Scaling up Aqueous Enteric Coating with Hypromellose Acetate Succinate (HPMCAS)

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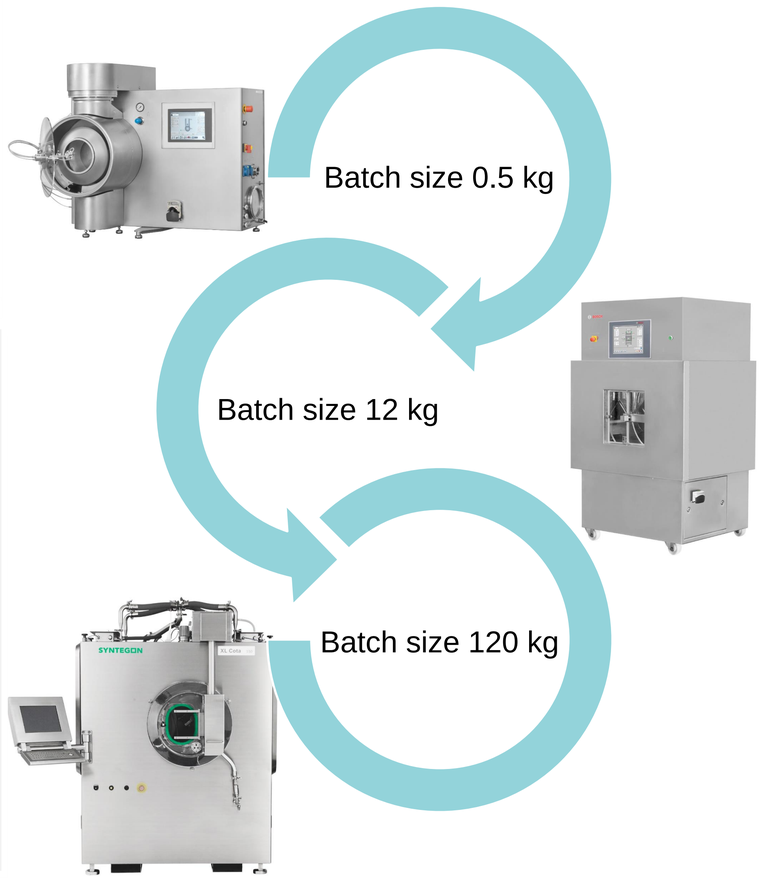
Introduction

Enteric coating is widely applied to protect acid-labile drugs from degradation in the gastric environment, or to protect the gastric mucosa from irritating drugs.[1] HPMCAS is one of the polymers applied in enteric coating. Several formulation pathways for aqueous enteric coating using Hypromellose Acetate Succinate (HPMCAS, Shin-Etsu AQOAT®) are available. The partially ammonia neutralized dispersion [2] enables a higher polymer solid content (12 %) compared to aqueous dispersion coating [3] (7 %), resulting in reduced process time. However, information about scale-up of the partially ammonia neutralized formulation is limited. This study describes the scale-up of the partly ammonia neutralized enteric coating dispersion from lab to production scale.

Materials and Methods

Acetaminophen tablets (10 % acetaminophen, 507.9 mg, 10 mm, round, R11.78, hardness = 332 N, friability = 0.18 %) were produced on a SYNTEGON rotary tablet press TPR200. The coating suspension (table 1) was prepared according to Shin-Etsu technical information A 037 [2] (dispersion viscosity 130 mPa·s, pH = 5.4, filtered through a 200 µm sieve before coating, a video on the dispersion preparation is available on YouTube [4]). Tablet coating was carried out in three different SYNTEGON perforated pan coaters (Figure 1): Solidlab 1 (0.5 kg, lab scale), Solidlab 2 (12 kg, pilot scale), and XL Cota 150 (120 kg, production scale). Tablet hardness and tablet dissolution were tested on an Erweka TBH225 and Erweka DT720 dissolution tester equipped with UV analysis (USP dissolution test pH half buffer change method A procedure, n=6; USP acid stage pH=1.2, 750 mL, 37 ºC, λ=280 nm, apparatus 2, 50 rpm; USP buffer stage pH=6.8, 1000 mL, 37 ºC, λ=243 nm, apparatus 2, 50 rpm). The surface of coated tablets and the thickness of the film were analyzed using a JEOL JSM-IT100 scanning electron microscope.

