tablet coating

Delivering solutions: How film-coating technology is addressing modern pharmaceutical industry trends

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This article discusses how film coating technology is helping solid oral dosage manufacturers adopt continuous processes and meet the needs of pediatric patients.

Film-coating technology has undergone a steady evolution over the last half century. At the beginning, film coating was limited to some extent by the need to rely on the use of organic solvents. However, beginning in the late 1970s, technological improvements in processing equipment and related technologies enabled a gradual adoption of aqueous coating formulations, a trend that facilitated an increase in the number of film-coated products introduced into the marketplace.

Still, early aqueous coating formulations were limited both in scope and in technical performance because they primarily used the same cellulosic polymers that had formed the backbone of the earlier organic-solvent-based formulations. However, innovations in formulation design during the early 1980s, supported first by the introduction of fully-formulated coatings and later by the expanded focus on non-cellulosic polymers (such as vinyl polymers), have enabled the industry to overcome the shortcomings of early aqueous formulations. Innovation in aqueous film-coating technology has continued, and aqueous coatings are available today that can produce high-quality film-coated products when sprayed at up to 35 percent solids (w/w) while significantly reducing processing cost and time.

This article will show how modern coating formulations are successfully addressing industry trends, including:

- High-solids coatings that can drastically reduce processing times and facilitate the use of continuous coating processes.
- Specialized taste-masking coatings designed to meet the challenges imposed by pediatric dosage form development.

Improving process economics and meeting the challenges of continuous coating processes

As previously mentioned, early aqueous film coating formulations had many shortcomings, not least of which was the fact that the attainable sprayable solids content was limited to approximately 10 percent w/w. This low solids content, coupled with the reduced volatility of water compared to organic solvents, often resulted in extended processing times and increased stability issues for moisture-sensitive products. Another technical issue was related to the higher surface tension of water compared to organic solvents, which made it more difficult to ensure that the coating solution wetted the tablet surface enough to provide adequate film adhesion.

These challenges became less important as coating suppliers introduced new types of polymers into their coating formulations and the sprayable solids content gradually increased to 15 to 18 percent w/w. Ongoing innovations have further increased the sprayable solids content, initially to 20 to 25 percent w/w and, more recently, to 30 to 35 percent w/w. These developments have drastically reduced coating process times and facilitated the successful introduction of continuous coating processes.

The data shown in Figure 1 illustrate how increased sprayable solids content can reduce processing time, in this case using a pilot-scale (40-kilogram batch size) O'Hara LabCoat IIX coater. The figure compares the performance of a standard HPMC-based coating formulation

Figure 1

Impact of sprayable coating solids on coating process time using an O'Hara LabCoat IIX coater fitted with a 30-inch pan (40-kilogram charge)

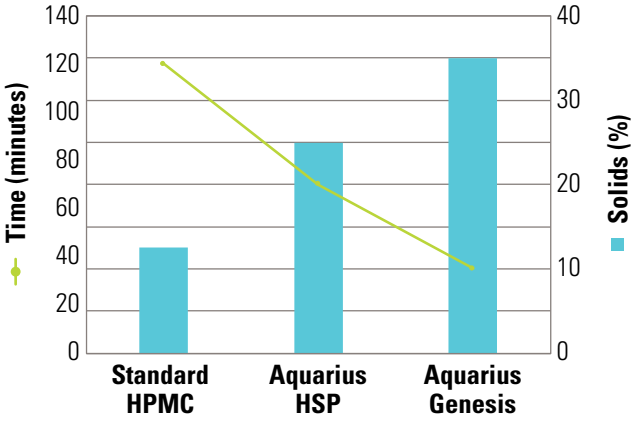


Figure 2

Examples of tablets coated using an O'Hara LabCoat IIX coater fitted with a 30-inch pan

a. Standard HPMC coating (Aquarius Prime, 12.5 percent solids)

b. Intermediate solids coating (Aquarius Preferred HSP, 20 percent solids)

c. Ultra-high solids coating (Aquarius Genesis, 35 percent solids)

