid compositions accessible by COSMO-RS, including multiple compounds mixtures and organic-organic interfaces. It provides a sound picture of the relevant interactions of the molecules at the interface. Several examples application will be presented.



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Intelligent formulation design to minimise losses due to rain

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The world's population is increasing rapidly and higher calorific diets are becoming more common; as a consequence the demand for grain is predicted to increase by more than 50% by 2050 without a significant increase in the available agricultural land. Maximising the productivity of the available agricultural land is key to maintaining food security and agrochemicals continue to be a key enabler for the efficiency gains required. However, agrochemicals can be susceptible to significant losses and thus often require further chemical to be applied to compensate. Sources of such losses include spray drift, poor spray retention/capture by the target, poor penetration through the plant cuticle, photolytic, hydrolytic or microbial breakdown and wash-off due to rain. Formulation can play a key role in preventing such losses and maximizing the delivery of the agrochemical active ingredient to the target site. In this contribution we share developments in state of the art for testing the rainfastness of a formulation and highlight the progress in intelligent formulation design such capability allows.

Influence of crosslinked alginate in highly concentrated emulsion stability and drug release

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Highly concentrated emulsions, also known as high internal phase ratio emulsions (HIPRE) are emulsions in which the volume fraction of the dispersed phase is higher than 0.74, the maximum volume fraction of close-packed mono-disperse spheres [1]. The characteristic properties of highly concentrated emulsions make them interesting as new drug delivery systems [2]. The incorporation of polymers in the continuous or in the dispersed phase of these emulsions may confer specific properties. Alginate is a natural anionic polysaccharide that consists of linear chains of α-L-guluronic acid and β-D-mannuronic acid residues joined by 1, 4-glycosidic linkages. Alginate has been used in drug delivery systems due to its biocompatibility, water solubility, sol-gel transition properties, mucoadhesion, biodegradability, film formation properties, low cost and availability. Soluble sodium alginate can be physically crosslinked using calcium chloride. Divalent cations, such as calcium ions, interact with the negatively charged carboxyl groups from the guluronic blocks of alginate to form the so-called "egg-box" structure [3]. The aim of this research was to study the influence of crosslinked calcium alginate in the stability and release properties of O/W and W/O HIPREs in order to develop nanostructured drug delivery systems.

Calcium alginate colloidal solutions were prepared by mixing sodium alginate and calcium chloride solutions at constant ratios. The influence of the order of incorporation of sodium alginate and calcium chloride to the aqueous phase of O/W and W/O HIPREs was determined. The results obtained showed a slight increase in the stability of O/W emulsions with sodium alginate at 1% (w/v) and calcium chloride (0.015% v/v) solutions as aqueous phase. A lipophilic non steroidal anti-inflammatory drug, ketoprofen, and a hydrophilic antibiotic, clindamicine, were added to selected HIPREs. Drug release from O/W and W/O HIPREs was studied at 37ºC by the dialysis bag method. The presence of alginate and the order of incorporation of calcium chloride and sodium alginate influenced significantly ketoprofen release profiles from O/W HIPREs; in contrast, alginate showed a lower influence on clindamicine release from both W/O and O/W HIPREs.

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Development of microgels from aqueous mixtures of Gelatin and CMC for encapsulation of Probiotics

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Abstract

In this study we have focused on studying the effects of temperature, and pH on the phase separation behaviour of type B pigskin gelatin/ sodium carboxy methyl cellulose (NaCMC). The mixtures showed compatible, associative, and segregative phase separation behaviours. Associative phase separation, resulting in morphologies changing from compatible solution to liquid coacervate and further to solid precipitate with decreasing pH were observed using optical microscope: olympus model BX51TRF-6, coupled to a digital camera olympus DP73. As gelatin is a protein which can be negatively or positively charged by varying the pH and charge density, phase separation of both these biopolymers is based on thermodynamic incompatibility in solutions. The phase separation changes with the variation in concentration of biopolymers too. Temperature dependence contributes to the fact that it should not exceed the gelation temperature of the protein. Gelatin and anionic polysaccharide (NaCMC) when interact form complexes depending on the isoelectric point. The range of pH studies done included both higher, and lower pH than (PI) of the gelatin, (4.95-5.2) and pKa of NaCMC (4.2). At very low (<3.0) and high pH (> 12.0) emulsion like droplets were formed where as at other pH (4.2-11.00) weaker complexes are formed. The particles obtained will be used for the encapsulation of probiotic bacteria and their sustained release in the intestine.

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Design and mechanics of nanostructured aggregates via spray drying

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Nanoparticle-based coatings or aggregate structures enable the controlled and simplified realization of high quality products in the chemical, pharmaceutical, food and dye industry. The desired product properties are specified by material characteristics of the particles and the resulting aggregate or coating structures. Apart from the nanoparticle synthesis, their controlled processing into well-defined, partially hierarchical nanostructures is a major challenge in research and development. Spray drying processes are suitable for the production of novel nanoparticulate hybrid materials with hierarchical structures [1]. Hereby, the defined formation of these nanostructures is realized by optimized formulation and process strategies and parameters. Beside other formulation strategies and the process parameters of the drying process, the structure formation during the spray drying process and the resultant micromechanical properties of the aggregates depend on the particle-particle interactions, the surface functionalization [2], the mono- or polydisperse particle size distributions and the particle morphology.

In this study, the effect of various monodisperse primary particle sizes, mixtures of different particle sizes, particle materials and surface functionalization on the colloidal structure formation and micromechanical properties of silica model aggregates were investigated and compared to theoretical considerations. The silica nanoparticles were synthesized by the Stöber method with primary particle sizes between 50 and 500 nm. Additionally, latex particles with different particle sizes (between 20 nm and 500 nm) were used to produce porous structures via a template process (removal by tempering or leaching using a solvent). The model aggregates were produced by a spray drying process and stressed with a flat punch indenter tip via nanoindentation. Since a classification during the spray drying process for different particle materials and mixtures of various particle sizes was observed, the structure formation of aggregates during the spray drying process differs considerably. As a result, various core-shell aggregates with different structure and surface functionalizationas well as highly different mechanical properties, e.g. aggregate strength and elastic-plastic deformation, were produced.

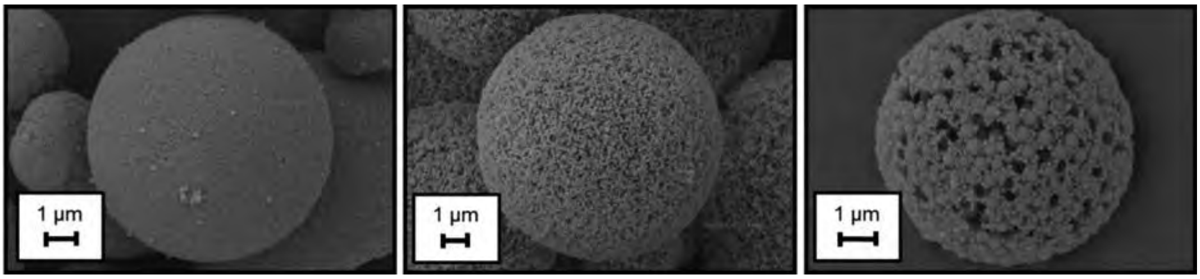

Figure 1 Silica aggregates with 150 nm primary particles (left), porous aggregate (center) and porous core-shell aggregate with 150 nm and 500 nm primary particles (right)

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Hot Melt Extrusion: Influence of Operating Parameters and Screw Geometry on Residence Time Distribution and Product's Crystallinity

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Hot melt extrusion (HME) is gaining more and more interest and has become an established processing method, e.g. for dispersing poorly water-soluble drug substances in solid excipients, either in the crystalline or the amorphous state [1]. Although HME is a well-recognized manufacturing process the influence of different operating parameters of the extruder as well as the influence of screw geometry on, firstly, residence time distribution and, secondly, on quality of the final product is not yet fully understood. Furthermore, in-line information about drug substance's concentration variability in the hot melt or its residence time distribution is hardly available.

Different pre-blended bulks with the drug substances ***Paracetamol***, ***Celecoxib***, and ***Carba-mazepine*** together with the biopolymer ***Soluplus***® were fed into a loss-in-weight feeder and dosed into the first barrel of a twin-screw extruder (***ZSE 18HPE, Leistritz GmbH)***. The geometry of the twin screw elements were varied to result in different shear intensities and therefore in higher energy input during the extrusion. Variation of the temperature profile in the extrusion barrel also influenced the energy input–but without added shear intensity.

In-line measurements to study the residence time distribution of the drug substances were conducted with an UV vis spectroscopic system (Colvistec–InSpectro X2). The probe of the in-line UV vis system was directly mounted into the hot melt–after the twin screws but before the discharge die. Using the in-line measurements the mean residence time, the Bodenstein number and changes in the UV vis spectrum were determined; with differential scanning calorimetry the crystallinity of the drug product after cooling was determined.

In addition, further experiments with the same formulations but with a novel mini-extruder were carried out. The novel mini-extruder was designed and built at the ***FHNW Institute for Pharma Technology.*** The results showed clearly the advantages of a twin screw setup in pilot scale (above mentioned extruder) compared to the smaller extrusion system, with its intrinsic process limitations due to its simplified construction.

The results demonstrate that in-line UV vis spectroscopic monitoring is a powerful PAT tool for process development as well as for process control. Furthermore, the results of the comparison of the two extruders in different scales deepened the understanding of scale-up/-down procedures.

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Designing a lipid microstructure on an inorganic carrier for solid drug dispersion formulation

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Regarding the increasing number of poorly water-soluble drug compound candidates, solid dispersions (SDs) is considered as one of the most successful formulation strategies. By molecular or amorphous dispersion of such compounds in a solid matrix, bioavailability and solubility can be greatly improved [1]. Among the different solid dispersions (SDs) preparation techniques, hot-melt extrusion (HME) has become a common manufacturing process over the last decades. The active ingredient is typically embedded in a carrier that is composed of a polymer and other excipients such as plasticizers or fillers [2]. Besides commonly used polymers (cellulose derivates or polyethylene oxides), other excipients can be used as carriers. Few reports showed that as with the melt-adsorption method, stable melt-extruded amorphous SDs could be obtained by adsorbing an acidic compound on an inorganic carrier [3]. It was observed that intermolecular interactions between the compounds acidic moiety and the silanol groups and Al3^{+}/Mg^{2+} ions of aluminum magnesium silicate (AMS) were driving the amorphization and stabilization of the drugs.

The aim of this study was to employ similar molecular interactions, however, to design a novel kind of matrix for oral delivery. It was intended to combine an acidic lipid (stearic acid; SA), a polymer (hydroxypropylcellulose) and an adsorbent (AMS) to obtain designed lipid microdomains (DLMs) for delivery systems by HME (Fig. 1). X-ray powder diffraction and atomic force microscopy analyses showed that the presence of AMS implied a disruption in SA crystallinity after HME. Creation of the desired interactions between SA and AMS functional groups was confirmed by Fourier-transform infrared spectroscopy. Finally, we showed that the DLMs, composed of amorphous lipid, could host a poorly water-soluble model compound, i.e. β-carotene (BC).

Figure.1. Schematic of interactions involved in the designed lipid microdomains (DLM) delivery system

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Synthesis of controlled-size nanovesicles

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Nanovesicles are commonly used as colloidal carriers to encapsulate different compounds for food, pharmaceutical, cosmetic and biomedical applications.

Several methods can be selected to produce these vesicles, but control over their size and polydispersity is not always possible.

In this work, controlled-size nanovesicles were produced by using a modified ethanol injection method.

Two types of vesicles were prepared, liposomes and niosomes, formulated with phosphatidylcholine and Span 60-Cholesterol, respectively.

An initial screening design with two levels (Plackett-Burman) was applied in order to determine the most important factors on vesicles preparation by the ethanol injection method.

Then, an experimental design was performed to study the influence of these factors on the characteristics of resulting vesicles.

Vesicles stability was studied by multiple light scattering technology and by measuring the encapsulation efficiency of different compounds (lipophilic and hydrophilic).

Equations, which are able to predict mean vesicle size, in the range of 54-142 nm for liposomes and 235-379 nm for niosomes with PDI values between 0.066-0.307, were obtained from the experimental design.

Optimization of surfactans in a microemulsion system for oral administration by design of experiments

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In recent years, the development and optimization of microemulsions (ME) have improved by using new techniques such as design of experiments (DOE). This method provides more information about the effects of the composition and other variables compared to traditional methods, such as PIT or HLB. One of the most important applications of ME is the oral administration of hydrophobic compounds such as essential oils. They are oily plant products with promising therapeutic properties. ***Artemisia absinthium*** is one of the most widespread plant varieties in the genus Artemisia L., in Europe, whose steam distillation extracts have shown promising anthelmintic properties. Nevertheless, the oily characteristics of these extracts requires the development of different formulations which can improve its dosage and oral bioavailability.

The aim of this work was to analyze the effect of the composition on the droplet size and conductivity in different mixtures of polysorbate 80®: propylene glycol (1.5:1), water and an ***Artemisia absinthium*** steam distillation extract, using the DOE method. The effect of water content on the viscosity of the system was also elucidated.

In previous studies, the compatibility of excipients with the extract, and the range of concentrations to establish the ME area was analyzed. In this work, a study of mixtures by a Simple Lattice method with a predefined range was conducted. Surfactant mixture (50–100%) (SM), distilled water (0%–50%) (DW) and the extract (0%–50%) (O). 19 formulations were prepared, and analyzed using a Zetasizer® NanoZS equipment, to determine their average droplet size and their conductivity at 25 °C. Viscosity of several samples was also analyzed using a MCR 102 rheometer.

A cubic model was developed to evaluate the effect of the components on the droplet size in the microemulsion system. On the other hand, conductivity data were fitted to a quadratic model. Two equations were developed from both statistical models, in which main coefficients indicated the interaction between system composition and the parameters measured: droplet size and conductivity (table 1).

	SM	O	DW	R-Squared	Adj R-Squared
Droplet size	0,819	-7,336	19,463	0,9974	0,9928
Conductivity	6,371	2,647	262,767	0,9927	0,9882

Table 1. Main coefficients from both models.

It was shown that water had the largest influence on droplet size as it causes swelling. Distilled water also affected the system conductivity due to the non-ionic nature of the other components. Finally, viscosity and conductivity indicated that increasing water content in the system caused changes in the system ultrastructure, from a W/O ME, an O/W ME and a bicontinuous state.

The main conclusion is that DOE method can be used for the development of ME, as it provides information about the components and their effects on the system, as part of the optimization process.

Synthesis of highly mesoporous films by means electrodeposition in microemulsions containing ionic liquid

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Herein, we present a novel method of preparation of very highly mesoporous films based on the electrodeposition of metals or alloys by using microemulsions containing ionic liquids. Ionic Liquid-in-Water (IL/W) microemulsions with a IL low proportion (IL: 1-butyl-3-methylimidazolium hexafluorophosphate aka bmimPF$_6$) dispersed in an electrolytic bath containing the precursors of the metals or alloys (W) and stabilized by a surfactant (Triton X-100) have been selected in order to confer the enough conductivity to permit the electrodeposition at significant deposition rates. The presence of IL droplets induces the formation of highly mesoporous films. The preparation method is described in Figure 1. Pt, Co_3Pt and $CoPt_3$ porous films, with pores in the 30-40 nm range and excellent durability in both acidic and alkaline aggressive media have been prepared. These films, with a very high active surface, have been demonstrated to be very efficient for the catalysis of methanol electro-oxidation in alkaline media. Therefore, their catalytic performance and the fast, simple, inexpensive and environmentally friendly synthesis procedure, make these porous films excellent candidates for the commercial exploitation of direct methanol fuel cells. Moreover, the synthesized porous films can be detached from the substrate by thermal shock and their magnetic properties (in the case of Co_3Pt and $CoPt_3$) allow the easy manipulation of the catalysts by magnetic fields.

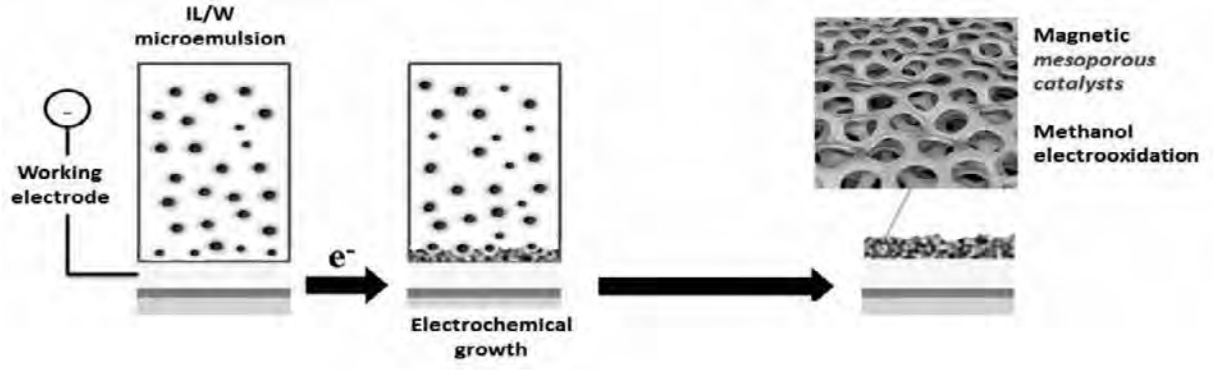

Figure 1. Scheme of the electrochemical procedure developed to obtain mesoporous films, catalysts for methanol electro-oxidation.

