Bioencapsulation Research Group

Bioencapsulation Innovations

July 2014

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22th International Conference on Bioencapsulation

September 17-19, 2014
Bratislava, Slovakia
http://bioencapsulation.net/ 2014_Bratislava/

2nd South American Workshop on Microencapsulation

November 24-26, 2014
Joao Pessoa, Brazil
http://bioencapsulation.net/2014_Joao_Pessoa

EDITORIAL

MICROENCAPSULATION : 17TH INDUSTRIAL CONVENTION

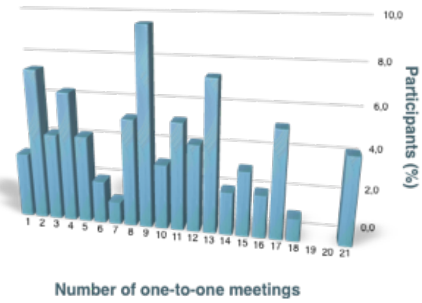
Held in Brussels on April 23-25, 2014, our last industrial event was a record of success. The meeting was articulated around 12 oral presentations presented by industrial and university experts and an exhibition from providers of services or equipments in the realm of microencapsulation.

A friendly atmosphere favoured the contact between attendees, especially during the convention diner, which took place in the former Waucquez Warehouse, a gem of Art Nouveau by grand master Victor Horta, now devoted to a cartoon museum, the Belgian Comic Strip Center.

But the success of the convention was largely due to the one-to-one meetings, i.e. a unique opportunity to meet many potential partners during 40 minutes and to establish advanced contacts for the future.

Based on the own pre-selection of each participant, with the help of a unique and fast tool allowing optimisation including «on-site» up-dating and printing of individual participants agendas, several hundreds of one-to-one meetings were organized. In mean, each attendee participated to 10 individual meetings, in addition of many informal discussions during coffee breaks and lunches.

The success was so great that we had to put another few extra time slots, allowing some participants to accumulate up to 21 meetings.



Next microencapsulation industrial convention will be organized during april 2015 in Eindoven, the Netherlands with the help of TNO. Please be sure to already mark the date on your calendar and be so kind to pass this information along to your colleagues.

Denis Poncelet

Oniris & Capaulae, France

BRG President

denis.poncelet@bioencapsulation.net

CALENDAR

PROGRAM 2014

August

Translational Nanomedicine

August 27-29, 2014 - Angers, France
http://www.transnanomedicine.com

September

Success in Animal Cell Encapsulation

September 4-5, 2014 - Zurich, Switzerland
http://www.buchi.com/training

Course on Microencapsulation

Wednesday 10 – Friday 12 September 2014
http://store.leeds.ac.uk/browse/extra_info.asp?compid=1&modid=2&deptid=41&catid=29&prodid=450

22th International Conference on Bioencapsulation

September 17-19, 2014 - Bratislava, Slovakia
http://bioencapsulation.net/2014_Bratislava/

3rd International Meeting on Pharmaceutical Sciences

September 18-19, 2014 - Cordoba , Argentina
http://http://ricifa.com.ar

Continuous Granulation

September 23-25, 2014 - Binzen, Germany
http://ttc-binzen.de/cm/index.php?id=714

Benefiq2014

September 23-25, 2014 - Quebec, Canada
http://www.benefiq.ca/en/

Club Emulsion 2014

29-30 Septembre 2014 - Argenteuil, France
http://clubemulsion2014.wix.com/club-emulsion-2014

October

International workshop New trends in encapsulation of bioactive compounds

October 1-2, 2014 – Santiago de Chile
http://www.foodpropertiesgroup.USACH.cl

20th International Symposium on Microencapsulation

October 1-3, 2015 – Boston, USA
http://www.northeastern.edu/ims2015/

SFNano Workshop 2014 : Relevant tools and models for translation of advanced drug delivery

October 2-4, 2014 - Porto, Portugal
http://www.sfnano.fr/?page_id=3224&lang=fr

Pan Coating

October 7-9, 2014 - Binzen, Germany
http://ttc-binzen.de/cm/index.php?id=719&L=0

November

Pellets and Micropellets for oral multi-dosage forms

November 25-27, 2014 - Binzen, Germany
http://ttc-binzen.de/cm/index.php?id=769&L=0

2nd South American Workshop on Microencapsulation

November26-28, 2014 - Joa Pessao, Brazil
Web site available soon
see http://bioencapsulation.net/

December

16th Journée de formulation

December 9-10, 2014 - Villeneuve d'Ascq, France
More information :
veronique.rataj@univ-lille1.fr
p.org@wanadoo.fr (site web ?)

FUTURE EVENTS

Bioencapsulation Research Group

22th International Conference on Bioencapsulation

&

21st Bratislava International Conference on Macromolecules

September 17-19, 2014 - Bratislava, Slovakia

http://bioencapsulation.net/2014_Bratislava/

Bioencapsulation Research Group

2nd South American Workshop on Microencapsulation

November 24-26, 2014 - Joao Pessoa, Brazil

followed by a two days student training

http://bioencapsulation.net/2014_Joao_Pessoa

Deadlines

For oral contributions and grant requests
August 30, 2014
For poster contribution
September 30, 2014

Bioencapsulation Research Group

18th Microencapsulation Convention on Microencapsulation

April 2015 - Eindhoven, Netherlands

Web site availbale end of September

Bioencapsulation Research Group

23th International Conference on Bioencapsulation

September 2015 - Delft, Netherlands

Web site availbale end of September

International Microencapsulation Society

20th International Symposium on Microencapsulation

October 1-3, 2015 - Boston, USA

http://www.northeastern.edu/ims2015/

ARTICLE

CREASPHER: A NEW TECHNOLOGY DEVELOPED FOR FOOD AND HEALTH

Adeline Callet, Hervé Huilier - Creathes, Belfort - France

SCOPE

CREASPHER is a Creathes' proprietary technology, involving emulsion solidification by « flash freezing ». It permits to prevent active products from oxidation, to protect flavors and to deliver actives in specific areas (e.g.: in gastro-intestinal tract, on skin at a chosen temperature ...). CREASPHER can be used to incorporate oily substances (pure or mixed) in an oily matrix material which can be incorporated in aqueous phase making a stable dispersion. This technology is completely green as absolutely no chemical reaction is involved during the encapsulation process.

CONTEXT

In food industry, problems involved are essentially related to formulation, protection, compatibility between products, taste masking which means directly linked to galenic and organoleptic properties of products.

Lots of technologies already exist but frequently induce high particle size, not indicated for therapeutical use. In this domain, advanced technologies provide controlled and targeted release without texture problems, but or not suitable for health applications because of the benefit-risk balance: residual solvent, CMR substances like glutaraldehyde, formaldehyde...

With the development of therapeutic innovations, new technologies have emerged to meet new needs (size reduction, use of different materials ...). However, other criteria are not met, such as small size or texture problems reduction.

creathes
Create the Solution OnDemand

Nowadays, applications related to health are not only medical but also well-being. The aging population is bringing new needs such as decrease of nutrients absorption, change in eating habits, skin problems (dehydration)... For these kinds of applications, risk-benefit balance could not be valid anymore as risks are almost non-existent. As more and more benefits need to be brought, we have to develop other ways to integrate new functionality in products.

The issue is to develop a technology allowing vectorization-diffusion-protection and suppress this benefit-risk balance. Several existing technologies can meet this challenge, but problems related to texture and particle size are still present.

AS AN ALTERNATIVE TO PRILLING AND GELATION

CREASPHER is also an alternative to these existing technologies such as prilling, spray-drying or gelation. For example, prilling can provide capsules with 70-100 µm minimum PSD, but not suitable for food or cosmetic industries. Through our full mastery of the particle size, very small microcapsules are obtained in the range of 0.5 to 40 µm (figure 1). By this way, issues on stability, texture or grainy touch can be easily overcome and some specific applications can be reached.