Figure 3

Typical viscosity profiles of evaluated coatings

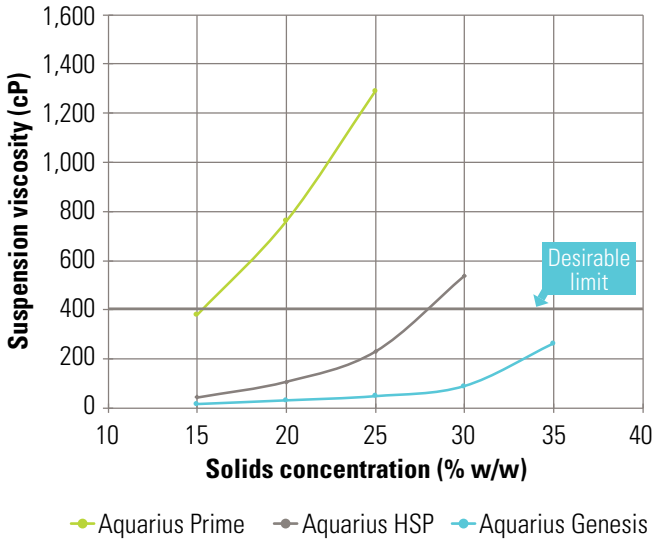


Table 1

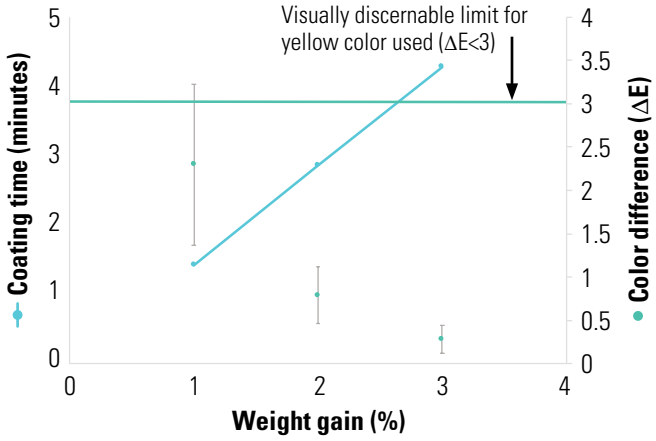
Coating process time for 3 percent weight gain (O'Hara LabCoat IIX coater with a 19-inch pan configured to simulate a segment of an O'Hara FCC 500 continuous coater)

Coating	Solids (%)	Time (minutes)
Aquarius Prime	12.5	22
Aquarius HSP*	20	11
Aquarius Genesis	35	5

* Achieved a throughput rate of 450 kg/h in an FCC 500 continuous coater

Figure 4

Visual coating uniformity for coating sprayed at 35 percent solids using a GEA ConsiGma coater (N=20)



(sprayed at 12.5 percent w/w solids) to that of an intermediately high-solids film coating formulation (Aquarius Preferred HSP, sprayed at 20 percent w/w solids) and an ultra-high-solids film coating formulation (Aquarius Genesis, sprayed at 35 percent w/w solids).

As the figure shows, the processing time required to achieve a 3 percent weight gain went from 120 minutes at 12.5 percent solids to 70 minutes at 20 percent solids to 38 minutes at 35 percent solids [1]. This reduced processing time can not only improve process economics, but it also reduces the tablets' exposure to potentially stressful conditions such as relatively high processing temperatures and mechanical agitation. Also, the shorter processing time did not compromise product quality, as indicated by the tablet samples shown in Figure 2. These results are primarily due to advances in polymer science that have allowed for a substantial reduction in coating suspension viscosity, as shown in Figure 3.

Another important benefit of reduced processing time is that it allows for a continuous coating process. Large-volume continuous coating processes (capable of achieving throughputs of 500 to 2,000 kg/h) have been in operation in a somewhat limited fashion for more than a decade. More recently, the pharmaceutical industry has begun to shift its focus toward fully continuous manufacturing processes, which require coating process throughputs in the range of 40 to 120 kg/h. Existing coating machines such as the O'Hara FCC 75, GEA ConsiGma, and others are capable of achieving these throughput rates, and available high-solids coatings can support this industry trend as well.