Hierarchical self-assemble of bacteria using pickering effect and layer by layer technique

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In the last decade, hierarchical organization of matter has been received attention in chemistry, physics and biology as an interdisciplinary subject. Mimicking the atoms, hierarchical dimensions from pico to macro level has been studied to define design parameters of self-assembled system such as size, shape and surface chemisrty.[1] Furthermore, one of the theories regarding the development of multicellular organisms proposes a self-assembling of individual cells in a programmable way.[2,3] We investigate ways to hierarchically self-assemble bacteria using pickering stabilized foams[4,5] and surface modification of bacteria via layer by layer method[6]. Such a system could be a promising candidate for a variety of applications such as cell based delivery systems, foam stabilizing formulations, and a possible opportunity for multi strain encapsulation of probiotics. ***Lactobacillus acidophilus*** were used as model bacteria. A negatively charged edible surfactant sodium stearoyl lactylate (SSL) was used to stabilize foam. Since the cell membrane of bacteria is naturally negatively charged, chitosan was chosen as a naturally occurring biopolymer to introduce positive surface charges to bacteria below pH 6.5. Results show that positively charged bacteria were mostly self-assembled around air bubbles which were stabilized by SSL (Figure 1). Therefore, combination of layer by layer method and pickering systems can potentially be utilized in bottom up construction of more complex hierarchical structures.

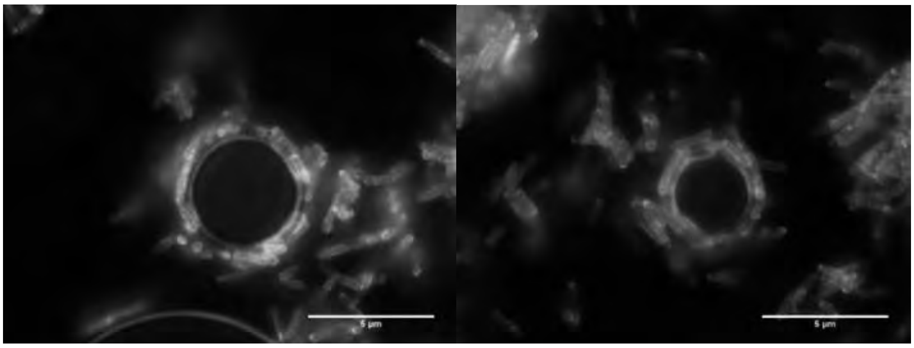

Figure.1. Flourescence microscope pictures of FITC-labelled chitosan coated bacteria templated on air bubbles which were formed by A) 5 mM, B) 15 mM SSL containing solutions.

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The Faster and Better Systematic Investigation of Both the Raw Material and Process Space

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Formulation sciences play a key role in the development of new products (formulate your innovation) and optimization of existing products (innovate your formulation). Typical challenges inherent to formulation are:

- Bans on commonly used additives / raw materials.
- Additives / raw materials with lack of biodegradability.
- Facing the consequences of REACH regulations.
- Never really questioned the composition and process of your formulations.
- Push to release innovative highly effective products quickly.
- Need to produce more formulations in less time.
- Growing pressure for sourcing of sustainable materials.
- Facing quality issues of production batches.
- …

Consequently, a large number of formulations are necessary to develop a new product or to re-formulate existing products. These challenges highlight the need for High-Throughput and High-Output formulation.

This talk will focus on the challenges presented by systematically investigating both the raw materials and the process space for efficient, reliable scale-up. Success stories towards meeting these challenges will be highlighted with a selection of High-Throughput and High-Output case studies; e.g.:

- Sun screen and eye cream formulation.
- Lipstick formulation and color matching.
- Liquid detergent formulation and testing.
- Lubricant formulation and testing.
- Battery paste and electrolyte formulation, application, testing.
- Paints & coatings formulation, application and testing.

Adsorption capacity evaluation of a lipopeptide biosurfactant on human hair

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Nowadays, surfactants are used in a wide variety of applications in several fields, such as cosmetic and health care, environmental issues and, generally, as detergents. They present valuable characteristics since they can decrease water surface tension and solubilize molecules that cannot be eliminated in an aqueous media in normal conditions. Due to their surface active nature, synthetic surfactants can result toxic in the media in which they are applied. These drawbacks can be overcome by using biosurfactants, since they result environmentally friendly because of their biodegradability and low toxicity. Therefore, it would be interesting to replace synthetic detergents by biosurfactants in cosmetic and personal care formulations. From this point of view, Vecino et al., [1] have extracted biosurfactants from an industrial stream of corn wet milling industry, consisting of a lipopeptide that could have important applications in the formulation of natural shampoos. This biosurfactant is able to reduce the surface tension of water in more than 30 units. Thus, the aim of this work was to study the adsorption of this biosurfactant in human hair.

Biosurfactant was extracted from corn steep liquor using the methodology proposed by Vecino et al. [1], obtaining a biosurfactant extract that was dissolved in water at its critical micelle concentration. After that, samples of hair were added to this solution using a liquid-solid ratio of 50:1. Adsorption experiments were carried out at 20ºC, pH 6 at 200 rpm during 30 min. At different intervals of time, samples of biosurfactant solution were obtained and their surface tensions were measured.

The results showed that after 30 min, part of the biosurfactant was adsorbed onto the hair, thus samples increased their surface tension from 43.4 mN/m up to 52.8 mN/m. These are very promising results because they open the door for obtaining more biocompatible an ecofriendly shampoos. Moreover, this biosurfactant could increase the strength of damaged hair by incorporating lipopeptides to the hair fiber, although more studies would be needed in order to corroborate this fact.

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Characterization of ionic nature of biosurfactant extracted from corn steep liquor using ionic exchange resins

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Resins have been used for years for the purification and characterization of ionic substances. The use of these resins allows not only remove impurities or increase the concentration of metabolites from industrial streams, but also allows define their ionic structure. In general, surfactants can be classified as non-ionic, anionic, cationic or amphoteric, what is going to define their future application at industrial scale. For example, anionic surfactants present the greatest wetting and emulsifying properties, while cationic ones have excellent antibacterial properties as well as good emulsifier capacities. Otherwise, amphoteric surfactants, which may have anionic or cationic properties depending on pH, are widely used in personal care products because of their less irritability to skin and eyes in comparison with other types of surfactants. Although in the literature it is possible to find many works about the production and potential application of biosurfactants in cosmetic, pharmaceutical and personal care industries, there are almost not works about the ionic nature of these surface-active compounds. Therefore, the aim of this work is to characterize the ionic nature of the biosurfactant extracted from corn steep liquor in order to define its more adequate application at industrial scale. Biosurfactant was extracted from corn steep liquor using the methodology proposed by Vecino et al. [1], obtaining a biosurfactant extract that was dissolved in water under its critical micellar concentration. After that, Amberlite IRA 400 (an anionic exchange resin) and Amberlite IR 120 (a cationic exchange resin) were added to the aqueous solution, containing the biosurfactant, using a solid:liquid ratio of 1:8. Ionic exchange experiments were carried out at 25ºC and 200 rpm during 16 min. At different intervals of time, samples of biosurfactant solutions were obtained and their surface tensions were measured.

Using Amberlite IRA 400, the results showed, that after 16 min, 100% of the biosurfactant was removed from the solution, thus samples increased their surface tension from 47.7 mN/m up to 72.6 mN/m, the same surface tension as water. Furthermore, the results obtained after using the cationic resin showed that biosurfactant was also partially captured by Amberlite IR 120. Thus it can be speculated that the biosurfactant extracted from corn steep liquor is an amphoteric detergent. This fact could be interesting in terms of stablishing its applications, because, as it was said, amphoteric surfactants are used to diminishing irritating effects of other chemical surfactants in cleansing products.

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Emulsification of viscous mineral oil by catastrophic phase inversion with non ionic surfactants.

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The influence of process and formulation conditions on catastrophic phase inversion of viscous mineral oil has been studied. Measurement of torque and conductivity allows to determine the catastrophic phase inversion point (PIP) and multiple w/O/W emulsion formation (Figure 1).

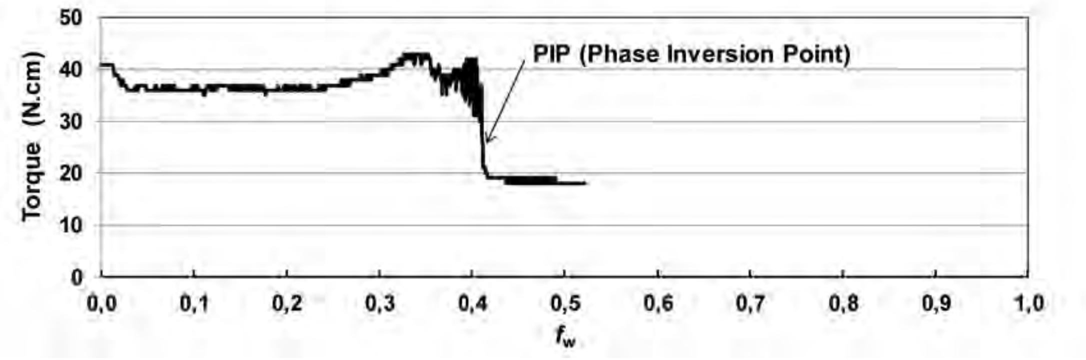

Figure 1. Variation of torque (N.cm) during addition of water in mineral oil and determination of the PIP (Phase Inversion Point).

Catastrophic inversion from water-in-oil emulsion (W/O) to oil-in water emulsion (O/W) is obtained by dispersed phase (W) addition. During this water addition, a dynamic balance between coalescence and breakup is established. However, as breakup is a unary process, proportional to the number of droplets per unit, and coalescence is a binary process proportional to the number of droplets per unit volume squared, the coalescence rate increases faster than the breakup rate with increasing volume fraction of dispersed phase.

Thus, effects of process (water flow rate, stirring speed) and formulation (nature of surfactant) conditions on the PIP have been studied.

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Essential oil-water emulsions containing a biosurfactant from *Lactobacillus paracasei*

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Surfactants play important roles in cosmetic products due to diverse properties including as emulsifier, foaming, wetting, detergency and solubilizer agents, among others. However, the market for beauty and personal care products based on natural ingredients has shown a relevant growth. In this sense, biosurfactants being non-toxic, biodegradable and ecofriendly natural compounds are suitable replacers of the chemical-based surfactants showing equal or better performances [1]. In addition, essential oils are natural ingredients extracted from plants that also are interesting ingredients for novel cosmetic formulations. The aim of this study was to formulate oil-water emulsions using a biosurfactant from ***Lactobacillus paracasei*** in combination with several essential oils (wheat germ, almond, rosemary and jojoba oil). The biosurfactant was produced in a 2-L Applikon bioreactor using a glucose-based fermentation media (supplemented with 10 g/L of yeast extract and 10 g/L of corn steep liquor) during 24h, 37 ºC, pH=5.85 and 150 rpm. After this period, the cells were recovered and washed with distilled water (2 times) and afterwards used to extract the biosurfactant in phosphate buffer-saline solution [2]. Then, the biosurfactant aqueous solution (2 mL) was mixed with the essential oils (2 mL) using an IKA T25 Ultra-Turrax homogenizer during 2 min at 18000 rpm. Subsequently, the volume (EV,%) and the stability (ES,%) of the emulsions were measured during 15 days. A Leica DMI 3000B Inverted microscope equipped with a LEICA DFC450C camera was used to observe the emulsion droplets [3]. The best formulation was obtained with an almond oil-water emulsion, which gave 52.5±3.5% and 76.7±4.7% of EV and ES respectively; whereas the jojoba oil-water emulsion was not stable after 15 days. The results gathered in this work suggest the potential use of the biosurfactant from ***L. paracasei*** in natural cosmetic products; however further toxicity assays are necessary. Additionally, the EU Cosmetic Regulation still does not account for the incorporation of this type of ingredients.

ACKNOWLEDGMENTS

This study was supported by the Portuguese Foundation for Science and Technology (FCT) under the scope of the strategic funding of UID/BIO/04469/2013 unit, COMPETE 2020 (POCI-01-0145-FEDER-006684) and the project RECI/BBB-EBI/0179/2012 (FCOMP-01-0124-FEDER-027462), as well as Xanel Vecino post-doctoral grant (SFRH/BPD/101476/2014). Also, the authors acknowledge the financial support from Spanish Ministry of Economy and Competitiveness (FEDER funds under the project CTM2015-68904); and Andrea Ferreira acknowledges to the Region Aquitaine Limousin Poitou-Charentes for her Erasmus+ internship.

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The influence of the medium composition on the biosurfactants produced by *Lactobacillus paracasei*

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Lactic acid bacteria is an interesting group of microorganisms for the production of biosurfactants. In addition, these bacteria are generally recognized as safe by the American Food and Drug Administration. An example is the ***Lactobacillus paracasei*** that was isolated from a Portuguese dairy industry and has been previously reported by Gudiña and collaborators [1] for the production of biosurfactants. The biosurfactants produced by LAB are cell-bound biosurfactants contrarily to the most well-known extracellular biosurfactants produced by ***Pseudomonas*** or ***Bacillus*** species. The main bottleneck of their industrial production and application is related with the production and recovery costs. Therefore, many studies are focusing on the use of renewable agro-industrial wastes as carbon sources in the fermentative processes [2]. The aim of this work was the production and characterization of biosurfactants by ***L. paracasei*** using a lignocellulosic residue (vineyard pruning waste) as carbon source. The vineyard pruning waste was subjected to a fractionation process to obtain cellulose, which was next submitted to a saccharification step with enzymes in order to convert cellulose in a glucose-based fermentation media. Once this glucose solution was obtained, it was further supplemented with 10 g/L of yeast extract and 10 g/L of corn steep liquor. The fermentation process was carried out in a 2-L Applikon bioreactor during 24 h, at 37ºC, pH=5.85 and 150 rpm. Finally, the cells were recovered and washed, and the biosurfactant was extracted (with phosphate buffer saline solution). Next, the biosurfactant content in sugars, proteins and fatty acids was determined and compared to the same contents obtained while using a synthetic lactose-based medium (control). The chemical analysis revealed that the biosurfactant obtained from the culture grown on glucose from vineyard pruning waste was a mixture of carbohydrate, protein and lipid in the combination 1:4:4.5, respectively. This composition is in good agreement with data reported by other authors using cellulosic sugars to produce biosurfactants by lactobacilli strains. Vecino and collaborators [3] found that the biosurfactant produced by ***L. pentosus***, grown on hemicellulosic sugars from vineyard pruning waste, is a glycolipopeptide. However, Pinto et al. [4] reported that the biosurfactant from ***L. paracasei*** (the strain herein used) produces a glycoprotein biosurfactant when grown in MRS-Lac medium (lactose-based media). Based on the results gathered in this work, it can be speculated that the composition of biosurfactants can change according to the type of carbon source used in their production. This finding opens the door to the production of different types of biosurfactants from the same strain using different carbon sources.

ACKNOWLEDGMENTS

This study was supported by the Portuguese Foundation for Science and Technology (FCT) under the scope of the strategic funding of UID/BIO/04469/2013 unit, COMPETE 2020 (POCI-01-0145-FEDER-006684) and the project RECI/BBB-EBI/0179/2012 (FCOMP-01-0124-FEDER-027462), as well as Xanel Vecino post-doctoral grant (SFRH/BPD/101476/2014). Also, the authors acknowledge the financial support from Spanish Ministry of Economy and Competitiveness (FEDER funds under the project CTM2015-68904).

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P 50

Hafnia-silica cryogels: Catalytical properties controlled by their porous structure

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(-)-Menthol is a fine chemical widely used in the manufacture of pharmaceutical, cosmetics and other compounds [1]. In the last years, the research has been focused on the proposal of different routes for the cyclization of citronellal to isopulegol, a previous and crucial step to synthesize (-)-menthol [2]. One of the main targets is to develope heterogeneous catalysts that provide high conversion but also with the suitable stereoselectivity to the desired diasteriomer. With this aim, HfO_2-SiO_2 materials have been studied as promising catalysts for the synthesis of isopulegol. These mixed oxides were prepared by a sol-gel method and a variety of aqueous-alcoholic systems have been examinated [3]. This work has been focused on their porous and textural structure, studying if such structures could control the catalytical properties of cryogels. The structures of mixed oxides was established by nitrogen sorption measurements (Figure 1) and the results show clearly that the alcoholic solvent had a decisive influence on the specific surface area and porosity. The surface area increased from Hf-Si8-A (466 $m^2 \cdot g^{-1}$ in ethanol) to Hf-Si8-B (604 $m^2 \cdot g^{-1}$ in isopropyl alcohol) and to Hf-Si8-C (684 $m^2 \cdot g^{-1}$ in ***tert***-butyl alcohol). The same trend was observed in the pore diameter (from 2.5-3 nm to 5-6 nm) and the total pore volume (from 0.30 to 1.06 cm^3/g).