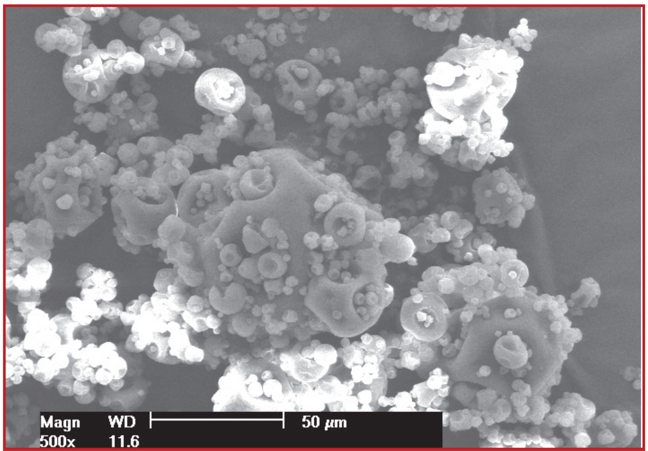


Figure 1: SEM picture of CREASPHER capsules

CREASPHER is a proprietary technology (Huilier, 2013) involving emulsion solidification by "flash crystallization". It permits to prevent active products from oxidation, to protect flavors and to deliver actives in specific areas (e.g.: in gastro-intestinal tract, on skin at a chosen temperature...). CREASPHER can be used to incorporate oily substances (pure or mixed) in an oily matrix material which can be incorporated in aqueous phase making a stable dispersion.

Moreover, CREASPHER does not use any chemical mechanism, but only phase change phenomena. INCI formula used is 100% indicated for food and medical applications, and could also be used for organic products. All materials used are completely safe, without any toxicity even concerning surfactants. Not involving chemical reaction and secondary product, it could also be integrate into GMP processes.

APPLICATIONS

This technology is available for several applications such as food, animal feed, nutraceutics... PSD could be chosen from 0.5 to 40 µm, depending on the expected applications.

Microcapsules are presented in a water dispersion form (table 1, figure 2A) and can be spray-dried. Powder form is preferred for food use, whereas liquid form is highly used for creams and textile deposit.

Table 1: Data for CREASPHER in liquid form (slurry)

	Data
Particle size distribution	d(0.5) can be adjusted in 0.5 to 30 µm range
Dry content	35-40 %
pH	4.5-5
Aspect	Slurry, white color, no odor
Viscosity	100 cP < v < 1000 cP

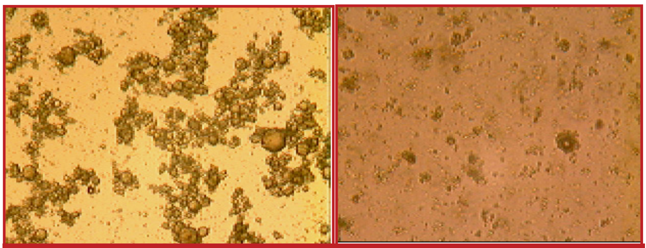


Figure 2: Optical microscopy picture of CREASPHER slurry (A) and powder (B)

This CREASPHER powder form (table 2, figure 2B) can be used either directly in a solid product or can be dispersed in aqueous phases. It exists into an instant version, which exhibits auto-dispersible properties for beverages or other liquid products...

Table 2: Data for CREASPHER in powder form

	Data
Particle size distribution for powder	50-80 µm
Particle size distribution for capsules	d(0,5) can be adjusted in 0.5 to 30 µm range
Humidity rate	3-7 %
Density	0.3-0.5
Aspect	Powder, no color, no odor

It can also be deposit on textile and fabrics (figure 3) for use in medical devices (e.g.: skin moisturizing, actives delivery ...) for skin-related diseases or affections due to dehydration (dermatosis, dermatitis, ichthyosis ...).

Figure 3: CREASPHER capsules on textiles (optical microscopy)

PROPERTIES AND HEALTH FRIENDLY

Stability has been checked with several core materials and did not show any issue after 6 weeks at 40°C. Physical stability has also been tested. Sedimentation did not occur while creaming can occur (depending on PSD, particles density).

Release of the encapsulated core product (figure 4) can occur: either by diffusion through the shell material in different scale times and intensity for volatile products (figure 5). Release preferably occurs when there is no more water residues in the product (evaporation), and/or under pressure or mechanical stimulus.

CREASPHER resists to pH conditions from 3 up to 9. Temperature stability depends on shell material properties. Typically, the temperature range is about 55-70°C (melting point of shell material).

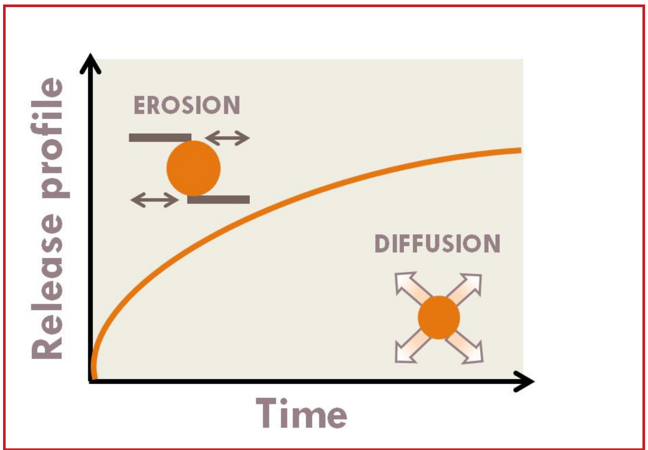


Figure 4: Schematic representation of the content delivery

All materials used for CREASPHER formulation are completed indicated for food and health use (Anderson, 1986; Feldman, 1979).

REFERENCES!

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Feldman EB, et al., « Effects of tristearin, triolein and safflower oil diets on cholesterol balance in rats. » The Journal of Nutrition, 1979, 109 (12), 2226-2236

Huilier H., « Alternative method for microencapsulation of active ingredients », WO2014041001 (A1), 2013

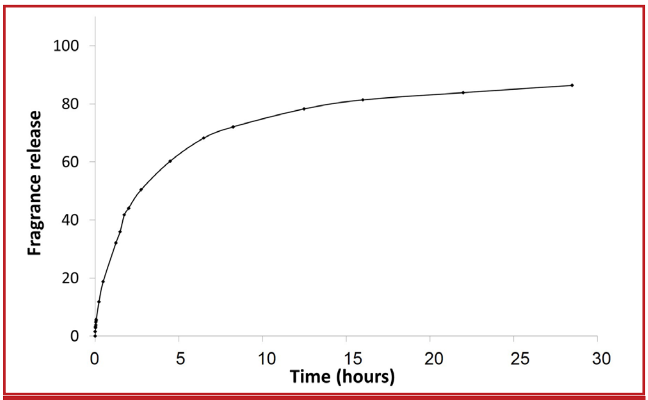

Figure 5: Fragrance release out of CREASPHER capsules

ADELINE CALLET

adeline.callet@creathes.com

Graduated at the University of Strasbourg, Adeline CALLET is a chemistry engineer and has a PhD in chemistry and physics. With a master degree in Innovation project management, she's now working as R&D project manager at CREATHES, providing technical solutions, especially in encapsulation and formulation.

For further information, *www.creathes.com*.

ARTICLE

ENCAPSULATION OF NANOPARTICLES FOR CATALYSIS APPLICATIONS

Stéphanie D. Lambert, University of Liege, Chem Eng – Nanomat, Catalysis, Electrochem, Belgium

INTRODUCTION

Ni-Cu/SIO$_2$ cogelled xerogel catalysts for selective hydrodechlorination of 1,2-dichloroethane into ethylene

There is an increasing demand for technology that will convert chlorocarbons as by-products of industrial processes into more useful or environmentally benign products. For example, hydrodechlorination of chlorinated organics is a particularly attractive alternative compared with incineration of wastes from the chlorine industry from both economic and environmental points of view (Kalnes, 1988). Several authors demonstrated the ability of bimetallic catalysts, composed of metals from Groups VIII and IB, to convert chlorinated alkanes selectively into less or not chlorinated alkenes. Here it is presented catalytic activity and selectivities of 1,2-dichloroethane hydrodechlorination over Ni-Cu/SiO$_2$ cogelled xerogel catalysts and the relationships between catalytic activity and surface properties of bimetallic catalysts. To understand the mechanism of hydrodechlorination of 1,2-dichloroethane on a supported alloy, the surface composition of Ni-Cu alloy is measured from H_2 chemisorption, XRD and TEM.

