TABLE 22.3
Comparison of Drug Release from an Osmotic Controlled Release Tablet Containing Solid Dispersion as Compared to That from an Osmotic Controlled Release Tablet with Crystalline Drug That Had Not Been Manipulated

	Drug Concentration (μg/mL)	Drug Concentration (μg/mL)
Time (h)	**CR w/ Solid Dispersion**	**CR w/o Solid Dispersion**
0	0	0
1	1.3	0
2	12.8	1.8
4	46.5	4.9
8	82.7	7.5
19.5	55.9	7.9

Source: Appel, L. E. et al., Controlled release by extrusion of solid amorphous dispersions of drugs, U.S. Patent 6706283, 2004.

The human GI tract is lined by a layer of *mucus* synthesized by cells that form part of the epithelium. Mucus is composed mostly of water, cross-linked mucins, electrolytes (inorganic salts and carbohydrates), and other substances depending on the location (Marriott and Gregory 1990). Mucins are high molecular weight glycoproteins that have protein backbones covered by covalently bonded oligosaccharide side chains (Longer et al. 1985). Mucin macromolecules form gel-like mucous layers through noncovalent bonding between mucin side chains (Bansil et al. 1995). These oligosaccharide side chains are terminated with sialic acid, which renders a negative charge for mucins in the pH > 3 environment (Bansil et al. 1995). The mucus gel layer is constantly being replaced, and the estimated turnover time of GI mucus layer is believed between 6 and 48 h (Marriott and Hughes 1990; Khanvilkar et al. 2001).

Mucoadhesive drug delivery systems employ natural and synthetic polymers as bioadhesion components. The polymers studied for mucoadhesive drug delivery are summarized in Table 22.4. Most of these polymers are hydrophilic and have similar mechanisms, which provide for their mucosal bioadhesion characteristics. These properties are hydrophilicity (low aqueous surface contact angle), rich in hydrogen bonding groups such as hydroxyl and carboxylic groups (bonding to mucosal surface), and polymer chain flexibility (diffusion and interpenetration of mucosal surface). The most common bioadhesive polymers are synthetic poly(acrylic acid) (PAA), poly(methacrylic acid) (PMA), poly(methyl methacrylate) (PMMA) polymers, and natural polymers such as chitosan and hyaluronic acid and hyaluronan (Ch'ng et al. 1985; Park and Robinson 1987; Lehr et al. 1992; Henriksen et al. 1996; Pritchard et al. 1996). Many efforts have been made to improve the bioadhesive properties of these materials by grafting adhesion promoters such as carbohydrates or PEG onto these polymers (Garcia-Gonzalez et al. 1993; De Ascentiis et al. 1995; Shojaei and Li 1995; Serra et al. 2006). Such modification has produced many PAA, PMA, PMMA, and chitosan derivatives (listed in Table 22.4) for use in mucoadhesive drug delivery. Most of the polymer modifications enhance adhesion of the polymer to mucosal surface through improved wetting, adsorption, interpenetration, and entanglement. In recent years, new bioadhesive polymers containing thiol groups have been produced (Bernkop-Schnurch et al. 1999; Marschütz and Bernkop-Schnürch 2002). These thiolated polymers (thiomers) have strong mucoadhesive properties owing to their ability to form disulfide bonds between the thiomer and cysteine-rich subdomains of the mucus gel layer (Marschütz and Bernkop-Schnürch 2002; Roldo et al. 2004). Thiomers such as thiolated chitosan and PAA exhibited nearly 20- and 140-fold improvements in mucoadhesive properties relative to the nonthiolated ones, respectively (Clausen and Bernkop-Schnürch 2000; Kast et al. 2003).