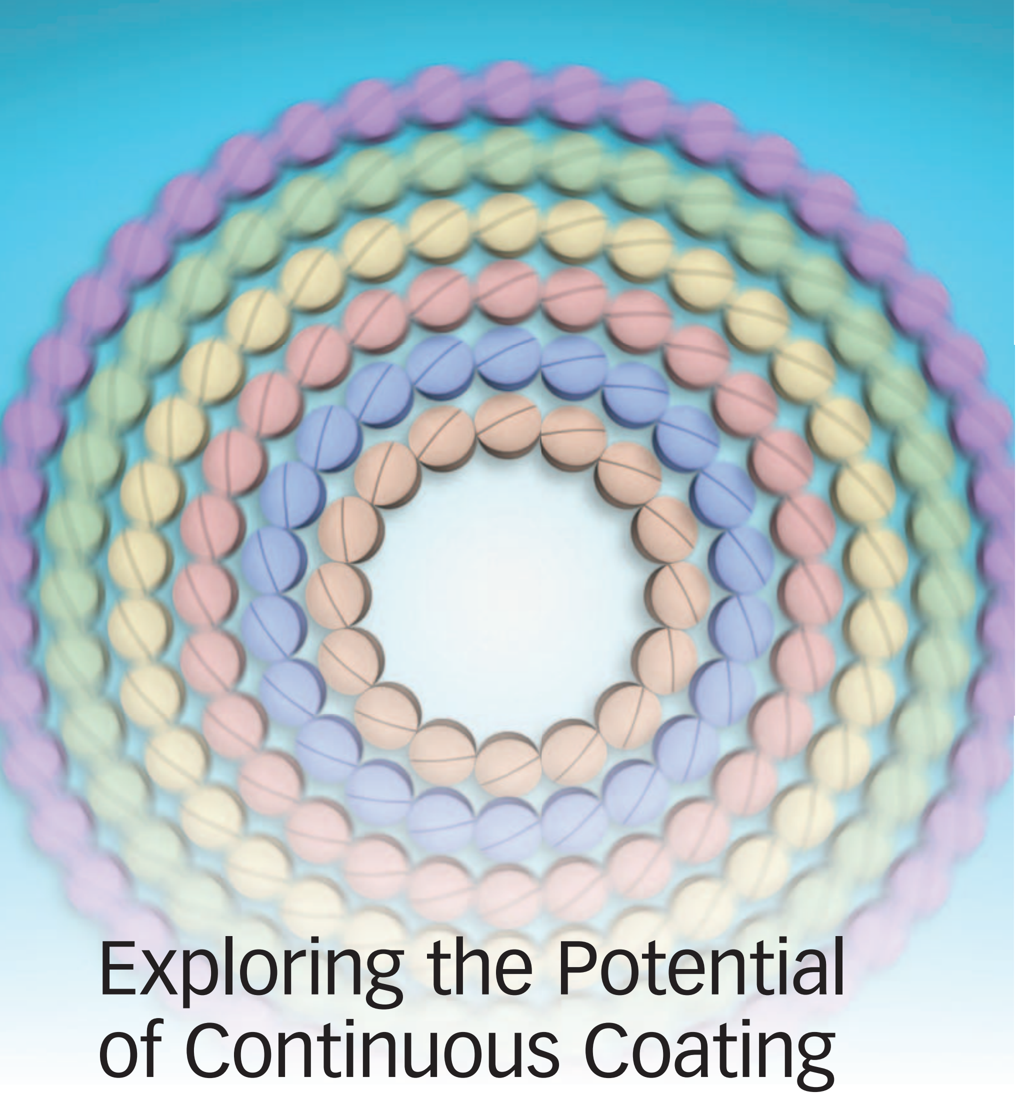

Exploring the Potential of Continuous Coating

Industy experts share insights on the advances in tablet coating technologies and the potential of continuous coating in solid-dosage manufacturing.

A Q&A by
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Tablets are coated for several reasons, such as to improve appearance; for taste- and odour-masking purposes; to protect the API from moisture, oxygen, or the gastric environment of the stomach (e.g., using acid-resistant enteric coating); to separate incompatible substances; and to control drug release, among others. As the industry continues to explore the advantages of switching from batch manufacturing to continuous processes, *Pharmaceutical Technology Europe* spoke to Ali Rajabi-Siahboomi, chief scientific officer at Colorcon; Charlie Cunningham, senior manager, Product Development, Colorcon; Martin Hack, vice-president and general manager, L.B. Bohle; and Hubertus Rehbaum, manager, Scientific Operations, L.B. Bohle, to gain insight on the advances in coating technologies and the potential of continuous coating in the production of solid-dosage forms.

Tablet coating process

PTE: What are the steps involved in a typical tablet coating process? How do you control the different variables affecting the quality attributes of the coated tablets, such as uniformity and functionality of the coating?

