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particle coating

Using conical rotor technology to coat small mulitparticulate dosage forms

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This article presents several brief case studies that describe how conical rotor technology can apply APIs and other dry powders to small cores for use in multiparticluate dosage forms. The equipment also applies traditional solutions/suspensions, sometimes using unconventional methods. In each case, conical rotor processing can shorten process times and improve results over conventional coating methods.

Rotor technology has been used to process multiparticulate pharmaceutical materials for many years, and it is ideal for processing small particles. It provides excellent mixing, smooth ordered flow, and concurrent tangential spray.

Rotor technology has, however, shown several limitations, including small capacities, ineffective drying, and difficult-to-control airflow, which have kept rotor-based equipment from wide production use. That has changed, however, with the arrival of conical rotor technology. The equipment offers larger batch sizes, provides a fixed rotor-stator gap for fine airflow control, and can efficiently introduce large amounts of drying air into the rotor system.

These advances have eliminated many of the issues that plagued flat rotors and allow conical rotor equipment to perform as a one-pot system for processing small particles. When paired with precise powder delivery, conical rotor technology is the fastest, most efficient way to apply dry coatings of active pharmaceutical ingredients (APIs) and polymer coatings to small particles. It also performs traditional solution/suspension coating.

The case studies that follow illustrate the versatility and high-yield performance of conical rotor technology.

API and dry powder coating

Methods. Powder layering begins with a core material, usually a sphere made of sugar, starch, microcystalline cellu-

A conical rotor processor [1] with feeder (left) and controls

lose (MCC), or salt, but the process is not limited to those materials. Onto this core, an API is dispersed via a precise powder feeder. For best results, the API powder must be either micronized or very finely divided, ideally to an average particle size of less than 40 microns. As the feeder disperses the powder, a spray gun applies a solution that binds the active to the outer surface of the core material. A proper balance between the powder feed rate and the binder spray rate produces a coating with precise API levels and the correct particle size. It's also possible to greatly reduce coating time compared to conventional coating methods.

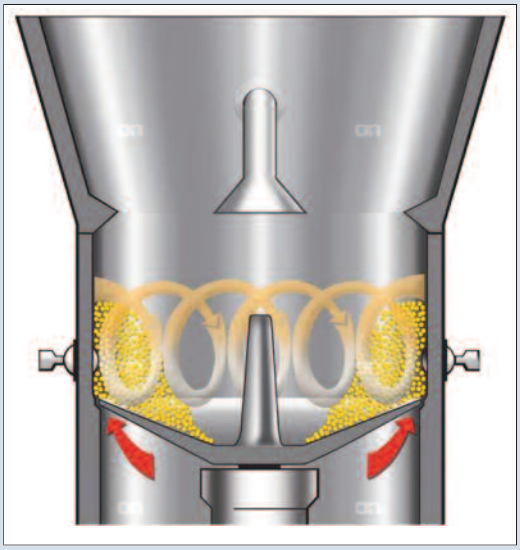
Applying the active powder in dry form significantly reduces process time because the API is applied at 100 percent of its solid weight instead of the 10 to 30 percent solid weight of a solution or suspension. With no need to dissolve or suspend the active in a liquid, dry application eliminates the need to prepare solutions, which saves time. The process also reduces or eliminates the need for organic solvents in many cases. Furthermore, it can produce layered beads that comprise multiple actives and polymers, allowing you to create unique dosing and delivery options. The process also achieves very narrow particle size distributions.

In this case study—as in the studies that follow—a conical rotor processor with a 35-centimeter-diameter rotor [1] was selected. In this study, the goal was to achieve a uniform, smooth, 75 percent loading of flurbiprofen onto 35- to 40-mesh sugar spheres. The binder was a 5 percent solution of polyvinylpyrrolidone (PVP K30, BASF, Florham Park, NJ). After layering the API, a coating of polymer (Eudragit RS 30 D, Evonik, Piscataway, NJ) was applied to achieve a sustained-release dosage.

