

Abstract Submitted
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Preventing Small Molecule Nucleation and Crystallization by Sequestering in a Micelle Corona¹ ZIANG LI, LINDSAY JOHNSON, RALM RICARTE, LETITIA YAO, MARC HILLMYER, FRANK BATES, TIMOTHY LODGE, Univ of Minnesota - Twin Cities — We exploited a blend of hydroxypropyl methylcellulose acetate succinate and poly(N-isopropylacrylamide) (PNIPAm) to improve the solubility and dissolution of a rapidly crystallizing model drug molecule phenytoin and observed synergistic effect in vitro at constant drug loading by varying the blending ratio. Dynamic and static light scattering experiments showed that PNIPAm self-assembled into micelles in aqueous solution. We believe that adding these PNIPAm micelles inhibited both nucleation and crystal growth of phenytoin based on the polarized light micrographs taken from the dissolution media. The drug-polymer intermolecular interaction was revealed by nuclear Overhauser effect spectroscopy and further quantified by diffusion ordered spectroscopy. We found that the phenytoin molecules were sequestered in aqueous solution by partitioning into the corona of the micelle. The blend strategy through the use of self-assembled micelles showcased in this study offers a new platform for designing advanced excipients for oral drug delivery.

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