An example of such a formulation follows:

	Active/Excipients	mg/tablet	Comment
(i)	API	250.0	Required
(ii)	MCC	87.2	Diluent/compressibility enhancer/disintegrant/ dissolution aid
(iii)	Povidone	10.0	Binder (2.5%)
(iv)	Starch	20.0	Disintegrant (5%)
(v)	Citric acid	8.0	Stabilizer
(vi)	Starch (as paste)	20.0	Binder (5%)
(vii)	Stearic acid	4.0	Lubricant (1%)
(viii)	Magnesium stearate	0.8	Lubricant (0.2%)
(ix)	Purified water	q.s.	Granulation liquid

The Handbook of Pharmaceutical Excipients [45] should be consulted to confirm the quantities of the excipients selected.

This formulation is then scaled up in size to 10,000 to 20,000 units to provide sufficient samples for stability assessment. The physical/chemical testing is repeated to confirm that the larger batch provides comparable data with that yielded by the smaller trial.

Manufacturing Method

Items (i) to (iv), screened through an appropriate mesh (e.g., 20 mesh), are added to a suitably sized granulator/mixer bowl and mixed for 5 min under conditions of high-speed mix and shear. The citric acid (item (v)) is dissolved in a portion of purified water (ix) in a suitable stainless steel container. The starch (item (vi)) is added to form a slurry and then additional boiling purified water is added and vigorously stirred until a paste is formed. The paste is allowed to cool to ambient temperature and then added to the previously mixed powders and granulated for 5 min under controlled conditions using approximately 10% to 30% by weight of the granulating vehicle. The granules are dried in a fluidized bed drier [50°C–60°C] to a moisture level not exceeding 2% loss on drying. The dried granules are milled and transferred to a suitable tumble blender. Stearic acid (item (vii)) is screened through a 40 mesh and blended with the granule for 10 min before the addition of magnesium stearate (also prescreened through a 40 mesh) with final blending effected for 5 min.

Granules should be analyzed for LOD, bulk and tapped density, and sieve analysis. The resultant granules are compressed to a target weight of 400 mg.

Tablets should be compressed at three hardness ranges (low [2–8 kP], target [6–10 kP], and high [11–17 kP]) and friability, hardness, thickness, disintegration, and dissolution profiles determined.

It is important that tablets meet all physical and chemical acceptance criteria at both the lower and higher ends of the hardness range.

Results revealed that the target hardness generic formulation (Test 1) has a dissolution profile similar to Brand Lot 2, which is slower than Brand Lot 3 (faster-releasing Brand Lot) and faster than Brand Lot 1 (slowest-releasing Brand Lot) (Figure 4.6).