EXPERIMENTAL

Samples containing various amounts of nickel and copper are xerogels prepared by a one-step sol-gel procedure, which consists in the cogelation of the silica precursor, tetraethoxysilane (TEOS), with organically substituted alkoxides capable of forming chelates with nickel and copper ions (Lambert, 2008). All the reagents are with industrial grade. The resulting alcogels were dried under vacuum at 80°C, calcined in air at 400°C, and finally reduced in hydrogen at 450°C. All samples were tested for 1,2-dichloroethane hydrodechlorination. For each catalytic experiment, 0.11 g of catalyst pellets, sieved between 250 and 500 µm, were tested. The total flow of the reactant mixture was 0.45 mmol s-1 and consisted of CH_2Cl-CH_2Cl (0.011 mmol s-1), H_2 (0.023 mmol s-1), and He (0.42 mmol s-1). The temperature was successively kept at 200, 250, 300, 350 and 300°C. The effluent was analyzed every 15 min.

The combination of results from H_2 chemisorption, XRD and TEM allowed calculating the surface composition of the nickel-copper particles in all cogelled xerogel catalysts. Values obtained indicate a very pronounced surface enrichment with copper (Lambert).

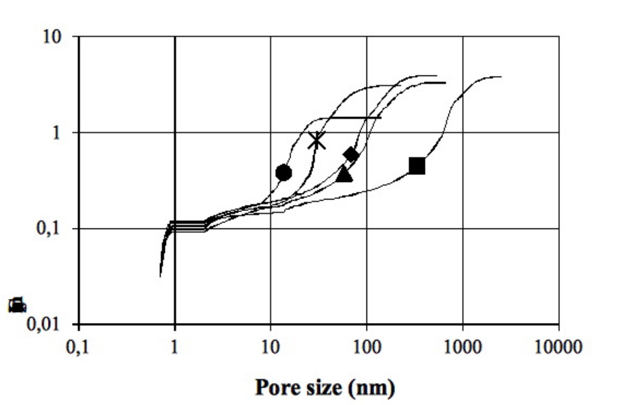

Figure 1 : Pore size distributions of samples Ni100 (X), Ni67-Cu33 (♦), Ni50-Cu50 (▲), Ni33-Cu67 (●) and Cu100 (■).

RESULTS AND DISCUSSION

Textural curves were obtained from nitrogen adsorption-desorption isotherms and mercury porosimetry measurements. All the samples are characterized by a narrow micropore size distribution around 0.8 nm inside SiO$_2$ particles, a broad porous distribution between 2 and several hundred nm outside SiO$_2$ particles and cumulated volumes equal from 1 to 7 cm^3/g (comparable to aerogels) (Figure 1) (Lambert, 2006).

The cogelation synthesis procedure described in this study allows obtaining highly dispersed Ni-Cu/SiO$_2$ cogelled xerogel catalysts. These samples contain Ni-Cu alloy crystallites with sizes of 1.6-3.4 nm, and which are located inside microporous silica particles (Figure 2).

The combination of results from the calculation of H_2 chemisorption, XRD measurements and transmission electron microscopy al-

Table 1. Ni and Cu loadings in Ni-Cu/SiO$_2$ cogelled xerogel catalysts.

Sample	Actual metal loading by mass balance: Ni (wt%)	Actual metal loading by mass balance: Cu (wt%)	Cu/(Ni+Cu)[b] (at.%)	X_{N_s}[c] (at.%)
Ni100	0.83	-[a]	0	100
Ni67-Cu33	0.83	0.45	37	33
Ni50-Cu50	0.83	0.90	54	23
Ni33-Cu67	0.82	1.79	70	10
Cu100	-[a]	0.90	100	0

[a]nonexistent.

[b]Cu/(Ni+Cu) is the metal atomic ratio.

[c]fraction of Ni atoms present at the surface of Ni-Cu alloy particles.

Table 1. Actual metal loading and surface composition of Ni-Cu nanoparticles in cogelled xerogel catalysts.

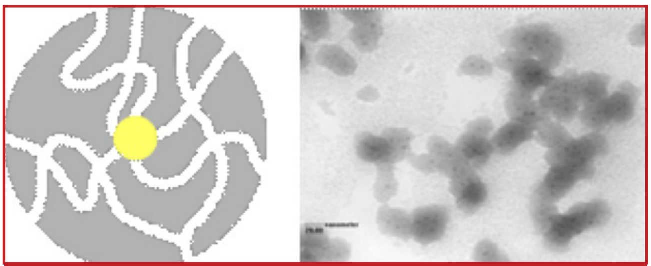

Figure 2 : On the right, scheme of a microporous silica particle (grey) with a Ni-Cu nanoparticle in the center (yellow); on the left, TEM micrograph of Ni33-Cu67 sample (350.000 ×).

lowed calculating the surface composition of the nickel-copper particles in Ni-Cu/SiO_2 cogelled xerogel catalysts. Values obtained indicate a very pronounced surface enrichment with copper. The copper concentration, which is higher at the surface in comparison with the bulk of the alloy, results from a surface energy of copper, which is slightly lower than the surface energy of nickel. Furthermore, the surface enrichment with Cu could result from a preferential localization of Cu atoms on low coordination sites. (Table 1).

While 1,2-dichloroethane hydrodechlorination over pure nickel mainly produces ethane, increasing copper content in bimetallic catalysts results in an increase in ethylene selectivity (Figures 3 and 4). Used alone, copper deactivates rapidly due to its covering by chlorine atoms. Thanks to its activation power of hydrogen by dissociative chemisorption, nickel present in the Ni-Cu alloy supplies hydrogen atoms for the regeneration of the chlorinated copper surfaces into metallic copper.

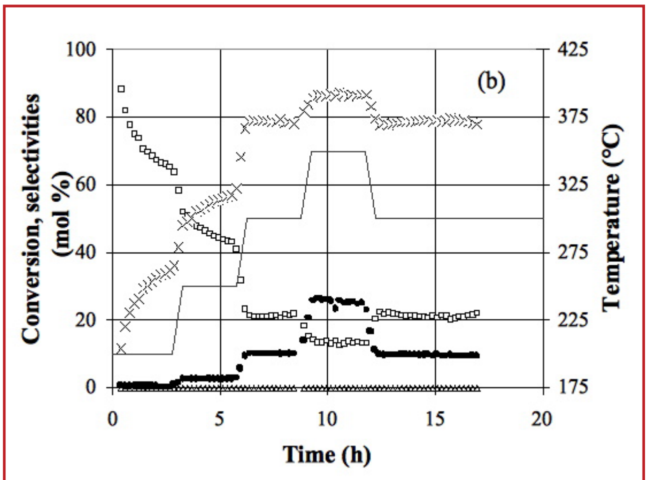

Figure 3: 1,2-dichloroethane hydrodechlorination for sample Ni50-Cu50. (●) $ClCH_2$-CH_2Cl conversion, (X) C2H4 selectivity, (□) C_2H_6 selectivity, (Δ) C_2H_5Cl selectivity, (—) Temperature.

The specific consumption rate of 1,2-dichloroethane decreases when copper loading increases. The turnover frequency, that is, the number of catalytic cycle per active site (nickel atom and its surrounding copper atoms) and per second, seems to be independent of surface composition of alloy particles.

Conclusions

The ultimate aim of this study was to prepare with a very simplified synthesis procedure and industrial grade rea-

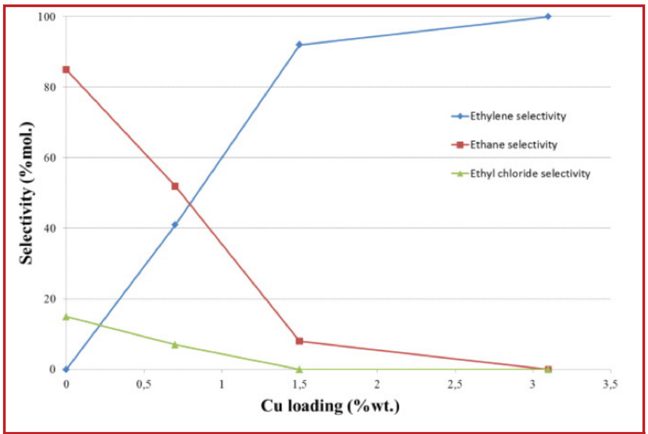

Figure 4: C_2H_4, C_2H_6 and C_2H_5Cl selectivities as a function of copper loading.

gents, highly dispersed Ni-Cu/SiO_2 catalysts. Furthermore, these catalysts had to be very active and selective for 1,2-dichloroethane hydrodechlorination into ethylene. This aim is reached because these bimetallic catalysts product only ethylene during catalytic tests of 75 hours without deactivation. Furthermore, the chemicals purity seems to have no influence on textural properties and catalytic performances of Ni-Cu/SiO_2 cogelled xerogel catalysts. So the use of industrial reagents is encouraging for the follow of the study concerning the extrapolating of the synthesis of metallic cogelled catalysts to an industrial scale.

