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Nanoparticles Made from PNIPAM-G-PEO Double Hydrophilic Copolymers for Temperature-Controlled Drug Delivery

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Abstract: The aim of this work is to design and develop thermo-responsive nanosized drug delivery systems based on poly(Nisopropylacrylamide)-q-poly(ethylene oxide) (PNIPAM-q-PEO) double hydrophilic graft copolymers. The PNIPAM-q-PEO copolymers are able to self-assemble in water into nanoparticles above the LCST of the thermo-responsive PNIPAM backbone and to disassemble and rapidly release the entrapped drugs upon cooling. However, their drug delivery applications are often hindered by their low loading capacity as the drugs to be encapsulated do not dissolve in water. In order to overcome this limitation, here we applied a low-temperature procedure with ethanol as an alternative route to the formation and loading a model hydrophobic drug, Indomethacin (IMC), into PNIPAM-g-PEO nanoparticles. The rationale for this approach was that ethanol dissolves both IMC and the copolymer and its mixing with water may induce micellization of PNIPAM-g-PEO at temperatures lower than the LCST. The influence of the volume fraction of ethanol and the temperature on the aggregation characteristics of PNIPAM-g-PEO copolymers (2.7 mol% PEO) was investigated by means of DLS, TEM and rheological dynamic oscillatory tests. The studies showed rich phase behavior at T < LCST, incl. the formation of highly solvated 500-1000 nm complex structures, 30-70 nm micelles and polymersomes as well as giant polymersomes, as the fraction of added ethanol increased. We believe that the PNIPAM-g-PEO self-assembly is favored due to the different solvation of its constituting blocks in ethanol-water mixtures. The incorporation of IMC led to alteration of the physicochemical and morphological characteristics of the blank nanoparticles. In this case, only monodisperse polymersomes and micelles were observed in the solutions with an average diameter less than 65 nm and substantial drug loading (DLC ~117 - 146 wt%). Indomethacin release from the nanoparticles was responsive to temperature changes, being much faster at a temperature of 42oC compared to that of 37oC under otherwise the same conditions. The results obtained suggest that these PNIPAM-g-PEO nanoparticles could be potential in mild hyper-thermic delivery of nonsteroidal anti-inflammatory drugs.

Keywords: drug delivery, nanoparticles, poly(N-isopropylacryl amide)-g-poly(ethylene oxide), thermo-responsive **Conference Title:** ICPPT 2016: International Conference on Pharmacology and Pharmaceutical Technology

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