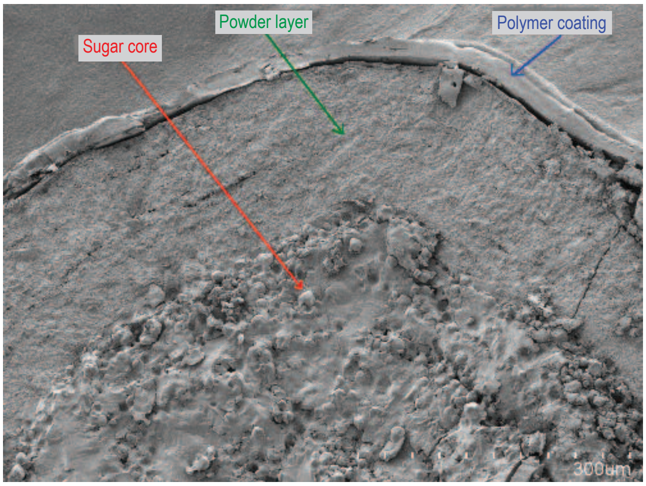
Process. Starting with 500 grams of sugar spheres in the rotor, 2,000 grams of micronized flurbiprofen powder were dry-coated onto the spheres at an average rate of 40 grams per minute (g/min). The PVP binder solution was sprayed at 15 g/min. The rotor operated at 200 rpm, and airflow during the coating portion of the trial was 10 cubic feet per minute (cfm). After the spheres were coated with the active, they were dried until they reached 35°C. Airflow of 80 cfm was provided by an accelerated drying apparatus [2], which introduces a large amount of air atop the product instead of through the rotor-stator gap. By introducing air from the top, a large drying capacity is obtained without fluidizing the product, as would normally occur if the drying air were introduced through the rotor-stator gap (Figure 1).

Figure 1

Introducing drying air from the top instead of through the rotor-stator gap eliminates fluidization and boosts drying capacity.



Results. The process created a very uniform coating (photo below), with 99.1 percent usable yield of finished material. The finished beads contained 75 percent API loading. No organic solvents were used, and the process was complete in 65 minutes. Achieving an identical weight gain using a Wurster coater would have taken upward of 300 minutes, required organic solvents, and entailed several steps to prepare the solution.



Cross-section of a sugar sphere dry-coated with API and then spray-coated with a sustained-release polymer

Polymers and dry powder coating

Methods. In addition to applying an API to an inert core, a conical rotor processor can apply a polymer powder to an active core to achieve the desired release profile. When coating with polymers, a plasticizer solution that both binds and plasticizes the polymer is used instead of a standard binder solution. Again, a balance between the powder's feed rate and the solution spray rate is required and, once attained, the conical rotor processor allows you to achieve precise coating levels and correct particle sizes faster than is possible using traditional coating methods.

As with API layering, applying the polymer as a dry powder saves significant time over applying it via a solution or suspension. It also reduces or eliminates the need for organic solvents, and the process provides very narrow particle size distributions with no agglomeration. Process yields are as high as 99 percent, and the coating is uniform.

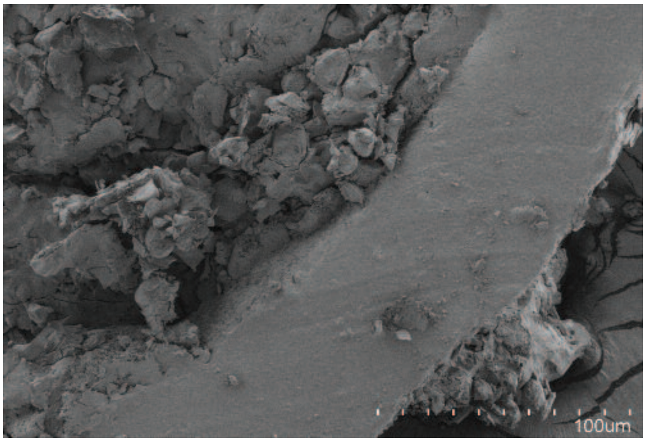
In each of the following three studies, the goal was to coat sugar or starch beads with 60 milligrams of API (acetaminophen) for each gram of bead. The API served as a marker when conducting dissolution and taste tests. Dry polymer was layered onto the beads using a precise powder feeder (KT-20, K-Tron, Pitman, NJ), and the active beads were coated with ethylcellulose (Ethocel Premium 10 FP, Dow Chemical, Midland, MI), a sustained-release polymer; hypromellose acetate succinate—HPMC-AS— (Aqoat, Shin-Etsu, New York, NY), an enteric polymer; and a taste-masking polymer (Eudragit E PO, Evonik). To adhere the polymers to the beads and plasticize them, a suspension of either triethyl citrate (TEC) or dibutyl sebacate (DBS) was used after it was emulsified in water using Tween 80.

