151e The Effects of Pharmaceuticals and Cell Media on the Micellar Structure and Gelation Behavior of Peo-Ppo-Peo Copolymers

Praveen K. Sharma and Surita R. Bhatia

Pluronics® consisting of poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) have generated significant interest for drug delivery and tissue engineering applications due to their ability to form thermoreversible gels. In water, these copolymers form micelles that become partly ordered into a cubic gel state. The effects of various hydrophobic pharmaceutical solutes on the micellar structure and gelation behavior of Pluronic® F127 have been studied. In general, small-angle neutron scattering data showed increases in the micelle size and intermicellar interaction distance and decreases in the aggregation number in the presence of most of the drugs. These changes were analyzed using a design of experiments approach and correlated with two physicochemical properties of the solutes: the apparent micelle-water partition coefficient and the solubility in 10 wt% Pluronic® F127, measured by ultraviolet spectroscopy. Dynamic light scattering showed changes in the critical micelle concentration (CMC) in the presence of the pharmaceuticals; however, there did not appear to be a clear trend. The liquid-to-gel and gel-to-liquid transition temperatures were measured for a series of copolymer solutions containing the pharmaceuticals. In general, the liquid-to-gel transition temperature was found to be lower in the presence of the solutes, and was only dependent on the solubility. It was concluded that the mechanism of gelation was likely to be related to the micellar volume fraction reaching a critical value. Furthermore, the findings of the study allow predictions to be made of the micellar structure and gelation behavior in the presence of other hydrophobic pharmaceuticals, which has major implications on the assessment of suitability and performance for new compounds in development, for drug delivery applications.

Changes in the micellar structure caused by the presence of cell media components were also investigated. A decrease in the CMC and an increase in the aggregation number were observed in the presence of the cell media, suggesting an enhancement of the gelation process. More significantly, large intermicellar interactions were observed at low copolymer concentrations in cell media, indicating a greater degree of order and accounting for the lower gelation temperatures observed in cell media. This has implications on the transport of nutrients to encapsulated cells in tissue engineering.