Scaling up fluidised bed coating of sustained release microparticles at high spray rate using the MicroCoat™ technology

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Introduction

Scaling up fluidised bed coating of microparticles with particle size smaller than 150 µm is a challenge because of the high tendency of particle agglomeration.

Consequently, the production yield of coating trials are unsatisfactory and low spray rate is typically applied leading to long duration of coating process.

The aim of this study is to scale up fluidise bed coating of microparticles at high spray rate using aqueous sustained release polymer dispersions by applying the proprietary MicroCoat™ technology.

Methods

Scaling up microparticle coating using the MicroCoat™ technology

Metoprolol succinate layered microcrystalline cellulose cores (Cellets® 100, D_{50} 144µm) were coated using aqueous Eudragit® NM 30 D dispersion (Evonik AG, Germany) containing 100% talc (w/w, based on dry polymer) as anti-tacking agent.

The coating trials in a Mini-Glatt were conducted with and without the application of the MicroCoat™ technology, whereby a dry powder glidant (magnesium stearate) was periodically added to the coating chamber during the coating process[1].

The coating process was scaled up in a MultiLab® fluidised bed processor (Glatt GmbH, Germany) using placebo Cellets® 100 and the same coating formulation (Table 1).

The product yield was calculated based on the percentage of non-agglomerated, free flowing particles after discharge.

Table 1. Process parameters for polymer coating using Mini-Glatt and MultiLab® systems

	Mini-Glatt	MultiLab®
Batch Size	100g	1kg
Product Temp.	28-30°C	28-30°C
Max. Spray Rate	2.3g/min	10g/min
Final weight gain	120%	40%
With/without MicroCoat™	Both	With

Particle Size Measurement

Sieve analysis was conducted for the coated particles by sieve shaking for 10 min at 70 amplitude. Laser diffraction particle size analysis was performed using a Sympatec particles sizer or Malvern MasterSizer.

Drug Release Measurement

Drug release from coated microparticles was determined in 500mL pH 6.8 phosphate buffer using a USP II apparatus (Copley Scientific, UK) at a paddle speed of 50rpm for 20h. Metoprolol succinate absorbance was measured at λ 274nm. Temperature was controlled at 37±0.5° C. Drug release was measured in triplicate.

Results

Microparticle coating with and without the MicroCoat™ Technology

Significant particle agglomeration and aggregation was observed resulting in a low production yield of 55% without applying the MicroCoat™ technology. 15 and 29% of particles were stuck in the down-flow bed or the filter housing, respectively (Figure 1).

The coated particles showed non-uniform size distribution with smaller particles collected from the down-flow zone (D_{50} 195 µm) and the filter housing (D_{50} 173µm) and much larger particles as free-flowing particles after discharge (D_{50} 285µm) (Figure 2).

Metoprolol release from the particles stuck in the filter housing and down-flow zone was immediate indicating insufficient coating. In contrast, drug release from the free-flowing particles was slow, incomplete and with large variation, suggesting over-coating (Figure 3).

Applying the MicroCoat™ technology completely eliminated particle agglomeration, with no stuck particles found in the filter housing or the down-flow bed (Figure 1). Extremely high production yield was achieved at 99.8%.

The coated particles showed narrow and uniform size distribution (D_{50} 229 µm) (Figure 2). Uniform metoprolol release was achieved from coated particles with complete drug release at 20 h (Figure 3).

Scaling up of microparticle coating with the MicroCoat™ Technology

The coating process was successfully scaled up using the Glatt MultiLab®. High spray rate (10g/min) was achieved. No particle agglomeration or sticking on equipment was noticed with 100% production yield and 92% spray efficiency. The coated particles showed uniform and narrow particle size distribution with 100% particles below 250 and D_{50} of 177µm (Figure 4).

Results

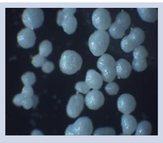
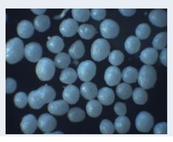
MicroCoat™	Down Flow Bed	Filter Housing	Light Microscopy
Without			
With			

Figure 1. Equipment appearance and light microscopy of coated microparticles following coating without (top) and with (bottom) MIcroCoat™ technology