Process: Sustained-release polymer and dry powder coating. Starting with 1,000 grams of 40- to 45-mesh acetaminophen-loaded beads in the processor, 425 grams of ethylcellulose were fed onto the rotating beads as the 30 percent TEC-water suspension was sprayed. The ethylcellulose powder was applied at 12 g/min, while the TEC suspension was sprayed at 10 g/min. The ethylcellulose addition was complete in 32 minutes, after which the beads were dried for 15 minutes to 37°C, for a total process time of only 52 minutes.

Results: Sustained-release polymer and dry powder coating. The finished beads were uniform and showed no signs of agglomeration. The addition of the plasticizer throughout the powder layering process helped create a uniform film on each bead (photo above). By eliminating the need to dissolve the polymers in a solvent and spray them onto the beads, the process saved significant time compared to conventional methods.

Precise airflow control allowed the finely divided polymer to remain in the product bed and provided high application efficiency, resulting in a total process efficiency of 98.4 percent. Dissolution testing showed 6-hour delayed-release of the acetaminophen (Figure 2).

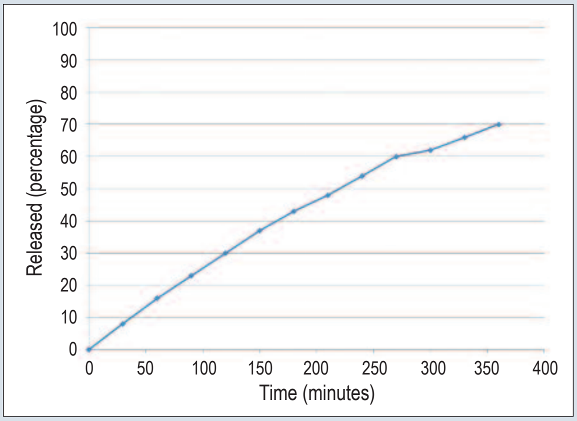
Process: Enteric-release polymer and dry powder coating. Starting with 1,000 grams of 40- to 45-mesh acetaminophen-loaded beads in the processor, 425 grams of HPMC-AS were fed onto the rotating beads, as a 30 percent TEC-water suspension was sprayed simultaneously. The HPMC-AS powder was applied at a rate of 14 g/min, while the TEC suspension was sprayed at 11 g/min. The HPMC-AS addition was complete in 28 minutes, after which the beads were dried for 15 minutes to a product temperature of 40°C for a total process time of only 47 minutes.



Cross-section of acetaminophen-loaded beads coated with ethylcellulose.

FIGURE 2

Release profile of acetaminophen-loaded beads coated with ethylcellulose (sustained release)



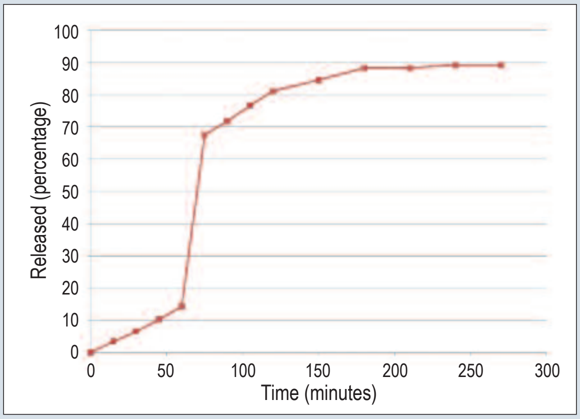
Results: Enteric-release polymer and dry powder coating. The finished beads were extremely uniform and smooth, with no signs of agglomeration. The final efficiency of the trial was 97.2 percent. Dissolution testing showed enteric protection was achieved, with slight leakage of the API during the 60-minute acidic phase (Figure 3).

Process: Taste-masking polymer and dry powder coating. In taste-masking applications that use multiparticulates, the desired particle size is often very small to prevent disagreeable mouth-feel. Coating such small particles often leads to problems, including long spray times and agglomeration, during the coating processes. Applying a taste-masking polymer in dry form using a conical rotor system eliminates those issues and achieves very small finished particles.

