OVERVIEW

Polymeric surfactants are finding increasing use in pharmaceutical applications. Although polymeric micelles have mostly been studied as delivery systems for anticancer drugs, they could be used to transport plasmid DNA (Katayose and Kataoka, 1997, 1998), antisense oligonucleotides (Kataoka et al., 1996), or for the delivery of diagnostic agents to a specific organ in the body (Park et al., 2002; Torchilin, 2002). The structures of the copolymers vary widely and include random copolymers, grafted copolymers, and the most commonly used block copolymers (Kataoda et al., 1993; Kwon and Okano, 1996, 1999; Alakahov and Kabanov, 1998; Kwon, 1998, 2003; Seymour et al., 1998). Novel polymer chemistries, including drugs covalently bound to the hydrophobic blocks of micelle-forming block copolymer conjugates Kwon and Okano, 1996, 1999) have shown success in clinical trials. In all cases, the relative hydrophilic/lipophilic balance is achieved by using a combination of hydrophilic and hydrophobic monomers. In a solvent compatible with one monomer but incompatible with the other, micelles form with the poorly soluble monomers forming the core and the easily soluble monomers forming the corona (Xing and Mattice, 1998).

The advantages of polymers over conventional surfactants include their lower toxicity, ability to prevent the adsorption of proteins such as immunoglobuins (Abuchowski et al., 1977), and ability to prevent adhesion of the drug vehicle onto the surfaces of phagocytes. The latter phenomena would otherwise lead to the clearance of drug vehicles. Therefore, polymeric micelles possess great potential for extending the circulation time of a drug (Kwon and Kataoka, 1995; Kwon, 2003; Aliabadi and Lavasanifar, 2006). To date, several polymeric micellar formulations have reached preclinical and clinical trials, and one of paclitaxel micellar formulation has been approved for clinical use.

CLASSIFICATION OF COPOLYMERS

Copolymers are defined as polymers composed of several different monomer units and are classified into four types by monomer organization: random copolymers, alternating copolymers, graft copolymers, star copolymers, and block copolymers (Nagarajan and Ganesh, 1989a,b; Yokoyama, 1992). If A is defined as a monomer unit soluble in the solvent and B as a solvent-phobic monomer unit, the five types of copolymers can be pictured as in Figure 13.1. For the purposes of this chapter, monomer A will always be a water-soluble monomer, and B will refer to water-insoluble monomers.

Random copolymers are characterized by the statistical placement of comonomer repeating units along the backbone chain. Alternating copolymers, as the name suggests, are characterized by the alternate placement of monomers. Graft copolymers are made of chemically linked pairs of homopolymers and resemble a comb. Block copolymers are composed of terminally connected structures.