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STÉPHANIE D. LAMBERT

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She received the M.Sc. in Chemical Engineering from the University of Liege in 1999 and Ph.D. in Applied Sciences in the same university in 2003. She worked as a researcher engineer at Nanocyl Society in 2004. In 2005, she joined the Department of Chemical Engineering of the University of Illinois at Chicago. From 2009, she became permanent as an Associate Professor and a FRS-FNRS Research Associate in the University of Liege.

ARTICLE

INORGANIC MICROENCAPSULATION OF BIOCATALYSTS

F. Galeone, N. Wautier, L. Marteaux – Dow Corning Europe S.A

INORGANIC IMMOBILIZATION AND ENCAPSULATION OF BIOCATALYSTS

Biocatalysts catalyze the transformations of organic compounds in living cells. The true active species are enzymes that can be used isolated or inside the cells. Because of the cost associated to their isolation, researchers are trying to delay their denaturation and reuse them by different ways.

A first approach consists in their immobilization onto inorganic substrates like silica by physical adsorption, covalent bonding on –SiOH groups, by coupling SiOH with -NH2, -CN, epoxy groups or by alkylation or arylation of hydroxyl group by cyanuric chloride derivatives (Pierre, 2004).

A second approach is the encapsulation into silica or organo-modified silica monoliths obtained by the cost effective "water glass" route (1) or by the more robust "sol-gel" process (2). The former route has major constraints in terms of pH and pI on enzymes stability. The later route is more robust and less demanding on the enzyme conformation if the released alcohol can be rapidly eliminated from the reaction environment (E = Enzyme).

(1) $E + Na_2SiO_3 + HCl - (x\text{-}1)\ H_20 \longrightarrow E + SiO_2 xH_20 + 2\ NaCl$

(2) $E + Si(OR)_4 + 2\ H_20 \longrightarrow E + SiO_2 + 2\ ROH$

Another constraint of the encapsulation approach is the shrinkage of the xerogel upon the drying stage of the wet gel. One can mitigate the shrinking by reducing the amount of silanol- silanol interactions by hydrophobisation and obtain an ambigel. Another strategy is the use of supercritical drying by CO2 at 31°C and 1072 PSI to obtain an aerogel (Figure 1).

The encapsulation of biocatalyst by the sol-gel route found many industrial applications as biosensors for glucose, cholesterol, urea, lactate...assays. The end-points can be electrochemical or optical. In the former case the gel contains conducting particles like graphite, metal powders, mediators or co-reagents and a current is measured. In the later case the enzymes are labeled with chromophoric or fluorescent groups or a molecule reacting to pH or O2 levels changes and a light emission or absorption is measured. The technology is also used for the synthesis of chiral compounds, chromatographic columns, and biocompatible implants and even in ammonia free hair colorants (Plos and Lagrange, 2002).

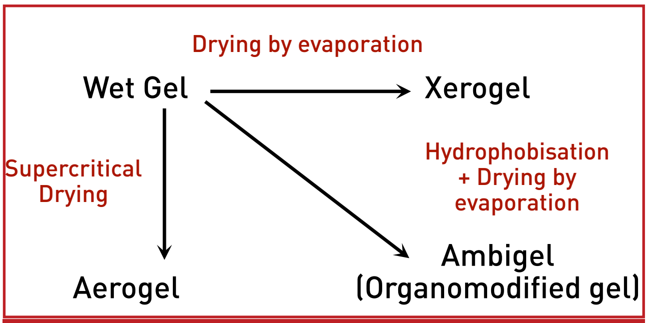

Figure 1: Strategies to reduce shrinkage of wet gels

BIOCATALYST MICROENCAPSULATION

Because of the limited surfaces developed by monoliths, their use finds their own limitations in industrial applications wherein transformation rate is critical. One way to meet this requirement is to significantly increase the interfacial exchange surface between the biocatalyst and its substrate medium. An option is to microencapsulate the biocatalyst into a nano or microcapsule in suspension in the substrate media (Barbe, 2010). Since most biocatalysts are active in water-based environment, the state of the art solution should be a W/O/W colloidal system. However W/O/W multiple emulsions are very unstable. Indeed on top of the intrinsic entropic instability of emulsions, they have to face osmotic pressure gradient between the internal and the external water phases. One way to mitigate the later is to increase the elastic modulus (G') of the oil phase. One approach is to use sol-gel precursors like alkoxysilanes as the initial oil phase (Marteaux, 2006). Their hydrolysis (a) and condensation (b) (Iler, 1979):

(a) $TEOS + 4\ H_20 \rightarrow Si(OH)_4 + 4\ C_2H_5OH$

(b) $Si(OH)_4 \rightarrow SiO_2 + 2\ H_20$

(a+b) $TEOS + 2\ H_20 \rightarrow SiO_2 + 4\ C_2H_5OH$

will transform the oil phase into a silica or an organo-modified silica phase leading to a W/Silica or organo-modified

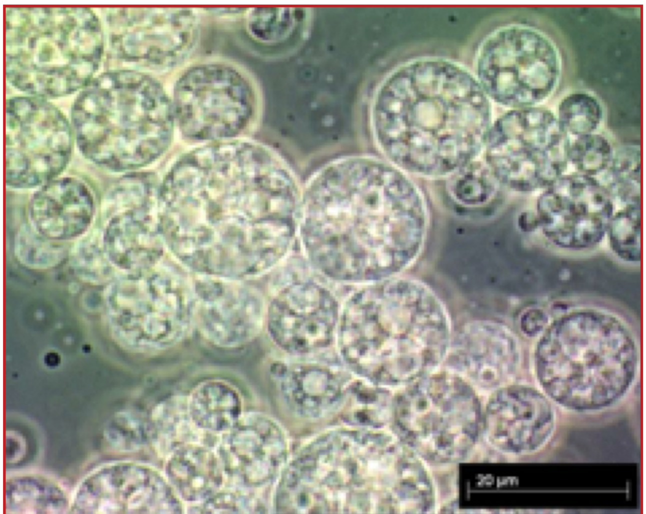

Figure 2: W/Silica/W polynuclear microcapsule suspension

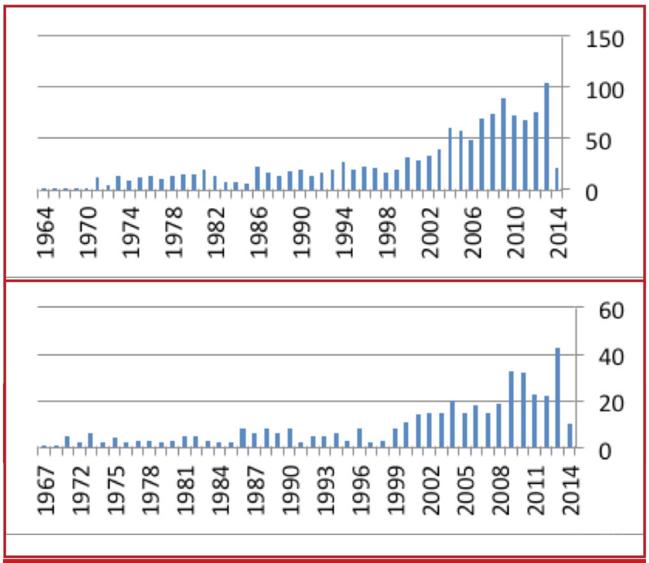

Figure 3: Publications (top) and patents (Bottom) on Enzyme containing microcapsules. Source SciFinder

silica/W polynuclear microcapsule suspension (Figure 2).

As the structure of the silica shell produced depends on many physical parameters like, temperature, pH, ionic strength etc...the use of this mild chemistry is delicate (Brinker, 1990). The hydrolysis and condensation reactions described above are further complicated by the presence of a surfactants to template the silica shells as well as the presence of a dispersed oil in a large excess of water. The large excess of water is a reaction condition that is very rarely studied by the sol-gel research community

In the case of biocatalyst microencapsulation, the internal water phase contains the biocatalyst, preferably water soluble enzymes and its co-factor, and the external phase the substrate. The goal is that the polynuclear microcapsule is acting as a microbioreactor wherein the substrate can diffuse in the internal water phase, be transformed by the biocatalyst in a product that can diffuse out to the external water phase.

