To Determine the Dosing Disk and Encapsulation Speed for Encapsulation of a Drug Product Using Automated Encapsulator

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PURPOSE

The purpose of this research work was:

1) to determine the dosing disk for automated encapsulator in order to obtain the target fill weight during the encapsulation
2) to optimize the encapsulation speed for the encapsulation process

OBJECTIVE(S)

The overall objective of the research work was to determine the optimal equipment setting for an encapsulation process using automated encapsulator

METHOD(S)

- Placebo Direct blend was prepared followed by encapsulation using automatic encapsulator (Bosch 1700). The placebo formulation was selected for this trial as drug load is very low (maximum 1%) and it is representative of the active formulation.
- One common blend was manufactured at a scale of 80 kg comprising diluent, Super Disintegrant, lubricant. The blending was performed using 325 L tote using Gallay tote blender.
- The common blend was split into three batches, where Batch A, Batch B and Batch C were encapsulated with 12 mm, 11.5 mm and 10 mm Size 4 dosing disk respectively using similar fill weight. Each batch was encapsulated at three different encapsulation speeds i.e. 800 (low), 900 (medium) and 1000 (high) caps / min.
- The capsules were polished, and metal checked in-line using Combo Capsule Polisher/ Metal detector; and further check-weighed using Bosch check weigher fitted with Size 4 change parts. The trials were assessed for filling the capsules with target fill weight with minimal weight variation.

RESULT(S)

Physical properties of the blend:

- The physical properties of the final blend (PSD, Bulk/tap density and flow) resulted in acceptable characteristics. The PSD data shows that 70% of the particles were beyond 140 mesh (higher fines) screen. The formulation consists of Microcrystalline cellulose and is a major contributor towards the fines in the blend. Although the flow was characterized as being poor, there were no flow issues encountered during encapsulation.

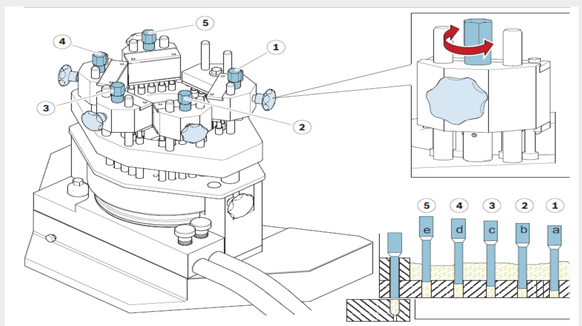
Encapsulation:

- No technical issues were encountered during the encapsulation of Batch A and B, however for Batch C, the fill weight could not be achieved. Hence, no further evaluation was performed on Batch C.
- For Batch A and B, the encapsulation process was stable and consistent (≈ 2 hr. 15 minutes in duration) at three different encapsulation speeds producing a minimal number of rejects. The results show that no significant differences between both batches at different encapsulation speeds. The RSD was less than 2% indicating that the weights were well controlled throughout the encapsulation process. Both Batch A and B batch showed lower % rejects at higher speed (1000 caps/ min) compared to 900 and 800 caps/ min.
- The filled capsules showed no visual defects based on level II AQL criteria for appearance. Overall, the results pertaining to the filled capsules indicate a stable encapsulation process. However, from the % rejects the Batch A showed better weight controls over Batch B. Therefore, based on these results, it is suggested to use 12 mm dosing disc and a target speed of 900 capsules / minute (with ± 100 caps/minute range) for future trials.

Table 1: Physical test results of the direct blend

Test	Data / Process Stage	Direct Blend for Encapsulation
Particle Size Distribution (% Retained)	Mesh Size	Final Blend
	#40 Mesh (425 µm)	0.4
	#60 Mesh (250 µm)	0.5
	#80 Mesh (180 µm)	9.8
	#100 Mesh (149 µm)	8.9
	#140 Mesh (150 µm)	44.3
	#270 Mesh (90 µm)	5.7
	Pan	30.4
Bulk/Tapped Density	Bulk density (g/ml)	0.383 / 0.383
	Tapped density (g/ml)	0.521 / 0.521
	Hausner ratio	1.363 /1.350
	Compressibility Index (%)	26.61 / 25.93
	Flow Character	Poor
Flow	Flow Angle	36.6°
	Flow Index	0.45
	Flow Quality	Poor

Figure 1: Tamping pin adjustment for obtaining target weight using automated encapsulator



CONCLUSION(S)

- The evaluation of the quality of the manufacturing process and product was based on weight control during encapsulation at different speed using different dosing discs.
- Properties of blend and capsules that were of particular interest includes bulk / tapped density, particle size distribution, capsule appearance, closed length and weight variation and hence they are considered as critical quality attributes of the encapsulated drug product.
- In conclusion, the encapsulation trials conducted at three different speeds using 12 mm and 11.5 mm dosing disc had no technical concerns except for 10.5 mm dosing disc. The 10.5 mm dosing disc failed to achieve the target fill weight and may not be suitable for this product. Based on the results, 12 mm dosing disc and 900 ± 100 capsules/minute encapsulation speed is recommended for all future trials.

REFERENCES:

1. Wagner, B., Brinz, T., Otterbach, S. and Khinast, J., 2018. Rapid automated process development of a continuous capsule-filling process. International journal of pharmaceutics, 546(1-2), pp.154-165.

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