In this process, beads made of MCC (Celphere 102, Asahi Kasei, New York, NY) were used. The beads, with an average size of 160 microns, were dry-coated with acetaminophen powder until they reached 60 milligrams of active for each gram of bead. Next, the conical rotor system was loaded with 1,000 grams of the API-loaded beads, they were coated with 1,000 grams of a taste-masking

FIGURE 3

Release profile of acetaminophen-loaded beads coated with HPMC-AS (enteric release)



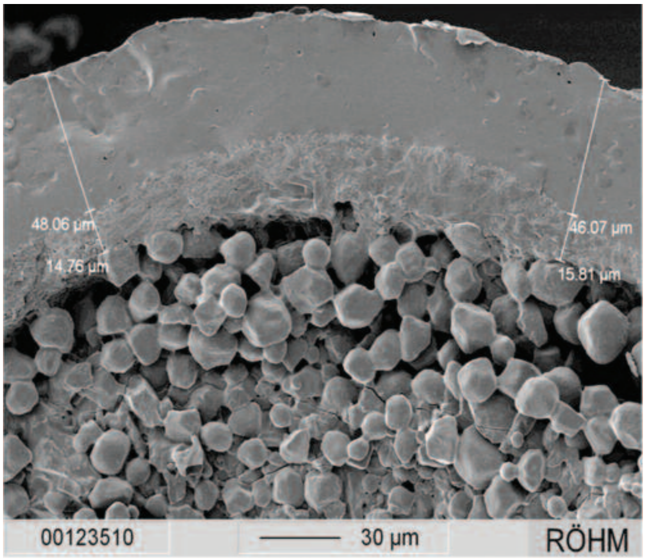
polymer (Eudragit E PO) using the powder feeder while a 10 percent suspension of DBS and water—serving as a plasticizing solution—was applied. The polymer was applied at 20 g/min, and the DBS suspension was sprayed at 10 g/min. A 100 percent weight gain was achieved in 50 minutes of processing time and 15 minutes of accelerated drying.

Results: Taste-masking polymer and dry powder coating. Cross-sectional images from a scanning electron microscope show clear evidence of a uniform film on the surface of each bead, with no cracking or holes (photo above). Taste masking was evaluated by a panel of seven volunteers who placed 300 milligrams of the coated pellets on their tongue for 60 seconds. It was determined that complete taste masking was accomplished at coating weight gains of 25 percent and higher. Dissolution tests showed that 100 percent of the API was released within 5 minutes of testing in the pH 1.2 media, as was expected of the polymer system. The finished particle size averaged 250 microns.

Solution/suspension spray coating

Methods. When spray-coating in traditional rotor equipment, the API or polymer is dissolved or suspended into a liquid and sprayed onto a multiparticulate core, similar to a conventional Wurster process. Conical rotor technology, however, allows glidants such as talc to be added as dry powders via a feeder. This eliminates them from the solution, thereby increasing spray rates, minimizing clogs in the spray gun and solution line, and reducing the amount of glidant required. The conical rotor system produced very high coating uniformity and yields, with excellent film quality and dissolution results. Coating with a solution/suspension requires higher process airflow than does dry coating with an active or polymer, and that was provided by an accelerated drying apparatus [2].

Process. After 1,000 grams of acetaminophen-loaded beads were placed into the conical rotor system, a 10 percent solution of an enteric polymer (Eudragit L-100 55) in acetone was sprayed onto them while talc was applied at a rate of 1.5 g/min via the powder feeder. The process



Cross-section of an API-loaded bead coated with a taste-masking polymer shows a uniform film on the surface and no cracking or holes.

achieved spray rates as high as 80 g/min.

Results. The coating surface was very smooth and dissolution profiles met the target. Process yield was more than 97 percent.

By applying the glidant in dry form instead of suspending it in the coating solution, the amount of glidant required was reduced by almost 50 percent from what the polymer manufacturer recommended. With no glidant in the solution, spray rates were higher than what a comparably sized Wurster coater could have achieved. Dry application of the talc also eliminated buildup in the solution supply lines and clogs at the spray gun, greatly reducing process and cleaning times.

Conclusions

These examples demonstrate that conical rotor processing is a viable alternative to today's conventional coating methods. The key advantages of the conical rotor in each of the processes described include significantly shorter process times and fewer material requirements (organic solvents, glidants, etc.), which can decrease costs and increase productivity. Other advantages include high process yields, high content uniformity, a unique ability to create multilayer multiparticulates very quickly, and the ability to apply functional polymers in dry form or via a traditional solution/suspension spray with great speed and efficiency. *T&C*

References

1. Granurex GXR-35 from Freund-Vector.
2. Granurex Drying Accelerator Duct system.

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