Nutrition & Biosciences

TM PB108-1

AQUACOAT® ECD: COATING PROCESS CONSIDERATIONS

Technical Memorandum

At DuPont, we aim to help our pharma customers with both every day challenges and future solutions. Armed with essential excipients and vital expertise, our broad portfolio is designed to deliver performance and cost advantages in various oral solid dosage forms.

The coating process

Extended-release pseudolatex film coating requires good control of a dynamic process environment with optimization of the following steps[1]:

1. Formation of appropriately-sized droplets
2. Droplet contact with the substrate
3. Spreading of the droplets on the substrate
4. Water evaporation and coalescence of the latex particles

Process equilibrium must be established such that the droplets adhere to the surface of the substrate upon contact and coalesce into a continuous coating film. At the same time, the coating dried at a rate that avoids overwetting but without hindering latex particle coalescence, which depends on the capillary pressure of water within the coating.

Equipment

The equipment used in coating can be classified into two categories:

1. Pan coaters (pan or perforated pan), generally used for tablet coating
2. Fluid bed coaters, generally used for powder, pellet and mini-tablet coating

Critical Process Parameters (CPPs) and recommended process ranges for each of these two equipment categories are discussed in Table 1.

Table 1. Recommended parameter ranges for the coating process

Process Parameters	Criticality	Recommended Range (Fluid bed)	Recommended Range (Pan coater)
Inlet temperature	This temperature dictates the rate of water evaporation. Very high drying rates will not allow the coating solution to spread evenly and will inhibit polymer deformation and coalescence.	55-65°C	55-65°C
Product temperature	A determinant of heat transfer and water evaporation rates, very high product temperature can result in over-rapid drying rates that negatively impact coalescence. Product temperature is thus critical to achieving process consistency and successful scale-up.	40-45°C	40-45°C
Air volume	This variable is the air volume needed to suspend pellets in the Wurster column. Lower air volume can result in varying coating film thickness and sticking, while too-high air volume can cause pellet attrition. For pan coating, this parameter indicates the air volume needed to prevent tablet sticking and achieve a uniform coating.	60-70 m3/hr	220-260 CFM (374-442 m3/hr)
Spray rate	This defines the amount of coating solution sprayed per minute. It affects the solution droplet size and the rate at which droplets are spread on pellets, and thus impacts product temperature. A higher spray rate can lower the product temperature, also lowering the rate of water evaporation. Spray rate must be adjusted based on the pellet or tablet size.	3-10 g/min	3-10 g/min
Atomizing air pressure	This affects droplet size and hence the consistency of the coating process.	1.0-1.2 bar	20-30 psi (1.4-2.0 bar)
Dew point/ Absolute humidity	This is a measure of humidity during coating. Dew point can be influenced through the use of high-humidity inlet air or a lower solid-content coating solution. It is a critical attribute as higher humidity during the process facilitates film coalescence.	8-10°C (No control) Absolute humidity 7-10 g/kg	No control

For fluid bed coaters, recommendations are based on a Niro-1 unit and a batch size of 800 g-1 kg. For pan coaters, recommendations are based on Thomas Engineering Compu-Lab equipment with a 14 inch perforated pan and a batch size of 1-1.2 kg.

The coalescence process

Polymer particles are deposited on the surface of the core material during the spraying of the aqueous dispersion coating. Under optimal conditions above a minimum film forming temperature (MFFT), water evaporation concentrates the polymer particles into a closely-packed arrangement on the substrate surface, and the capillary force of the interstitial water deforms the particles to coalesce and produce a dense, continuous film (Figure 1).

However, aggressive drying may remove the interstitial water before coalescence is complete. Complete film coalescence is critical to achieving stable dissolution profiles, otherwise further gradual coalescence may occur, which risks release profile changes over longer-term storage[2].

