# POLYMER-DRUG ENCAPSULATION COMPATIBILITY USING NANOMETRIC POLYMERIC MICELLES BASED ON COPOLYMERS OF PEG AND/OR POLYLYSINE WITH PCL

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## ABSTRACT

Nanoparticle sustained drug delivery systems offer several advantages over conventional delivery such as maintenance of optimum therapeutic concentration of drug in the blood or cell, elimination of frequent dosing and better patient compliance. Amphiphilic block and graft copolymers consisting of hydrophobic and hydrophilic moieties have been synthesized for that purpose. These amphiphiles give rise to nanomeric micelles which .[1] The typical morphology adopted by the micelles are either spherical or cylindrical. The chemical nature of the micelles affects its interaction with the drug it can encapsulate. Better drug retention in the micelle core is a key to ensure prolonged circulation time and eventually maximize drug accumulation at the target site via the enhanced permeation and retention effect. The hydrophobic nature of the micelle interior increases the drug solubility dramatically through hydrophobic–hydrophobic interactions.

In a previous study, we showed that novel block PCL-PolyLysine (PolyLys) copolymers self-assemble into nanometer-size core-shell micelles[2] (cmc = 0.3 mg/ml) and can be loaded with drugs that reside in the hydrophobic core of the micelles.[3] To investigate the effect of combined hydrophilic blocks on drug loading, block copolymers based on PEG and PolyLys coupled with PCL have now been synthesized. The resulting micelles were successfully loaded with anti-inflammatory ketoprofen as model drug (Table 1). The effect of anchoring of glucitol sugar moieties onto the PolyLys segments as side groups on drug loading was also investigated and the results compared with β-cyclodextrin(Table 1). PolyLys-b-PCL copolymer has a loading efficiency of 13%. Polymer-drug interaction here occurs both via entrapment in the hydrophobic core and ionic interaction between PolyLys$NH_3^+$ and $COO^-$ on ketoprofen. For comparison sake, ketoprofen was conjugated to polyLys alone and as expected, a lower drug loading efficiency was noted as compared to the copolymer micelles. The presence of glucitol moieties on PolyLys segments, on the other hand, limits conjugation thereby leading to decrease in loading efficiency (7%). A ter-polymer consisting of two hydrophilic blocks, PEG and PolyLys together with a hydrophobic block (PCL) also self-assemble in solution did not bring about significant changes in drug loading efficiency. Cyclodextrin which is known to encapsulate drugs via an inclusion mechanism[4] showed a lower loading efficiency compared to our micellar systems.

Table 1. Loading efficiency and possible polymer-drug interactions

| Polymeric System | Loading Efficiency | Binding Mode |
|---|---|---|
| Poly(Lysine) | 12% | Conjugation (Ionic Bonding) |
| Poly (Lys-*b*-CL) | 13% | Entrapment and Conjugation |
| Poly(Lys-*g*-Glu)-*b*-CL | 7% | Entrapment |
| PEG-*b*-Polylys-*b*-PCL | 9% | Entrapment |
| Cyclodextrin | 6.9% | Inclusion |

References:

1. Yokoyama, M. (2010) *Expert Opin Drug Deliv*, **2010**, *7(2)*, 145-158.
2. Motala-Timol, S.; Jhurry, D.; Zhou, J.; Bhaw-Luximon, A.; Mohun, G.; Ritter, H. *Macromolecules*, **2008**, *41(15)*, 5571-76.
3. Jhurry, D.; Bhaw-Luximon, A.; Lochee, Y.; Ancharaz, B.; Veeren, A.; Jeetah, R. *European Cells and Materials*, **2010**, 19(1), 36.
4. Rasheed, A.; Kumar, C.K.A.; Sravanthi, V.V.N.S.S. *Sci Pharm*, **2008**, *76*, 567–598.