Pharmacopoeial tests

The pharmacopoeial tests for assessing the quality of most powdered and granular dosage forms are very similar. The role of these tests is indicated by its title; details of procedures and standards can be found in the latest appropriate pharmacopeia.

Uniformity of dosage units. Single-dose oral powders should comply with a pharmacopoeial test for uniformity of dosage units or, where justified and authorized, with the tests for uniformity of content and/or uniformity of mass.

Uniformity of mass. Single-dose oral powders need to comply with a test for uniformity of mass of single-dose preparations. If the product complies with the uniformity of content test for all active substances, the test for uniformity of mass is not required.

Uniformity of content. In the case where the oral powder contains a particularly active drug, single-dose oral powders must comply with a test for uniformity of content of active drug(s) in single-dose preparations. After shaking, empty each container as completely as possible; the test is carried out on the individual contents. As an example, the BP defines an active substance as one where a single-dose of powder or granules contains an amount of active substance less than 2 mg, or less than 2 per cent of the total mass of the single-dose preparation.

Uniformity of mass of delivered doses from multidose containers. Oral powders and granules supplied in multidose containers must comply with this test.

Drug release. Where appropriate (e.g. coated granules, modified-release granules, gastro-resistant granules) the rate and extent of release of the active drug(s) must be quantified and compared with the required specification.

Granules used as an intermediate in tablet manufacture

As indicated earlier in this chapter, by far the largest portion of pharmaceutical granules that are made will have a short lifetime before they are incorporated into tablets (mainly) or hard-gelatin capsule dosage forms. The methods of manufacture of granules are basically the same irrespective of the fate of the granules. However, in the context of manufacturing tablets, the mechanical properties of the granules and the way in which they deform and bond are critical in the tableting process. The remainder of this chapter discusses in more detail the way in which granules are formed and how their structure influences their compactability. Current manufacturing methods are also discussed.

Pharmaceutical technology of granule production

Pharmaceutical granulation processes

Granulation methods can be divided into two types: *wet* methods which utilize a liquid in the process and *dry* methods in which no liquid is used.

In a suitable formulation a number of different excipients will be needed in addition to the drug. The common types used are diluents, to produce a unit dose weight of suitable size, and disintegrating agents which are added to aid the break-up of the granule when it reaches a liquid medium, e.g. on ingestion by the patient. An adhesive (also known as a binder) in the form of a dry powder may also be added, particularly if dry granulation is employed. All ingredients will be mixed before granulation.

Dry granulation

In the dry methods of granulation, the primary powder particles are aggregated at high pressure. There are two main intermediate processes. Either the production of a large tablet (known as a '*slug*') in a heavy-duty tableting press (a process known as *slugging*) or the powder is squeezed between two rollers to produce a sheet or flakes of material (*roller compaction*). In both cases, the intermediate product is broken using a suitable milling technique to produce granular material which is usually sieved to separate the desired size fraction. The unused fine material may be reworked to avoid waste. This dry method may be used for drugs which do not compress well after wet granulation or those which are sensitive to moisture.

Wet granulation (involving wet massing)

Wet granulation involves the massing of a mix of dry *primary powder particles* using a *granulating fluid*.