The optimized coating process should be developed by considering the temperature, time and humidity effects that impact film coalescence. Higher temperature increases polymer mobility, facilitating polymer particle coalescence, but may remove interstitial water from coating before coalescence is complete. Higher humidity during coating reduces the risk of over-drying and enhances coalescence, as water is an efficient plasticizer for ethyl cellulose polymers [3, 4]. Humidity during coating may be controlled by conditioning the inlet air or by adding more water to the aqueous dispersion (i.e., reducing solid content).

Figure 2 shows the effects of curing time, temperature and humidity on film coalescence and the resulting dissolution profile. For Aquacoat® ECD, dry heat at 40-45°C is not enough to achieve complete coalescence.

Figure 1. Coalescence process

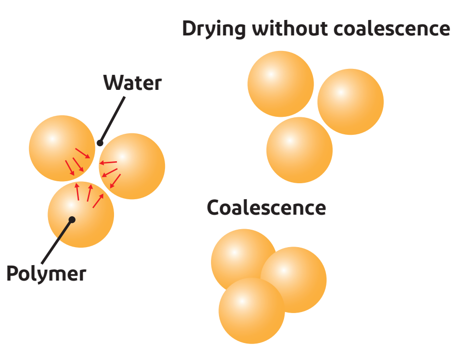
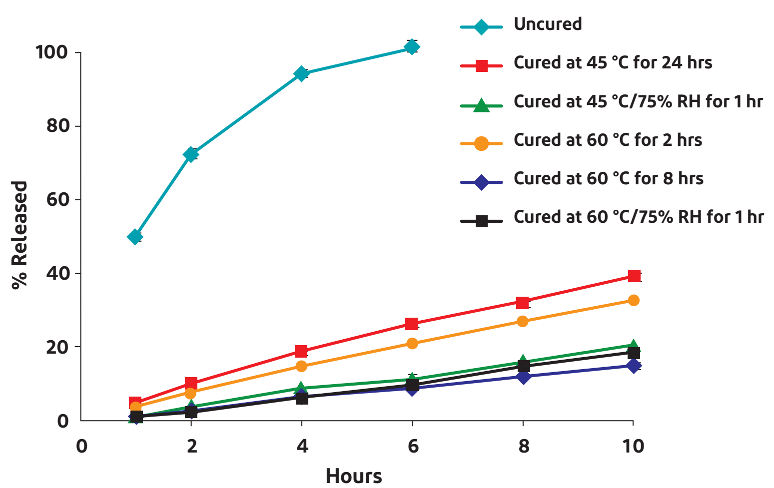


Table 2. Recommended parameter ranges for the coating process

Approach	Recommended conditions	Pros and cons
Oven usage	60°C for 2-8 hours	This adds another processing step.
In-process curing in fluid bed or pan coater		
Dry curing	Product temperature 57-60°C for 1-2 hours	This is carried out after the coating process with no need for an additional processing step.
Continued water spraying after application of the aqueous dispersion	• Product temperature of 57-59°C to create absolute humidity of 17-20 g/kg • 1-2 hours of water application • Water spray-rate and amount dependent on equipment scale	This is carried out after the coating process with no need for an additional processing step. Water facilitates coalescence through capillary pressure, reducing both MFFT as well as the electrostatic charge generated during curing. Water spraying further reduces the time needed to achieve complete coalescence.
Humidity treatment of equipment input air	• Use of higher humidity air (e.g. 40-45°C dew point, absolute humidity of 40-60 g/kg) and/or: • Use of a coating dispersion with lower solid content (e.g. <15% w/w) to create a higher-humidity environment.	There is no need for an additional curing step as coalescence is achieved during the coating process.