Scale steps



Coating Suspension

- Preparation within 30 minutes!
- See video on YouTube [4].
- Suspension viscosity 130 mPa·s, pH=5.41.
- This coating suspension was sprayed until 8 % polymer weight gain.

Shin-Etsu AQOAT® coating formulation

Material	w/w [%]
Shin-Etsu AQOAT® AS-MF	12
Sodium lauryl sulfate (SLS)	0.36
Ammonia (NH_3 pure 100%)	0.04
Triethyl citrate (TEC)	1.8
Talc	3.6
TiO_2	1.0
Water	81.2
Total	100

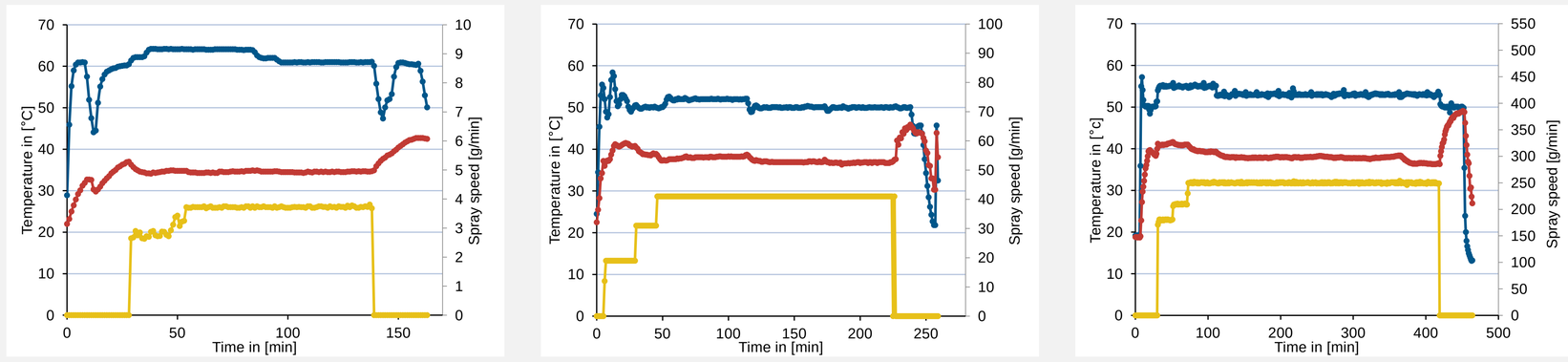
1. Add SLS to water and stir until a clear solution is observed.
2. Add Shin-Etsu AQOAT® and stir for 10 minutes.
3. Add Ammonia and stir for 5 minutes.
4. Disperse talc and TiO_2 in water with Ultra Turrax in another vessel.
5. Add the talc and TiO_2 suspension to the vessel with polymer and stir for 5 minutes.
6. Add TEC and stir for 5 minutes.
7. Sieve through 0.2 mm sieve.

Coating Parameters and Process

Model	Solidlab 1	Solidlab 2	XL Cota 150
Number of nozzle(s)	1	1	3
Nozzle diameter [mm]	0.5	1.2	1.2
Batch size [kg]	0.5	12	120
Drum speed [rpm]	20	14	7
Air flow [m³/h]	50	380	1800
Inlet temp. set point [°C]	61	50	52
Tablet bed temp. [°C]	34	34	34
Outlet temp. [°C]	35	37	38
Spray rate [g/min]	4	40	250
Relative spray rate [g min^{-1} kg^{-1}]	8	3.3	2.1
Spray pressure [bar]	0.7	1.6	2.2
Total process time [hour]	2.7	4.3	7.7

- The tablets were first heated up to a core temperature of 36-38 °C.
- Initial spray speed was lower until a first layer was formed. The tablet bed temperature was kept at 36 °C.
- After 20 minutes spraying, the spray speed was increased.
- In the drying step, the coated tablets were dried at a tablet bed temperature of 38-40 °C for 20 minutes.
- All coating trials proceeded smoothly.