Looking at the prior art in enzyme microencapsulation we notice that the topic is getting more and more interest reaching a total of 1323 hits (Figure 3 top).

The patent portion of it is about one third which is translating the high industrial interest in the field (Figure 3 bottom).

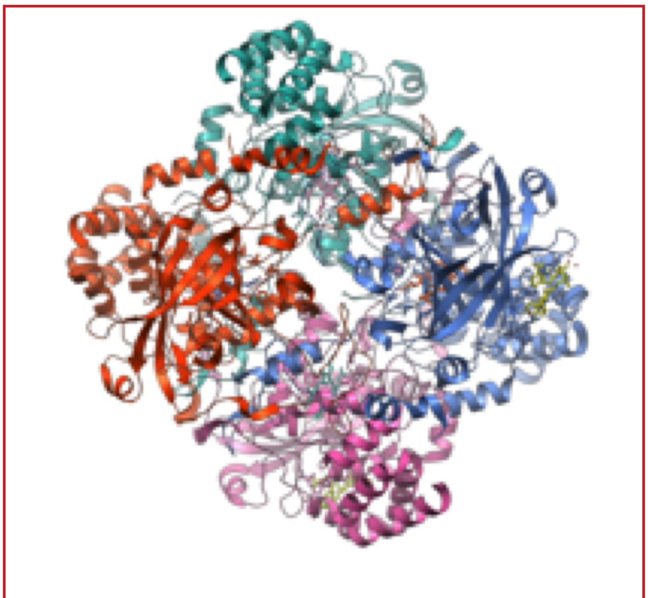

Figure 4: Catalase from human erythrocyte. Source Vossman

MICROENCAPSULATION OF CATALASE FROM ASPERGILLUS NIGER.

Catalase (Figure 4) is an oxydo-reductase enzyme catalyzing the transformation of hydrogen peroxide into water and oxygen:

$$H_2O_2 + Fe(III)\text{-}C \rightarrow H_2O + O{=}Fe(IV)\text{-}C$$

$$H_2O_2 + H_2O + O{=}Fe(IV)\text{-}C \rightarrow O_2 + Fe(III)\text{-}C$$

$$2\,H_2O_2 \rightarrow 2\,H_2O + O_2$$

Catalase contains four sub units of polypeptide chains and four porphyrin hemes for a total Mw. of about 345000 g/mole. Its Stokes radius is 5.83 +/-0.49 nm. Its reaction rate is only limited by substrate diffusion allowing ~200.000 reactions/second.

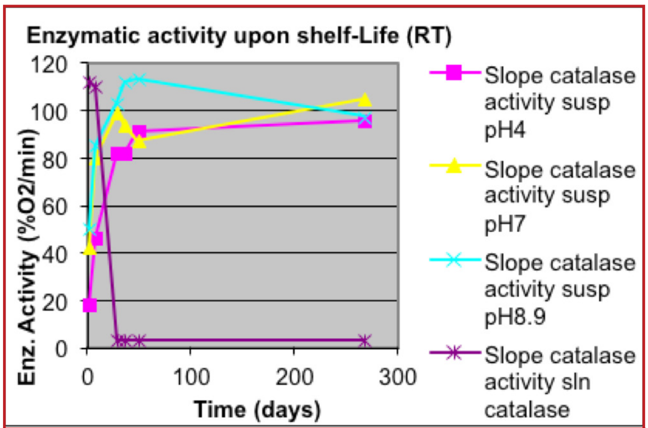

Figure 6: Catalase activity upon its polynuclear microcapsules suspensions shelf-life.

Catalase has been microencapsulated according to the process described in US8734840B2 (Marteaux, 2006). The authors did not observed measurable loss of Catalase from the internal water to the external water phase upon aging by both protein assay and Catalase activity measurement of the external water phase. All the microencapsulated Catalase was fully encapsulated at pH 4, 7 and 8.9. The Catalase activity was measured in a 50 mM phosphate buffer having a pI of 110 mM, and a pH of 7.The concentration in hydrogen peroxide was 40 mM and the concentration of microencapsulated Catalase was 9 ppm. The oxygen concentration was measured using an oxygen Poket Meter Oxi 340i equipped with a specific oxygen electrode Cellox 325.

The enzymatic activity of the suspensions obtained at pH 4, 7 and 8,9 have been monitored upon shelf-life (Figure 5).

The ability to measure a significant increase of oxygen concentration once the Catalase containing suspension is added to the hydrogen peroxide reactive medium indicates that it can diffuse in and the oxygen can diffuse out of the silica matrix. The microencapsulation of Catalase from

ARTICLE

Aspergillus niger into silica polynuclear microcapsules extends its half-life time from 2 weeks RT to one year RT.

CONCLUSIONS

While sol-gel encapsulation of biocatalyst in monolith and coatings is a quite mature field of activity with many industrial applications, inorganic microencapsulation of biocatalyst is still a promising incubating field. To conduct hydrolysis and condensation of alkoxysilane from a multiple W/TEOS/W emulsion mitigate the risk of enzyme denaturation due to gel shrinkage and/or high ethanol concentrations. More specifically the microencapsulation of Catalase from Aspergillus niger into silica polynuclear microcapsules extends its half-life time from 2 weeks RT to one year RT. Silica-Based polynuclear microcapsules can act as an enzymatic microreactor wherein low Mw. substrates and low Mw. reactants can go in and out of it.

The concept can most likely be extended to other biocatalyst like cells, bacteria, fungi, yeast, viruses and cells organelles but cannot work in applications where a close contact between the enzyme and the substrate is required.

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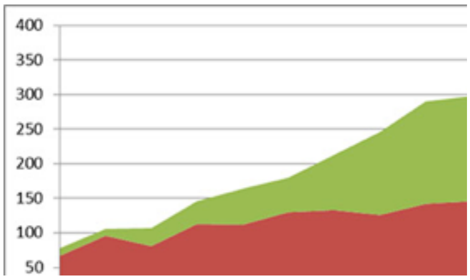
INDUSTRIAL NEWS

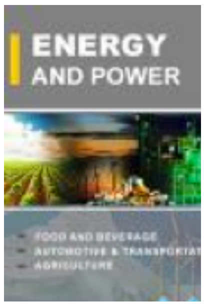
FORMULATION DEVELOPMENT
Trends & Opportunities in Particle Design Technologies



This article discusses the observed trends in particle design and engineering technologies, as well as the main factors and opportunities driving the principal technological advances in the biopharmaceutical industry around this topic.
Edited by Cecilia Van Cauwenberghe, Senior Research Analyst with Frost & Sullivan's Technical Insights practice.

More information on http://bit.ly/1nb6ELw

Food Encapsulation Market by Technology, Shell Materials & Core Phase - Global Trends & Forecasts to 2018



Published: January 2014 - Markets and Markets

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To offer an alternative to traditional spray drying process, Dinnissen has developed a fluid bed drying unit to contact precisely pre-dried liquid with hot air allowing to significantly lower energy consumption and optimum retention of colour, flavour and vitamins. During the final drying process, Dinnissen makes use of the double-shafted paddle mechanism built into the Drying Unit to gently suspend powders, granules, and granulates in the air.

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INDUSTRIAL NEWS

Book on encapsulation of food ingredients & for food processes has a total of 18562 downloads so far!

Since its online publication on October 30, 2009, there has been a total of 18562 chapter downloads for my book on 'Encapsulation Technologies' on SpringerLink. Massive! Klaas-Jan Zuidan, co-editor, thanks the contributors from both academia & industry for this success. It is one of the top 25% most downloaded eBooks in the relevant Springer eBook Collection in 2013.

Further information: http://lnkd.in/dXYWkjG

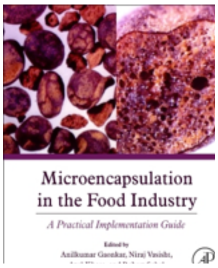
Encapsulated biocide 3AEY world licencing

GM Avocats & Solicitors
Franchising, Licensing & Multi-Channel Strategies

The legal firm GM Avocats assisted the company TerpeneTech Ltd (UK) in their world strategy for sub-licencing encapsulation technology for the mass-consumption market and agro-food in biocides. TerpeneTech is an English company, holder of a licence for two patents, utilising cell wall glucans to encapsulate terpene active ingredients, developed by Eden Research PLC, a biotech research company.

