

The high structural integrity of PEO-PBLA micelles, along with slow release of AmB, may be due to the solid-like cores of PEO-*b*-PBLA micelles (Kwon et al., 1993a,b). Strong secondary interactions along with the bulky benzyl side chains in the cores of PEO-*b*-PBLA micelles lead to high core viscosity (Kwon et al., 1993a,b), which may deter micelle breakup and AmB release. For polymeric micelles with core-forming poly(styrene) blocks (phenyl side chains), there is no intermicellar exchange of diblock copolymers at 25°C (Wang et al., 1992). On the other hand, detergent micelles have liquid-like cores, and in this case intermicellar exchange happens in the order of μ s (Yu et al., 1998).

Finally, freeze-dried, AmB-loaded PEO-*b*-PBLA micelles easily dissolved within a few seconds in aqueous solutions. This contrasts with the behavior of PEO-*b*-PBLA and AmB, both of which are insoluble when directly placed in water. TEM reveals that the PEO-*b*-PBLA micelles remain intact, and the size distribution confirms the absence of any secondary aggregation that may have resulted from the freeze-drying and reconstitution processes. Further, the resultant AmB-loaded PEO-*b*-PBLA micelles cause no hemolysis at 10 μ g/mL, indicating that AmB is still present inside the polymeric micelles. An AmB level of 5.0 mg/mL was obtained; this is 10,000 times the solubility of AmB. Thus, reconstitution of freeze-dried micelles allows high AmB levels in solution. It is the same with doxorubicin-loaded PEO-*b*-PBLA micelles (Kwon et al., 1997).

Yu et al. (1998) were able to increase the *in vitro* antifungal efficiency of amphotericin B while at the same time decreasing its hemolytic activity by loading the drug into polymeric micelles. It was suggested that polymeric micelles could stabilize amphotericin B against autooxidation and/or enhance membrane perturbation of fungal cells.

TRIBLOCK POLYMERIC MICELLES

Solubilization of insoluble drugs using poloxamers (Pluronics), PEO-*b*-PPO-*b*-PEO triblock copolymers, has been extensively studied. Kabanov et al. (1992) designed and formulated targeted drug delivery systems for the hydrophobic neuroleptic haloperidol. Other drugs studied include tropicamide, a poorly water-soluble mydriatic/cycloplegic drug (Saettone et al., 1988); allopurinol (Hamza and Kata, 1989); diazepam (Lin, 1987); and naproxen (Suh and Jun, 1996). A brief summary of the highlights of each of these studies is given subsequently.

Micelles for drug targeting were prepared using polymeric surfactant PEO-*b*-PPO-*b*-PEO block copolymers such as Pluronic P-85, F-64, L-68, and L-101 (Kabanov et al., 1992). Haloperidol was dissolved in Pluronic micelle solutions at pH 6, and the solutions were incubated at 37°C for 1 h. The drug was incorporated into the inner hydrophobic core formed by PPO blocks. The polymeric micellar solubilization of low molecular weight compounds, such as fluorescein isothiocyanate (FITC) and haloperidol, was characterized using various techniques including fluorescence, ultracentrifugation, and quasielastic light scattering. In a majority of cases, the diameter of Pluronic micelles including those containing solubilized compounds ranged from 12 to 36 nm.

To target these microcontainers to a certain cell, the Pluronic molecules were conjugated with antibodies against a target-specific antigen or with protein ligands selectively interacting with target cell receptors. These conjugates were then incorporated into the drug-containing micelles by simple mixing of the corresponding components. Solubilization of FITC in Pluronic micelles shows its distribution in animal (mouse) tissues. Unconjugated micelles concentrate in the lung. Conjugation of FITC-containing micelles with insulin vector results in increase of FITC penetration in all tissues including the brain. Specific targeting of the brain occurred when the Pluronic was conjugated with antibodies to the antigen of brain glial cells (α 2-glycoprotein). When haloperidol was solubilized in these conjugated micelles, there was a drastic increase of drug effect. This result indicates that vector-containing Pluronic micelles provide an effective transport of solubilized neuroleptics across blood-brain barrier.

Solubilization of tropicamide, a poorly water-soluble mydriatic/cycloplegic drug, by poloxamers or Pluronics was studied (Saettone et al., 1988). The polymers evaluated as solubilizers for the drug