Solidlab 1 | Solidlab 2 | XL Cota 150

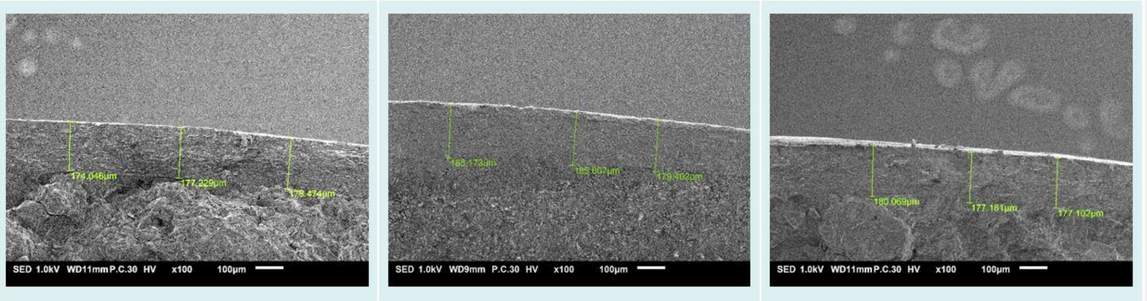


Process charts from scale-up

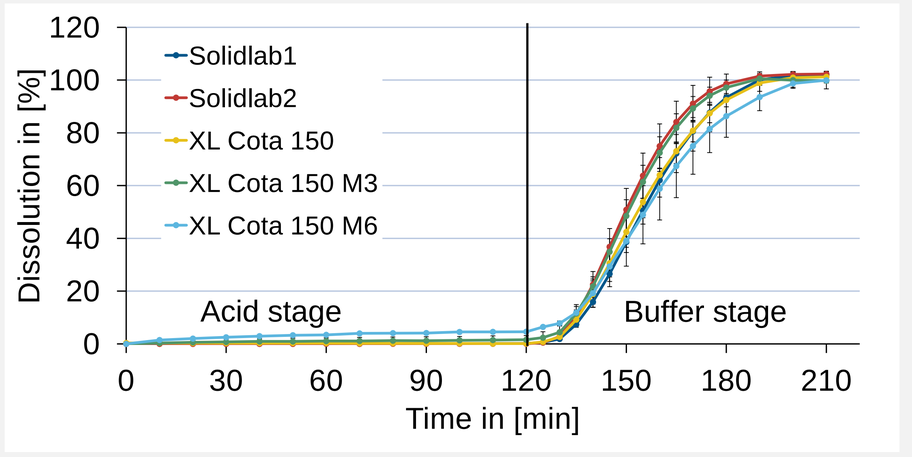
Analysis

SEM Analysis

Solidlab 1	Solidlab 2	XL Cota 150
8.04 %Polymer weight gain.	8.02 %Polymer weight gain.	8.02 %Polymer weight gain.



- Coated tablets show no release in acid stage and rapid API release profile in buffer stage.
- Coated tablets had smooth surface without defects.
- Coating layer thickness is 180 µm (8 % Polymer WG, 14 g/cm²).



Dissolution test (n=6)

Summary

- Paracetamol tablets were coated with Shin-Etsu AQOAT® on Syntegon perforated coating machines.
- The scale up processes were carried out successfully. Total coating process for 120 kg of tablets on the XL Cota 150 was finished within 8 hours.
- 60 ºC hot water was sufficient to clean the machines. No detergent was needed.
- The coated tablets passed the USP dissolution test.
- All coated tablets passed the USP dissolution test after 6 month in climate cabinet (storage conditions T=40 ºC and RH=75 %).

References

1. Seo, K.S.; Bajracharya, R.; Lee, S.H. and Han, H.K. Pharmaceutical Application of Tablet Film Coating. Pharmaceutics, 12, 853 (2020).
2. Shin-Etsu Technical Information A-037.
3. Shin-Etsu Technical Information A-057.
4. Scan me to watch the video on YouTube.

Acknowledgement: We thank Syntegon for their support of the trials on their side.