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Short communication

Assessment of pellet mixture segregation during machine capsule filling

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Introduction

Pellet capsule filling process supports possible combining of different types of pellets, which however can exhibit different physical properties. Since pellets are considered to have excellent flow properties, they are generally considered to be filled into capsules easily, but at the same time they are also much more subjected to potential segregation processes (Chopra et al., 2022). In experimental segregation studies researchers experimentally treated various materials under vibration conditions (Jain et al., 2013), but not pharmaceutical pellets. Studies of pellet encapsulation are also rare in the literature.

Materials and methods

Four different types of pellets were used (Table 1): two sizes of sugar spheres (NP1 and NP2), film-coated pellets colored by Tartrazine (TP) and bigger, prolonged release pellets (PR). Pellets were evaluated for their size using Camsizer XT. Their bulk and tapped density were analyzed and Carr index and Hausner Ratio were calculated. Revolution Powder Analyzer was used to evaluate flow properties of pellets. Surface of pellets samples was evaluated with SEM, while particle surface roughness (Sa) was assessed with the use of confocal microscopy. Two-component pellet mixtures, composed of two different types of pellets and 0.3% Talc as antiadhesive, were prepared in 20 L mixing bin at 22 rpm and 5 min of mixing time. Capsule filling was than performed using pilot scale Bosch GKF 702 capsule filling machine (Table 1). In the first set of experiments (set A) a mixture was dispensed to hopper directly from the mixing bin and in the second set of experiments (set B) vacuum transport was used.

Table 1. Performed capsule filling experiments with pellet component ratios and properties

Exp.	Mixture composition	Assumed difference in properties
P1_A/B	PR:TP (1:1)	(Δ D(4,3)~400 µm), ≠ Sa
P2_A/B	PR:NP1 (1:1)	(Δ D(4,3)~400 µm), ≠ Sa
P3_A/B	TP:NP1 (1:1)	Same size, ≠ Sa
P4_A/B	TP:NP2 (1:1)	(Δ D(4,3)~100 µm), ≠ Sa

Optical method, which was able to systematically assess the ratio of the components in the capsules during the entire capsule filling process, was developed, validated and used to demonstrate time-dependent segregation trends during the entire encapsulation process with average ratios demonstrating trends of global segregation, and SD values local inhomogeneity of capsulated pellet mixtures.

Results and discussion

In all experiments where pellets of different sizes were mixed and filling process was carried out directly from the capsule machine hopper, the observed global trend of segregation is present (Fig. 1). First and last capsules are dominated by larger component, and during the middle of filling process the component mass ratio reverses in favor of smaller pellets. Larger particles in the first capsules can most likely be attributed to segregation due to air entrainment/ fluidization during the free fall. In the next phase, during machine run causing external vibrations,

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percolation mechanism likely prevailed, due to which the smaller particles traveled downstream the particle bed faster than the larger ones. In experiment P3_A where the same sized pellet components were mixed (TP and NP1) (Table 2), the mass ratio of pellet components NP1 to TP is around 1 throughout the whole process and as expected the global segregation is not present.

Table 2. Results of pellet component evaluations in terms of particle size, flow properties estimates and surface roughness

Comp.	D(4,3)	Carr index	Hausner ratio	Angle of repose	Sa
	[µm]	[%]	[/]	[°]	[µm]
NP1	690	3.70	1.04	29.9	0.34±0.05
NP2	824	3.70	1.04	30.3	0.35±0.05
PR	1100	1.72	1.02	25.4	0.37±0.08
TP	714	8.47	1.09	30.1	0.29±0.05

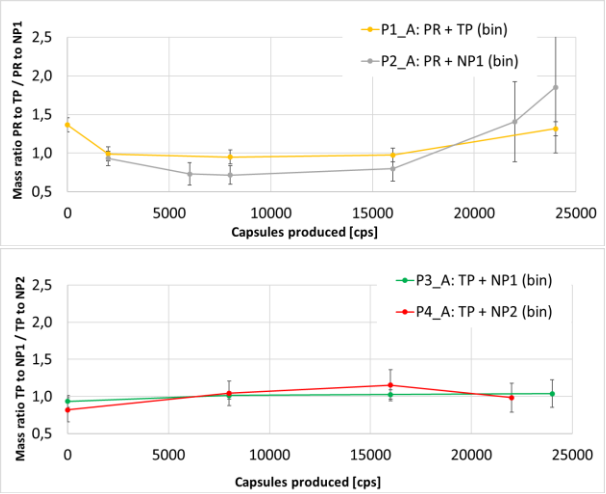

Fig. 1. Mass ratios of pellet components in capsules through the capsule filling process for all Exp. where mixture was dispensed directly from the mixing bin (A).

Comparing capsule filling experiments P1_A and P2_A, the global segregation is more pronounced in case of combining uncoated and coated pellets (P2, component mass ratio varied from 0.72 to 1.85). In case of combining only coated pellets (P1), mass ratios were between 0.95 and 1.37. As both second components (TP and NP1) in mixture with PR pellet component were of practically the same size, one can deduce that higher interparticle friction between both coated pellet types (PR and TP) was higher in comparison with the coated and uncoated pellet system (PR and NP1) as segregation was less pronounced in case of experiment P1_A. Components of Exp. P3_A (TP and NP1) had the same size and different surface properties (Table 2), but the segregation of the mixture was not observed, which demonstrates dominant influence of size differences. Surface related component properties will however modify the extent of segregation.

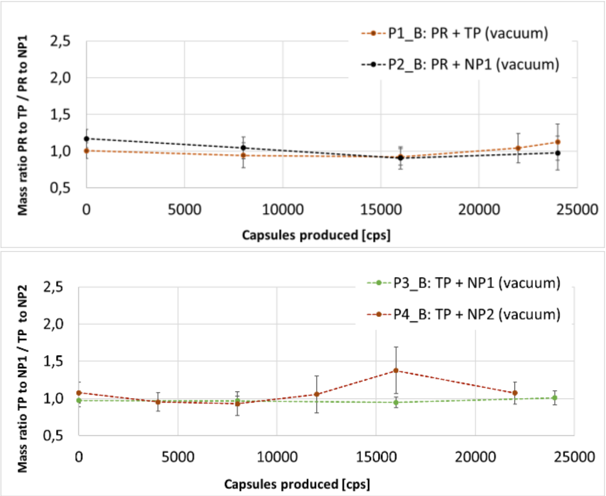

Fig. 2. Mass ratios of pellet components in capsules through the capsule filling process for all experiments, where vacuum transport was used (B)

In the case of using vacuum transport system (Fig 2), the global segregation was substantially reduced in capsule filling experiments P1_B and P2_B and for experiments P3_A and P3_B, the results are comparable for both ways of filling. In the case of the P4 experiments set, vacuum transport caused greater segregation than the gravity filling from a mixing bin (Fig. 1, Fig. 2).

Conclusion

Optical method, which was able to systematically assess the ratio of the components in the capsules during the entire capsule filling process, was developed and used to demonstrate time-dependent segregation trends during the entire encapsulation process. The results prove that global segregation and local inhomogeneity can only be avoided if we combine pellets of comparable sizes.

References

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