matrix substrate or surrounded by a water-insoluble coating with one or more pore-forming agents (McClelland and Zentner 1990). The core is then surrounded with a semipermeable membrane to regulate the drug release.

Simvastatin, a HMG CoA reductase inhibitor, is highly effective in the reduction of blood cholesterol levels in humans and has neither acidic nor basic functionalities. The drug is poorly soluble in water with a value of 30 μg/mL at 20°C. A solubility modulated controlled delivery system was prepared by first preparing a controlled release sodium dodecyl sulfate (SDS) surfactant particles to modulate the drug solubility. The SDS granules were prepared with lactose at a 1:1 ratio in a fluid bed granulator and were coated with a microporous layer that allowed continuous release of SDS over the time. Next, using a wet granulation method, the drug was mixed with controlled-release SDS (C.R. SDS granules) and other excipients to further form drug-containing granules. The dried granules were then compressed into core tablets using a tablet press. A microporous coat containing CA butyrate 318–20 dissolved in an acetone/methanol solvent mixture and a pore former (sorbitol dissolved in a water/methanol solvent blend) was applied to the core tablet to form a membrane of sufficient thickness to provide a continuous release of simvastatin for 4–24 h.

Osmotically Controlled Release of Solid Dispersions

Controlled release of poorly soluble drugs may also be achieved by using solid-solution or solid-dispersion preparation techniques in combination with osmotically controlled release concepts (Appel et al. 2004). These delivery systems consist of a core with an osmotic agent and the drug in the form of a solid dispersion with the major portion of the mixture being amorphous and stabilized with ionizable and nonionizable cellulosic polymers (e.g., carboxymethylcellulose [CMC] and its sodium salt, hydroxypropyl-methylcellulose phthalate [HPMCP], or HPMCAS). A water-permeable membrane is coated onto the drug-containing core with at least one delivery orifice that allows drug release. The amorphous solid dispersion of the drug may be prepared by various techniques, such as hot-melt mixing/extrusion, solvent-based spray drying, and spray coating.

A poorly water-soluble glycogen phosphorylase inhibitor with solubility of about 1 mg/mL was processed into a solid dispersion with 10 wt% drug and 90 wt% HPMCAS using a solvent-based (acetone) spray-drying method. The resulting solid-dispersion particles with a mean diameter of 5–20 microns were shown to be essentially amorphous by a powder X-ray diffraction analysis. The solid-dispersion particles were further processed by mixing with other tablet excipients such as microcrystalline cellulose, poly(ethylene oxide) with a molecular weight of 600,000, and a lubricant; these were compressed into tablets containing 30 wt% of the solid dispersion. The cores were then coated with a water-permeable membrane comprising 70/30 wt% CA and PEG 3350 that was dissolved in 68/22 wt% acetone/water. The coated cores were drilled either mechanically or by laser to form an exit orifice for drug release. The study showed a tenfold increase in the total amount of the drugs available in solution after releasing from an osmotic CR tablet containing solid dispersion as compared to that from an osmotic CR tablet comprising unmanipulated, crystalline drug, as indicated in Table 22.3.

Bioadhesive Sustained- and Controlled-Release Drug Delivery Systems

Bioadhesive drug delivery systems refer to those delivering drugs through adhesion to physiological surfaces of the body. The bioadhesive sustained- and controlled-release drug delivery systems discussed in this section, however are focused on mucoadhesive or mucosal-adhesive drug delivery systems. Mucoadhesive drug delivery systems have historically been used to deliver drugs locally at sites such as the eye, the oral, and nasal cavities as well as systemically through the GI track (Mathiowitz et al. 1999). Bioadhesives have been increasingly used in the oral sustained/controlled drug delivery systems. The bioadhesive sustained/controlled drug delivery systems can improve drug bioavailability through intimate contact of the dosage forms with mucosal surfaces and as such can increase the duration of action through prolonging the transition time in the GI track (Park and Robinson 1984).