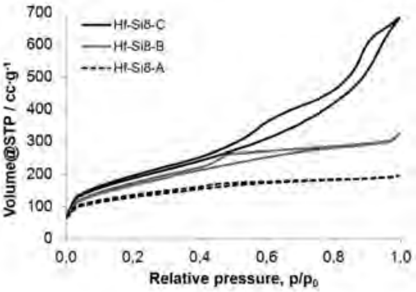

Figure 1. Nitrogen sorption for cryogels Hf-Si8-A (prepared in ethanol), Hf-Si8-B (prepared in isopropyl alcohol) and Hf-Si8-C (prepared in ***tert***-butyl alcohol); STP: Standard Temperature and Pressure

For catalytical applications in these systems, the conversion but also the diastereoselectivity (ds) are crucial. ***Tert***-butyl alcohol (Hf-Si8-C) provided catalysts with the highest values for citronellal cyclization (Conversion=93±3%, ds=74±2%). In summary, catalysts with remarkable catalytic activity were obtained. Moreover, the results obtained showed that porosity is a key parameter to determine the properties of these hafnia-silica catalysts.

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Emulsification properties of steviol glycosides

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Rebaudioside A (Reb. A) is a steviol glycoside extracted from the leaves of ***Stevia rebaudiana*** Bertoni. Due to its natural origin and high sweetness intensity and low caloric density, it is considered a natural high intensity sweetener. Its addition however results in some undesired taste attributes, such as bitterness and a lingering aftertaste. The hypothesis is that this off-taste originates from the hydrophobic steviol backbone in the Reb. A molecule. This hydrophobic backbone gives Reb. A potential to be used as an emulsifier and the hypothesis is that the off-taste can be masked by concentrating Reb. A on the oil/water interface in an oil in water emulsion.

In order to test Reb. A's potential to be homogenised in MCT and water, measurements on the interfacial tension between solutions of Reb. A and MCT were performed (see Figure 1). These results were compared to the effect of Gum Arabic (GA), a known emulsifier, on the interfacial tension. Reb. A lowered the interfacial tension more than GA, although this is likely to be due to the higher complexity of the GA molecule, which leads to a longer time required to reach an equilibrium. More detailed study is needed to determine reliable reference values. Although an effect on the interfacial tension does not give direct proof for emulsification properties, it does give an indication of the potential of Reb. A to be used as an emulsifier.

To test whether the incorporation of Reb. A in an emulsion has an impact on the taste of Reb. A in beverages, emulsions with Reb. A and different types of oil were made and tested for their sensory attributes. Initial trials were performed with orange oil, deodorised lemon oil, extra virgin olive oil and sunflower oil. As the first three of these oils brought an extra flavour to the beverages themselves and sunflower oil oxidised over time, their applicability is limited to these specific beverage products. Therefore further experiments were performed with Medium Chain Triglycerides (MCT).

First experiments with MCT showed promise, so more extensive sensory tests were performed with a lemon and a 'fruit punch' flavoured water. Respondents were asked to rate the overall taste, sweetness, aftertaste, bitterness and lingering. Although the 'fruit punch' flavoured samples with only Reb. A performed significantly worse than sugar sweetened samples, the emulsification with MCT seemed to slightly (although not statistically significant) improve the sensory properties of Reb. A sweetened samples. The overall taste of lemon flavoured samples with Reb. A was closer to that of a sample sweetened with sugar, likely because the matrix in these beverages is different and fits better to taste of Reb. A. The emulsification does however not seem to improve the taste of lemon flavoured samples sweetened with Reb. A.

Emulsification of Reb. A does not universally remove the off-taste associated to Reb. A in beverages. Further work is needed to investigate in details physico-chemical properties of Reb A. emulsions and their impact on bitterness perception in humans.

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Phase Behavior of a Diglycerol-Based Surfactant: Formation of Stable Hexosome Dispersions for Drug Delivery Applications

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Glycerol-based nonionic surfactants attract considerable attention in food, pharmaceutical and cosmetic industries due to their biocompatibility and biodegradability as compared with other conventional nonionic surfactants.[1] However, there have been few studies of the phase behavior of these commercial surfactants despite of their industrial relevance. In this context, the aim of this work was to study the phase behavior of a commercially available diglycerol-mono-isostearate surfactant (**C41V**) by phase diagram determinations. Its potential as an oral drug delivery system has also been evaluated. C41V forms an inverse hexagonal liquid crystal (H_{II}) that coexists with an excess of water. H_{II} can be dispersed as small structured particles (hexosomes); their particle size can be tuned and stability enhanced by using block copolymers (e.g. Pluronic **F127**). The hexosome nanostructure and particle size was assessed by Small Angle X-ray Scattering (SAXS) and Dynamic Light Scattering (DLS), respectively (Figure 1). A model drug was encapsulated in the lipophilic domain of the hexosomes and the release to a receptor solution at different pH values was studied. Higher release rates were found at basic pH. This behavior could be attributed to the alkali-catalysed hydrolysis of the surfactant ester bond.

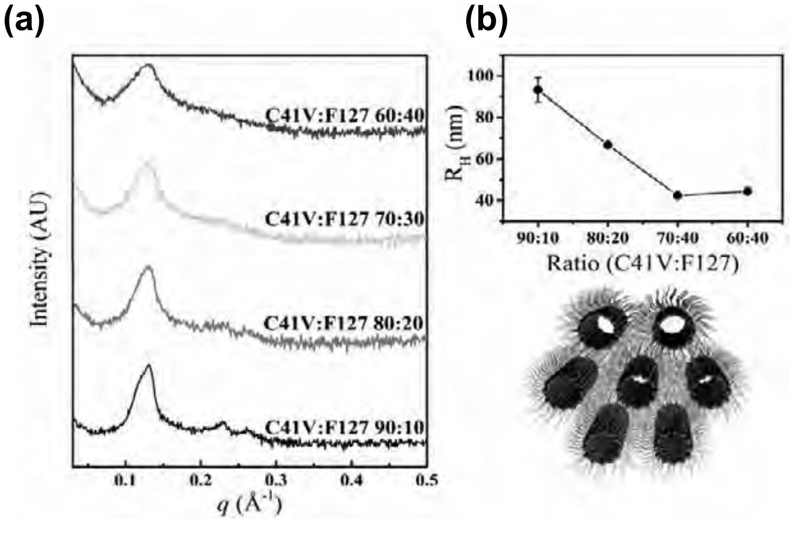

Figure 1. (a) SAXS patterns of a 5 wt% C41V dispersion as a function of C14V:block copolymer (F127) weight ratio(b) Hexosome particle size as a function of C41V:F127 ratio of a 5 wt% of C41V dispersion. The schematic structure of the inverse hexagonal phase is also shown.

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Towards functional foods through engineering of β-galactosidase carriers

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One way to treat lactose intolerance consists in using exogenous β-galactosidase. Upon administration, the enzyme needs to be encapsulated into a carrier in order to be protected from the acidic pH of the stomach, which can compromise its structural integrity, and from the deactivating environment in the small intestine caused by the presence of inhibitors (e.g. glucose, galactose) and proteases.

Recently, silica materials were proposed as carriers for food delivery applications, being biocompatible, biodegradable and generally regarded as safe (GRAS). After the discovery of organized mesoporous silica, the synthesis of inorganic materials with controlled porous structures was widely studied. The synthetic routes to obtain silica materials with dual meso-macroporosity remain a challenge in which colloidal templating emerged as an efficient way to control the pore size range and the particle shape.

Recently, Solid Lipid Nanoparticles (SLNs) revealed to be appropriate templates to obtain porous silica materials through sol-gel synthesis [1], as well as promising drug carriers [2]. Besides this, biomolecular entrapment in silica supports has won a lot of interest. This type of encapsulation has expanded the field of the drug delivery strategies.

Thereby, we present a synthetic approach for the preparation of meso-macroporous silica materials based on hard SLN templates for enzyme entrapment applications. These SLNs are previously produced mechanically in the desired size from a direct emulsion of O/W by ultrasonication.

The entrapment of enzymes such as lactase in porous materials became a clever way to facilitate solid formulation intended for the administration of dietary supplements that relieve lactose intolerance discomfort. With that in mind lactase can be encapsulated in a carrier system and added to dairy products.

Thus, our goal is to entrap lactase enzymes such as beta-galactosidase (EC 3.2.1.23) in the previously described silica materials. The encapsulation method is a post-entrapment of the enzyme in the empty silica material through physisorption.

We characterize the effectiveness of the enzyme adsorption and the stability of the material over the immobilization process by small angle X-ray scattering (SAXS), nitrogen adsorption, zeta potential and infrared spectroscopy techniques. The loading of the enzyme was promoted by the meso-macroporosity, which improved the diffusion of the enzyme towards the silica support.

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Formulation of a nano-emulsions-based system for loading and releasing of Ketoprofen

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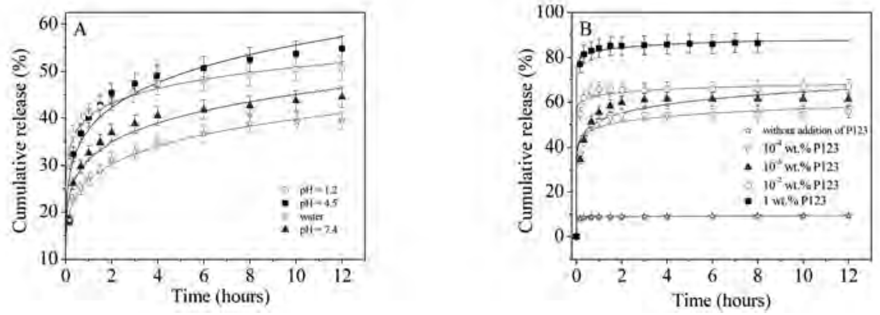
The growing demand of more efficient medicines forces to adapt drug delivery systems because of the low solubility of many active pharmaceutic ingredients in biocompatible solvents. For example, the water solubility of ketoprofen, which is effective and well-tolerated in the treatment of acute and chronic pain of both rheumatic and traumatic origin as well as postoperative pain [1,2], is only 0.0213 mg.mL^{-1}. Different strategies have been developed to overcome this drawback and one of the most popular approaches is the entrapment of a drug molecule into inert vehicles. Various systems based on micelles, microemulsions, emulsions and even inorganic materials, have been formulated for this purpose. Here, a new nanocarrier for loading and releasing of drugs is reported and ketoprofen was used as a model drug. More precisely, the carrier is a hybrid material prepared by combining O/W nano-emulsions, into which the drug has been solubilized, with mesostructured silica. This organic-inorganic hybrid material shows a controlled release of the drug, depending on pH. If the drug is impregnated into the bare hierarchical meso/macroporous dual silica material, obtained after removal of organic components by extraction, only 8 wt.% of ketoprofen is released in a phosphate buffer media (pH 7.4), probably due to its low solubility in the aqueous phase. The drug solubility and the release strongly increase by adding Pluronic micelles in the receptor phase, suggesting a micelle-promoted and assisted release mechanism. Whatever the vehicle, release profiles of ketoprofen always follow the Korsmeyer–Peppas model with a diffusional release exponent value lower than 0.5, characteristic of a pseudo-Fickian release mechanism. Moreover, the release of ketoprofen is better controlled from the hybrid nanocarrier than from the hierarchical bare porous silica. Results concerning the formulation of the nanocarrier using biocompatible products will be also presented.



Profiles of the cumulative release of ketoprofen from the hybrid material as a function of the receptor solution pH (A) and from the hierarchical bare silica as a function of the P123 concentration added in the receptor solution (B).

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Mucoadhesive property of paclitaxel encapsulated into copaiba oil containing-poly(isobutylcyanoacrylate) nanocapsules coated with chitosan

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Cancer remains a major cause of death and its incidence increases over the years [1]. Paclitaxel is an antitumor drug used in treatments against a wide spectrum of cancers . Unfortunately, its efficacy is hampered due to unfavorable profile of the drug molecule for an efficient in vivo delivery. Indeed, this drug is insoluble in aqueous based medium that composed biological fluids and it is metabolized over absorption by epithelial cells of the gut mucosa showing a limited oral bioavailability (<10%) [4]. Formulation strategies based on the use of nanoparticles can be proposed to overcome these limitations . The work was aimed to formulate mucoadhesive nanocapsules (NC) containing paclitaxel in copaiba oil and to evaluate their mucoadhesive property on gut mucosa of rats in vitro. Chitosan was used in the composition of the NC to confer mucoadhesive property. Formulation of the NC prepared by interfacial polymerization of isobutylcyanoacrylate was optimized using a statistical interaction approach by varying concentrations in copaiba oil, isobutylcyanoacrylate and paclitaxel. Optimal formulation of paclitaxel-loaded NC showed hydrodynamic diameter of 486 ± 3 nm with a narrow PdI of 0.17 and appeared spherical by transmission electron microscopy. Zeta potential was + 37 ± 0.3 mV consistently with the presence of chitosan on the NC surface. Encapsulation efficiency and drug loading of paclitaxel were 74 ± 1% and 1.70 ± 0.02%, respectively. Dispersions of NCs were stable after six months storage at 4°C and for 120 min in simulated gastric medium. In the presence of mucins, NCs were aggregated supporting that they were mucoadhesive (Figure 1). Consistently, the NC promoted retention of [3H]-paclitaxel-on rat intestinal mucosa mounted in Ussing Chamber. Taking together, results are encouraging to pursue the evaluation of the chitosan-coated NCs as an oral formulation for the delivery of paclitaxel designing a new treatment for cancer with possible synergetic anticancer effect with anticancer components found in copaiba oil.

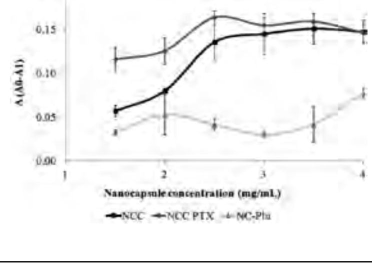

Figure 1- *in-vitro* mucin aggregation test evaluating mucoadhesive properties of the NCs. NCC: Copaiba oil-loaded chitosan-poly (isobutylcyanocrylate) core-shell NCs; NCC PTX: Paclitaxel into NCC; NC-Plu: Copaiba oil-loaded Pluronic-poly (isobutylcyanocrylate) NCs.

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Nanoemulsion (NE) containing hydrogel formulations of tacrolimus for the treatment of psoriasis

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Purpose:

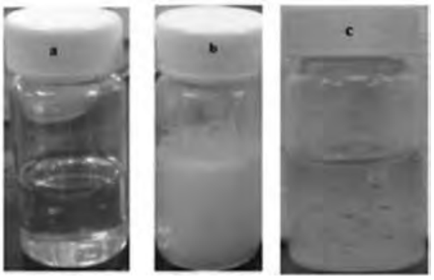
The objective of this study was to formulate, optimize and characterize a thermodynamically stable nanoemulsion formulation for transdermal delivery of tacrolimus to improve its bioavailability and permeability through the skin.

Methods:

Solubility determination of tacrolimus in various oils, surfactants and co-surfactants was determined by dissolving excess amount of tacrolimus in 2 ml of each of the selected oils, surfactants and co-surfactants in 5 ml stoppered vials**.** Based on the solubility and miscibility studies combination of oil phase (Glyceryl mono oleate), surfactant (Tween 80) and co-surfactant (Propylene glycol) were chosen to construct the pseudoternary phase diagram by aqueous titration method. Surfactant and co-surfactant (Smix) were mixed in different volume ratios (1:1, 1:2, and 2:1). Nanoemulsion formulations with different combination from phase diagrams were selected.To overcome the problem of metastable formulation, physical stability tests were performed. The droplet size, polydispersity index, zeta potential, pH, electrical conductance, viscosity, refractive index of optimized batches were determined. Optimized nanoemulsion formulation was converted into hydrogel by using carbopol 934. In vitro skin permeation studies were performed using Franz diffusion cell with an effective diffusional area 2.56 cm^2 and the capacity of the receiver compartment 10 ml using rat skin.

Results:

The mean droplet size of nanoemulsion formulations was found to be 115 nm and polydisperlibity index was 0.391. Drug content was determined by developed RP-HPLC method. The zeta potential of the optimized formulation was less than -30 mV. In vitro skin permeation studies were performed for the permeation of drug from formulations and marketed tacrolimus ointment. The flux of optimized formulation was significantly increased in comparison to the marketed tacrolimus ointment (Control).



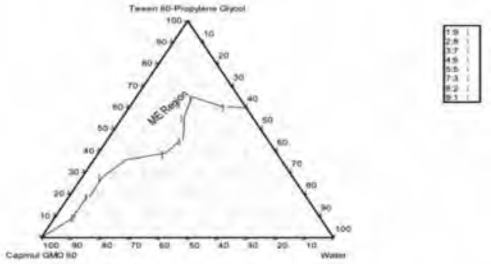


Figure 1. a) Transparent NE, b) turbid emulsion, c) gel (left to right)

Conclusion:

The optimized nanoemulsion containing hydrogel formulation increased the permeation of tacrolimus through the skin compared to the control. Developed system of nanoemulsion based hydrogels can serve as potential drug delivery system for increasing the bioavailability and better patient acceptability in the treatment of psoriasis.

