If one then assumes that the solute surface area (S) and the volume of dissolution medium (V) remain constant, Equation 17.17 can be rewritten as

$$\frac{dc}{dt} = K \tag{17.18}$$

This explains the observance of zero-order kinetics under sink conditions.

Hixson and Crowell's Cubic Root Law

To account for cases where the surface area is changing during the course of the dissolution process, such as for solute crystals and traditional solid dosage forms, Hixson and Crowell developed the *cubic root law*. Instead of modeling on the basis of the rate of change in the concentration of a solute, they sought to describe dissolution in terms of the rate of change in weight of the solute. This was accomplished by multiplying both sides of Equation 17.11 by the volume of the dissolution medium (V), which yields

$$\frac{dw}{dt} = K_2 S\left(c_s - c_t\right) \tag{17.19}$$

where dw/dt is the rate of change in weight of the solute, K_2 is k_1V, and w is the weight of undissolved crystal at time t. Note that in this equation, the surface area (S) is no longer constant but is now variable.

Provided that there is no change in the shape of the drug crystal as it dissolves, its surface varies as the two-thirds power of its volume (v), that is,

$$S \propto v^{2/3} \tag{17.20}$$

Since $v = w/d$, where d is the density of the solute, then

$$S = k_4 w^{2/3} \tag{17.21}$$

where k_4 takes into account the density of the solute and contains a shape constant that is dependent on crystal morphology. Substitution for S in Equation 17.19 gives

$$\frac{dw}{dt} = K_2\left(k_4 w^{2/3}\right)\left(c_s - c_t\right) \tag{17.22}$$

For the special case where the change in concentration is negligible, (c_s – c_t) is constant, and therefore, the rate of dissolution is dependent on surface area alone and Equation 17.19 can be rewritten as

$$\frac{dw}{dt} = k_3 w^{2/3} \tag{17.23}$$

Since the change in solute concentration is negligible, w can be approximated by w_0, the weight of undissolved solute crystals at time 0. This is a reasonable approximation when the initial amount of solute is less than one-twentieth (1/20) of its solubility. Integration of Equation 17.23 under these conditions gives the cubic root law, which can be written as follows:

$$K_4 t = w_0^{1/3} - w^{1/3} \tag{17.24}$$