Hack (L.B. Bohle): The coating processes currently used in the pharmaceutical industry vary from simple taste- or colour-masking up to highly complex multilayer functional coatings. But as tablets become more sophisticated therapeutic systems (e.g., with controlled release mechanisms or combined APIs), manufacturers must pay closer attention to the quality of the coating. To achieve the required high-quality standards, process parameters such as air flow, spray rate, spray gun position, and tablet bed movement must be taken into account. By using equipment with reliable hardware components and fine-tuned control loops, those critical process parameters can be kept in the design space, ensuring the targeted product quality. In addition to using laboratory analysis to monitor the process, Raman or near infrared (NIR) spectroscopy will also play an important part in ensuring the final product and process quality.

Rajabi-Siahboomi (Colorcon): In my view, all tablets should be coated, whether for trade-dress purposes or for the functional properties mentioned above. The tablet must have a robust formulation with good mechanical strength to withstand the handling, transport, and film-coating processes. Therefore, robust formulation and physical design of tablets are crucial for film-coating success. Tablets with good hardness, low friability, appropriate shape, and low propensity for moisture uptake are desirable.

The film-coating process is fairly complex but can be broken down into three primary control areas:

- *Coating application.* The coating dispersion is delivered to the spray guns and atomized using compressed air into fine droplets for deposition to the tablet surfaces. The viscosity of the coating formulation, number of spray guns (depending on scale of coating pan), atomization, and air-pattern conditions all play a role in how smoothly and uniformly the coating will be applied to the tablet surface. The solids concentration of the dispersion influences coating process time, coating uniformity, and ultimately, the quality of the finished tablet surface.
- *Thermodynamics.* The drying air parameters of temperature, humidity, and volume (air flow) must be carefully balanced with the spray rates for the liquid-dispersion coating application. As the coating dispersion is applied continuously, maintaining appropriate temperature and air

Nicholas Eveleigh/Getty Images; Dan Ward volume versus the coating spray rate is important. The right balance will prevent coating defects related to over-wetting (tablet-to-tablet sticking), or over-dry conditions (spray-drying).

- *Mechanical movement.* Tablets are typically coated in rotating, perforated drums, ranging in diameter from 10" at laboratory scale to more than 60" at production scale, with batch sizes from a few hundred grams up to several hundred kilograms. The speed of pan rotation governs how many passes an individual tablet will pass through the spray zone in a given coating cycle and has a great influence on coating uniformity. Appropriate design of baffles within the pan also facilitate tablet movement and mixing to influence coating uniformity.

Scaling up

PTE: What about scaling up the coating process?

Hack (L.B. Bohle): When scaling up a coating process, the three unit operations of a film-coating process—which are mixing, spraying/ film building, and drying, operated simultaneously within a coating pan during a film-coating process—must be understood. Important parameters are the drum rotation speed, the ratio of the air and liquid flows (as process air flow and coating solution spray rate), and the tablet bed temperature.

When scaling up, normally, the tablet bed temperature or exhaust air temperature is kept constant. The reason is to have the same film building temperature of the polymer of the coating solution. The spray droplets spread on the tablet surface, and film building is generated with a certain temperature. Also, the ratio between mass flow of process air and mass flow of coating solution (spray rate) should be equal to have the same thermodynamic condition for the drying. The drum rotation speed should be scaled in a way that the tablet velocity—while tablets move through the spray zone—is almost the same in laboratory scale, pilot scale, and production scale. Other parameters such as atomizing air flow and pattern air flow and the distance of the spray nozzle tips to the tablet bed surface need to be adjusted properly for even spray performance in each scale.

Geometrical similarity of the selected coating drum from laboratory to production size is useful too. Special spray nozzles (laboratory, pilot, or production coater) designed for different coater sizes (spray rates and droplet sizes) are recommended for successful scale up.

Coating technologies

PTE: Can you tell us more about the recent advances in coating technologies and their impact on continuous coating?

Rajabi-Siahboomi (Colorcon): In the past, continuous coaters were most often employed for high-volume products with tablet throughput rates in the range of 500 kg to over 1000 kg per hour. The scale of equipment is now being modified to meet lower production capacity demands, ranging from 50 kg to 500 kg per hour. New mechanisms have also been developed to eliminate the start-up and shut-down product losses associated with earlier continuous coater equipment. Studies evaluating these improvements conducted in an O'Hara Fastcoat continuous coating system showed consistent colour uniformity for all tablets from start-up through shut-down. Some machine manufacturers have developed novel approaches to coating in semi-continuous modes. In one example, the GEA ConsiGma coater is able to coat small, 3-kg sub-batches rapidly, with a high degree of accuracy. Using this method, each sub-batch is able to be tracked from the upstream continuous tableting process, and critical coating attributes can be monitored in real-time. Use of in-line, process analytical technology (PAT)-based Raman analytics during coating ensures product quality of each sub-batch.

Film-coating formulation technology is also advancing with the use of lower-viscosity polymers that provide significantly improved process efficiency compared with more traditional hypromellose-based coating systems. A benefit of low-viscosity coating formulations is the ability for application of the coating dispersion at significantly higher solids concentration compared to traditional coatings, resulting in considerably shorter process times.