Two simultaneous processes of extraction and solubilization of astaxanthin by dilutable microemulsions

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The consumption of food supplements from natural sources, to maintain the body health has been increasing during the last years. Astaxanthin (3,3'-dihydroxy-β-carotene-d-d'-dione(is natural carotenoid antioxidant with a variety of health benefits.

The main and almost exclusive source of astaxanthin is ***Hematococcus Pluvialis*** microalgae with ca 38000 PPM astaxanthin. However, it has low solubility in water, resulting in extremely low oral bioavailability.

We solubilized astaxanthin within a food-grade, fully dilutable microemulsions and characterized the empty and the loaded systems. The nanostructure of the both empty and loaded-ME inverted from O/W droplets (0-20 wt% water) to bicontinuous domains (20-60 wt% water) and finally to swollen direct micelles (> 60 wt%).

Astaxanthin solubilization contributed to the system's order (cosmotropic effect) in particular within the bicontinuous nanostructures. However the high order comes at the expense of the solubilization capacity.

We utilize the ME as a medium for the extraction of astaxanthin from wet or dried microalgae. We examined the effect of different parameters on the extraction. For one step extraction of 10 minutes at RT we obtained a concentration of 0.56%(w/w) of astaxanthin in the ME concentrate (no water added) and a yield of 79%. Recycling the loaded ME from the first round of extraction for second and third extraction cycles with fresh biomass nearly doubled and tripled (respectively) the concentration of astaxanthin in the ME increasing its capacity to up to 1.6%(w/w). Correspondingly, the yield of each cycle was approximately the same and reached 73%.

PLGA nanoparticles as a novel approach for ophthalmic delivery of pranoprofen: *in vitro* cytotoxicity studies

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Pranoprofen (PF) is a non-steroidal anti-inflammatory drug that can be used as a safe and effective alternative anti-inflammatory treatment following strabismus and/or cataract surgery [1]. Although this drug has shown high anti-inflammatory and analgesic efficiency, the pharmaceutical use of PF is limited due to its inadequate biopharmaceutical profile. [2].

PF is commercially available in the form of eye-drops. However, this traditional dosage form cannot be considered optimal in the treatment of ocular diseases due to the fact that most of the drug is removed from the surface of the eye, following the instillation, by various mechanisms. Moreover, the relatively impermeable corneal barrier restricts the entry of foreign substances. As a result, less than 5% of the administered drug penetrates the cornea and reaches intraocular tissues[3]. To improve these inconvenient, we formulated PF in nanoparticles (NPs) as innovative strategy to improve the biopharmaceutical profile of PF for ophthalmic administration. The optimized PF-F1NPs suspensions showed an average size appropriate for ocular administration (around 350 nm) and high entrapment efficiency (80%) [4].This formulation was selected to evaluate ***in vitro*** cytotoxicity using the method described by Fangueiro et al[5]. Y-79 human retinoblastoma cell line was using to evaluate the cytotoxicity of the PF-F1NPs formulations which were compared with Blank NPs and with the free drug solution (PF dissolved in PBS).

Cell cytotoxicity assays revealed little or no toxicity for concentrations up to 300 μg/mL of free drug but when loaded into PF-F1NPs formulations toxicity was achieved earlier. In these experiments, concentrations up to 300 μg/mL are considered safe as they do not reduce cell viability below 70% of the control [6]. The results obtained from cytotoxicity assays could be attributed to the fact that free drug in solution can undergo degradation, leading to others molecules less toxic and, consequently these molecules not affect the cell viability in the same extension as drug entrapped in NP (protected from water) and continuously released in a stable form that can interact negatively (causing toxicity) with cells.

From all the results obtained in this research, it could be concluded that the ocular administration of the PF-F1NPs formulations could be an effective system and appropriate for ocular application of PF, improving the biopharmaceutical profile of this drug.

Acknowledgement

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Cross-Linked microgels, produced by water-in-water-emulsions, as delivery system for enzymes

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The research work has focused on the preparation and characterization of microgel particles, obtained by cross-linking in the disperse phase of water-in-water (W/W) emulsions, with the final aim of studying the microgels as carriers for the delivery of enzymes.

The first system was composed of water, gelatin and maltodextrin, because of its excellent biocompatibility and the easy formation of W/W emulsions in this system, due to mutual immiscibility between gelatin and maltodextrin. Stable gelatin-in-maltodextrin emulsions have been prepared by dispersing the gelatin aqueous phase into the maltodextrin aqueous phase. Genipin, a biocompatible cross-linker, has been added to cross-link into the gelatin-based aqueous droplets, and thus obtaining stable microgel dispersions of 10-20 µm (Fig.1a). The microgels have been purified and freeze dried, which lead to leaf-like structured macroporous particles (Fig. 1b). The influence of cross-linker concentration and pH on microgel properties have being tested. High genipin concentrations (10 mM) increase bond formation between polymer chains, leading to rigid particles with low swelling ratios. Higher microgel swelling ratios have been observed at pH < 4 and pH > 8, because gelatin proteinaceous chains are electrostatically charged at those pH values, leading to repulsion between adjacent chains and producing expansion of the microgel network.

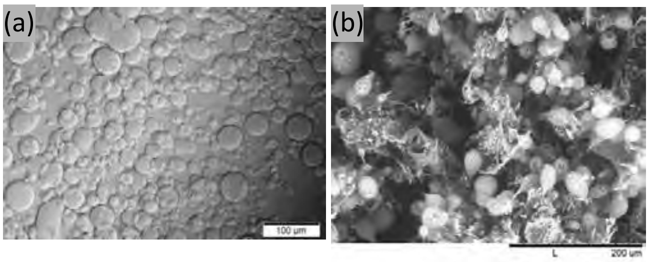

Fig. 1. Microscopic image (a) of gelatin microgel dispersion and scanning electron microscope image after freeze-drying the sample (b)

The second studied system was composed of water, carboxymethylcellulose (CMC) and bovine serum albumin (BSA). This system, which also formed W/W emulsions, allowed to obtain microgels, around 5-10 µm, by emulsifying CMC droplets dispersed into a BSA aqueous phase. CMC exhibited low swelling at acidic pH or if ionically crosslinked by Fe^{3+}. Ionic crosslinking can be made reversible at pH<pKa (4.3), as the protonation of the carboxyl groups of CMC, leads to dissociation of the Fe^{3+} ions from the polymer. This behavior makes cross-linked CMC microgels very interesting for oral drug delivery to the intestine: The microgels could remain both, in a neutral/basic solution ***ex-vivo*** and later in the acidic environment of the stomach unswollen, but might swell in the intestine, due to the loss of ionic crosslinks inside the stomach.

Enzyme activity within gelatin macrogel cross-linked with genipin has been studied. The activity of enzyme remained active during at least 2 days inside gel stored at 4 ºC with 1 mM Genipin. Detailed influence of genipin concentration, storage time and pH, but also encapsulation efficiency into microgels, are subject to current study.

POSTERS
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Hyaluronan hydrogels with ionic liquids based on ketoprofen as drug delivery systems

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Ionic liquids (ILs) have been recognized as an alternative to conventional solvents and they are becoming increasingly useful in a wide range of fields in chemistry leaning toward biology. ILs make a unique architectural platform on which the properties of both cation and anion can be independently modified, providing tunability in the design of new functional materials as well as pharmaceutical and biological ingredients. In this context, their use enables to modulate the properties of active pharmaceutical ingredients (APIs) with novel performance enhancement and delivery options. Three ILs based on ketoprofen (KP), non-steroidal anti-inflammatory drug, were prepared using anion exchange procedure in non-aqueous media (**Fig. 1**) [1].

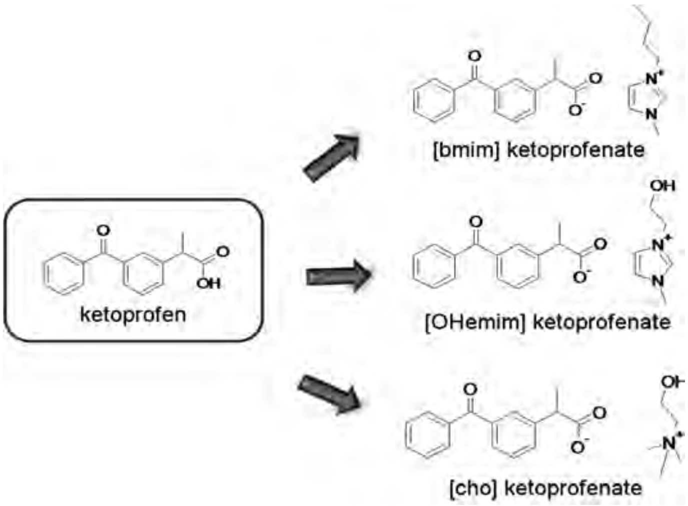

Fig. 1 Three ILs consisting in KP salts.

The aim of this work was to study the release properties of ILs based on KP salts obtained by ionic exchange. These ILs were incorporated to hyaluronan (HA) hydrogels crosslinked with butanediol diglycidyl ether (BDDE). HA hydrogels were selected due to their physicochemical and mechanical properties that show that these materials can be considered as good candidates to be used as drug delivery systems and for implants development [2]. The influence of ILs on hydrogels swelling ratio and drug release has been studied. Differences in KP release can be related to drug solubility and hydrogels crosslinking.

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Formulation of low containing surfactant o/w microemulsion with high volume fraction of copaiba oil: a rational approach based on a match of solubility parameters between surfactant and oil components

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The present study aimed to develop an O/W microemulsion (ME) including a high volume fraction of oil with a low amount of surfactant. MEs are interesting systems. They are thermodynamically stable and are considered as pharmaceutical formulation to promote delivery of hydrophobic compounds with therapeutic activities [1, 2]. In general, the obtaining of MEs requires the incorporation of a large amount of surfactants. This can be the cause of toxicity . While ME are still formulated on empirically basis, it was postulated that W/O microemulsion with a low concentration of surfactant(s) but having a high volume fraction could be formulated using a rational approach based on a match of solubility parameters between components of the oil and the lipophilic part of surfactants. Solubility parameters of a series of surfactants and of main components of copaiba oil, a natural oil with therapeutic activities used in traditional medicine, were calculated according to the Hansen approach [5] (equations 1,2). The required HLB of the oil (HLB_0) was calculated with equation 3.

$$\delta_{d}=\frac{\Sigma F_{di}}{V}\quad \delta_{p}=\frac{\sqrt{\Sigma F_{pi}^{2}}}{V}\quad \delta_{h}=\sqrt{\frac{\Sigma E_{hi}}{V}}\qquad (Eq1)\qquad\qquad \delta_{t}^{2}=\delta_{d}^{2}+\delta_{p}^{2}+\delta_{h}^{2}\qquad (Eq2)$$

$$HLB_{0}=\frac{20}{1+K/\,[\delta_{d}^{2}+0.25\,\delta_{p}^{2}+0.25\,\delta_{h}^{2}]_{L}}\qquad (Eq3)$$

Solubility parameters of surfactants showing the best match with those of copaiba oil components were selected. Blends at different were prepared to match the required HLB of the oil. The minimum concentration of surfactant blend required to obtain a ME was determined by titration of a mixture containing 75% water and 25 % copaiba oil at 25°C. Transparent and isotropic ME were obtained with copaiba essential oil at final composition of oil 19.6 %, Pluronic F-68® 0.15 %, Brij O10® 13.55 %, and milli-Q® water 66.7% (w/w). The hydrodynamic diameter of the droplets was 42 ± 0.5 nm with unimodal distribution (PDI= 0.13 ± 0.01). The approach based on chemical match oil components and lipophilic part of surfactants and evaluated by comparing their solubility parameters was suitable to formulate MEs characterized with a high oil/surfactant ratio (1.43) and oil volume fraction (19.6 %) as compared with MEs of the literature. The approach previously applied optimizing formulation of emulsions and inverse MEs [6] can also apply formulating O/W MEs with high volume fraction of complex oils and low surfactant content.

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Physical aging of emulsions containing coated tio$_2$-nanoparticles: interaction between nanoparticles and other ingredients

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TiO^2-nanoparticles (NPs) are usually added to cosmetic emulsions because they procure a good UV-protection[1]. In this study, two natures of NPs surfaces were explored: a hydrophilic silica-coated particle and a hydrophobic one covered with a large organic coating. During emulsion aging and depending on their surface nature and properties, NPs might interact with the formula by inducing adsorption of formula's compounds[2] or by undergoing coatings damages. These phenomena may change the nanoparticle surface properties, their behavior in emulsion, and finally, led to the emulsions destabilization. The impact of TiO^2-NP surfaces on the physical aging of emulsions was here studied.

For this purpose, three emulsions were formulated differing only by the presence and type of NPs: one NP-free as blank, and two containing hydrophilic and hydrophobic commercial TiO^2-NPs, respectively. The emulsification process was optimized to obtain a blank emulsion physically stable and to improve the NPs dispersions. Effects of coatings on fresh emulsions were depicted on the micro and macro scales by several physico-chemical methods. Then, emulsions physical evolutions on normal or accelerate aging conditions were monitored.

Droplets sizes were similar between the three fresh emulsions, whereas slight differences in term of networks organization highlighted the impact of the coating nature on the emulsion microstructure. However, initial emulsions properties looked similar by applying rheological and textural analyses. Although the blank emulsion and the one with hydrophilic NPs remained similar after the aging step, the microstructure of the emulsion with hydrophobic NPs quickly evolved: aggregates of both droplets and NPs made the formula less homogeneous. As will be illustrated, this evolution in term of colloids sizes strongly affects the functional properties, as viscosity, consistency or spreading quality of this aged emulsion.

These results revealed the impact of coating nature in this kind of complex media. After innovative NPs extractions[3] from fresh and aged formulae, their surfaces were characterized. By an original physico-chemical approach, quick surface modifications were evidenced thanks to an original physico-chemical approach; changings of the surface charges and wettability of particles were shown. These variations might cause the differences in term of stability between emulsions.

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Flow focusing microfluidic emulsification: Formulation variables impact in flow behavior

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Emulsions are thermodynamically unstable mixtures of two immiscible liquids in the presence of a surfactant. The physicochemical environment (i.e. salinity, presence of alcohols, temperature, nature surfactant and oil phase) affects the final emulsion properties. The effect of all intensive variables was gathered in the generalized formulation variable called hydrophilic-lipophilic balance[1] (HLD), proposed by Salager et al. When HLD = 0, the surfactant has the same affinity for oil and the water: the so-called "optimal formulation". When HLD> 0, the system is hydrophobic (W/O) and for HLD <0, the system is hydrophilic (O/W emulsions).

Changes in formulation parameters affect the force balance that occurs at the interface. When emulsions are formed by microfluidic chip on a "flow focusing"[2] geometry, the changes in HLD affect both the droplet size and flow behavior of the fluids.

Pre-equilibrium time, salinity and oil nature influence on flow properties of Surfactant/Oil/Water systems was studied. Pre-equilibrium time and salinity effect were studied for sodium dodecyl sulfate/toluene/water system and temperature and oil nature were studied for alkyl poly-ethoxylated surfactant/oil/water system. The borders of different flow zones change for each formulation variable. For both systems, ionic and non-ionic surfactant, a jet-flow pattern was found in the vicinity of "optimal formulation" independently of the continuous phase flow and of the studied formulation variable. These results shown that "HLD approach", often used on the emulsions formulation, could be extrapolated on microfluidics domain. Obtain stable dispersions and complete the actual physical conceptions are the final objective of this project.

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Solid crystal suspensions: an approach for dissolution rate enhancement of efavirenz by hot melt extrusion.

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The improvement of the solubility and bioavailability of poorly water-soluble drugs has been the important issue in front of pharmaceutical scientists for many years. Recently solid crystal suspensions (SCS) approach has been reported by scientists to improve the solubility of poorly water soluble drugs, in which the crystalline drug are ground and dispersed in a highly water soluble crystalline carrier by a hot melt extrusion process. (1-2)

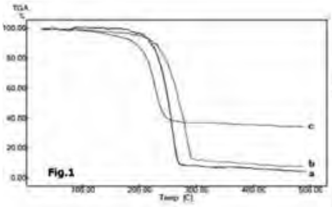

Fig.1

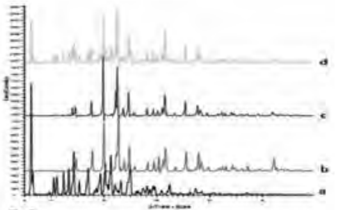

Fig.2

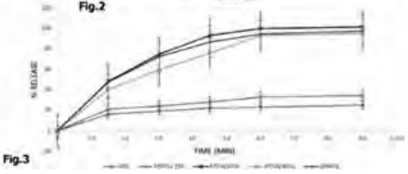

Fig.3

Fig 1) TGA analysis
Fig 2) XRD diffractograms
Fig 3) *In-vitro* dissolution study

In this context, we have explored polyols i.e. xylitol as crystalline highly water soluble carrier system to improve solubility and dissolution of Efavirenz (EFV). EFV is an oral non-nucleoside reverse transcriptase inhibitor for the treatment of HIV-type 1 disease. EFV (20 & 60% w/w) was premixed with xylitol (XYLISORB®300) using a V-Shell blender. These binary mixtures were extruded using a co-rotating twin-screw extruder (Thermo Fisher Scientific HAAKE MiniLab II) at screw speeds of 50-150 rpm and a temperature range of 92-98°C to obtain extrudates i.e. solid crystal suspensions. The extrudates were milled and passed through ASTM #35 mesh. TGA, DSC and PXRD studies were performed to characterize the physical form of EFV in extrudates. Hot stage microscopy (HSM) was conducted to determine the thermal transitions of drug upon heating. Milled extrudates equivalent to 100 mg EFV were filled into capsules. Dissolution studies were performed for pure EFV, physical mixtures, and the extruded formulations along with EFAVIR® as per USP monograph.