More information (French) : http://bit.ly/VP9kcf

Microencapsulation in the Food Industry : A Practical Implementation Guide



Editor(s): A. Gaonkar, N. Vasisht, A. Khare and R. Sobel
Expected Release Date: 22 Jul 2014
Academic Press, ISBN : 9780124045682
Pages: 590

More information :http://bit.ly/1rbiYk7

TNO has developed an innovative spray-drying technique

TNO has developed a spray-drying technique that atomises the fluid with proprietary high-viscosity inkjet printing technology. This allows the formation of highly uniform powders and encapsulates, which results in high quality products. And in turn the uniform droplet/powder size leads to an energy reduction of 63%. They are currently looking for partners to test the print-drying technology with industrially relevant formulations and products.

More information : http://bit.ly/1qZoCrW

Textiles : from cosmetics to medical applications of microcapsules

Slimming without diet, tanning without self-tanner creams is a dream no more with cosmeto-textiles. One novel application is the « kama-sousdrap », a bed sheet releasing aphrodisiac aromas. However, the application of microcapsules to textiles now extends to the medical field such as an anti tennis-elbow delivery system or skin allergy reduction through the release of moisturizer.

More information (in French) : http://bit.ly/1sCgFXv

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ARTICLE

OPTIMISATION OF INDUSTRIAL MICROCAPSULE PRODUCTION

Denis Poncelet, Oniris & Capsulae, Nantes, France & Jean-Paul Simon, O.B.E., Brussels, Belgium

INTRODUCTION

Hundreds of papers are published every year on the development and the application of microcapsules. However, most works are realized at the laboratory scale without considering the real conditions of production at industrial scale.

Most universities and research centers have more and more limited fundings, and developing a research at even pilot scale is out of their capacity. The transfer from laboratory to production plant is then mainly done internally and confidentially by industrials. However, those often do not have time neither budget to carry out the full process development and optimization. Most microcapsule production are then run under non-optimum conditions and based on the operator's experience rather than reliable conditions.

In the last few years, we developed some processes at pilot scale and also helped some industrials to optimize their process. Without revealing some confidential information, we report here some works done, taking as example the fluid bed coating.

PROCESS CONTROL OF FLUID BED COATING

Fluid bed coating consists in fluidizing particles in a rector and spraying a coating polymer solution on the particles. The fluidization air provokes drying at the surface of the particles and the dried polymer forms a coating around the particles (Figure 1). To promote a better particle circulation, more air is passing in the center of the reactor in a configuration called Wurster (Figure 1).

The fluidization air is preheated to favor quick drying of the coating around the particles (Figure 2, line A-B). During evaporation, no new energy is provided. Consequently, the warm air provides evaporation enthalpy. The air cools down and uptakes the humidity (Figure 2, line B-C). The residual humidity at the surface of the particles is directly in equilibrium with the humidity in the air surrounding the particles.

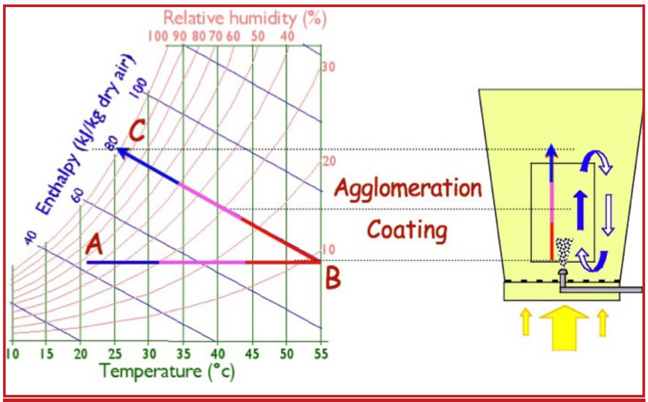

Figure 2 : temperature evolution in the fluid bed.

Agglomeration of the particles takes place while the temperature is over the glass transition temperature of the coating material, which decreases quickly as the water activity in the coating increases. To avoid agglomeration, the operator must select conditions where the drying is fast enough for the coating material being always under the glass transition temperature/humidity. He generally misses detailed information about the optimum conditions and then has to rely on his own feeling, i.e. the sound emitted by the reactor which changes while agglomeration starts.

We have run an experimental plan coating microcrystalline cellulose particle with arabic gum solution, trying to dtermine some criterion for detecting pre-agglomeration state. This set of experiments shown a drop of pressure over the fluid bed before agglomeration starts while parameters such as temperature and humidity change only after agglomeration. We have then built a simple model (Figure 3) allowing starting and stopping the coating solution pump, based on a pressure drop signal (Prata, 2012). Using such control, we avoided agglomeration while allowing mainly double coating speed compared to a manual control.

One drawback of this first model is that the pressure drop criterion depended of the types of reactor, particles and

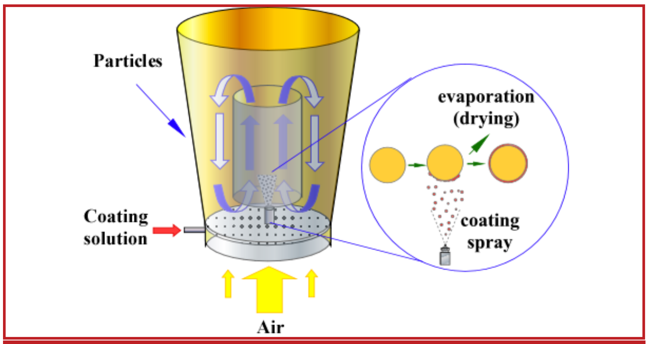

Figure 1 : Fluid bed coating in Wurster reactor

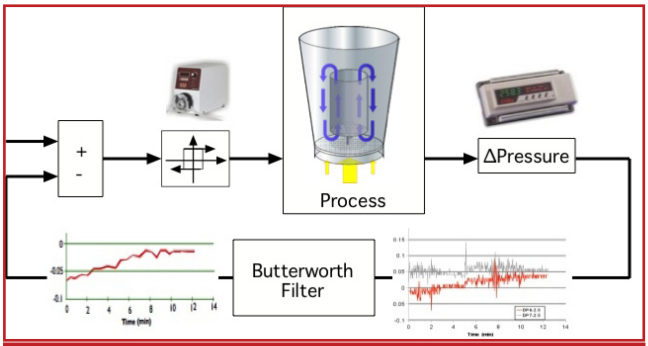

Figure 3 : Bang-Bang control process of fluid bed coating

coating. The control was also based on a on/off principle. We then developed a new model that searches automatically the optimum running conditions by modulating the pump speed. This model is in the phase of validation, and we are also collaborating with other groups to extend the control to the fluidization air flow, not only on the coating solution flow.

FLUID BED COATER DESIGN

Wurster reactor is considered as the best configuration as it promotes good particle circulation, and the spray is done in the particle flow allowing good contact. This results in a better quality coating than for example top spray coating. However, we found some drawback to this configuration.

While starting the fluidization, air is passing through the particles. At a certain flow, air starts to expand the particle bed but the fluidization is relatively unstable. This is indicated by a pressure drop fluctuation through the bed. With optimum airflow rate, pressure drop becomes stable. At too high flow, the turbulence provokes again fluctuation of the pressure drop. We observed that the optimum airflow window is relatively small while using the Wurster configuration.

In the central zone of the Wurster, temperature is the compromise between warming by the airflow and cooling by evaporation. The temperature in this zone is often 20 °c lower than the airflow temperature. However, in the annular zone, no evaporation takes place and the temperature may raise to the air flow temperature, i.e. 20° higher than in the central zone (Figure 4).

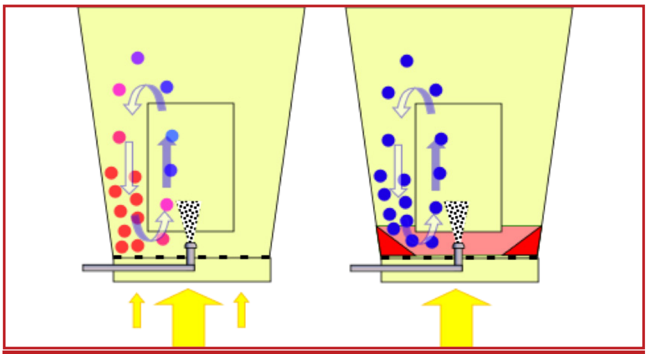

Figure 4 : the Wurster and Spouted bed configuration

We tested another configuration called spouted bed (Figure 4). No air is supposed to pass in the annular zone and we observed that the temperature was homogeneous over the reactor and 20 °c lower than the airflow temperature. Spouted bed are generally advised for large particles (over 1 mm), but even for small one (500 µm) we observed a stable fluidization over a large range of air flow. This would allow to keep a good fluidization while modulating the drying capacity.