Rehbaum (L.B. Bohle): For the coating process, two different approaches are currently being applied. Some vendors have presented truly continuous coaters, for which a continuous product flow into the long coating drum and a continuous product flow out of the drum is characteristic. R&D at L.B. Bohle, however, has shown that at this point, a truly continuous coating process does not meet the requirements for functional coatings. For tablet coating, the time that each tablet is exposed to the process directly affects the quality of the coating. Therefore, a narrow residence time distribution, ideally a spike, is the key to achieving an outstanding coating uniformity. As the travel time of all tablet cores through a truly continuous coater cannot be controlled sufficiently using inserts or other guiding elements inside the drum, L.B. Bohle has decided to follow the concept of a fast-batch coating design with our KOCO machine family. In this approach, by optimizing the charging and discharging as well as the coating process in terms of spray rate, air flow, and tablet-bed formation, we are able to achieve a high throughput at constant, spike-shaped residence time distributions.

There is another reason to decouple the coating process from the upstream continuous manufacturing of the tablet core, which is the tablet core relaxation time. For the majority of products, the core needs to be given a sufficient time to expand after the compression process. Feeding the tablet cores from the de-duster directly into a truly continuous coater does not allow the cores to expand before applying the film coat. This implies that the expansion of the tablet core will continue with the film coat in place, leading to cracks in the coating layer. For functional coating, such defects are unacceptable. As a result, the tablet core expansion step, which interrupts the continuous product stream of a continuous production line between the tablet press and the coater, makes the advantage of a truly continuous coater to keep the product stream continuous obsolete.

Continous versus batch coating

PTE: How does continuous coating compare with the traditional batch coating?

Cunningham (Colorcon): Compared to batch coaters, the commercially available continuous coating machines have pan diameters that are half, or less, than the diameter of manufacturing-scale batch coaters; but the length of the pan can be as long as 15 feet. However, the resultant tablet-bed depth, which is low, is more consistent with laboratory or pilot-scale batch coating pans; this shallower bed depth ensures greater frequency of tablet presentation to the spray zone.

In recent work, Colorcon studied the effect of tablet residence time and uniformity of tablet progression and coating variability in a Thomas Engineering Flex CTC continuous coater. We were able to conclude that individual tablets progressed uniformly through the continuous process at production rates of up to 850 kg per hour with relatively small variability in transit times and superior coating weight and colour uniformity compared to the traditional batch coater process.

In another study conducted in a Driam Driaconti-T continuous cycled coater, we evaluated the performance of a novel film-coating formulation developed by Colorcon capable of application at solids concentrations up to 35% w/w solids. Although this coater employs elongated rotating drum technology, the drum is divided into individual coating segments, giving it the advantages of small-scale batch production. In this coater, with production rates of 110–180 kg/hour, we also found that coating uniformity was significantly improved over batch coaters.

The common theme around all currently available continuous and semi-continuous coater technology is a significantly reduced coating cycle time and reduced exposure of the tablets to the coating environment.

Rehbaum (L.B. Bohle): At this point, we do not see advantages in truly continuous coating, as indicated previously. However, based on experience with our KOCO machine family, we can achieve shorter cycle times and higher throughput, while maintaining the coating uniformity.

PTE: What aspects of continuous coating still need to be addressed by the industry?

Cunningham (Colorcon): With continued innovation in equipment design, some of the past limitations in throughput rate are being addressed. Equipment is now available to meet a wide range of production capacity demands. Although current film-coating formulation technology provides satisfactory results in these machines, new, low-viscosity coating formulations are being developed to maximize coating efficiency. Linking continuous coating processes to newly evolving continuous tablet manufacturing lines is underway, and continued technology development is needed for 'real-time' PAT monitoring of coated tablet quality attributes to ensure seamless quality from start to finish in continuous tablet manufacture. Although there may not be an issue with the regulators, another aspect to be considered is the definition of a batch while manufacturing using continuous processing. A batch can be defined on a time or material lot basis, depending on specific product manufacturing flows. These may be related to a mindset change for manufacturers as well as the need for clarification from the regulators.

Hack (L.B. Bohle): Currently, truly continuous coating from our perspective is limited to simple taste masking or colour coatings, as long as the tablet core is not required to expand or the film coating has highly elastic properties. One of the limitations is because of the wide residence time distribution, which results in poor coating uniformity. To be able to overcome this limitation, new ways to control the flow of all (100%) tablet cores are needed. Some vendors have suggested solutions with compartments and mechanical barriers or inserts to guide the tablet bed flow. Unfortunately, from our experience, none of these measures can ensure a spike-shaped residence time distribution. The efforts to overcome this limitation only provide benefits if the coating process can be an integral part of the continuous material flow. If the expansion behaviour of the tablet cores forestalls the seamless transfer of the core from tablet press/de-duster to the coating process, there is no benefit in using truly continuous coaters. PTE