The TGA studies inferred suitability of componenets for HME processing. XRD studies indicated that both carrier and drug maintained in crystalline state after the extrusion process, which was further confirmed by DSC. HSM was conducted to visually determine the thermal transitions and extent of drug melting in coformers. DSC results are in good agreement with HSM findings. (2) FTIR imaging analysis showed partial miscibility and inhomogeneous system of EFV with xylitol. The melt extrudates with 60% drug loading showed a 5.5-fold higher release rate compared to pure drug. The API particles become intimately mixed and entirely surrounded by highly hydrophilic xylitol resulting improved solubiltiy and dissolution that is also due to the particle size reduction due to HME process. All extruded formulations were found stable as per ICH guidelines for a period of six months. In conclusión, formulation of crystal suspensions by HME technology significantly increased solubility of EFV. This technique/process provided an alternative approach for enhancing solubility of other poorly water-soluble drugs using xylitol as a primary matrix carrier.

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Formulation and optimization of emulsions based on fennel essential oil and eo/bo block copolymer surfactant

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The influence of EO/BO block copolymer surfactant concentration in the range (1-5 wt%) and energy input on the emulsion stability and droplet size distribution of fennel essential oil-in-water emulsions has been studied.

Fennel essential oil is an interesting promising material to be used for emulsion formulation with applications in cosmetics, food industry and agrochemicals. In the latter field, these emulsions may be used as matrices for pesticides, where fennel essential oil plays the role of an eco-friendly solvent.

A two-factor central composite design was conducted in order to optimize the emulsion formulation and processing. Emulsion stability has been studied as function of ageing time, by multiple light scattering (Turbiscan Lab-expert, Formulaction) and laser diffraction (Mastersizer X, Malvern). The surface response methodology allowed us to obtain a formulation comprising minimum droplet size and maximum stability by using a single step rotor/stator homogenizer process.

It was observed that creaming was the main destabilization process. In order to improve emulsion stability the influence of high pressure homogenization (M110P, Microfluidics, Massachusetts, USA) was studied. Nevertheless, although lower droplet sizes were obtained, emulsions were more unstable maybe due to Ostwald ripening phenomena.

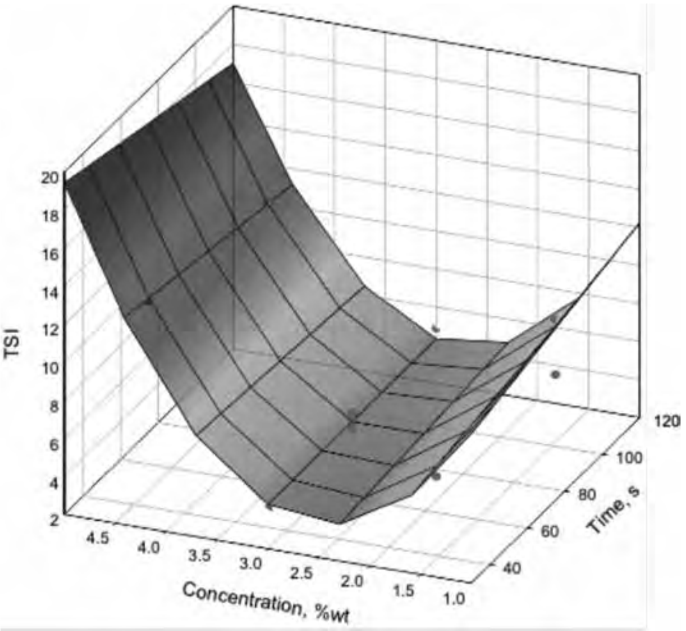

Figure 1. Response surface 3D plots of Turbiscan Stability Index as a function of EO/BO block copolymer surfactant concentration and processing time for emulsions at t = 0.

Modelling the micellization behavior of ionic surfactants

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Surfactants are amphiphilic molecules consisting of two blocks, generally referred to as hydrophilic head and hydrophobic tail. Due to their ability to lower the surface tension between two phases, surfactants are employed as detergents, wetting agents and emulsifiers. Additionally, they tend to self-assemble to form complex structures, such as micelles or, at higher concentrations, liquid crystalline phases, which find application as nanoreactors and material's templates, respectively. [1]

In this work, we investigate the micellization behavior of a cationic surfactant (Varisoft RTM 50) of relatively low critical micelle concentration (*CMC*). To this end, we propose an effective short-range correction to the long-range Coulomb interactions that allows to reproduce very accurately the degree of ionization of the micelles as obtained by experiments. Our theoretical framework is validated by extensive molecular simulations that provide insight into the structural properties of the micellar aggregates obtained.

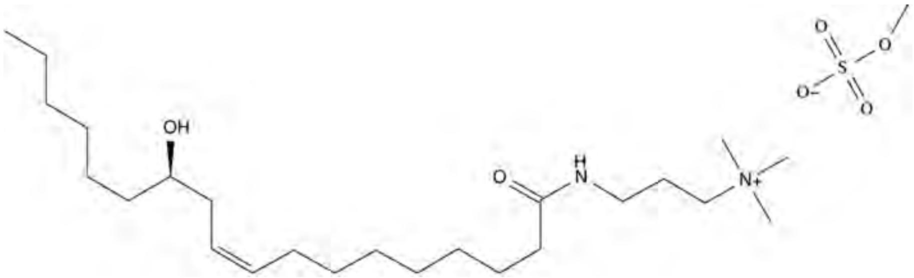

Figure 1. Chemical structure of Ricinoleamidopropyltrimonium methosulfate,commercially sold as Varisoft RTM50.

While our simulation results indicate the presence of monodisperse spherical micelles at concentrations close to the *CMC,* larger micelles are formed at higher concentrations, revealing a transition to a bidisperse distribution with the micelles keeping a spherical shape. These findings are in excellent agreement with our conductivity measurements, which confirmed the presence of a second *CMC* at a very similar surfactant concentration.

Keywords:

Micelles, CMC, Lattice, Monte Carlo

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Problem of cmc determination for amphiphilic molecules having a krafft point

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Since the beginning of 20th century, numerous experimental studies have been conducted on surfactants. Progress of experimental investigations and modern instantaneous internet access to a large part of relevant scientific literature makes now possible to gather a widespread amount of data. This database provides surfactant information about solubility and spontaneous organization at room temperature, which would be valuable for many industrial applications. However, analysis of literature data pointed out some significant discrepancies regarding Critical Micellar Concentration (CMC) values of octyl-α-glucoside (C8αGlc) and dodecyl-β-glucoside (C12βGlc) [1,3] surfactants, for which some measurements were carried out at room temperature, but under the Kraft Point (Tk), when surfactant is in an hydrated crystalline state.

The present work deals with the effect of temperature and solubility state of surfactant molecules on the results obtained with various analytical methods employed to determine CMC values. Methods based on the evolution of surface tension with surfactant concentration, and on change in absorbance related to preferential solubilization of a dye into the micelle, were used [4]. Characteristic amphiphilic sugar-based surfactants were studied: dodecyl-β, octyl-α and octyl-β-D-glucoside [1]. Differential scanning calorimetry (DSC), in addition to the visual observations, allowed the determination of the Tk of each molecule.

The results show that discontinuity of standard curves obtained by surface tension versus surfactant concentration are frequently misinterpreted as a CMC value, but can also be observed in the appearance of crystals (CAC), and in fact seem to reflect their solubility limit. In parallel, the results obtained by colorimetry and dynamic light scattering were used to verify the presence of micelles in solution.

This work illustrates the importance of carefully considering the question of the solubility of surfactant molecules, and checking the effect of experimental temperature conditions, as well as the protocol of sample preparation, during the CMC determination by tensiometry. It also highlights the necessity to use complementary methods to verify the presence of micelles in solution and define unambiguously the CMC, particularly for molecules with a Tk above room temperature.

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Influence of physicochemical interactions between particles and organic compounds on mineral foams stability

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Reducing energy consumption and greenhouse gas emission became a major concern in all domains and also in the construction sector. Cement based mineral foams appears to be an effective solution to these issues. Such foams can be produced by industrial processes from water, cement, organic compounds (surfactants, superplasticizers…) and other components as filler or sand [1]. However, the production of these materials can be difficult because of the kinetic competition between foam stability and cement setting. Cement based mineral foams are extremely complex materials because of the number of components and all their interactions. The objective of our study is to get insight into the interactions between mineral and organic compounds and to understand their role in the stabilizing mechanisms.

Our strategy is to use a surfactant exhibiting a characteristic peak in UV-visible spectroscopy namely sodium dodecylbenzene sulfonate (SDBS) in order to determine its function and position in the complex system. We first worked on unfoamed slurries to understand the behavior of the cement suspensions in presence of surfactant and the interaction between the mineral particles and the molecules of surfactant. Then we studied the foamed materials in order to study the effect of the surfactant on the stability and the characteristic parameters of the cement based mineral foams.

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Adequate Flow Properties for Consistent Tableting: A Case Study on Lactose and MCC

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Powder flow is a key to the robust tablet production process [1]. In general, poor powder flow of an excipient mix results in tablet weight variations, poor content uniformity and inconsistent tablet properties. Each excipient plays therefore an important role in determining the flow behavior of the total powder mixture. The main objective of this study is to investigate the flow behavior of various excipients and the tabletability in placebo composition.

A ring shear cell tester (Brookfield PFT, UK) was used for measuring the powder flow properties. Particle size distributions, bulk and tapped densities were measured following the USP method. Excipients, lubricated with 0.5% w/w magnesium stearate, were compressed to a 225 mg tablet on a ZPS08 (Shanghai Tianxiang, China) tableting press equipped with a gravimetric feeder system. Tabletting was performed using two types of tooling [a round flat beveled 7 mm tooling and an elongated (14 mm*6 mm) tooling].

SuperTab® 24AN (anhydrous granulated) and other directly compressible lactose types showed the lowest variation in tablet weights. Similar results were noted for directly compressible Pharmacel®102. Interestingly, Pharmacel® 101 and 102, excipients with low bulk densities, showed good flow behavior in this experiment. Low bulk density can cause inconsistent die filling, which is reflected in the tablet weight variation (Table 1). Addition of lactose to MCC can overcome this issue by offering superior flow. The differences in tablet weight variation found between tooling shapes are likely due to the ability to overcome arching of an elongated tablet.

Table 1: A summary of the typical physical parameters, theoretical conical hopper arching diameters and tableting results of the different excipients tested in this study.

Products	Particle Size (micron), n=3			Density (g/ml), n=3		HR	CI	FFC, n=3	Tablet wt RSD (mean +/- SD, n=13-14)	
	X10	X50	X90	Bulk	Tapped				round	elongate
SuperTab® 21AN	12.2 (0.1)	159 (1)	351 (17)	710 (28)	896 (37)	1.26	20.8	10	0.89 (0.19)	0.92 (0.19)
SuperTab® 22AN	64.7 (0.3)	223 (1)	394 (2)	670 (8)	786 (9)	1.17	14.8	40	0.52 (0.11)	0.61 (0.12)
SuperTab® 24AN	42.6 (0.3)	129 (1)	275 (10)	502 (16)	620 (22)	1.24	19.0	30	0.52 (0.07)	0.46 (0.09)
SuperTab® 30GR	41.8 (0.7)	140 (3)	302 (16)	548 (22)	671 (30)	1.23	18.3	30	0.63 (0.07)	0.52 (0.08)
Pharmacel® 101	19.5 (0.4)	66.3 (2)	135 (6)	294 (12)	442 (15)	1.50	33.5	6.8	0.98 (0.40)	0.96 (0.26)
Pharmacel® 102	29.2 (0.4)	94.2 (2)	190 (8)	317 (9)	450 (17)	1.42	29.6	11	0.94 (0.17)	0.86 (0.12)

FFC= flow function coefficient

The SuperTab® grades with higher densities lead to less weight variation than the less dense Pharmacel® 101 grade and can be used alone or in combination to provide adequate flow properties required for high speed tableting in formulation.

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Classification of oils using the phase inversion temperature of $C_{10}E_4$/n-octane/water emulsions and comparison with required HLB.

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The evaluation of the required hydrophilic lipophilic balance of several oils has been studied with the use of a new concept of classification of surfactants based on the phase inversion temperature called the PIT-slope. In 1964, Shinoda et al. discovered that a whole emulsion system can be characterized by measuring the evolution of conductivity with temperature [1]. This method has recently been exploited by Ontiveros et al. in order to classify surfactants [2, 3] and is called the PIT-slope. The extensive property of the PIT-slope was demonstrated on five couples of surfactants from different chemical structure (**Fig 1**). This characterization facilitates the formulation of mixtures of surfactants of desire hydrophilicity in order to determine the required-PIT-slope of several oils. Required-PIT-slope of five oils has been investigated and results were discussed with respect to the HLB and required-HLB of Griffin.

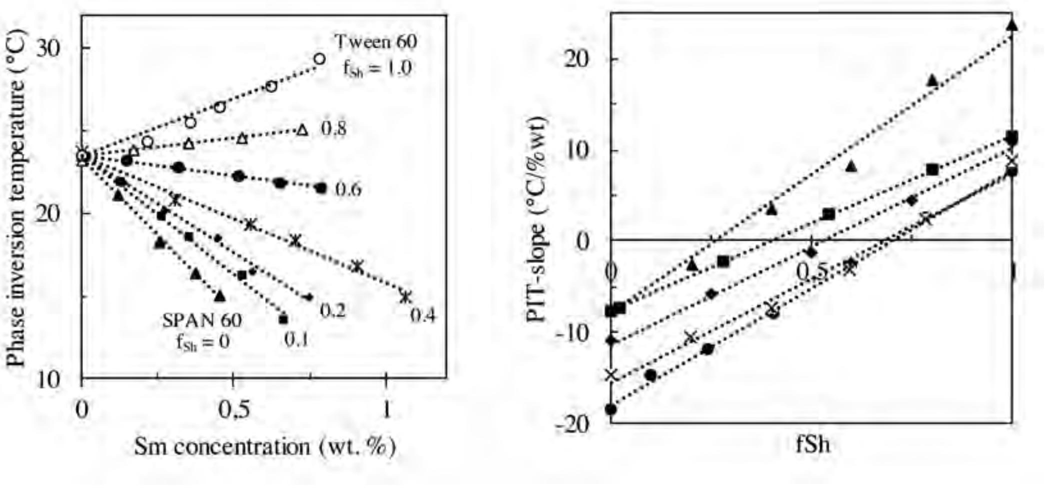

Figure 1. Left: PIT variation for several ratios of a mixture of SPAN 60/ Tween 60. Right: Linearity of the PIT slope with molar fraction of five mixtures of surfactants

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Compared impacts of xanthan gum content and oil phase ratio on the stretching properties of cosmetic emulsions

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Stretching is a texturing property of cosmetics [1]–[3] defined as "amount sample deforms or strings rather than breaks when fingers are separated" [1] meaning: the stringier a product, the longer its filaments. This attribute is therefore related to the sample's extensional properties. Emulsions and solutions containing xanthan exhibit high stretchability and even more so for the emulsions [4], [5]. In order to determine why, the present work explores the effects of xanthan gum and oil phase ratio on stretching properties of oil-in-water (O/W) emulsions varying in their micro- and macrostructure.

For this purpose, fourteen O/W emulsions were developed, varying through their oil phase content (from 10 to 30%) and amount (w/w) of xanthan (up to 1%). A series of aqueous solutions containing xanthan (up to 3%) was prepared to evaluate the stretching properties of the polymer alone. Formulation protocols were specifically developed in order to obtain stable products over several months, with well-defined physicochemical properties.

An imitative test of the sensory assessment has been set up to compress and stretch fluids at a controlled speed to form a filament using a texture analyzer TA.XT Plus [4]. Microscopic and macroscopic analyses were conducted in order to characterize each product (static light scattering, rheology, texture analysis…). Lastly, a statistical analysis was conducted.

This study highlights the polymeric agent and the emollient's roles on stretchability: the effect of xanthan is predominant since stretchability increases with the amount of gum but its effect quite lessens with the content of oil phase. Each of those two parameters implies some differences in terms of droplets size distribution and rheological and texture behaviors. While there is no connection between stretchability and microstructure, connections clearly exist with instrumental results such as consistency and resistance to strain. Lastly, compared to emulsions, even solutions with higher concentrations of xanthan still exhibit lesser stretchability which really means that the emulsions ingredients enhance the polysaccharide intrinsic stretchability.