Figure 2: Effects of time, temperature and humidity on drug release

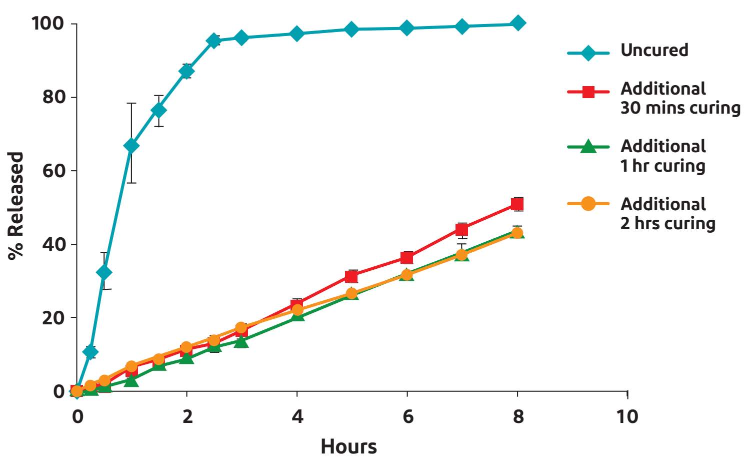


Theophylline pellets coated with Aquacoat® ECD at a coating level of 3% w/w; dissolution medium pH 6.8 phosphate buffer

Full coalescence was achieved at 45°C/75% RH over 1 hour, at 60°C for 8 hours and at 60°C/75% RH over 1 hour. Complete film coalescence can be achieved in the fluid bed with appropriate temperature and humidity control, to avoid the need for a separate curing step (Figure 3). Table 2 describes various acceptable approaches to achieve complete film coalescence.

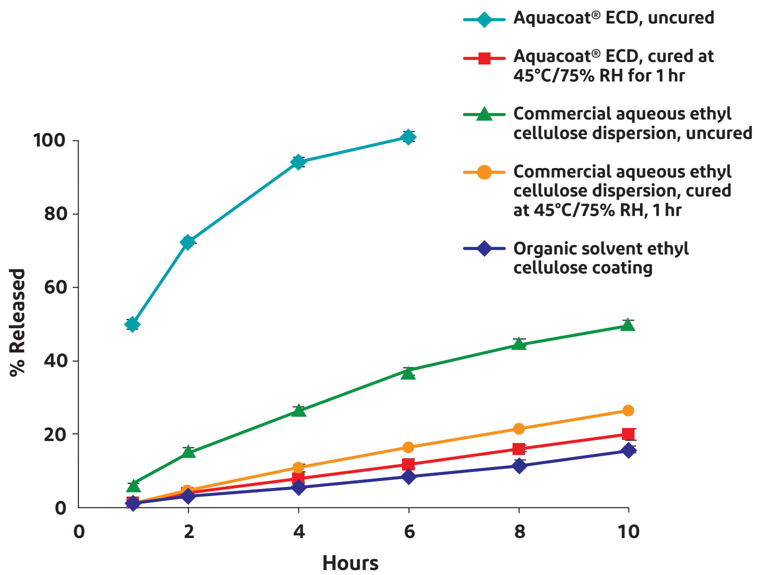
All pseudolatex ethyl cellulose-based coatings must be fully coalesced to ensure stable drug release profiles. Consistent, reproducible release profiles require a continuous coating film that is formed through the process of particle coalescence. A robust coating process must be designed to reliably achieve a stable, fully-coalesced film. This is true of any aqueous ethyl cellulose dispersion. Figure 4 compares the dissolution profiles of two aqueous ethyl cellulose dispersions types against that of an organic solvent ethyl cellulose coating system. The organic solvent release profile can be used as the reference standard for a fully-coalesced aqueous system. Complete coalescence is the most critical attribute of aqueous latex systems to achieve robust product performance.

Figure 3: In-process film coalescence



Theophylline pellets coated with Aquacoat® ECD and PEG-PVP graft copolymer in the ratio of 85:15 at a 15% w/w coating level; in-process curing at 57°C with 15% relative humidity

Figure 4: Effect of curing on various aqueous ethyl cellulose coating systems



Theopylline pellets coated with commercial aqueous ethyl cellulose dispersion (Type A and B) at a coating level of 3% w/w; dissolution medium pH 6.8 phosphate buffer

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