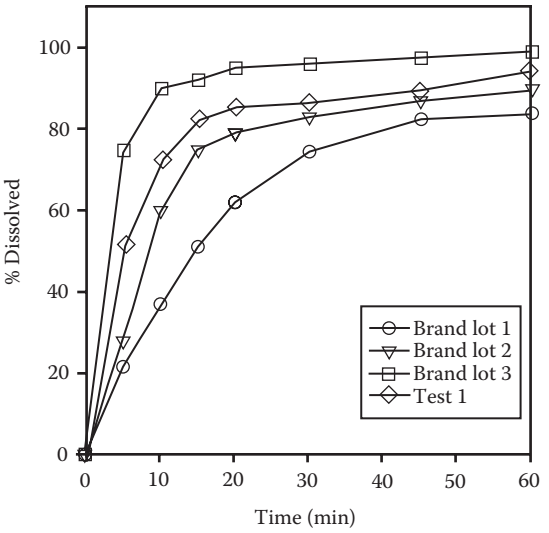

FIGURE 4.6 Comparative dissolution profiles of a generic product with a specific target hardness value versus three different brand lots of the same commercially available product.

Range Studies—Investigation of Formulation and Process Variables

Should the formulation prove stable under "accelerated" conditions of high temperature/humidity, "range studies" should be progressed to verify and assess the robustness of the formulation and process of manufacture.

The batch size should be the same as was employed for formulation development (2000–5000 units), and the campaign must contain a "control" batch, so that differences in excipient level and process of manufacture can be correctly interpreted.

Formulation Variables

Effect of binder level. Consider the effect of increasing/decreasing the binder level (e.g., by 1% of the total weight of this formulation). Provision for varying the binder level must be accommodated by reducing/increasing the amount of diluent to maintain a consistent tablet weight. Bulk and tapped density as well as sieve analysis of the final blend should be determined. In addition, granule flow and compressibility must be carefully monitored. Friability, disintegration, and dissolution rate testing must be performed in each case.

Figure 4.7 depicts the dissolution results that show that the effects of binder level variation by 1% were not significant.

However, nonuniform flow was observed in the tablets containing a lower binder concentration. This, together with the fact that the in vitro release rate did not decrease with increased binder concentration, demonstrates that an adequate amount of binder has been used.

Effect of disintegrant level. Similar experiments to those described above but increasing and decreasing instead, the level of disintegrant (starch) by a specified