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Clear food solutions of Rebaudioside A and Sodium Oleate at neutral pH

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Herein, we present a novel method for the preparation of highly translucent and macroscopically stable aqueous long chain soap solutions at neutral pH values. This is for the first time that a long-chain soap could be really solubilised in water at neutral pH. The consequences for manifold now possible applications is evident, e.g. in food and cosmetics, whenever neutral pH values are mandatory.

Using the food emulsifier sodium oleate (NaOl), clear and stable aqueous solutions can only be obtained at pH values higher than 10. A decrease in the pH value leads to turbid and unstable solutions [1, 2]. This effect is not compatible with the formulation of stable aqueous drinkable formulations with a pH value lower than 8.5. In this work, we report on the effect of the edible bio-surfactant and high efficiency sweetener Rebaudioside A ("Stevia"), on the macroscopic and microscopic phase behavior of simple aqueous sodium oleate solutions at varying pH values. The macroscopic phase behavior was investigated by visual observation and turbidity measurements. The microscopic phase behavior was analyzed by acid-base titration curves, phase-contrast and electron microscopy.

We observed very interesting changes in microscopic and macroscopic phase behavior of the mixed NaOl/RebA/water systems compared to the pure aqueous NaOl system. In particular, it turned out that even at neutral pH, such systems are completely clear and stable for more than 50 days at room temperature. Figure 1 shows the difference in the macroscopic appearance of aqueous 1 wt % NaOl solutions at different neutralization states Θ_P of NaOl without RebA (A) and with additional 0.8 wt% RebA (B). With soaps having a chain-melting temperature above room temperature, such as sodium dodecanoate and tetradecanoate, the effect of RebA was not observed due to the formation of crystals. At last, these findings were applied to prepare stable, highly translucent and drinkable aqueous solutions of omega-3-fatty acids at a pH value of 7.5.

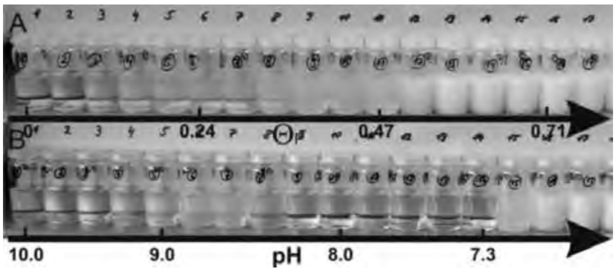

Figure 1: The macroscopic appearance of aqueous 1 wt % NaOl solutions at different neutralization states Θ_P of the soap without RebA (photo A) and with additional 0.8 wt% RebA (photo B) after 21 days of aging. The pH scale is only valid for the lower picture, since the addition of RebA reduces the pH value of aqueous NaOl solutions at a given neutralization state Θ_P.

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Dynamic interfacial tensions and emulsifying properties of some secondary alkanesulfonates

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Secondary alcanesulfonates (S.A.S) are biodegradable surfactants largely used as active matter in detergent formulations [1]. Their detergent properties compare well with those of linear alkylbenzenesulfonates (LAS), whereas, their aqueous solubility and ultimate biodegradation rate are slightly higher. As photosulfochlorination reaction is an efficient method to transform n-alkanes into alkanesulfonyl chlorides wich lead to secondary alkanesulfonates after hydrolysis, n-dodecanesulfonyl chlorides are prepared by photosulfochlorination of n-dodecane according to a new process instead of gas mixture [2]. Under different reaction conditions, samples of SAS with different isomeric distributions were obtained. The micellar behaviours of such compounds have already been investigated [3].They show interesting foaming power characterized by metastable and dry foam [4].

This paper deals with the dynamic interfacial tensions, and emulsifying properties of some samples of the synthesized SAS . These properties are compared in relation to the isomeric distribution of the samples. The results obtained for these surfactants are also compared with those of a commercial sample of SAS (Hostapur 60).

Before studying the emulsifying properties of these anionic surfactants, we have measured the dynamic interfacial tensions at oil-surfactant solution interfaces using as oil systems sunflower oil and mineral oil. The results compare well with those of the commercial secondary alkanesulfonates (hostapur 60), the surfactants lower effeciently the surface tensions at water-oil interfaces in only few seconds. Oil in water (O/W) emulsions were prepared using our surfactants and a commercial one (Hostapur 60), with three oils. We followed the O/W emulsion ageing by photodensitometry in order to compare the capacity of the synthesized surfactants to stabilize oil droplets. Under fixed conditions of emulsification, our surfactants give more stable emulsions than the commercial reference. These investigations showed the importance of the surfactant type on the stability of obtained emulsions and could define the kind of surfactant applications.

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Antimicrobial study of biosurfactants from *Lactobacillus* strains against skin pathogens

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Human skin microflora is composed by resident, temporarily resident and transient microbial species. Therefore, gram-positive bacteria from the genera ***Propionibacterium***, ***Staphylococcus***, ***Micrococcus***, ***Corynebacterium*** and ***Acinetobacter*** are the majority microorganisms present in the resident microflora [1]. For instance, ***Staphylococcus epidermidis*** is the main constituent of skin microflora, which protects the human skin from infections; whereas ***Staphylococcus aureus*** is a common transient species, which causes skin infections [2]. Anti-bacterial preservatives such as triclosan, methylparaben or bronopol, among others, are currently used as ingredients in the skin and oral care cosmetic products. However, there is a growing demand for cosmetics free of synthetic preservatives [3]. In this sense, biosurfactants from lactic acid bacteria, which are generally recognized as safe by the American Food and Drug Administration, are natural compounds that exhibit antimicrobial activity and therefore, could be used as an alternative to the chemically synthetized preservatives. The aim of this study was to evaluate the antimicrobial activity of biosurfactants obtained from two different ***Lactobacillus*** strains (***L. pentosus and L. paracasei***) against skin pathogenic microorganisms. The biosurfactants were obtained according to the procedures described by Vecino et al. [4] and Gudiña et al. [5]. Afterwards, antimicrobial assays were carried out following the method proposed by Gudiña et al. [5]. The ***L. paracasei*** biosurfactant showed a considerable antimicrobial activity against ***S. aureus*** (around 83% at the highest concentration tested, 50 mg/mL), whereas the ***L. pentosus*** biosurfactant was less efficient exhibiting around 67% inhibition against the same organism. The same trend was observed against ***S. epidermidis***, the ***L. paracasei*** biosurfactant was more efficient (100% inhibition) than the ***L. pentosus*** one (40% inhibition). These results are in accordance with other studies reported in the literature. For instance, Madhu and Prapulla [6] showed that the ***L. plantarum*** biosurfactant was able to inhibit the growth of ***S. aureus***. Gudiña and collaborators [7] showed that ***L. agilis*** biosurfactants exhibit antimicrobial activity against ***S. aureus*** (around 20%) at low biosurfactant concentrations (5 mg/mL). The results gathered in this study clearly highlight the potential of these biosurfactants as preservative ingredients in cosmetic formulations.

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Salt tolerance of commercial surfactants and prediction of the cloud point of nonionic surfactants in presence of salt

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Surfactants have solubilizing, emulsifying and detergent properties which make them essential compounds in end-use products. In certain applications e.g. detergency, hair care products or oil recovery, anionic surfactants such as sulfates and carboxylates are known to precipitate because of the presence of mono- or di-valent ions in hard water. Consequently these surfactants turn inefficient with regard to its application.[1] Compared to ionic surfactants, non-ionic surfactants are considered to be less sensitive to the presence of electrolytes. However those which exhibit a cloud point (temperature at which the non-ionic surfactant precipitates), may decrease their solubility and thus their properties in the presence of salt.[2]

Considering this problematic, the aim of this work is to identify and to classify ionic surfactant head groups according to their salt-tolerance (i.e. the amount of salt required to precipitate a surfactant) and to predict the evolution of the cloud point of non ionic surfactants in presence of salt.

The salt-tolerance of various commercial ionic and non-ionic surfactants are compared and then a ranking with the corresponding salt-tolerance characteristics is established. As a result, it appears that for extended carboxylic surfactants, the presence of ethylene oxyde groups increases significantly the resistance to mono- and di-valent ions.

The second part of this work consists of studying the evolution of the cloud point of C_iE_j non-ionic surfactants in the presence of salt. It appears that the cloud point evolves linearly only for weight percentages of salt lower than 5 wt.%. For this concentration range, the value of the slope of the linear part of the curve, noted a_S, correspond to the salt sensitivity of the surfactant. Predict this value would be very helpful to anticipate if a non-ionic surfactant is soluble in hard water. It exists a correlation between the structure of the surfactant and the salt sensitivity a_S which allows to calculate an estimated salt coefficient $a_{S(est)}$ depending only on the number of carbon i and the number of ethylene oxide j. This calculated salt coefficient is then compared to experimental $a_{S.}$

Furthermore, the calculation of $a_{S(est)}$ is extended to widely used commercial non-ionic surfactants, such as Tween and ethoxylated carboxylic acids. Knowing the cloud point of these surfactants without salt, $a_{S(est)}$ is then used to predict the evolution of the cloud point in up to 5 wt. % of salt. The comparison between experimental and calculated values highlights the accuracy of the prediction.

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Characterisation of the head group and hydrophobic regions of glycosides vesicles' membrane using steady state fluorescence technique

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The vesicles' membrane behaviors of synthetic glycosides in hydrophilic and hydrophobic regions were characterized using two fluorescent probes, nile red (NR) and 1,6 diphenyl-1,3,5-hexatriene (DPH), as local reporters in the membrane. Nile red (NR) is used to probe the polar head group region and the latter to probe the hydrophobic region. The properties of the membrane were modified by incorporation of three lipidic modifiers: oleic acid, lecithin and Tween 80. These modifiers destabilize the lipid bilayer to increase flexibility to form deformable vesicles able to improve penetration of drug into the skin to achieve delivery of therapeutic amount for topical drug carrier. Polarity of both hydrophilic and hydrophobic regions was estimated based on parallel study in different solvents.

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In vitro half-life and binding of bevacizumab from nipaam hydrogels

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One of the most important goals in ophthalmic drug development is to extend the duration of action of protein therapeutics such as antibodies in the back of the eye to treat blinding diseases. With an aging population, there is a need to develop longer acting formulations that can decrease the frequency for intravitreal (IVT) injections. In an effort to increase the intraocular half-life of bevacizumab, we now report the preparation of an injectable N-Isopropylacrylamide (NIPAAM) ***in situ*** forming gel that is prepared in the presence of bevacizumab. The ***in vitro*** ocular half-life and binding activity of bevacizumab were determined in an effort to optimise the cross-link density of the NIPAAM gel.

Bevacizumab (1.0 mL; 25.0 mg/mL, pharmaceutical preparation) was mixed with NIPAAM (40.0 mg) and ammonium per sulfate (APS, 4.0 mg). Different amounts (~4, 8 and 12 µL) of poly(ethylene glycol) diacrylate (PEG-DA) crosslinker were added to the polymerisation mixture. Upon addition of ***N***,***N***,***N***,***N***-tetramethylethylenediamine (TEMED), and the mixtures were incubated for ~24 hours at 4°C. Both injection and gel formation of the bevacizumab loaded gels were separately evaluated in our ***in vitro*** model, known at the PK-Eye™[1]. This 2-compartment ocular aqueous outflow model provides the means to estimate human protein clearance times. The use of animals to evaluate therapeutic proteins is severely limited due to the formation of anti-drug antibodies (ADAs).

To determine half-life, bevacizumab-NIPAAM gels (2.5 mg, 100 µL) which had been prepared with different amounts of PEGDA were injected into the posterior cavity of the PK-Eye which was then used with an inflow of 2.0 µL/min(37°C). To obtain comparative data more quickly, PBS, rather than simulated vitreous was used in the posterior cavity of our model to determine release kinetics. Samples were analysed by HPLC (280 nm) to calculate the release kinetics. Binding properties of released bevacizumab were evaluated against its ligand (vascular endothelial growth factor, VEGF) using surface plasmon resonance (SPR).

Bevacizumab from the gels prepared with different amounts of PEGDA (4 uL, 8 uL and 12 uL) displayed a $t_{1/2}$ of approximately ~2.01 ± 0.01, 3.66 ± 1.21 and 2.55 ± 0.03 days respectively. These studies showed continuous release of bevacizumab after a month. In contrast, a gel-free dose of bevacizumab (2.5 mg) displayed a $t_{1/2}$ of 2.3 ± 0.8 days. Samples collected throughout the 4-week study were also evaluated by SPR which indicated that bevacizumab maintained its binding properties after release from in the gels.

In conclusion, these studies indicate that it is possible to extend the duration of protein release using a thermoresponsive gel that is prepared in the presence of the protein.

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Non-emulsifiers for completion brines: adapting chemical formulations to brazilian oilfield challenges

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During workover and completion operations, oil-based, water-based and acid-based fluids are injected into the well, entering formation pores and reaching oil reserves [1]. Depending on the flow intensity and ambient conditions, these fluids may interact with oil to form viscous emulsions, causing several problems in the reservoir and ultimately a decline in oil production [2]. Non-emulsifiers, when added to brines and acid solutions, are supposed to act as a barrier on the interface between the oil and the fluid, preventing emulsion formation and helping to maintain fluid's properties and preserving the oil in the reservoir. Lately, Brazilian fields have faced challenges that resulted into the use of different fluids and brines and also different types of oil to be dealt with. Thus, the purpose of this work was to adapt some of techniques of emulsion breakage to develop novel non-emulsifiers formulations that cope with current technical and environmental requirements regarding emulsion prevention for oil exploration in Brazil. Several formulations have been evaluated in order to better understand the effect of different parameters on the emulsion prevention of brines during completion operations. A Design of Experiments (DoE) approach has been prepared in order to test different formulations (varying solvent and co-surfactant natures and content) in different scenarios: brines with different salts and oils with different °API.

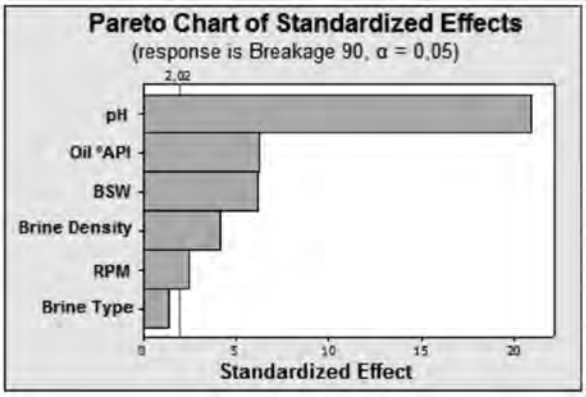

Figure 1. Pareto Chart of effects for the Design of Experiments (DoE).

All those parameters were taken into account and enabled the design of an optimized formulation for the application. Once evaluated through adapted bottle tests, the toxicity of most promising formulations was performed. It has been found that solvent and surfactant types and concentrations have great effect on emulsion prevention. Further, another DoE approach has been prepared in order to understand how different scenarios impact on emulsion prevention: the novel formulation was tested against brines with different salts and different oils (°API). The effect of parameters such as oil density, BSW, brine pH, brine type and agitation could be evaluated and a mechanism of action for the high performance non-emulsifier could be investigated, as well as a novel non-emulsifier developed.

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Preparation and characterization of iota carragenaan spheres gelled by calcium ions. Comparative study between rheometer and texturometer characterization

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Hydrocolloids are composed by bonding of hydrophilic monomers forming polymers. These hydrocolloids have the ability of being hydrated and retain a huge amount of water by formation of hydrogen bonds. This water retention capacity gives the functional properties that can contribute to the stability and improvement of the sensory characteristics of a product [1], which has had a major impact on the food industry. In this work, it has been used iota carrageenan, a hydrocolloid extracted from red algae with thickening and gelling properties. Depending on the structure and physicochemical properties, iota carrageenan has the ability to bind calcium ions to form elastic gels.

The main aim of this work is the preparation and characterization of iota carrageenan spheres gelled by calcium ions. In order to study the texture of the spheres, an instrumental method that follows the principles of texture profile analysis (TPA) has been developed using a rheometer, and results have been compared with those obtained from a texturometer. To develop the instrumental method, the experimental conditions affecting the test were studied, and the conditions that made the results reliable and reproducible were fixed. Once the instrumental method was developed, the influence of calcium on the texture of spheres was studied, and it was determined that above a certain calcium concentration, it did not affected textural parameters, ie, there was a calcium saturation in the spheres. Likewise, the influence of iota carrageenan was studied, and it was found that increasing the iota carrageenan concentration increases the hardness of the spheres. As for the other textural parameters, it seems that they do not depend on the calcium or iota carrageenan concentrations.

Finally, with the rheological study of the gels with identical iota carrageenan concentrations as the spheres, it was possible to state that there is a certain correlation. The hardness of the spheres increases when the elastic behaviour of the gel increases.

