Under conditions where the initial amount of solute approaches the amount needed to produce a saturated solution (w_s), that is, when $w_s = w_0$, Hixson and Crowell derived the *negative two-thirds law*, which is given as follows:

$$K_5 t = v\left(w^{-2/3} - w_0^{-2/3}\right) \tag{17.25}$$

Dissolution of Monodisperse Systems (*z*-Law) under Nonsink Conditions

Yonezawa et al. (1994, 1995) derived a model on the basis of the Nernst equation to describe the rate of dissolution of a monodisperse system that can account for various initial amounts of solute, as long as it is less than that needed to saturate the solution. The *z*-law equation was derived from the Hixson–Crowell treatment under nonsink conditions. The general form of the *z*-law equation can be expressed as follows:

$$\left(\frac{M}{M_0}\right)^z = 1 - zk_z c_s St \tag{17.26}$$

where M_0 is the initial amount of solute for a monodisperse system, M is the amount at time t, $z = (1/3 - M_0/M_s)$, M_s is the amount of solute at saturation, and k_z is the dissolution rate constant. The cube root law Equation is obtained when M_0 is extremely small, and the negative two-thirds law is obtained in the case when $M_0 = M_s$.

Effect of Particle Size on Rate of Dissolution: Dissolution of Polydisperse Systems

Lu et al. (1993) developed refinements of the Noyes–Whitney-type equations, which included a time-dependent diffusion layer and also accounted for nonspherical particle geometry. Their program simulated initial particle size distributions on the basis of the log normal probability density function. The most accurate simulations were obtained by assuming cylindrical geometry with and without a time-dependent diffusion-layer thickness for fine (calculated mean particle size of 10.9 μm) and coarse (calculated mean particle size of 38.7 μm) hydrocortisone, respectively. The dissolution profiles for fine and coarse hydrocortisone are shown in Figure 17.2.

Other Factors Influencing Dissolution

1. The solubility of the drug will influence the rate of dissolution by determining the magnitude of the drug's concentration gradient ($c_s - c_t$).
2. Crystal morphology dictates the rate of dissolution along the different crystallographic axes. This dissolution anisotropy can be found in all but cubic crystals, which are isotropic.
3. Crystal defects and imperfections influence the crystal lattice energy. These defects, including dislocations, give rise to increased surface energy and may be a major factor in improving dissolution performance of poorly water-soluble, crystalline substances.
4. Polymorphism, where solute molecules crystallize in more than one form, with the polymorphs possessing different energies, will most likely give rise to different dissolution and solubility profiles. Polymorphs that have greater thermodynamic activity will dissolve faster than more stable ones, and this property has been exploited in the pharmaceutical industry in an attempt to increase therapeutic blood levels of insoluble or sparingly soluble drugs. In some instances, new polymorphs have been observed following size reduction processes.
5. Impurities (including surfactants, hydrates, solvates, complexes, and reactive additives) can greatly influence the rate of dissolution by modifying the crystal habit or by interfering with the interfacial transport of solute from the crystal to the bulk solution.
6. Physicochemical properties, such as density, viscosity, and wettability, influence ensemble properties (flocculation, flotation, and agglomeration), which in turn influence dissolution by perturbing the effective specific surface area.