A challenge of conducting development programs capable of supporting large-throughput coating processes is that companies typically have a limited amount of material available for the development process. One way to address this challenge is to configure a batch coater as a surrogate for the continuous process. For example, the O'Hara FCC 500 continuous coater uses a pan of similar diameter (19 inches) to those available for an O'Hara LabCoat IIX coater. Reconfiguring the latter to accommodate reduced bed depths and the process airflows and spray rates commensurate with those used in a segment of the FCC 500 can produce a suitable model for product development. Table 1 shows the processing times for various coatings applied using a LabCoat IIX fitted with a 19-inch pan and configured to simulate a segment of the FCC 500. The reduced process times are indicative of the potential throughput-rate increases such coatings can achieve.

Figure 4 shows the coating data for a continuous coater designed to support a continuous manufacturing process (GEA ConsiGma), using the Aquarius Genesis film coating at 35 percent solids [2]. The coater in this case is capable of attaining a throughput rate of 100 to 120 kg/h, with an individual sub-batch process time of 5 to 6 minutes. As the data show, the process can achieve a visually uniform coating with a weight gain of only 2 percent (because at 2 percent, the color difference [ΔE]

is <1.2, well below the visually detectable limit for this yellow color). In addition, coated tablet quality was more than acceptable, as shown in Figure 5.

Meeting the challenges of pediatric dosage form development

Historically, pediatric oral drug products were typically offered in the form of syrups or chewable tablets. More recently, regulatory agencies have placed greater demands on the development process, requiring that pediatric dosage forms be designed to meet the special needs of young patients. These requirements include that:

- The final product can be easily divided to match an individual patient's dosage requirements (depending on age, body size, and the particular disease state being treated).
- The formulation is effectively taste masked to facilitate compliance with the physician's and pharmacist's instructions. Additionally, the taste-masking method should not compromise the pharmacokinetic characteristics of the API (that is, taste masking should not change the product's drug release characteristics unless there is a specific requirement to do so).
- The developer conducts appropriate stability studies in cases where the final dose may need to be administered in food products, such as yogurt or applesauce.

Referring to the second requirement, taste masking has traditionally involved applying a polymer coating to a suitable dosage form (often in the form of multiparticulates). While many coatings can produce effective taste-masking characteristics, they often use polymers that are not particularly water soluble, so they could potentially change the product's drug-release behavior. Conversely, many coatings that are readily water soluble might prove less effective as taste-masking agents, especially when administering the final dosage form in the types of food products listed. As a result, balancing both pharmacokinetic and taste-masking requirements can be a challenge.

FIGURE 5

Coated tablet quality using a GEA ConsiGma coater

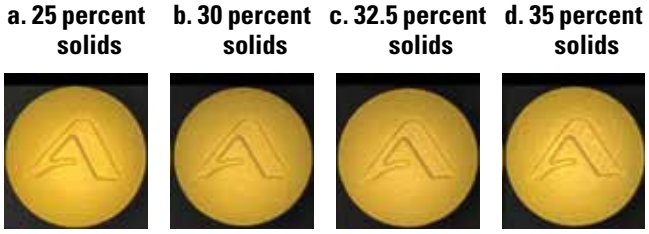


TABLE 2

Process conditions for coating mini-tablets (O'Hara fluid-bed coater fitted with a Wurster insert)

Inlet air temperature (°C)	Product temperature (°C)	Spray rate (g/min)	Atomizing air pressure (psi)	Air volume (cfm)
62-65	44-46	8-10	28-30	62-65

While many coatings can produce effective taste-masking characteristics, they often use polymers that are not particularly water soluble, so they could potentially change the product's drug-release behavior.

To illustrate how developers might address this challenge, a recent study examined the application of a specialized water-soluble film coating (Aquarius Protect) to mini-tablets containing cetirizine hydrochloride (20 percent drug content) [3]. For the sake of comparison, the study also evaluated a conventional HPMC-based film coating (Aquarius Prime). Each coating was applied at levels ranging from 10 to 30 percent (based on substrate weight) respectively, using an O'Hara laboratory-scale fluid-bed coater fitted with a Wurster insert and employing the coating process conditions listed in Table 2.

To assess the applied coatings' taste-masking capabilities, the study examined pure API, uncoated tablets containing the API, and both coated placebo and coated API-containing mini-tablets using an Astree e-Tongue system equipped with an Alpha MOS sensor set (comprising seven specific sensors: ZZ, AB, BA, BB, CA, DA, and JE). The sensors act as a surrogate for human taste buds, measuring changes in electric potentials that can be compared to physiological action potentials.

