

It is also important to control the particle size distribution of the granules because, although the individual components may not segregate, if there is a wide size distribution of the granules themselves, the granules may segregate. If this occurs in the hoppers of sachet-filling machines, capsule-filling machines or tableting machines, products having large weight variations will result. This is because these machines fill by volume rather than weight. If different regions in the hopper contain granules of different sizes (and hence different bulk density), a given volume from each region will contain a different weight of granules. This will lead to an unacceptable variability of the drug content within the batch of finished product even if the drug is evenly distributed, weight per weight, through individual granules.

To improve the flow properties of the mix

Many powders, because of their small size, irregular shape or surface characteristics, are cohesive and do not flow well. Poor powder flow will also often result in a wide weight variation within the final product due to variable fill of tablet dies, etc. The resulting granules produced from irregular particles will be larger and more isodiametric, both factors contributing to improved flow properties (discussed more fully in Chapter 12).

To improve the compaction characteristics of the mix

Some primary powder particles are difficult to compact into tablets even if a readily compactable adhesive is included in the blend. Granules of the same formulation are often more easily compacted and produce stronger tablets. This is associated with the method employed to produce the granule and its resulting structure. Often solute migration (see Chapter 29) may occur during the post-wet granulation drying stage and this can result in a binder-rich outer layer to the granules. This in turn leads to direct binder–binder bonding which assists the consolidation of weakly bonding materials.

Other reasons

The above are the primary reasons for the granulation of pharmaceutical products but there are others which may necessitate the granulation of powdered material:

- The granulation of powdered toxic materials will reduce the hazard associated with the generation of toxic dust that may arise during handling. Suitable precautions must be taken to ensure that such dust is not a hazard during the granulation process itself (notably during the mixing of the dry ingredients and during drying of the granules). The granules produced should be non-friable and have a suitable mechanical strength.
- Materials which are slightly hygroscopic may adhere and form a cake if stored as a powder. Granulation may reduce this hazard as the granules will be able to absorb some moisture and yet retain their flowability because of their size.
- Granules, having a greater bulk density than the parent powder mix, occupy less volume per unit weight. They are therefore more convenient for storage or shipment.

Powdered and granulated products as dosage forms

Powdered and granulated products are dispensed in many forms and these are discussed below. The advantages of this type of preparation as a dosage form are as follows:

1. Solid preparations are more chemically stable than liquid ones. The shelf-life of powders for antibiotic syrups, for example, is 2–3 years, but once they are reconstituted with water it is only 1–2 weeks. The instability observed in liquid preparations is usually the primary reason for presenting some injections as powders to be reconstituted just prior to use.
2. Powders and granules are a convenient form in which to dispense drugs with a high dose. The dose of Compound Magnesium Trisilicate Oral Powder is 1–5 g and, although it is feasible to manufacture tablets to supply this dose, it is often more acceptable to the patient to disperse a powder in water and swallow it as a draught.
3. Orally administered powders and granules of soluble medicaments have a faster dissolution rate than tablets or capsules, as these must first disintegrate before the drug dissolves. Drug release from such powdered or granulated preparations will therefore generally be faster than from the corresponding tablet or capsule.