Macedonian pharmaceutical bulletin, 69 (Suppl 1) 197 - 198 (2023)
Online ISSN 1857 - 8969
DOI: 10.33320/maced.pharm.bull.2023.69.03.097
Short communication

Fluid bed film coating of cohesive Geldart group C Ibuprofen Lysine powder

Katerina Arsova[1], Oja Ali Memed[2], Tamara Ivanovska[2], Elena Cvetkovska Bogatinovska[2], Lina Livrinska[1], Dusko Shalabalija[1], Maja Simonoska Crcarevska[1], Nikola Geskovski[1], Marija Glavas Dodov[1], Katerina Goracinova[1*]

[1]*Institute of Pharmaceutical Technology, Faculty of Pharmacy, University Ss Cyril and Methodius in Skopje, Mother Teresa 47, 1000 Skopje, N. Macedonia*
[2]*Research & Development, Alkaloid AD, bul. Aleksandar Makedonski 12, 1000 Skopje, N. Macedonia*

Introduction

The problem of poor flow properties and fluidization of fine and ultrafine bulk material (fine, d < 100 µm and ultra-fine, d < 10 µm) spans half a century accompanied with the efforts to find a solution to improve their processability while keeping the particles small. Ultrafine particles are dominated by cohesive forces (Van der Waals forces, electrostatic forces), and therefore when fluidized they develop channeling and cracks through which the gas tend to bypass the solid material thus resulting in poor contact and mixing accompanied with increased tendency to form agglomerates. To increase the efficacy of particle coating and decrease the degree of agglomeration for cohesive powders like Ibuprofen Lysine (IbuL, Hausner index 1.95, Geldart group C), the parameters affecting the process (coating solution, inlet air temperature, air flow rate, pressure of spraying liquid and spray rate) have to be carefully adjusted and optimized. Fluidization dynamics may also be improved by assisted fluidization technique using pulsation of the inlet flow to the fluidized bed, introduction of acoustic vibrations during fluidization and addition of external particles of Group A, B, D or nanoparticles to the bed of Group C particles to suppress hysteresis and reduce or overcome generation of agglomerates (Zhou and Zhu, 2021).

The objective of this study was to perform polymer film coating of a very fine cohesive pharmaceutical powder IbuL (d(50) 5.136 µm; d(90) 13.070 µm) via fluid bed processing using 0.5% aqueous hydroxypropyl methyl cellulose (HPMC) as a coating solution, while maintaining fluidization during the coating process with addition of external particles (1.0 mm glass beads, density of 2.50 g/cm3) to the fine powder as a fluidization aid. The influence of the coating process on the powder properties was explored by evaluating the powder flow properties, particle size & particle size distribution, and by analysis of the FTIR, NIR and Raman spectra of IbuL coated powders.

Materials and methods

Coating procedure was performed in Fluid bed - Wurster coater VFC-LAB MICRO FLO-COATER, (Freund-Vector Corporation, USA) with a classical air-distributor plate and a top-spray arrangement. 0.5% HPMC, Methocel E5, Dow Chemicals, was used as a coating solution. Fluidization behavior of the mixtures of the glass beads and the IbuL (Ph Eur grade) particles during the coating process were reproducible at a ratio of 1:1, airflow set at 105 LPM, inlet air temperature of 55 °C, nozzle atomization pressure 0.5 bars, pump speed 10 rpm (0.7g/min).

Raman spectra were recorded using ATR 3000DH (Optosky, China) instrument. Scans were performed using a fiberoptic probe under the following conditions: laser power 400mW, integration time 60s, resolution 8 cm^{-1}, range 190-2000 cm^{-1}. NIR spectra were recorded using MicroNIR 1700 ES (Viavi, USA) instrument under the following conditions: scan resolution 40 cm^{-1}, spectral range 11000-6000 cm^{-1}, integration time 10s. FTIR spectroscopy was performed using Diamond ATR-FTIR, Carry 600 (Agilent, Germany) under the following

*kago@ff.ukim.edu.mk

conditions: resolution 4 cm^{-1}, 32 scans per spectrum, and a range of 4000 to 650 cm^{-1}. Particle size analysis was performed on Mastersizer 2000 particle size analyzer (Malvern, UK), using Scirocco 2000 automated dry powder dispersion unit at dispersion pressure of 3 bars.]

