**From dextran-coverd nanoparticles to nanocapsules: how reactive surfactants based on dextran can help to control nanocapsule morphology?**

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***Abstract***

For biomedical applications the use of biocompatible and possibly biodegradable compounds is fundamental. In this respect, some polysaccharides and their derivatives are excellent candidates, due to their natural origin, and most likely their biodegradable and biocompatible character. For example they can be used to generate nanodevices such as polymeric nanoparticles made of a hydrophobic core and a hydrophilic coverage, which can be used for many applications from medical diagnostic to drug delivery.

From some decades, our laboratory is studying amphiphilic polysaccharides with attractive surfactant and self-assembly properties1. Lately, novel comb-like glycopolymers with well defined architecture have been developed using the ‘grafting from’ concept. In each case, controlled polymerization methods were used in homogeneous conditions from macroinitiator based on dextran. This produces grafted copolymers combining an hydrophilic dextran backbone with hydrophobic polymer grafts, either in polylactide2, 3 or in poly(methyl methacrylate)4, 5.

All of these glycopolymers display the capacity to self-organize in solution or at interfaces3, 6. Therefore they are able to stabilize submicronic emulsion6 or to be used to formulate biodegradable nanoparticles7. Others amphiphilic dextran derivatives have also been obtained by simple modification of native dextran8 and could be used as surfactants in miniemulsion polymerization to produce dextran-covered nanoparticles8, 9.

Extending these previous works on nanoparticles to nanocapsules, this talk will depict the use of reactive surfactant based on dextran to obtain dextran-covered nanocapsules. Nanocapsules with controlled properties for drug delivery applications were prepared by the combined use of miniemulsion polymerization, an advanced controlled radical polymerization technique (Activator Generated by Electron Transfer (AGET) ATRP) and an dextran-based inisurf (both surfactant and initiator during the polymerization) (Figure 1). These nanocapsules consist of a liquid core of Miglyol 810, an inner shell of poly(methyl methacrylate) (PMMA) and a dextran coverage. The inisurf is an amphiphilic dextran derivative, which stabilizes the miniemulsion as well as initiates the polymerization, resulting in nanocapsule formation. Thanks to the multifunctional character of the initiator located at the nanodroplet interface, PMMA-grafted-dextran copolymers are produced at the interface and their PMMA grafts constitute the inner polymeric core linked to the dextran coverage of the nanocapsules. The use of a controlled polymerization should facilitate the control of nanocapsule morphology and the anchorage of the particle coverage. In addition the inisurf avoids the use of additional free surfactant in the system and its removal after polymerization by extensive washing. Model kinetics were performed with a molecular initiator and model polysaccharidic surfactants in order to optimize polymerization conditions. The influence of different inisurfs and oil contents was studied on ATRP control, on nanocapsules size and morphology and on miniemulsion stability. TEM analyses have ascertained a core-shell structure.



Figure1: Nanocapsules produced by combined use of miniemulsion polymerization, (Activator Generated by Electron Transfer) AGET-ATRP and a polysaccharidic inisurf

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**References :**

1 C. Rouzes, R. Gref, M. Léonard, A.D. Delgado, E. Dellacherie, J. Biomed. Mater. Res **2000**, *50*, 557-565.

2 C. Nouvel, I. Ydens, P. Degée, P. Dubois, E. Dellacherie, J.-L. Six, J. Polym. Sci., Pol. Chem. **2004**, *42*, 2577-2588.

3 C. Nouvel, C. Frochot, V. Sadtler, P. Dubois, E. Dellacherie, J.-L. Six, Macromolecules, **2004**, *37*, 4981-4988.

4 L. Dupayage, M. Save, E. Dellacherie, C. Nouvel, J.-L. Six, J. Polym. Sci. Polym. Chem. **2008**, *46*, 7606–7620.

5 L. Dupayage, C. Nouvel, J.-L. Six, J. Polym. Sci., Polym. Chem. **2011**, *49*, 35–46

6 J. Raynaud, B. Choquenet, E. Marie, C. Nouvel, J.-L. Six, E. Dellacherie, A. Durand, Biomacromolecules **2008**, *9*, 1014-1021

7 C. Nouvel, J. Raynaud, E. Marie, E. Dellacherie, J.-L. Six, A. Durand, J. Colloid Interf. Sci. **2009**, *330*, 337–343.

**8** E. Rotureau, J. Raynaud, B. Choquenet, E. Marie, C. Nouvel, J.-L. Six, E. Dellacherie, A. Durand, Colloid Surf. A: **2008**, *331*, 84–90.

9 M. Wu, E. Dellacherie, A. Durand, E. Marie, Colloid Surface B, **2009**, *69*, 141-146.

***Biography***

Dr. Cecile Nouvel is an Associate professor of Polymer Chemistry at LCPM (Laboratory of Macromolecular Physical Chemistry), located at ENSIC Chemical Engineering School inside Lorraine University in NANCY, France. She got her MSc in Chemical Engineering at ENSIC in 1999, her Ph.D. in Chemical Engineering at INPL in NANCY. From 2002 to 2003, she spent one year in Steve Howdle’s Group as a postdoctoral research fellow working on the synthesis of new scCO2 surfactants, for use as stabilizer in dispersion polymerization. Since 2003, she joined LCPM as associate professor. During 6 months in 2009 and then one month in 2010, she was appointed visiting academic at University of New South Wales at center for advanced macromolecular design (CAMD) for collaboration with Pr T Davis and A Pr; M Stenzel. Currently Dr. Cecile Nouvel’s researches focus on the design of polymer for biomedical application and on the formulation of nano-objects for drug delivery.