This method allows researchers to examine the relative taste-masking effectiveness of formulation approaches, identifying the most likely candidates for ultimate assessment in human taste-masking studies. Test results are typically presented in the form of a principal component map. To interpret the results, it's necessary to assess the degree of separation between the pure API and uncoated samples containing the API and the coated API-containing samples (the further the degree of separation, the better). It's also necessary to study the relative closeness between the coated API-containing samples and the similarly coated placebo samples (in this case, the greater the similarity, the better).

As Figures 6 and 7 show, the coated API-containing mini-tablets produced the most effective taste-masking qualities at 15 and 20 percent when compared to the API comparator and at 20 percent when compared to the placebo comparator. An example of a principal component map is shown in Figure 8. In this case, testing was performed after 10 minutes mixing in the test fluid, where taste-masking effectiveness (compared to the API comparator) was greatest for mini-tablets coated with the Aquarius Protect film coating at 30 percent.

As previously stated, it's important to achieve effective taste masking without compromising drug release (unless a modified release characteristic is desirable). As shown in Figure 9, mini-tablets coated with a standard HPMC-based film coating (Aquarius Prime) and a special taste-masking film coating (Aquarius Protect) show similar dissolution behavior, and the dissolution profiles compare favorably to that of the uncoated mini-tablets, easily meeting the required Q value for the tested API.

Figure 6

Taste-masking effectiveness versus API comparator

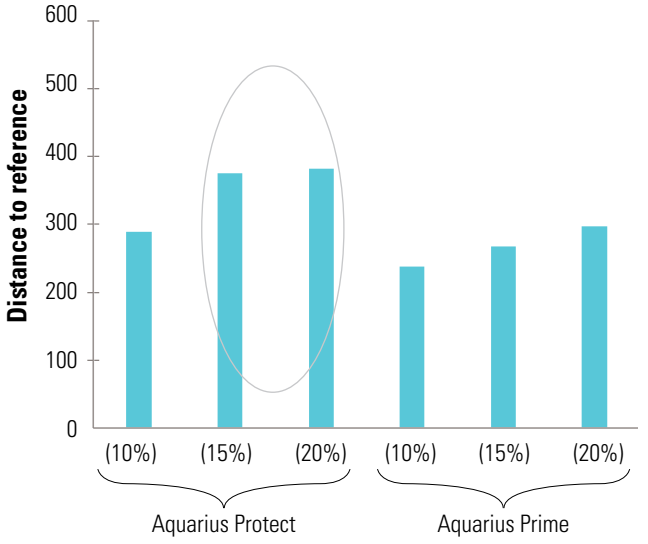


Figure 8

Principal component map (Testing performed after 10 minutes stirring in test fluid)