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Characterization of theophylline and budesonide encapsulated pla nanoparticles

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Theophylline and budesonide co-encapsulated poly (lactic acid) (PLA) nanoparticles were synthesized using a modified double emulsion solvent diffusion (DESD) method. The aim of the work was to investigate their effects on the human bronchial epithelial (16HBE14o-) cell line by studying the toxicity of the nanoparticles and the drug permeability [1, 2]. Further characterization was carried out by studying the in vitro pulmonary deposition using a multistage liquid impinger (MSLI) using a nebulized suspension of the nanoparticles and dry powder formulations using lactose carriers. At the highest concentration of nanoparticles suspension, the cell viability was reduced to approximately 70% of the controls for co-encapsulated nanoparticles ($p<0.05$). Reduced cell viability was only observed at a nanoparticle concentration of 5 mg/ml. The transport of the paracellular marker, FITC-dextran (FD4), across the 16HBE14o- cells was not altered when cells were treated with nanoparticle suspensions and drug solutions prepared at equivalent concentration, compared to the control ($p>0.05$). Initial studies indicated that the transport rate of theophylline and budesonide across 16HBE14o-cells was less when delivered using co-encapsulated nanoparticles than from their respective drug solutions at equivalent concentrations over a period of 24 hours. A total of 20% of theophylline and 5% budesonide were released, respectively from the nanoparticles. Approximately 100% of theophylline was delivered from equivalent theophylline solution and 20% of budesonide from equivalent concentration suspension. Comparisons were made between co- and mono-encapsulated theophylline and budesonide nanoparticles. Release profiles obtained using 16HBE14o- cells was compared to the release profiles obtained using Franz diffusion cells showing rate limiting step was the release of the drugs from the nanoparticles and not transport across cell/ artificial membrane. In vitro pulmonary deposition characterized using dry powders formulated using lactose as a carrier showed large nanoparticle deposition in the upper airways (20%) ideal for the treatment of local diseases such as asthma or COPD. Nebulized nanoparticle suspensions showed deposition throughout the upper and lower airways. The same concentration of nanoparticles was used for studying the in vitro deposition as dry powders and nebulized suspensions.

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Surface modification of calcium carbonate nanoparticles by fluorosurfactant

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Calcium carbonate ($CaCO_3$) has been frequently used as one of the major ingredients in plastics, rubber, paint, adhesive, sealant, pigments, coating, toothpaste, cosmetics, thermosetting resins, paper, food, and so on. However, one of the most problematic issues for the use of $CaCO_3$ is the hydrophilic property, and this problem makes $CaCO_3$ nanoparticles very difficult to be used widely. In this study, the effect of adsorption behavior of fluorosurfactant Zonyl® TBS (Dupont) on the wetting property of $CaCO_3$ substrate was investigated. Contact angle measurement, surface energy analysis, and floating test have been conducted to study the effect of surfactant adsorption on the wetting property of $CaCO_3$ substrate. In order to confirm surface modification of $CaCO_3$ nanoparticles by fluorosurfactant, FTIR spectroscopy, QCM-D analysis, XRF spectrometer and XPS analysis have been also used.

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Encapsulation and release study of active ingredients in mono-bilayer chitosan nano-microparticles

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This communication presents the results obtained from vitamin C release in chitosan nanoparticles and chitosan nanoparticles coated with alginate. The encapsulation method applied has been ionic gelation. The control variable that has been used for the release study of vitamin C is the encapsulation efficiency (EE) calculated in a 4 hour time range.

UV spectroscopy has been implemented for the quantification of the encapsulated vitamin C inside the nanoparticles and trapped in the surface. The effect of chitosan and alginate on the Vitamin C absorption spectrum has been taken in consideration. Moreover, due to the relatively easy degradability of vitamin C, the velocity of degradation in several acidic media has been studied. The obtained results from vitamin C degradability have been taken in consideration in order to calculate the encapsulation efficiency over time.

Intravenous human serum albumin (hsa)-bound artemether nanoformulation for treatment of severe malaria

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Severe malaria is life-threatening and requires the parenteral artemisinin based drug or quinine as monotherapy until patients can tolerate oral therapy. Intravenous (IV) artemether formulation has shown potentially better therapeutic efficacy than IV artesunate [1], however its poor water-solubility constitutes a challenge. Considering that: (1) malaria parasite infected erythrocytes import HSA from the plasma for survival [2]; and (2) IV nanoformulation has been successfully applied for clinical use, HSA-bound artemether nanoformulation is proposed and developed for IV treatment of severe malaria in this work. Emulsification and desolvation approaches were used in the production of the nanoformulations. In brief, artemether was dissolved in dichloromethane (emulsification) or acetone (desolvation), which was then mixed with aqueous HSA solution followed by ultrasonication. The obtained nanosuspension was evaporated, frozen and freeze dried to produce the nanoformulations. The mean particle size was below 50 nm, suitable for IV delivery as nanosuspension after reconstitution. Higher HSA concentration, lower drug concentration, faster freeze rate and longer ultrasonication time (up to 60 s) favoured the production of smaller particles. Comparatively, the emulsification method allowed for higher drug entrapment per the same concentration of HSA and required less organic solvent, less water and less energy and is therefore the preferred method.

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Development of nanoemulsions formulated from brazilian raw materials for dermocosmetic applications

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This study focuses on the development of nanoemulsions formulated from natural brazilian raw materials for dermocosmetic applications.

Nanoemulsions are introduced in cosmetic and pharmaceutical industries by the reason of their different interesting properties, due to their droplets average size of 100nm. Nanoemulsions are more stable than emulsions, it offers a better spreadability and transparency, and improve the delivery of active agents intradermal [1].

Different raw materials have been used to formulate the nanoemulsions. PEG castor oil derivatives are used as surfactant associated with the sorbitan monooleate. Copaiba oil (HLBr=10) and Calendula oil (HLBr=8) are used as oily phases. According to required HLB numbers, the amount of PEG castor oil derivatives and sorbitan monooleate have been calculated. Two different kinds of nanoemulsions have been formed (Copaiba nanoemulsions and Calendula nanoemulsions). Consequently, specific ingredients have been added to give them particular properties: Mango and Ucuuba butters and a mix of Spondias Monbin, Mangifera Indica and Musa Sapientum pulp extract, are used to give anti-aging properties to the Copaiba nanoemulsions; whereas, Aveia, Aloe Vera, Piptadenia Colubrina Peel extract and peach butter are employed for treatment of skin problems in the Calendula nanoemulsions.

Afterward, great nanoemulsions with colored reflects have been obtained. Copaiba nanoemulsions have a blue aspect, whereas Calendula nanoemulsions are pink and show a pearly shine when they are exposed to natural light.

To determine the impact of butter concentration on nanoemulsions properties, different assays have been made according to the rise of butter amount:

Particle size and opacity increase with the growth of Mango and Ucuuba butter percentage in the anti-aging Copaiba nanoemulsions. However they are all remained stable, with a low viscosity, and a bluish aspect.

Peach butter has been added in skin-problems-treatment Calendula nanoemulsions to measure the influence on opacity. A nanosizer has been used to measure particle size. It increases when the percentage of butter increases, until a particular point where the size considerably decreases In fact, liquid crystals, looking like malta crosses, emerged for addition of 12% of peach butter, and this leads to the decrease of particle size.

In conclusion, this research shows the interesting colored nanoemulsions that can be obtained from natural brazilian raw materials like Copaiba and Calendula oils, added to Castor oil derivatives. In the future, they could be used for development of dermocosmetic products that aimed the protection and cutaneous treatment.

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Formation and mechanical properties of thin coatings using modified, cross-linked nanoparticles

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Nanoparticles find their application in many fields in industry. An important branch is the improvement of surfaces by the use of nanoparticulate coatings.

The aim of this study is to investigate the use of different modified alumina and titania nanoparticles in thin coatings to achieve a defined coating structure as well as better mechanical product properties by cross-linking the particles during the drying step. To investigate the formation of such a network between the particles (exemplary shown in the TEM-pictures in the Figure below), the influence of the cross-linking additive on the particle network formation and the resulting coating characteristics are a main part of this research. The process chain in this study started with the dispersing of pyrogenic nanoparticles in a solvent followed by the modification as it is described by Kockmann et al. [1]. These suspensions were used to prepare the coating formulations by adding the cross-linking additive and characterized regarding particle size distribution, viscosity, stability as well as cross-linking kinetics. Afterwards nanoparticulate coatings were produced via dip coating and the properties, especially the mechanical properties, were determined.

Experiments with alumina (AluC, Evonik) as well as titania nanoparticles (P25, Evonik) show that the cross-linking-kinetics in the formulations can be influenced using different additive concentrations. More precisely, an optimum of the amount of additive in the formulation was identified regarding the strength of coatings and a first theoretical model for the cross-linking behaviour was established. Moreover, the abrasion resistance is higher by applying a high amount of the cross-linking additive. Apart from this strategy of cross-linking the particles by using the additive directly in the coating formulations, it is also possible to cross-link the particles by a subsequent process step. In this approach, the films with modified particles are coated afterwards with a solution, consisting of solvent and cross-linking additive. This enables the manipulation of individual product properties without interdependencies with other formulation and process parameters.

The results of this study show that the use of modified particles in combination with a suitable additive can significantly improve the particular structure and, thus, enhance the mechanical properties of thin nanoparticulate coatings.

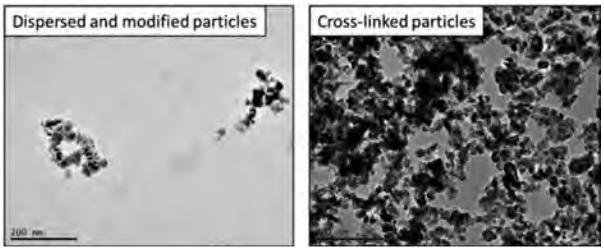

Figure 1 Dispersed and modified titania-nanoparticles without (left) and with cross-linking (right)

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Design and fabrication of radioisotope-based micro battery

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A radioisotope battery that converts the decay energy of a radioisotope into electricity offers advantages for application requiring a long lifetime without recharging and minimum maintenance [1]. In addition, it is used in many low-power applications because it can operate effectively under extreme environmental conditions such as in space and at deep sea.

For a beta-voltaic battery, beta rays emitted from a pure beta source such as ^{63}Ni, ^{147}Pm, and ^{3}T can cause the generation of an electron-hole pair (EHP) onto a semiconductor, and produce electricity. In addition, combining the solar or secondary cells and beta-voltaic batteries can produce a new hybrid battery system. In the case of secondary cells, the electricity generated from a beta-voltaic battery is stored in a secondary cell, and thus we can use the power stored in the secondary cell. Finally, a hybrid battery system that combines a CIGS (Cu-In-(Ga)-Se)-based solar cell with radioisotope batteries can be used as a power source for small equipment for the exploration of Lunar, Mars, and asteroids [2].

For the fabrication of a radioisotope battery, it is important to form a deposit of radioisotopes onto a substrate effectively. There are several methods for the deposition of radioisotopes onto a substrate, such as electroplating, electroless plating, and chemical vapor deposition [3]. ^{63}Ni, a pure beta-emitting source, is proper as the power source of a radioisotope battery because of its low energy spectrum (E_{evg}=17.4 KeV) and long half-life of 100.1 years. In this study, we fabricated a beta-voltaic micro battery and designed a radioisotope-based hybrid battery using ^{63}Ni as the energy source [4].

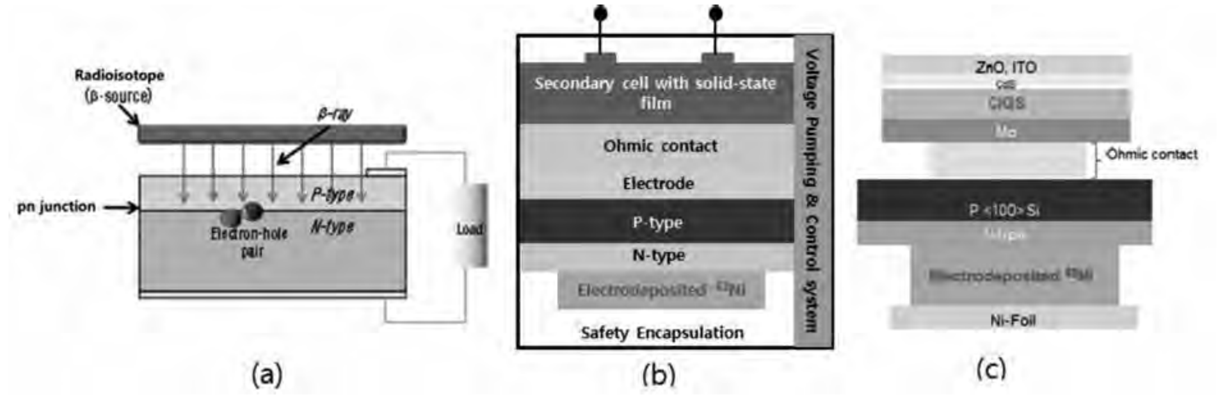

Figure 1. Schematic diagrams of (a) a beta-voltaic battery, and combined systems of beta-voltaic using ^{63}Ni with (b) a secondary cell and (c) photo-voltaic (solar cell).

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Scale-up of kneading processes for nanoparticulate suspensions

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Nanoparticles can be employed to improve the mechanical properties of fibre reinforced composites in aerospace applications. It could be shown that the improvement strongly depends on the disperse properties of the particles, which are mainly influenced by formulation and processing parameters. It is therefore crucial that industrial scale processes provide the same product quality as laboratory experiments. Therefore a scale up method for the dispersing process of boemithe nanoparticles and an epoxy resin which is used in aerospace applications is established, which utilizes formulation- and process parameters to achieve equal product quality and energy efficiency.

Kneaders find application in many industrial processes as a standard machine for mixing as well as dispersing via laminar shear flow, here for the processing of nanoparticulate suspensions. Despite the broad range of applications, little is published about scale up methods for kneading processes. The few available exemptions focus on special designs [1] or cover viscosity as the targeted property [2] as it is a key process parameter in many applications, e.g. in the rubber industry. But since viscosity depends on numerous parameters (e.g. temperature, shear rate, particle morphology and size) isn’t a universal parameter for describing the product quality of nanoparticulate suspensions.

The scale up concerning a similar final product quality utilizes the findings of Rumpf and Raasch [3] that the shear stress acting on a sphere in laminar flow is proportional to viscosity and shear rate. Even with geometrical differences between two systems adjusting the shear rate by means of rotational speed or changing the viscosity by varying temperature or solids content the same maximum shear stress ensures the same final, i.e. minimal particle size. However, the minimal particle size is only reached after extensive time and energy input. This is why in industrial applications, processes are usually aborted beforehand.

This is why a more sophisticated approach is established which aims to preserve the specific energy input required to reach the desired particle size. In analogy to the well-practiced scale up of stirred media mills [4], which is based on the preservation of a constant mean stress energy and an active specific energy, for kneaders also a constant mean stress intensity, i.e. mean shear stress is pursued. For the determination of the mean shear stress the kneading chamber geometry is divided into characteristic sections and for each section the shear rate regime is evaluated. The sections impact is rated by the frequency of their and the relative volume the section takes up. This provides a stress intensity distribution for each individual kneader from which a mean shear stress and, thus, mean stress intensity can be derived. If this mean stress intensity as well as the maximum stress intensity can be held constant for both process scales, both machines show the desired similar dispersion kinetics. The derived mean stress intensity is verified by a CFD simulation. The applicability of the approach is tested with dispersing experiments in two kneaders (0.3 l and 5 l volume).

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Development of a nanoemulsion for topical photodynamic therapy

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Topical photodynamic therapy (PDT) is a therapeutic modality that has been widely used in the local treatment of skin cancer. It involves the application of a photosensitizer that must cross the outermost skin layer, the stratum corneum, and reach the deeper layers of the skin where the tumor is located. When exposed to light at the wavelength of maximum absorption, the photosensitizer products are able to cause the death of the tumor cells by a series of photochemical reactions. A formulation that increases the photosensitizer penetration throughout the skin and the tumor cells is then an important part of a successful topical PDT. Nanoemulsions are heterogeneous dispersions of two immiscible liquids resulting in nanometric droplets of one of the liquids. The high superficial area occupied by these droplets and the components of the nanoemulsion can facilitate drugs skin penetration [1]. The aim of this work was to develop an oil-in-water nanoemulsion for topical administration of the photosensitizer zinc phthalocyanine (ZnPc) for further topical PDT. Nanoemulsions composed of a mixture of medium chain triglyceride (1.67%), polysorbate 80 (3.33%), poloxamer (0.1%) and water were produced by ultrasonic emulsification. Ultrasound was applied at the frequency of 20 kHz, 50% amplitude and pulse length of 1 s on, 1 s off for 5 min. The nanoemulsion was saturated with ZnPc 24 h after its preparation. This formulation was characterized by particle size, polydispersity index (PDI), zeta potential, pH and physical stability as a function of time. ZnPc was quantified in the formulation by a validated spectrofluorimetric assay at 610 nm/680 nm excitation/emission. Nanoemulsion developed was translucent; size, PDI and zeta potential were 86.4 ± 5.4 nm, 0.32 ± 0.05 and -11.8 ± 0.36 mV, respectively. The pH of the nanoemulsion was 6.78 ± 2.2. The nanoemulsion dispersion was stable (ANOVA, $P \geq 0.05$) during 60 days at 5°C ± 3°C (Figure 1).