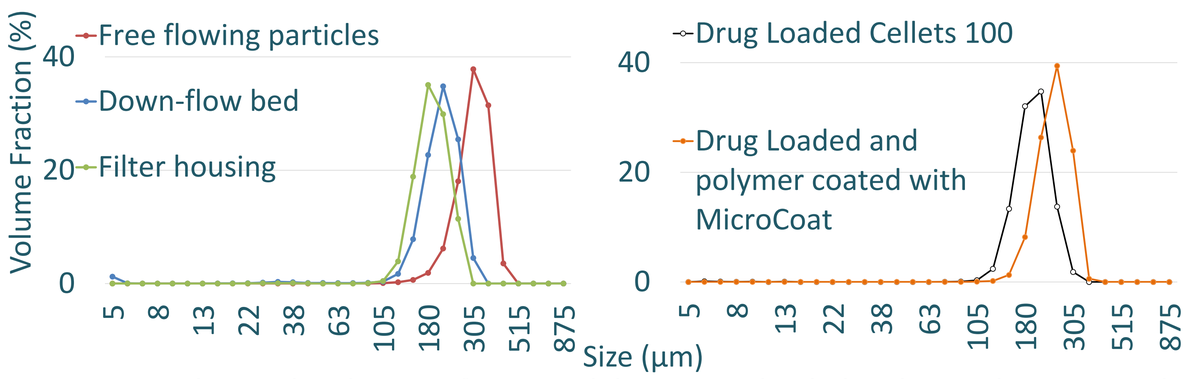


Figure 2. Particle size distribution of metoprolol succinate loaded and coated microparticles using Mini-Glatt by laser diffraction without (left) and with (right) MIcroCoat™ technology

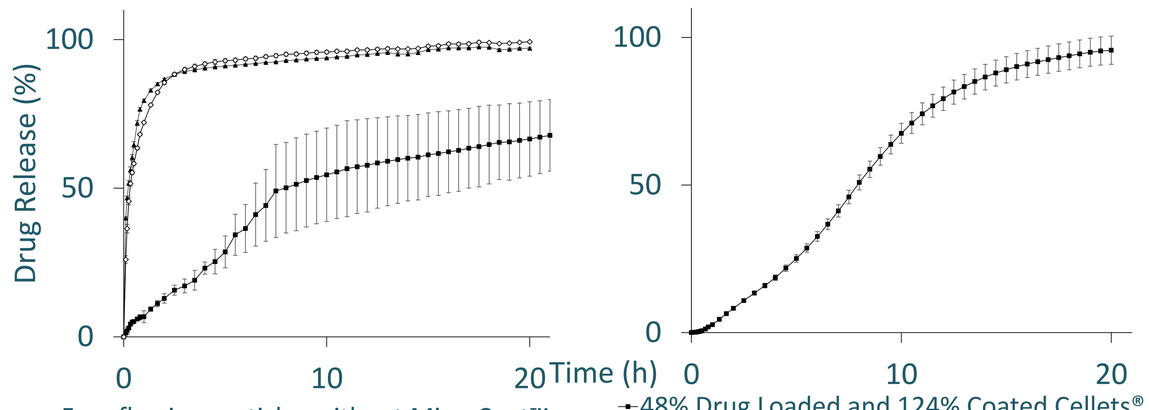


Figure 3. Metoprolol succinate released from coated microparticles using Mini-Glatt without (left) and with (right) MIcroCoat™ technology

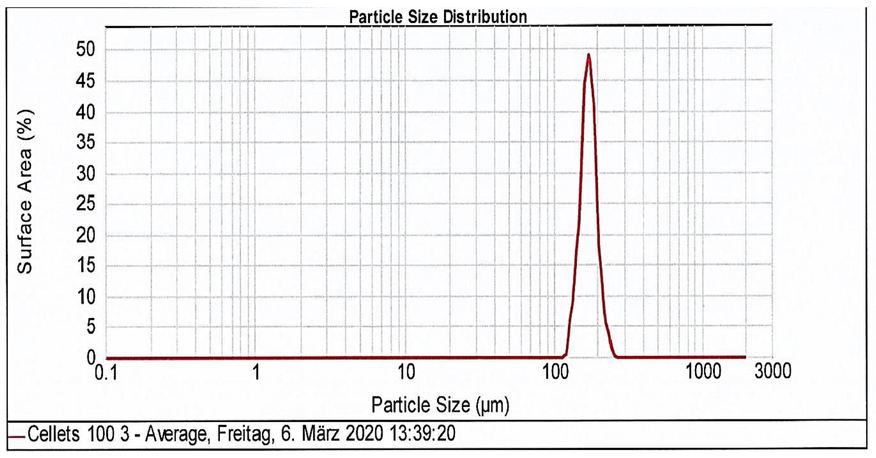


Figure 4 Particle size distribution of coated microparticles (Cellets® 100) using Glatt MultiLab® by laser diffraction

Conclusions

Significant challenge was encountered when coating microparticles smaller than 150 µm using conventional fluidised bed coating, with high proportion of particle agglomeration and sticking to equipment.

This issue was overcome by applying the novel MicroCoat™ technology, achieving high yield, uniform particle size distribution and consistent drug release profiles.

The coating process was successfully scaled up at high spray rate achieving 100% production yield and no particle agglomeration. The scalable production of sustained release microparticles offers a useful approach in developing age-appropriate paediatric formulations.

References

[1] Mohylyuk V, Patel K, Scott N, Richardson C, Murnane D, Liu F. Wurster Fluidised Bed Coating of Microparticles: Towards Scalable Production of Oral Sustained-Release Liquid Medicines for Patients with Swallowing Difficulties. AAPS PharmSciTech. 2019 21:3.