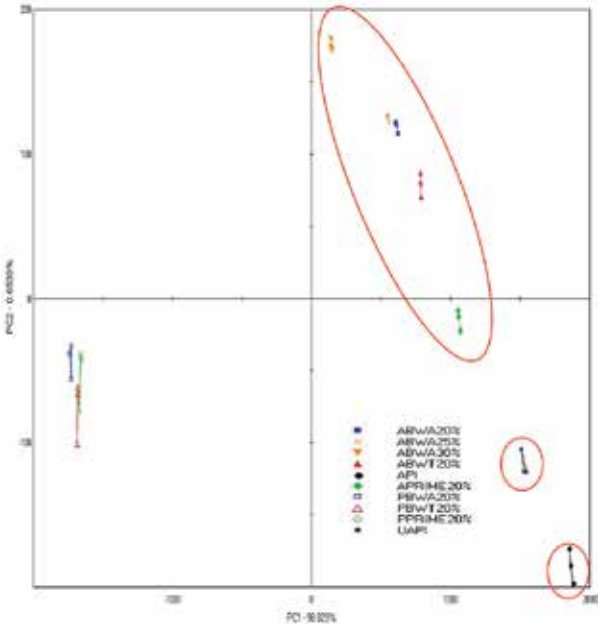


Figure 7

Taste-masking effectiveness versus coated placebo comparator

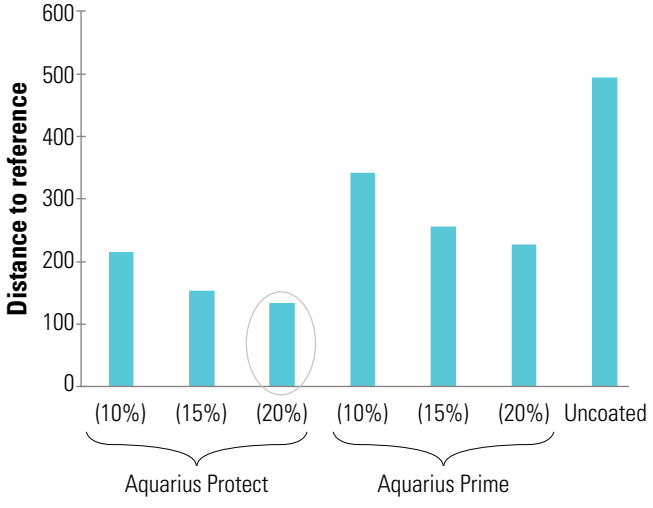
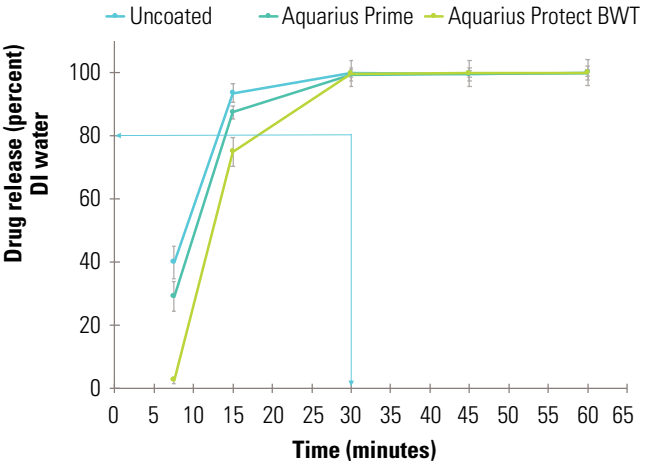


Figure 9

Dissolution profiles for uncoated and coated mini-tablets (20 percent weight gain)



To achieve the joint objective of effective taste masking and subsequent rapid API release once the dosage form is swallowed, the API release must be limited while the dosage form remains on the tongue. One way of assessing this requirement is to measure dissolution behavior in a limited amount of artificial saliva. This can be done using a µDiss Profiler dissolution apparatus, as shown in Figure 10. The data shown in Figure 11 were obtained using this apparatus (at 37°C, using a stirring rate of 100 rpm), employing 20 milliliters of artificial saliva. These data show that API release under these conditions can be restricted to varying degrees, depending on the amount of coating applied. For example, there was essentially no API release with a 30 percent coating level, even after 5 minutes exposure time. A 20 percent coating level was able to prevent API release for about 2 minutes.

Summary

The challenges facing manufacturers of solid oral dosage forms are continuously evolving, and film coatings must continue to evolve to help developers meet those challenges. While new and innovative raw materials typically face an onerous pathway to regulatory acceptance, essentially limiting coating formulations to materials already in common usage, the discussion in this article confirms that currently available film coatings continue to meet the needs of the industry's evolutionary trends. *T&C*

References

1. Kapish Karan, Thomas Dürig, and Stuart Porter. "Evaluation of a developmental high productivity high gloss coating system on the final appearance of coated tablets." (M0930-11-084). AAPS Annual Convention, Washington DC (Nov 2018).

2. Kapish Karan, Thomas Dürig, Ronald Hach, Andrew Birkmire, Jessica Anderson, and Jessica Zombek. "Evaluation of an ultra-high-speed high gloss film-coating system in the GEA ConsiGma Coater." (M1330-12-090). AAPS Annual Convention, Washington, DC (Nov 2018).

3. Stuart Porter, Kapish Karan, Ronald Hach, Quyen Schwing, Jeffery Williamson, and Nicole Mendonsa. "Facing the tastemasking challenges with pediatric oral solid dosage forms." (M5051). AAPS Annual Convention, San Diego, CA (Nov 2017).

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FIGURE 10

µDiss Profiler dissolution apparatus

FIGURE 11

Dissolution data for uncoated and coated mini-tablets using a µDiss Profiler dissolution apparatus