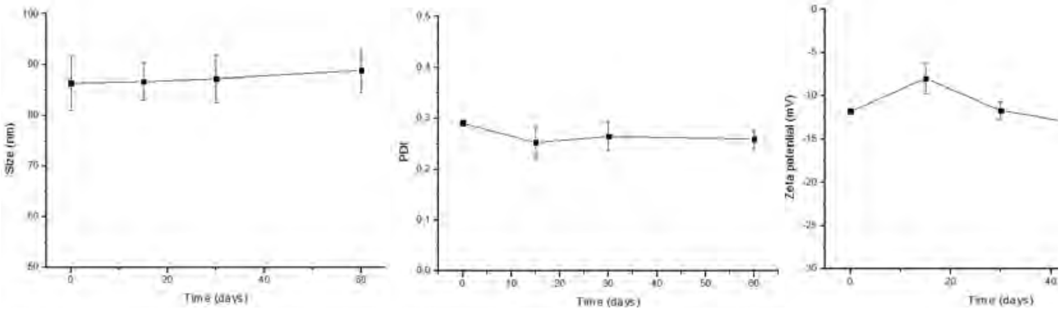

Figure 1. ZnPc nanoemulsion stability during 60 days at 5°C ± 3°C.

It was possible to incorporate 16.6 ± 2.2 µg/mL of ZnPc in the nanoemulsion. The concentration of ZnPc necessary to kill skin cancers cells by PDT is about 0.03 µg/mL [2]. Therefore, nanoemulsions containing ZnPc were successfully developed and showed adequate characteristics and stability.

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Effect of ionic strength and temperature on the critical micelle concentration of poloxamer 338

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To prepare pharmaceutical nanosuspensions starting from dry powders with supermicron sizes, ingredients, such as surfactants and stabilizers have to be added. An important quality criterion of these nanosuspensions is the absence of instability phenomena, such as Ostwald ripening. As the latter is affected by the presence of surfactant micelles, we investigated the influence of storage temperature and ionic strength on micelle formation.

The presented work focussed on poloxamer 338, a PEO-PPO-PEO surfactant that is for example used in Rilpivirine nanosuspensions [1]. Density measurements on aqueous solutions of poloxamer 338 showed a discontinuous profile as a function of temperature, which indicated a transition from a monomer solution, to a solution which also contained micelles (figure 1a). The experimental data revealed that micelle formation depended on both poloxamer concentration and temperature. Hereby, the critical micelle temperature (CMT) decreased with increasing concentration. In a next step, the effect of ionic strength on the onset of micelle formation was determined. The CMT decreased by about 20 degrees as the ionic strength was increased from ultrapure water to a phosphate buffered saline (PBS) solution that contained 118 mM of phosphate buffer in 1370 mM NaCl and 27 mM KCl.

The effect of micellisation on the solubilisation properties of the poloxamer surfactant solution was evaluated by colorimetric evaluation of the solubilisation of quinizarin, a poorly water soluble dye at 6.4, 20 and 40 °C [2]. The results clearly indicated that quinizarin solubilisation in ultrapure water only occurred in the presence of micelles, i.e. at 40 °C and a poloxamer concentration higher than 5 mg/ml. On the other hand, the aqueous phase remained colourless at both 6.4 and 20°C within the studied concentration range from 0 to 100 mg/ml. Figure 1b shows the effect of phosphate buffered saline (PBS) solution concentration on the absorbance of different poloxamer 338 solutions. It is noticed that a higher ionic strength (higher PBS concentration) enhances the absorbance of the poloxamer solutions.

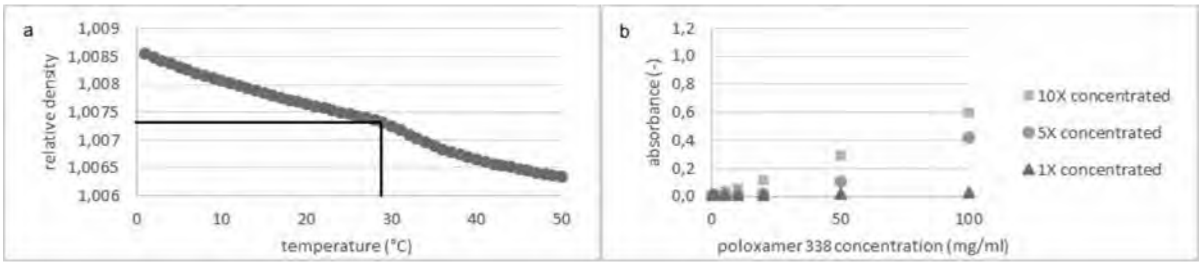

Figure 1: a: influence of temperature on the density of an aqueous 50 mg/ml poloxamer 338 solution relative to the density of ultrapure water. b: effect of PBS buffer concentration on the CMC of poloxamer 338 at 20 °C

This work shows that micelles are able to solubilize poorly water soluble compounds and that this solubilisation capacity is dependent on the ionic strength and temperature of the solution. Since an enhanced solubility of active ingredient in nanosuspensions might accelerate Ostwald-ripening, it is important to choose the appropriate storage temperature for a nanosupension with a certain ionic strength and surfactant concentration, and to consider the possible role of added ingredients (e.g. buffers), on the solubilisation properties of surfactants.

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Surfactants bilayers onto tio$_2$ p25 as hydrophobic compound carrier

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When ionic surfactants are adsorbed by opposite charged particles, a bilayer often occurs[1]. This phenomenon controls many processes, such as stabilization on solid dispersions[2], flotation[3], etc. The bilayer holds inside a hydrophobic region that can be used as a an hydrophobic compound carrier, and when necessary, can be triggered to release them in the media. However, to control the release, it is necessary to control the stability and the parameters that could break the bilayer.

In this work we have focused on the interaction of binary mixtures of surfactants on the surface of TiO_2 P25 in order to increase the stability of the bilayers formed. Surface tension, Z-potential, adsorption capacity, bilayer stability and adsolubilization power have been studied, in order to characterize the mixtures and to obtain stable combinations to be used as hydrophobic compound carriers. To explore the stability of different bilayers, the behavior of surfactant binary mixtures of sodium octyl sulfate (SOS), sodium dodecyl sulfate (SDS), decaethylene glycol monododecyl ether (C12EO10), trimethyloctylammonium bromide (OTAB), dodecyltrimethylammonium bromide (DTAB) and hexadecyltrimethylammonium bromide (CTAB) on P25 surface at different pH and at a constant ionic force using 10mM NaCl have been studied. The obtained results show a synergistic cooperative effect between surfactants having the same polarity, showing a decrease in the expected concentration to form the monolayer and the bilayer on the surface of the P25 nanoparticles.

A more remarkable decrease on expected concentration for the formation of surfactant bilayer happens when using ionic with non-ionic surfactant[4]. This effects of reducing the critical concentration to achieve the monolayer and the bilayer is even below the lower critical concentration of both surfactants individually.

In the other hand, when combining anionic with cationic surfactant, in a sequential addition order, it can be obtained a double bilayer[5] of surfactants. The second surfactant bilayer is then formed after the formation of the first surfactant bilayer of the opposite charge. It is found that the monolayer and the second bilayer is formed independently onto the first bilayer and its formation occurs without being affected by the previously formed bilayer.

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Investigation of new bio-based nanoparticles-in-microparticles formulations by spray-drying

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Various drug-delivery systems based on nanoparticles (NPs) and microparticles (MPs) were examined in the last decades. Nanoparticles-in-microparticles (NIMs) combine the advantages of both applications and their specific properties. However, most of the described methods for the preparation of such NIMs use emulsion based techniques. [1]

In this work, we present a novel combination of carbohydrate-based polymers as NIM systems by spray-drying. First, nanoparticles were synthesized via inverse mini-emulsion technique with the use of non-ionic surfactants. Chitosan or a functional methacrylamide was used as polymeric material for the nanoparticle synthesis. Next, the nanoparticles were dispersed in an inulin solution and processed by the spray-drying method. The obtained NIMs particles were characterized via scanning electron microscopy and dynamic and static light scattering methods.

Figure 1 shows spray-dried NIMs containing nanoparticles. The inulin NIMs showed a spherical shape with single nanoparticle attached to the surface. Further formulations with varying NPs, e.g. chitosan and different NP-to-inulin ratios have been investigated. In following steps, this system will be used to encapsulate pharmaceutical relevant substances in both formulations, the nanoparticles and microparticles. This allows new possibilities for the preparation of an asymmetrically loaded bio-based drug delivery system via spray-drying.

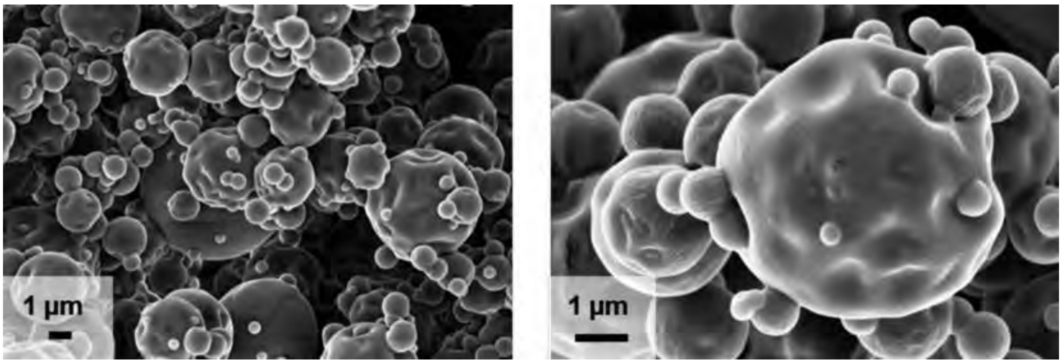

Figure 1: NIMs created by spray-drying containing nanoparticles in inulin capsules.

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Surface analysis of binary nanoparticles' systems as self-cleaning coatings.

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Self-cleaning properties have attracted interest for many applications, from home appliances to space and aircraft functional coatings. In the field of renewable energy conversion and specially solar applications systems demand high transparecy, enhanced mechanical properties and good adhesion properties among others. Thus, traditional self-cleaning systems present some disadvantages.

In this work, authors present an approach to face this challenge, using a combination of binary nanoparticles' systems. Development of coatings from commercial nanoparticles based on TiO_2-SiO_2 and CeO_2-Al_2O_3 systems, that were functionalised with different coupling agents are presented. Their surface properties and characteristics were carried out by means of XPS, SEM, drop shape analysis (sessile drop) as well as tribological properties. Also, we take in account the deposition method an its scalability.

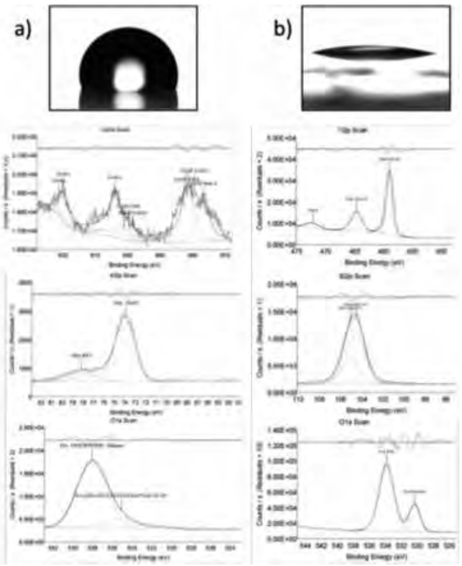

Figure 1. XPS spectra and contact angle (sessile drop) analysis of a) CeO2-Al2O3 and b) TiO2-SiO2 systems.

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Towards the preparation of functionalized graphene oxide for hydrophobic coatings

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Hydrophobic properties are a well-known phenomenon with an interesting application, such as self-cleaning coatings. Therefore, research for new hydrophobic materials and its application in this topic are demanded. Most of the hydrophobic materials are TiO_2 based with typical architectures. Graphene and its derivatives are of great interest since they can be synthesized from cheap sources, graphite for example.

One of these derivatives include octadecylamine, normally employing temperatures about 150°C for the functionalization [1]. In this work, we present a method, for the preparation of a series of functionalized N-octadecylamine graphene oxide (ODA-GO) films, achieving interesting hydrophobic properties when coated onto glass surfaces, using mild and low cost methods for the functionalization process. The films are deposited via spin coating followed by a thermal treatment of 60°C. Due to the dark tone presented on the films (figure 1), they could be used for tinted glass applications.

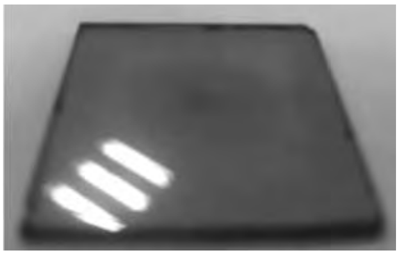

Figure 1. ODA-GO film casted onto glass via spin coating

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Polymeric nanoparticles stabilized by spray dryer

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Introduction: Nanoparticle (NP) production via spray-drying has been introduced as an attractive manufacturing process in the pharmaceutical industry due to its wide feasibility. However, spray-drying has been also used to increase drug solubility and bioavailability of active substances, modified release and to improve the stability. Recent advantages in the spray-drying led to new innovative technologies such as the Nano Spray Dryer B-90 developed by Büchi (Switzerland). This instrument based on vibration mesh spray technology, creating tiny droplets (before evaporation) in a size range of a smaller order of magnitude than in classical spray dryers. The main goal of this work was the production of Polymeric NPs from poly (D,L-lactide-***co***-glycolide) Resomer® 502H dried by Nano Spray B-90.

Materials and Methods: NPs were prepared by the solvent displacement technique using polyvinyl alcohol as surfactant, a matrix of RG502H, and acetone as organic solvent. Morphometric parameters (average particle size and polydispersity index (PI)) were determined by dynamic light scattering (DLS) and ZP by electrophoretic mobility. These assay were performed before and after the dried process. The formulation was spray-dried by using Nano Spray Dryer B-90. Briefly, fluid samples for spray-drying are atomized by a vibrating-mesh actuated by a piezoelectric element. Ejected droplets are dried in a co-current flow of a warm air, and the dried particles are then collected by an electrostatic particle collector. Technique condition were: Temperature of inlet, outlet and spray head were 30, 29 and 35ºC, respectively. It was optimized according to the characteristics of tested formulation, which does not allows to use high temperature, working with 110-113 l/min gas flow (compressed air), 100% spray rate. Sprayed assays used three kinds of mesh 4.0, 5.5 and 7.0 µm separately.

Results and Discussion: The average particle size ranges from 202,5 to 272±5nm and PI from 0.03 to 0.09 ± 0.021. The size showed discrete variations of the morphometry of the particles once resuspended after being subjected to the process of sprayed, with a suitable homogeneity of the sample, as it maintains a (PI) less than 0.100 characteristic of monodisperse systems. The ZP, which is a measure of the surface charge of the particles that influences the stability and mucoadhesion, range from -12 to -19,6 ± 0.23mV. It can be observed an increase (in absolute value) after process of spray drying, indicating a greater surface charge which could improve the system stability.

Conclusions: The Nano Spray dried constitutes a good alternative to freeze-drying method increasing NPs stability by remove water of the sample.

Acknowledgements:

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Topical delivery of a lipidic polyphenol from nano-emulsions and solid lipid nanosystems

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Flavonoids are a kind of polyphenols suitable for percutaneous absorption due to their anti-inflammatory effects and antioxidant properties and useful for preventing photo-oxidative damage [1]. However, it is needed to carry them in suitable formulations that provide high amount of the active retained in the skin and low penetration in the dermis.

The aim of the present study was to develop three nanostructured systems (nano-emulsion NE, nanostructured lipid carrier NLC and solid lipid nanoparticles SLN) containing a lipidic polyphenol (0.3% wt.) for topical application, and to study the influence of the formulation and the droplet size in the ***in vitro*** skin permeation through abdominal human skin.

Non-ionic surfactants, a polyoxyethylene derivate (HLB = 15) and a castor oil derivate (HLB ≈12) were used, and as oil phase an oil medium chain triglyceride and a solid lipid glyceryl derivate were selected. The formulations were prepared by the emulsification-sonication technique, and the droplet size (span) was determined by the cumulants method using the Vasco^{TM} particle size analyser (Cordouan Technologies, France). The droplet size and span were of 85.14 nm (0.95), 53.72 nm (1.16) and 589 nm (1.13) for NE, NLC and SLN, respectively.

For the skin permeation the MicroettePlus^{R} system (Hanson Research, USA) was used. The assays were performed at 32ºC ± 0.5, 400 rpm and a solution of phosphate buffered saline pH 7.2 (Na_2HPO_4 (0.0577 g/L), NaH_2PO_4 monohydrate (0.03173 g/L), NaCl (9.2 g/L) + 1% polysorbate 80) (sink conditions) as receptor medium. Skin (0.4 mm) from the same donor and after checking its integrity (Tewl), was used. At the end of the experiment, the rest of formulation was removed from the stratum corneum, the skin was washed 3 times with 0.6 mL of the receptor solution, and the solutions were kept at -20ºC for polyphenol quantification (HPLC-UV 290 nm).

According to the results obtained, the lipidic polyphenol from NLC and SLN showed the highest percentage permeated at 24h (0.83% ± 0.2 and 0.76% ± 0.32, respectively (n=4)), but SLN presented the highest amount of the active remaining in the skin (mass balance method). The droplet size does not seem to influence the skin permeation of the polyphenol assayed from the formulations developed.

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