Powder dissolution is another method that has been employed extensively. This method is particularly useful when the drug substances cannot readily be formed readily into disks by compression or when the particle size effect on dissolution needs to be studied. A variety of techniques for studying powder dissolution has been reported (Goldberg et al. 1965, Finholt 1974, Cakiryildiz et al. 1975, Lötter et al. 1983). Particles of hydrophobic substances tend to aggregate, and are often difficult to wet, causing a reduction in the effective surface area exposed to dissolution medium. For example, the dissolution rates of phenobarbital, aspirin, and phenacetin were found to increase unexpectedly with increasing particle size (Finholt 1974). This was attributed to the poor wettability of the drug substances. It was found that problems of flotation and aggregation of these drug substances could be overcome by adding 0.2% Tween 80 to the dissolution medium. The influence of aggregates on the dissolution process could also be eliminated effectively by deaggregating samples of insoluble drugs before they are introduced into the dissolution medium (Lötter et al. 1983).

The intrinsic dissolution and powder dissolution methods discussed earlier are typically used for the characterization of drug substances. For drug formulations, a USP apparatus such as the USP Apparatus 2 is more applicable. According to the Biopharmaceutics Classification Scheme (Amidon et al. 1995), drugs can be divided into four classes on the basis of their aqueous solubility and their ability to permeate the mucosa in the gut from the apical to the basolateral side. Low-solubility compounds are defined as those whose solubility in aqueous media is insufficient for the whole dose to be dissolved in the gastrointestinal (GI) contents under usual conditions. Since dissolution, for these substances, can depend on a wide variety of factors such surfactants, pH, buffer capacity, ionic strength, and volume available for dissolution, the media used for dissolution studies need to represent closely the prevailing conditions in the upper GI tract in order to achieve a meaningful *in vitro/in vivo* correlation.

Based on physiological parameters, media to simulate gastric and small intestinal conditions in the fed and fasted states have been suggested (Galia et al. 1996, Dressman et al. 1998). For many insoluble compounds, however, maintaining *sink* conditions may be very challenging. For ionizable compounds one may employ a totally aqueous medium by resorting to altering the pH. However, alternative strategies must be adopted for non-ionizable substances. Dissolution media containing solubilizing agents have been used to meet the requirement of *sink* conditions. However, one needs to be cautious in interpreting the results from these studies. A good *in vitro/in vivo* correlation needs to be established before the dissolution method can be used to predict the *in vivo* performance of drugs.

The addition of a co-solvent which increases the drug solubility in an aqueous-based dissolution medium has been widely employed to provide *sink* conditions for the dissolution of insoluble compounds (Poirier et al. 1981, Dodge et al. 1987, Corrigan 1991). When using this technique, the effects of the co-solvent on tablet disintegration and especially on the solubility and the dissolution rate of excipient(s) present in the dosage form need to be carefully considered to avoid anomalous release characteristics. Highly water-soluble excipients are often chosen for dosage forms containing insoluble compounds. Solubilities and dissolution rates of these water-soluble excipients, such as lactose, may decrease in the presence of co-solvents in sufficient concentration. Depending on the proportion of excipients in the formulation, drug dissolution in the co-solvent system may become controlled by the rate of dissolution of the less-soluble excipients. Theoretical models to predict the effect of co-solvent on the dissolution of a simple two-component drug-excipient compact are available in the literature (Corrigan 1991). Solubility and dissolution studies using Tolbutamide and lactose mixtures in water-ethanol mixtures provided results which were reasonably consistent with the theoretical models.

In developing dissolution method for poorly water-soluble drugs, besides selecting suitable pH in the dissolution medium, surfactants are often used to get suitable sink condition. However, special attention is needed in developing bio-relevant dissolution method with surfactants. Tang et al. (2001) used three different concentrations of sodium lauryl sulfate (SLS), 1%, 0.5%, and 0.25%,