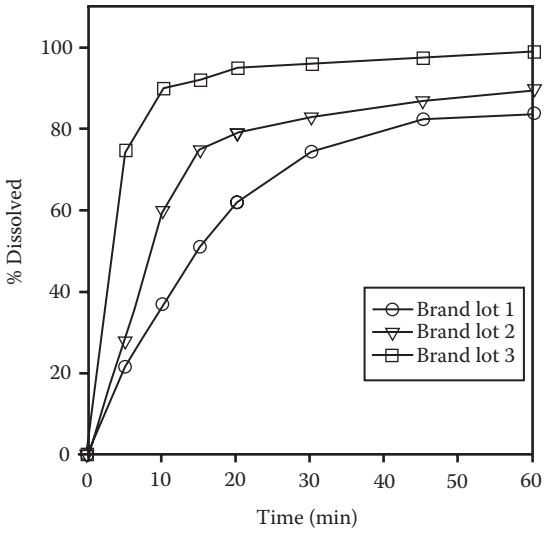

FIGURE 4.5 Comparative dissolution profiles of three different brand lots of the same commercially available product.

b. Comparative dissolution rate studies should be conducted on several different lots of commercially available product using an appropriate method (Figure 4.5). Dissolution test methods should be adequately discriminatory to identify true differences in dissolution rate and extent, if and where they do exist. Compendial methods (if shown to be discriminatory) are preferable.

Formulation Development

Formulation development is undertaken on comparatively small batches between 2000 and 5000 units. Physical data are captured from all batches (LOD, bulk/tapped density, sieve analysis [granule] and hardness, friability, disintegration, and compressibility characteristics [tablets]).

Once a satisfactory formulation from a physical characterization point-of-view has been arrived at, samples are submitted to the laboratory for chemical testing (dissolution profile, assay, content uniformity, etc.) as deemed appropriate.

It is recommended that dissolution-profile testing be undertaken on samples compressed at several hardnesses, so that the effect of varying the hardness on the dissolution profile can be established.

The development process is continued until one of the trial formulations demonstrates a close correlation to the Brandleader drug product as regards both physical and chemical results.