Dissolution Phenomena

The dissolution rate of a drug is usually determined experimentally. However, there is an abundance of theoretical and quantitative structure–activity relationship (QSAR) models (Grant and Higuchi, 1990) that provide estimates of the dissolution rates. The mass of the solute (m) at any given time can be defined as

$$m = Vc_t \tag{17.1}$$

where V is the volume of the bulk solution and c_t is the concentration of the solute at time t. It follows that

$$\frac{dm}{dt} = V\left(\frac{dc_t}{dt}\right) \tag{17.2}$$

where dm/dt is the rate of dissolution.

If one assumes that a given solid material is thoroughly wetted, it is known that the dissolution rate is strictly proportional to the specific surface area (S) of the dissolving solid, that is,

$$\frac{dm}{dt} \propto S \tag{17.3}$$

The dependence of dissolution rate to specific surface area is the basis for pursuing particle size reduction as a method of increasing the bioavailability of poorly water-soluble drugs.

The dissolution rate per unit surface area is referred to as the *intrinsic dissolution rate* or *mass flux* (J), and is given as

$$J = \left(\frac{dm}{dt}\right)\left(\frac{1}{S}\right) \tag{17.4}$$

The observed dissolution rate may be thought of as being composed of both transport and surface reaction processes. This being the case, then the observed rate constant (k_1) can be expressed as follows:

$$\frac{1}{k_1} = \frac{1}{k_T} + \frac{1}{k_R} \tag{17.5}$$

where k_T is the rate constant describing transport phenomena and k_R is that for reaction. Equation 17.5 can be rewritten as

$$k_1 = \frac{k_T k_R}{k_T + k_R} \tag{17.6}$$

When transport is rate-limiting, $k_T \ll k_R$, and Equations 17.5 and 17.6 reduce to

$$k_1 \sim k_T \tag{17.7}$$

When the surface reaction is rate-limiting, $k_R \ll k_T$, and Equations 17.5 and 17.6 reduce to

$$k_1 \sim k_R \tag{17.8}$$

Two of the simplest theories to explain the dissolution rate of solutes are the interfacial barrier model and the diffusion-layer model (Figures 17.1 and 17.2).