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Economical multiparticulates

Multiparticulates add important functions to solid dosage formulations. They provide reliable drug delivery, reduce the potential for abuse, and supply a platform for high-potency combination products. Made using conical rotor technology, these very small beads can also carry a large amount of API. That allows a given dose to be delivered in small tablets and capsules, which promotes patient compliance. Compact API loading also facilitates combination products because it allows two or more APIs to fit in an envelope that previously could hold just one. Conical rotor technology offers an economical method of producing multiparticulates.

With traditional methods—such as extrusion or wet massing followed by spheronization—the beads might be 800 to 1,200 microns and might attain 70 percent potency. With conical rotor methods—direct spherical agglomeration and powder layering—it is easy to produce beads of 150 to 500 microns that are 90 to 98 percent potent and that retain the smooth, dense characteristics that the older technology provided. When such beads are numerous and small, they increase the number of individual dose domains and improve packing density. And because small beads more closely match the size of the excipient particles, they are less prone to stress failure when compressed into a tablet.

Wurster technology, which clearly has improved in terms of application rates and minimum core size, also has drawbacks. Formulators must still contend with large volumes of solutions or suspensions to create layered beads that carry a high API load. Plus, the core particle is often inert, adding nothing to the final product's utility.

Direct spherical agglomeration using a conical rotor, however, can efficiently produce the core particle from the API, so no space is wasted in the final product. And onto that core the same equipment can apply more API at 100 percent solids via powder layering, no dilution required. This allows you to create beads of any size and potency and in an extremely narrow size distribution.

The conical rotor process also switches easily between modes, from agglomeration to film coating to powder layering with simple parametric changes. With that capability, the spherically agglomerated API core can be given a barrier film coating quickly, thereby separating incompatible APIs. Next, a powder layer of a second API can be applied, creating a multi-layer combination product in each bead.

Almost all API-layered beads are coated with a functional polymer to establish their release profile prior to encapsulation or compression. Traditional methods of applying a polymer require using a solvent system or an aqueous dispersion, but rarely do such coatings contain more than 15 percent polymer. Newer methods of polymer application can improve the economics of solid dosage manufacture.

Using conical rotor powder layering technology enables you to control the surface characteristics of the beads and apply aqueous methacrylate dispersions that have a polymer solids content as high as 40 percent, thereby reducing total application time by at least 60 percent compared to conventional methods. It is possible to economize even further by applying dry micronized polymer powders directly to API beads using only enough water and plasticizer to achieve proper coalescence of the polymer(s).

Even processes for applying nonfunctional coatings, such as those that taste-mask bitter APIs in rapidly dissolving oral delivery systems, can benefit from the conical rotor powder layering process. Consider crystalline APIs or agglomerates, which must typically be smaller than 100 microns to prevent gritty mouth-feel. Particles that small require high levels of polymer to mask off-tastes because they have large and irregular surface areas. But typical taste-masking formulas have a low solids content, so a long coating process is usually required. By using fine polymer powders and the conical rotor process, it is possible to achieve weight gains of 100 percent or more quickly and economically, saving hours of preparation and coating time.

The conical rotor process, with its inherent flexibility and ability to produce many, very small API-loaded beads, achieves a final product with very high uniformity, minimizes solution preparation, and ultimately leads to significant time savings. *T&C*

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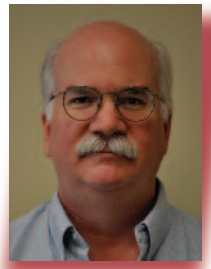

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