We tested the two configurations for encapsulation of probiotics, as temperature sensible indicator. Using the spouted bed allows a cell survival during coating process up to 2 times higher than with the Wurster configuration.

CONTINUOUS FLUID BED COATING

Working with continuous processes generally decreases the cost of production by a factor 3 (Teunou, 2004). However, the control and the optimization of continuous fluid bed pro-

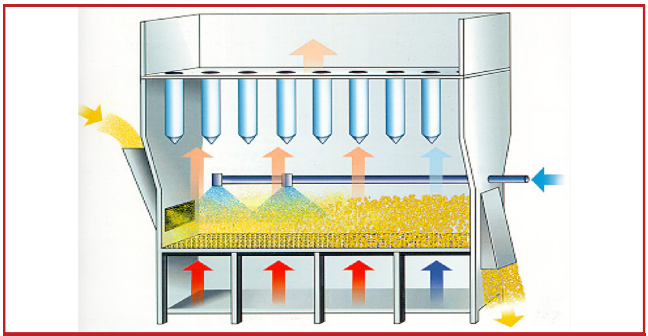

Figure 5 : Procell fluid bed coating reactor (Glatt ®)

cesses is difficult and industrials are aware to develop such systems. We helped one industrial to optimize a multi-layering coating process Procell recator (Figure 5, Glatt Gmbh). By better understanding the process conditions, developing energy and mass balance around the reactor, we succeeded to stabilize the process passing from 1 ton to 4.5 tons per week. The project is pursued actually expecting to reach 9 to 10 tons per week.

In another project we also doubled the production for a prilling process for feed applications and demonstrated that the laboratory dripping method may be scaled-up to several hundreds tons per year using a continuous process.

CONCLUSIONS

All these researches would not have been possible without strong collaborations between research laboratory and industry. Laboratories do not have access to the equipment while the industry does not have the human resources to develop such analyses.

ACKNOWLEDGE

The information collected in this article results from the work performed by (ex-)collaborators including Samira Elmafadi and Arnaud Picot (Capsulae, France), Ana Prata Soares (Unicamp, Brazil), Audrey Maudhuit (Phytosynthèse, France), Damien Cognac (SBII Nantes), Lionel Boillereaux (Oniris).

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ARTICLE

PROCESS IMPROVEMENT USING ENCAPSULATED BIOCATALYST

Jean-Paul Simon, O.B.E., Brussels, Belgium and Denis Poncelet, Oniris & Capsulae, Nantes, France

INTRODUCTION

While talking about encapsulation, the main objectives are generally immobilization, protection and controlled release. Occasionally, people are thinking to modify powder properties as flowdability or to provide a new functionality to a dispersed material.

However, immobilization of catalysts, more specifically biocatalysts, is an important issue and may provide a strong support for developing industrial processes. Batch processes remain the most usual approach, despite the higher performances of continuous processing. Using encapsulated biocatalysts is often the key to develop performant continuous processes.

In the 70th-80th, many authors claimed a process limitation due to the mass transfer inside the millimeter size capsules. However, many bioprocesses are not linked to very fast reactions (hours in relation to minutes in chemical processes). Moreover, the production of microcapsules has been improved allowing today to produce large quantities of capsules with a size down to even a few micrometers. The diffusional aspect is then no more a limitation.

This contribution shows some examples of potential use of encapsulated biocatalysts.

LACTIC BACTERIA CULTURES

Cultures of lactic bacteria have many industrial applications (Figure 1). They may be used for milk acidification, yogurt starter or probiotic production. Lactic bacteria are usually produced in a batch reactor while continuous processing would lead to largely higher volumetric productions.

Using free cells in a continuous reactor, the concentration of cells, X, is driven by :

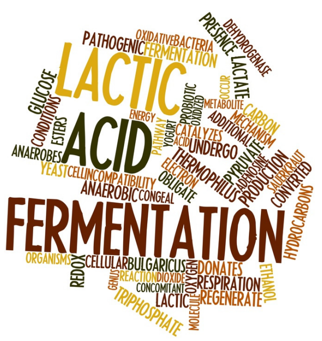

Figure 1 : Lactic bacteria - a large soectre of application

$$dX/dt = \text{cell growth-cell washout} = \mu X - F X \quad (1)$$

where μ is the growth rate and F the volumetric flow rate.

The growth rate is function of the substrate concentration, which itself is function of the quantity of substrate introduced in the reactor, thus the volumetric flow rate. We are then face to a challenge: to increase the cell growth, we must increase the flow rate, but then we also increase the cell washout. This limits the lactic bacteria concentration to 10^8 cells/mL.

Using encapsulated cells, for example in hydrogel beads, cell washout term disappears and the concentration of cells could increase up to 10^{10} or even 10^{11} cells/mL until either the microcapsules are full of cells, or some diffusional effects limit the growth (Champagne, 2006). As the microcapsules are full, the growth may be pursued but by releasing cells in the medium, leading often to higher free cells concentration that while using free cell reactor.

Encapsulation of lactic bacteria allows solving to other problems:

• lactic bacteria are very sensible to phage (virus) attacks. Entrapment of the cells in hydrogel beads offers a strong protection against phages (Champagne, 2006).

• In co-culture, a small difference of growth rate leads quickly to domination of one cell over the other. While encapsulated cells in different microcapsules, the relative concentration of cells could be controlled by the concentration of each type of capsules (Sodini-Gallot, 1995).

BEER PRODUCTION

The beer represents a market of 10^9 hectoliters/year worldwide (Figure 2). This is the largest consumed drink after the tea. Usual batch fermentation stands for one week for the first alcoholic fermentation and 3 weeks for the maturation. Labbat Brewies (Ontario, Canada) has developed a cell immobilization process in K-carrageenan beads allowing reduce the first fermentation to 2 days. Using static mixer system, it was possible to envisage very large production of beads (Descamps, 2004).

One of the main reasons for the second fermentation is linked to the production during the first fermentation of the alpha-acetolactate. This compound degrades spontaneously but very slowly to diacethyl, which leads to butter taste Further degradation of the diacethyl in acetoin solves the problem … after 3 weeks. Encapsulation of alpha-acetolactate de decarboxylase allows degrading alpha-acetolactate in less than 2 days (Dulieu, 2000).

Theoretically, a beer may be produced then in two days. However, beer is a complex product and research are still in progress to control its production in continuous reactor while providing the same taste then with batch reactor.

Figure 2 : Beer the most largest production of friendship drink

BIOREACTOR AERATION

Many useful fermentations are aerobic. However, the concentration of oxygen in water is very low (0,2 mM in regard to substrate concentration of tens of mM) and represents the limiting factor. Oxygen has to be provided continuously by bubbling air through the reactor. This represents a high energy consumption and provokes shear that may be detrimental to cells. Moreover, the oxygen transfer from bubble to the solution is slow. It may be represented by the oxygen specific time, T (inverse of the k_la), which is often ranges from a few minutes to tens of minutes for low or large agitated reactors.

Concentration of oxygen in air is around 9 mM, very similar to in perflurocarbons and slightly higher than in silicons (6mM). We tested oxygenation of a reactor using encapsulated silicons and found out that the oxygenation specific time was largely lower than with air (less than 5 seconds) without providing shear stress (Poncelet, 1993).

ENHANCING MASS TRANSFERT

As stated in the introduction, one drawback of using immobilized biocatalyst is the diffusional limitations. When the process it-self is slow, such as maturation of beer or secondary fermentation of champagne or cider, substrates and products could freely migrate through the capsules.

To reduce the mass transfer limitation, one could reduce the size of the capsules. Several authors stated that diffusion is often limited to a layer of 100 µm. By reducing the size of the capsules to a few hundreds micrometers, the process will not be limited by the diffusion. However, maintaining the microcapsules in the reactor is then challenge.