Results and discussion

Fluidization behavior of the mixtures of the glass beads and the Ibuprofen Lysine particles at the described process conditions were reproducible despite the large difference in particle sizes at a ratio not less than 1:1. Particles were fluidized as a very loose fragile clusters, not as an individual microparticles. The larger agglomerates were positioned at the bottom, and during the spray coating they were broken into smaller clusters which fluidized smoothly at the top of the fluidizing bed. Experimental results demonstrated that the spray rate and atomization air pressure were the factors differentiating between the coating and agglomeration. When these conditions are optimal particle coating can be achieved with acceptable agglomeration ratio. Having in mind that the effect of the atomization pressure on the droplet size is linear, in order to produce small droplets with narrow distribution and to avoid over wetting, the nozzle atomization pressure was increased to 0.5 bars and the liquid spray rate was decreased below 1g/min.

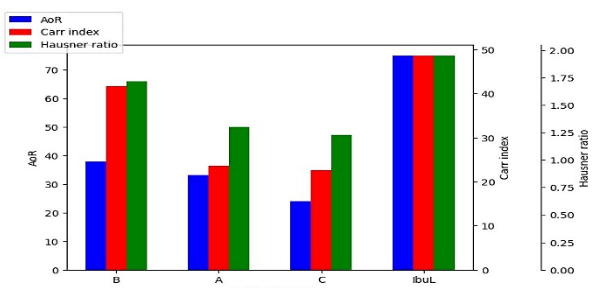

Fig. 1. Values of the Carr index, angle of repose (AoR) and Hausner ratio for IbuL and samples A, B and C.

The results from Angle of repose (AoR) of IbuL fluid bed coated powder analysis point to improved flow character from very, very poor (IbuL, AoR above 66^0) to fair (50g IbuL powder thin film coated with 108 mg HPMC, sample A, AoR=36.55^0) and good (50g IbuL powder thin film coated with 180 mg HPMC, sample B, AoR=32.820, Aor, Hausner ratio and Carr index are presented in Figure 1). In comparison, the AoR values for different types of microcrystalline cellulose for direct compression are in a range of 30 - 36 degrees. The particle size of coated Ibuprofen Lysine particles pointed to slight increase in the d(50) and acceptable agglomeration ratio of particles fluidized with addition of glass beads, compared to the particles coated without glass beads as a fluidization aid (Figure 2). The accumulated difference in volume frequency between coated IbuL and IbuL, used to evaluate the degree of agglomeration, pointed to a range of 5 (27 min process) – 7% (45 min process) agglomerates during the process of coating with addition of glass beads, or without glass beads addition 70 – 100% (27 or 1h process, respectively) (Zhou and Zhu, 2021).

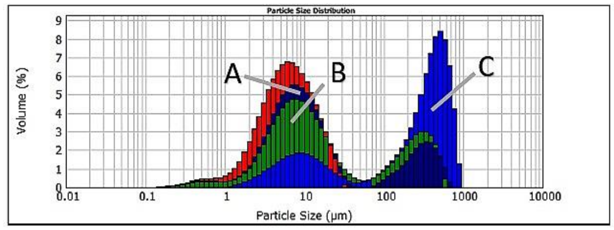

Fig. 2. Particle size distribution of IbuL (red), coated IbuL + fluidization aid (A - 27 min coating process; B - 45 min coating process), coated IbuL without fluidization aid (C - 27 min coating process)

IbuL peaks were dominant in the FTIR, Raman and NIR spectra of the thin film coated powders. The lack of characteristic absorption bands shifting or appearance of new bands suggest that neither chemical interaction nor hydrogen bonding occurred between ingredients. Raman spectra intensities were affected by the sample matrix effect, such as the particle size of the powder sample. In addition, this effect was seen in FT-NIR spectra where the y-axis was observed to be responsive to the difference in particle size with higher values for absorbance corresponding to larger particle size.

Conclusion

Our preliminary experiments point that Ibuprofen Lysine powder with a median diameter 5.136 micrometers can be coated with a thin film in a top spray fluidized bed granulator with acceptable agglomeration by addition of external particles in order to improve and maintain fluidization during the process. Thin film coating improved the flow properties of this cohesive particles from very, very poor to fair or good depending upon the level of coating. Experiments whether the increased level of coating will further improve the powder flow properties are still in progress

References

Zhou, Y., Zhu, J., 2021. A review of fluidization of Geldart Group C powders through nanoparticle modulation. Powder Technol., 381, 698-720. doi: 10.1016/j.powtec.2020.12.011