being more likely to be dislodged than those lying parallel to the surface.

Mixing of powders

Practical considerations

When mixing formulations in which there is a relatively low proportion of active ingredient(s), a more even distribution may be obtained by sequentially building up the amount of material in the mixer. This may be achieved by initially mixing the active component(s) with an approximately equal volume of diluent(s). Further amounts of diluents, equal to the amount of material in the mixer, can then be added and mixed, the process being continued until all material has been added. It may be more appropriate to preblend the active component with a diluent in a smaller mixer prior to transferring it to the main mixer in cases where the amount of active ingredient is very low.

Care must be taken to ensure that the volume of powder in the mixer is appropriate, as both over- and underfilling may significantly reduce mixing efficiency. In the case of overfilling, for example, sufficient bed dilation may not take place for diffusive mixing to occur to the required extent or the material may not be able to flow in a way that enables shear mixing to occur satisfactorily. Underfilling may mean the powder bed does not move in the required manner in the mixer or that an increased number of mixing operations may be needed for a batch of material.

The mixer used should produce the mixing mechanisms appropriate for the formulation. For example, diffusive mixing is generally preferable if potent drugs are to be mixed, and high shear is needed to break up aggregates of cohered material and ensure mixing at a particulate level. The impact or attrition forces generated if too-high shear forces are used may, however, damage fragile material and thus produce fines. The mixer design should be such that it is dust tight, can be easily cleaned and the product can be fully discharged. These features reduce the risk of cross-contamination between batches and protect the operator from the product.

In order to determine the appropriate mixing time, the process should be checked by removing and analysing representative samples after different mixing intervals. This may also indicate if segregation is occurring within the mixer and whether problems could occur if the mixing time is extended.

When particles rub past each other as they move within the mixer, static charges will be produced. These tend to result in 'clumping' and a reduction in diffusive mixing and cause material to adhere to machine or container surfaces. To avoid this, mixers should be suitably earthed to dissipate the static charge and the process should be carried out at a relative humidity greater (although not excessively) than approximately 40%.

Powder-mixing equipment

Tumbling mixers/blenders

Tumbling mixers are commonly used for mixing/blending granules or free-flowing powders. There are many different designs of tumbling mixer, e.g. double-cone, twin-shell, cube, Y-cone and drum mixers, some of which are shown diagrammatically in Figure 11.5. It is now common to use *intermediate bulk containers* (IBCs) as both the mixer bowl and to either feed the hopper of a tablet or a capsule machine, or act as the hopper itself. The shape of

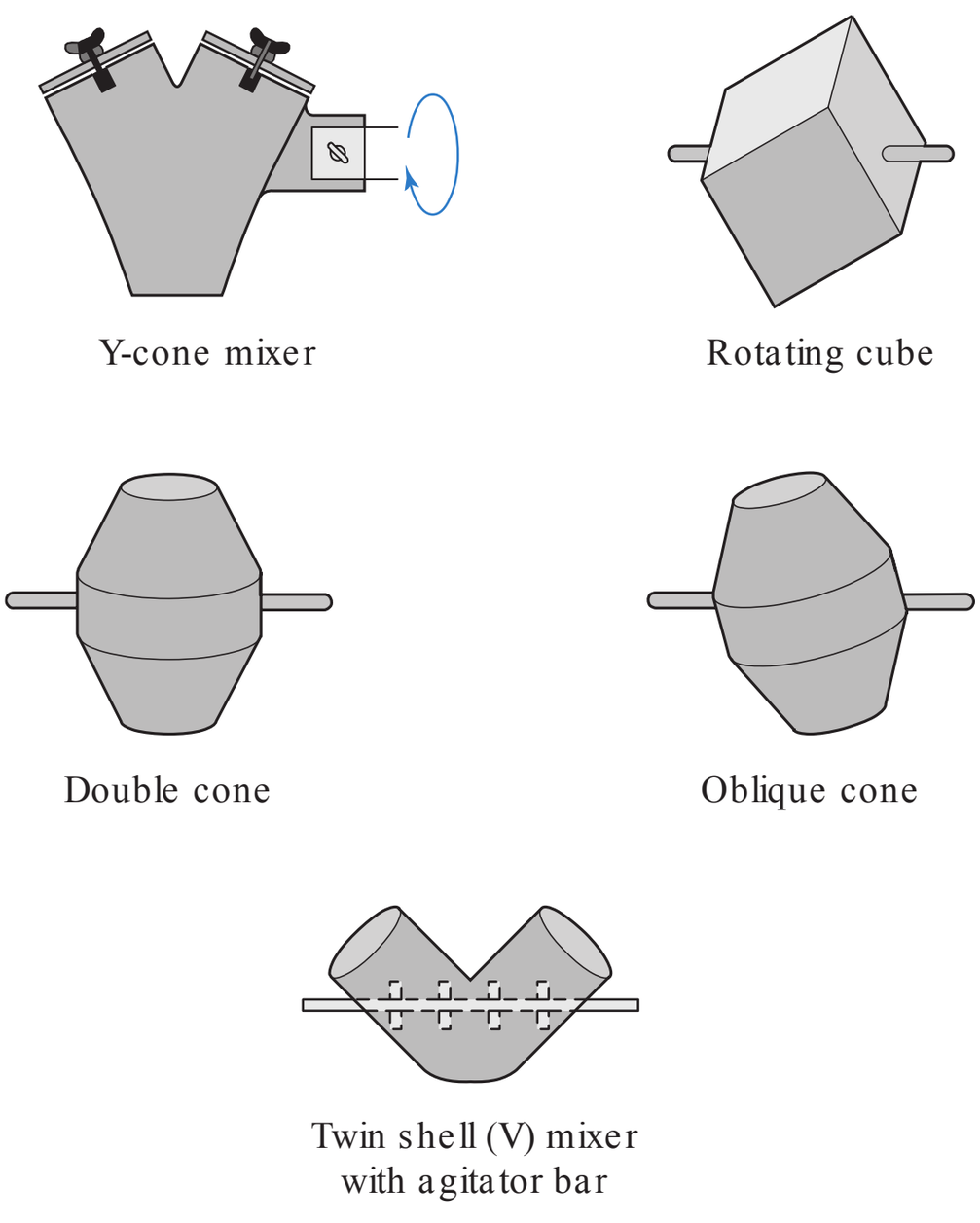

Fig. 11.5 • Different designs of tumbling mixers.