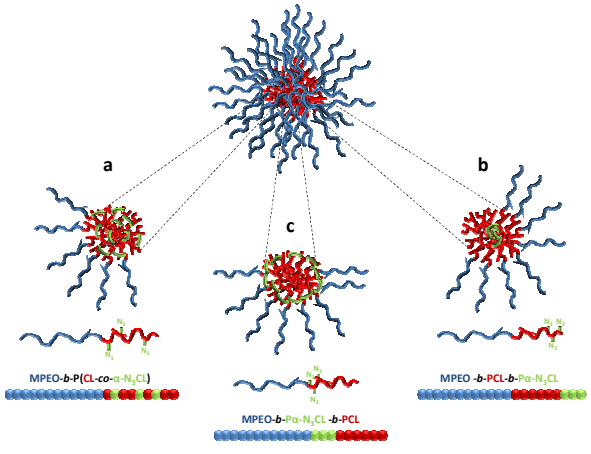
Disulfide Bridges, New Prospect in Drug Delivery Systems?

S. Cajot[1], F. Danhier[2], D. Schol[3], N. Lautram[4], C. Passirani[4], M.-C. Gillet - De Pauw[3], V. Préat[2], C. Jérôme[1]

[1] CERM, University of Liège, Allée de la Chimie 3 (B6a), 4000, Liège, Belgium
Phone: 00324/3663469 - Fax: 00324/3663497
E-mail: S.Cajot@ulg.ac.be
[2]LDRI, Université Catholique de Louvain, Belgium
[3]Laboratoire d'Histologie - Cytologie, University of Liège, Belgium
[4]INSERM U646, University of Angers, France

Over the last decade, polymer micelles attracted an increasing interest in drug pharmaceutical research because they could be used as efficient drug delivery systems. Micelles of amphiphilic block copolymers are supramolecular core-shell type assemblies of tens of nanometers in diameter. The micelles core is usually constructed with biodegradable hydrophobic polymers such as aliphatic polyesters, e.g. poly(ε-caprolactone) (PCL), which is used as reservoir for the incorporation of various lipophilic drugs. Water soluble poly(ethylene oxide) (PEO) is the most frequently used polymer to build the micelles corona. It is indeed very efficient to prevent protein adsorption on surfaces and to stabilize the micelles in the blood compartment, giving rise to particles invisible to the body defence system (so-called stealthy or long circulating particles).

Even if micelles get a high stability in aqueous media, the dissociation of micelles is not always avoided when they are injected in the blood compartment. The reversible cross-linking of the micelles by disulfide bridges will provide stability to micelles after the administration and the drug will be intracellularly released by breaking the disulfide bridges.
This work aims at reporting on the design of reversibly cross-linked micelles based on PEO-*b*-PCL copolymers by introducing disulfide bridges in the micelle core to provide higher stability. Different kinds of macromolecular architectures are employed to study their impact on the micelles and their biological behavior. These new functional copolymers were all successfully micellized, reversibly cross-linked and are stealthy, which show the efficiency of the developed cross-linking process and offer a set of nanocarriers to be tested further, as shown on the first biological tests[1].



[1] S. Cajot, N. Lautram, C. Passirani, C. Jérôme., *J. Control. Release*, **2011**, doi: 10.1016/j.jconrel.2011.03.026