The most easy system to separate the microcapsules from the liquid flow is by sedimentation. The settling velocity, v, is given by:

$$v = \frac{g(\rho_p - \rho_f)d^2}{18\mu} \qquad (2)$$

where g is gravity constant, ρ_p and ρ_f are the density of the particle and the fluid, d the diameter of the particules and µ the dynamic viscosity of the fluid.

While producing for example hydrogel beads, one could incorporate some inert filler and increase significantly the density and the settling velocity of the microcapsules (table 1). It is then possibly to compensate the size reduction by increasing the density of the microcapsules.

Size (mm)	Filler (%)	Density (g/L)	Settling velocity (m/s)
2	none	1,05	0,101
0,6	Sand 30 %	1,55	0,102

CONCLUSION

Microencapsulation of catalyst has a great potential for many (bio)processes but has be neglected due to prejudices. The evolution of the encapsulation technologies, especially regarding the size, structure and productivity, may bring back industrials to consider this solution for developing their processes.

ACKNOWLEDGE

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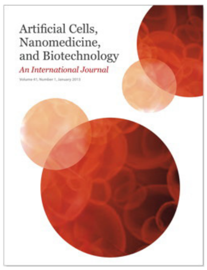

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- ***Chemical method for retrieval of cells encapsulated in alginate-polyethersulfone microcapsules***
  Barbara Kupikowska-Stobba , Dorota Lewińska , Marcin Grzeczkowicz
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- ***Small peptide-modified nanostructured lipid carriers distribution and targeting to EGFR-overexpressing tumor in vivo***
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- ***Synthesis and tyrosinase inhibitory properties of novel isoquinoline urea/thiourea derivatives***
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- ***Experiment research on inhibition of glioma with sTRAIL in vitro***
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- ***New coumarin derivatives as carbonic anhydrase inhibitors***
  Mert Olgun Karataş , Bülent Alici , Ümit Çakir , Engin Çetinkaya , Dudu Demir , Adem Ergün , Nahit Gençer , Oktay Arslan
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- ***Schiff bases attached L-glutamine and L-asparagine: First investigation on antimutagenic and antimicrobial analyses***
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THESIS SUMMARY

Investigation of process-structure-property relationships in dry particulate systems

ONDREJ KASPAR

Supervisor prof. Frantisek Stepanek
Date & Place 02-07-2014 – Prague , Czech Rep.
Affiliation ICT Prague, Czech Republic

My thesis deals with the preparation of composite particles by spray drying and batch wet granulation methods. In the case of spray drying, a unique cross-linking method of chitosan carriers by a 3-fluid kinetic nozzle and spray dryer Büchi B-290 was rigorously investigated. The determination of optimum values for all input parameters was followed by the encapsulation of different model active substances. The second part of this work deals with the influence of process parameters of batch high-shear wet granulation on the segregation of active pharmaceutical ingredient (API), particle size distribution and API release characteristic from granules. A novel methodology for the evaluation of porosity, pore size distribution and visualization from computer tomography (CT) data by image analysis was established.

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THESIS SUMMARY

Investigation of targeted particle adhesion to biological and non-biological substrates

VIOLA TOKAROVA

Supervisor Prof. Frantisek Stepanek, Ph.D.
Date & Place August 2014 – Prague, Czech Rep.
Affiliation ICT Prague, Czech Republic

The presented dissertation deals with the preparation and characterization of various types of structured nano- and micro-particles with a possible application in the pharmaceutical industry for targeted delivery of active substances. Adhesive properties of the particles are essential knowledge in targeted delivery and therefore a purpose designed adhesion cell was developed, which is used in particle adhesion determination to a certain type of the substrate. Ones of the presented nanoparticles are composed of silica with embedded magnetite and fluorescent dye inside the silica structure for multi-modal imaging. The targeted adhesion of such particles to a cancer cells are provided via specific antibody-antigen interaction. Antibody M75 is coupled on the surface of the particles and trans-membrane antigen CA IX is presented during cancer cell proliferation process.

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Microencapsulation by complex coacervation of whey proteins isolate and acacia gum

DELPHINE ACH

Supervisor Dr Y. Chevalier / Pr S. Briançon
Date & Place 06-10-2014 – Villeurbanne, France
Affiliation University Lyon 1, France

The purpose of this study was to improve the understanding of the microencapsulation process by complex coacervation. The work focused on the complex coacervation of whey proteins isolate and acacia gum. Few data are available on the mechanism of coacervation of these compounds. The composition of whey protein/acacia gum coacervates was determined by capillary gel electrophoresis. Coacervation depends on the protein/acacia gum ratio and an optimum pH was defined for each ratio. The microencapsulation of linseed oil was studied. The critical step of emulsification could be controlled by mixing parameters. An accurate description of successive steps of the process was proposed thanks to an in situ on line monitoring by a video probe immersed in the stirred vessel. Formation of complex coacervate particles, their deposition onto oil droplets, and encapsulation by a continuous shell are well-separated events taking place at well-defined pH values.

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JOB REQUESTS

Looking for a post-doctoral position

CLARA DOMBRE, PHD

As part of my Master's degree internship, I worked on the inclusion of essential oil in biopolymer matrix to develop a protective food packaging product. Thereafter, I did a PhD at the university of Montpellier in France, focussed on the barrier properties of polyethylene terephtalate bottles toward organic volatile compounds of wine as well as the the impact of aroma compound transfers on the aromatic profile of wine. These studies were under the directorship of Pascal Chalier. These experiences have given me sound and broad knowledge within the various niches of biochemistry of aroma compound, gaz and molecular transfer, or polymer characterisation. My PhD also helped me increase the quality of my approach to scientific rigor, as well as organization, patience and team work.I am seeking a post-doctoral position with focus on aroma compound transfer or other molecular transfer with application in the food, cosmetic or chemical industries.

Contact/Link

Clara Dombre, +33 6 6464 1335, *clara.dombre@gmail.com*

Looking for position in the field of food ingredient encapsulation

MR. ANKUR GOEL

M.Sc Food Science (McGill University)
Research Assistant (Fundamental & Applied Research – McCain Foods)
Ankur Goel has experience of working in the "Fundamental & Applied Research" group at McCain Foods Canada and also as a Senior Project leader at The Original Cakerie. He obtained his Bachelors in Biotechnology from Amity University (India) and Masters in Food Science from McGill University (Montreal, Canada).
He has worked on optimization of method for the characterization of nano encapsulation of bioactive molecules (protein/ polysaccharides) as ingredients, using ultra sonication. He is looking for further opportunities in the field of encapsulation. Please contact him with further details.

Contact/Link

Ankur Goel; *an_kur_g@yahoo.com* ; +1 (506)323 3192

Looking for a PhD position

CHLOÉ AMINE

Just graduated from the European School of Chemistry, Polymers and Materials (ECPM) at Strasbourg (France) (master degree) I'm currently performing a six months final internship at Sanofi (France). During this internship I had the opportunity to work on the derisking approach for fill & finish operations of biotechnology compounds. In this purpose I investigate the impact of shear on protein degradation during each step of the industrial process. The degradation was assessed by measurement of enzymatic activity but also using analytical devices such as DLS, FCM, HPLC-SEC, etc. During a previous internship I also had the opportunity to work on emulsions formation and stabilization using proteins as emulsifiers.
In order to be involved in a research project, to gain autonomy and to broaden my scientific knowledge I'm looking for a PhD position (from October 2014) focuses on bio encapsulation of biotechnology compounds for therapeutic or food industry applications.

Contact/Link

Amine Chloé, (+33) 7 81 81 81 02, *chloe1amine@gmail.com*

Postdoctoral Position

ANDREA SCHENKMAYEROVÁ, PHD.

Researcher in Biotechnology

My name is Andrea Schenkmayerová, I got a PhD. in Biotechnology at the Slovak University of Technology in Bratislava in August last year. Now I am searching for a PostDoc/working opportunity in a challenging international atmosphere to pursue my career.
My university studies were focused mainly on fermentation/biotransformation processes, immobilizations and biosensors development. I was using immobilized yeasts in organic compounds reduction, I was working on enzyme kinetics of alcohol dehydrogenase from Zymomonas mobilis, on acetone butanol fermentation, Baeyer-Villiger biooxidations and biotechnological production of 2-phenylacetic acid.
I have the ability to understand new issues very quickly and I prefer the application of the interdisciplinary approach in the laboratory. I am a team player, but I am able to act independently in solving problems even if they require novel approaches.

Contact/Link

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