



FIGURE 4.12 Comparative dissolution profiles showing the effect of increasing lubricant concentrations.

Process Variables

Typical variables that should be assessed include, among others, the granulation process (rate and quantity of granulation liquid addition, mixer and chopper conditions, over/under granulation, and the effects of over/under blending), dry-powder mixing time/speed, and the mesh size used for screening.

Samples from the resultant tablet batches should then be tested for compliance to specifications for hardness, disintegration, friability, and dissolution profile.

Effect of increasing lubricant mixing time. Doubling the mixing time should be evaluated to establish robustness. In this instance, no adverse effect on in vitro release profiles was seen (Figure 4.13).

Effect of increasing granulation time. Similarly, doubling the granulation time was evaluated for robustness and the in vitro release profile is depicted in Figure 4.14.

Once again, no marked changes to the dissolution profile were observed. In spite of satisfactory dissolution rates exhibited by the test formulations (Figures 4.13 and 4.14), the longer manufacturing times mitigate against using these process parameters for full-scale production.

Because the above series of trials challenging both the ranges of excipients and process variables provided results that confirmed that the formulation and process were sufficiently robust, and because data were available to demonstrate that the formulation was stable, exhibit-batch manufacture (comprising a minimum of 100,000 units or 10% of the envisaged commercial batch size, whichever is the greater) can now be embarked upon.