Mannosylated Amphiphilic And Degradable PEO-b-PCL Copolymers For Drug Delivery Systems: Preparation And Sugar Availability Characterizations

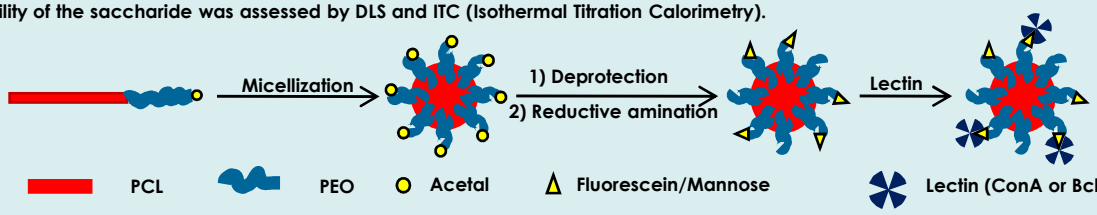
Hélène Freichels, Anne Imberty, Rachel Auzély-Velty, Christine Jérôme

H.Freichels@student.ulg.ac.be, University of Liège, Sart-Tilman, B6a, B-4000 Liège

Center for Education and Research on Macromolecules

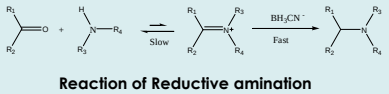
Introduction

Polymer micelles and nanoparticles attracted an increasing interest in pharmaceutical research because they can be used as efficient drug delivery systems. By end-capping the hydrophilic segment by a targeting moiety, the biodistribution can be modulated and can induce specific cellular uptake. In this study, the reductive amination reaction is used to attach this targeting agent. After optimisation of the reaction with amino fluorescein, a model amine, a mannosylated copolymer of PEO and PCL has been prepared and the surface availability of the saccharide was assessed by DLS and ITC (Isothermal Titration Calorimetry).

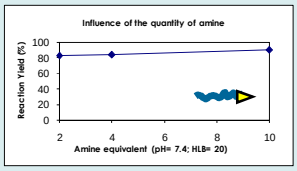


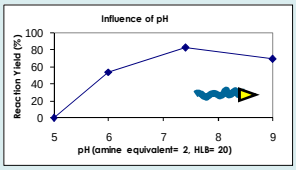
Results

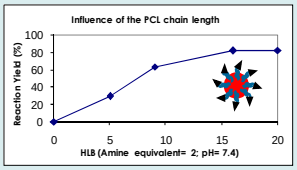
Optimisation of Reductive Amination



Reaction of Reductive amination



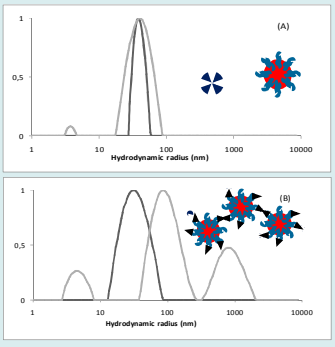




The optimal reaction parameters are 2 equivalents of amine at pH 7.4. The results indicated that the reaction yield decreases with the increase of the PCL chain length.

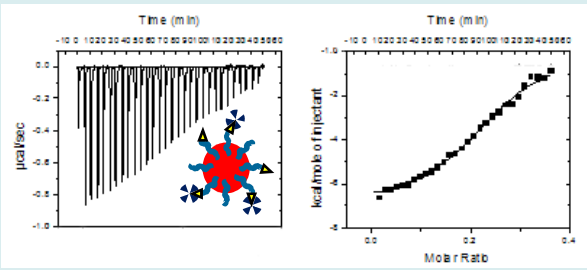
Interaction With Lectins

DLS Measurement (interaction with ConA lectin)



In black, micelles before adding ConA, in grey, after addition of ConA to the micellar solution (non-mannosylated (A), mannosylated (B)).

ITC Measurement (Interaction with BclA lectin)



Calorimetric data (up) and thermodynamic parameters calculated from ITC (down) for the titration the mannosylated micellar solution by BclA lectin

	Ka x 10^{-4} (M^{-1})	ΔH (kJ/mol)	TΔS (kJ/mol)	n (Man : lectin)
aMeMan	39 (±0.3)	-24 (±0.2)	7.7 (±0.3)	0.89 (±0.004)
Micelles	13.1 (±0.1)	-29 (±0.2)	4.0 (±0.7)	0.24 (±0.004)

Conclusions

In this study, after an optimisation of the reaction conditions, PEO-b-PCL have been succesfully functionalized by a mannose residue, a targeting agent. The qualitative DLS study shows that the sugar-copolymer material presented in this work is able to efficiently recognize mannose-binding model lectin ConA. The ITC allows to obtain the thermodynamics parameters of the interaction between the mannosylated micelles and the BclA lectin and, compared with the one obtain with the methylmannose, are of the same order of magniture, meaningful that the mechanism of binding is similar. The next step of this study will focus on targeted drug delivery using these bioeliminable mannose-decorated micelles as carrier systems.

Acknowledgments

CERM is much indebted to the « Région Wallonne » for the support in the frame of « VACCINOR » project.