Tailoring the Efficacy of Nimodipine Drug Delivery using Nanocarriers Based on A2B Miktoarm Star Polymers

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Abstract:

We report a nanocarrier based on A2B type miktoarm polymers (A = polyethylene glycol (PEG); B = polycaprolactone (PCL)) for nimodipine (NIM), a hydrophobic drug with very poor aqueous solubility that is commonly prescribed for the prevention and treatment of delayed ischemic neurological disorders. The A2B star polymers were constructed on a core with orthogonal functionalities that facilitated the performance of "click" chemistry followed by ring-opening polymerization. These star polymers assemble into spherical micelles into which NIM can be easily loaded by the co-solvent evaporation method. The micelles obtained from the star polymer PEG7752-PCL5800 showed NIM encapsulation efficiency of up to 78 wt% at a feed weight ratio of 5.0%. The loading efficiency of the micelles was dependent on the length of the PCL arm in the A2B miktoarm polymers. Aqueous solubility of NIM was increased by ~200 fold via micellar encapsulation. The in vitro release of NIM from the micelles was found to occur at a much slower rate than from its solution. Lipopolysaccharide induced nitric oxide production in N9 microglia cells was reduced in the presence of micelle-encapsulated NIM, as well as in the presence of micelles alone. The treatment of microglia with micelle-encapsulated NIM reduced the release of TNF-α, a pro-inflammatory cytokine. These results suggest that NIM-loaded miktoarm micelles could be useful in the treatment of neuroinflammation.

Published In:

Biomaterials, doi:10.1016/j.biomaterials.2010.07.039 , Vol. 31 , pp. 8382-8392