Membrane Reservoir Systems

Sustained or controlled release of water-insoluble drugs can be achieved through another type of diffusion-controlled system: the reservoir. Such systems comprise a drug core and a surrounding polymeric membrane that controls or modifies the drug-release rate. Since drug-release kinetics can be controlled by changing the characteristics of the polymeric material(s) used for the rate-controlling membrane, a zero-order release profile could be attainable with the design. Drug release from such a delivery system is mathematically described by Equation 22.13 for a simple slab-like system, and will vary depending on the geometry of the system (Higuchi 1961; Baker et al. 1974; Flynn et al. 1974; Good and Lee 1984).

$$\frac{dM_t}{dt} = \frac{ADK\Delta C}{d} \tag{22.13}$$

where dM_t/dt is the steady state release rate at time t, A the surface area of the reservoir system, D the diffusion coefficient, K the participant coefficient, ΔC the concentration difference across the membrane, and d is the diffusion layer thickness.

An example of such a reservoir matrix system is a rate-controlling membrane coated solid solution beads comprising: (1) a hydrophobic long-chain fatty acid or ester material; (2) a surfactant; and (3) a therapeutic agent that, in admixture, forms a solid solution at room temperature (Burnside et al. 2004). In this example, the model compound, acyclovir was formulated with the solubility-enhancing agent, Labrasol, and other excipients such as Compritol 888 (Gattefossé Corp., Paramus, NJ) and Talc to prepare granules or bead lets with particle sizes ranging from approximately 150–300 μm using a spray-melt method. The bead let size can be controlled by altering the drug-to-solubilizing agent ratio and/or changing the processing parameters. The acyclovir-containing bead lets were further coated with a rate-controlling polymer solution containing Eudragit L30D, hydroxypropyl methylcellulose acetate succinate (HPMCAS), and other coating additives. The release rate can be controlled by adjusting the composition of the coating formulation.

Osmotically Controlled Systems

In principle, the osmotically controlled system operates by a membrane diffusion-controlled mechanism. The drug release takes place through an orifice in the membrane through an osmotic pumping mechanism, where a semipermeable membrane such as cellulose acetate is utilized to regulate the osmotic permeation of water (Theeuwes 1975, 1980). The osmotically controlled delivery systems are capable of providing not only prolonged zero-order release but also programmable delivery profiles such as delayed, pulsatile, and ascending. The delivery rate from such an osmotically driven system is generally regulated by the osmotic pressure of the drug layer/core formulation with an elementary, single layer design or the osmotic pressure of the push layer with a multilayer design and by the water permeability of the semipermeable membrane. The controlled rate of drug release in the GI tract is independent of posture, pH, GI motility, and fed or fasting conditions. The biologically inert components of the delivery system remain intact during the transit through GI tract and are eliminated in the feces as an insoluble shell. Equation 22.14 can be used to describe and predict release rate from such an osmotic system from which the drug can be delivered in a liquid, solubilized form suspended in high molecular weight polymer, melt, or suspension:

$$\frac{dM}{dt} = \frac{A}{h} k\pi C \tag{22.14}$$

where dM/dt is the delivery rate of the solute (drug), A the membrane area, h the membrane thickness, k the constant, π the osmotic pressure, and C is the concentration of drug in the dispensed mass.