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Note

Some variables influencing rotoagglomeration in the multiprocessor MP-1

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Abstract

Pellets are of great interest to the pharmaceutical industry for variety reasons, e.g. flexibility in dosage form design and drug efficacy improvement. Rotoagglomeration is the novel method for their production using rotoprocessors or rotogranulators allowing one-piece equipment operation. However this process is sensitive and includes numerous variables that have to be optimalized for successful result—spherical pelets of desired properties. This paper is contributing to study some of them: liquid amount, its spray rate and input powder amount and their influence on lactose-microcrystalline celulose pellet properties. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Pellet; Rotary processor; Liquid saturation; Lactose; Microcrystalline cellulose; Roundness

Pelletization is the process of converting powders into spherical particles of desired size and mechanical properties. Such particles then can be coated successfully and are optimal for the controlled release medicaments. Pellets have good flow properties that are useful in exact metering processes, e.g. capsule filling (Vertommen et al., 1997). The currently popular methods for producing pellets are processes of extrusion and spheronization and suspension or solution layering on inactive seeds in fluid-bed equipment. Rotoagglomeration using centrifugal equipment allows formation, drying and coating, if desired, all in one equipment and in a continuous process.

Cetrifugal equipment (rotoprocessors, rotogranulators) consists of many components that are utilized in fluid bed units, e.g. air handling system, product chamber, expansion chamber, filtration device and spray systems. The uniqueness of centrifugal processing equipment lies mainly in the use of rotating discs (Goodhart, 1989). Combined action of three forces: centrifugal, fluidization air and gravitational, acting upon the product from different directions, generates a spiral rope-like material motion. Rapid turnover rate is responsible for the high efficiency of centrifugal equipment. Another distinct feature of centrifugal equipment is the spray method. The spray nozzle is immersed in the product and liquid is sprayed in the direction of pellet movement. This design partially accounts for the reproducibility and efficiency of the process.

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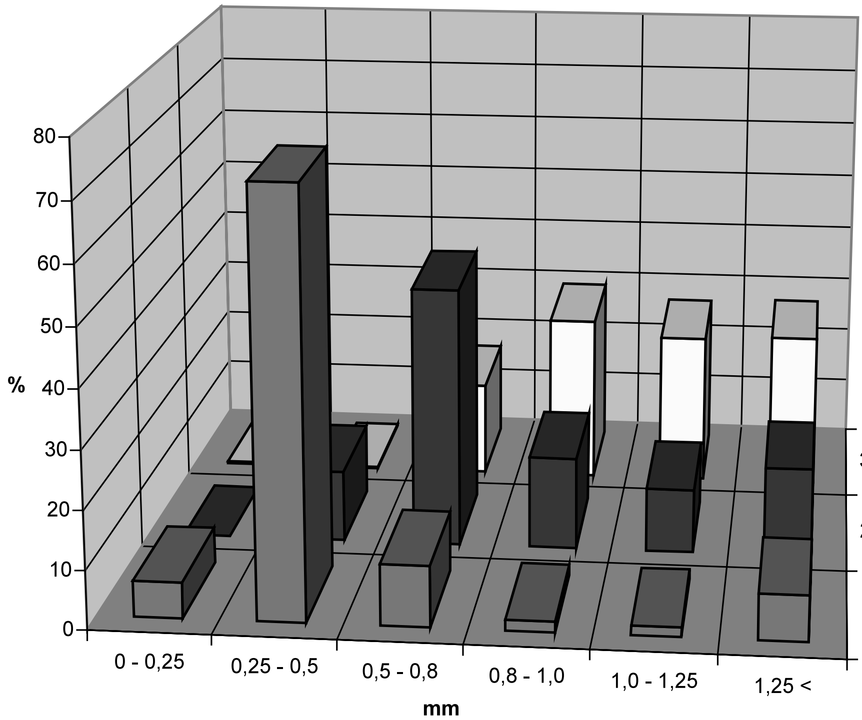

Fig. 1. The influence of the water content on the pellet size distribution.

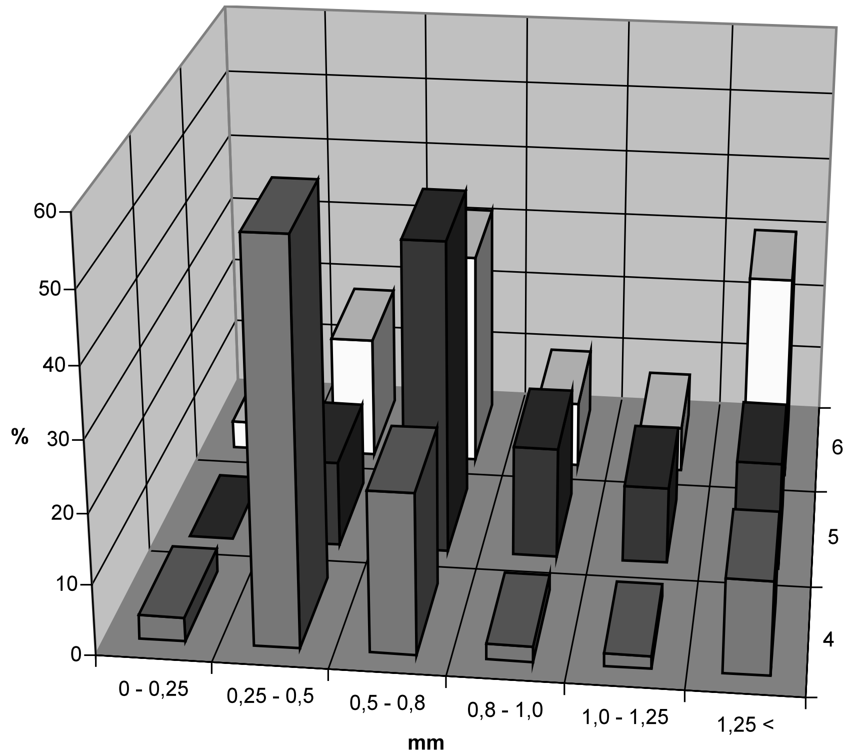

Fig. 2. The influence of the spray rate on the pellet size distribution.

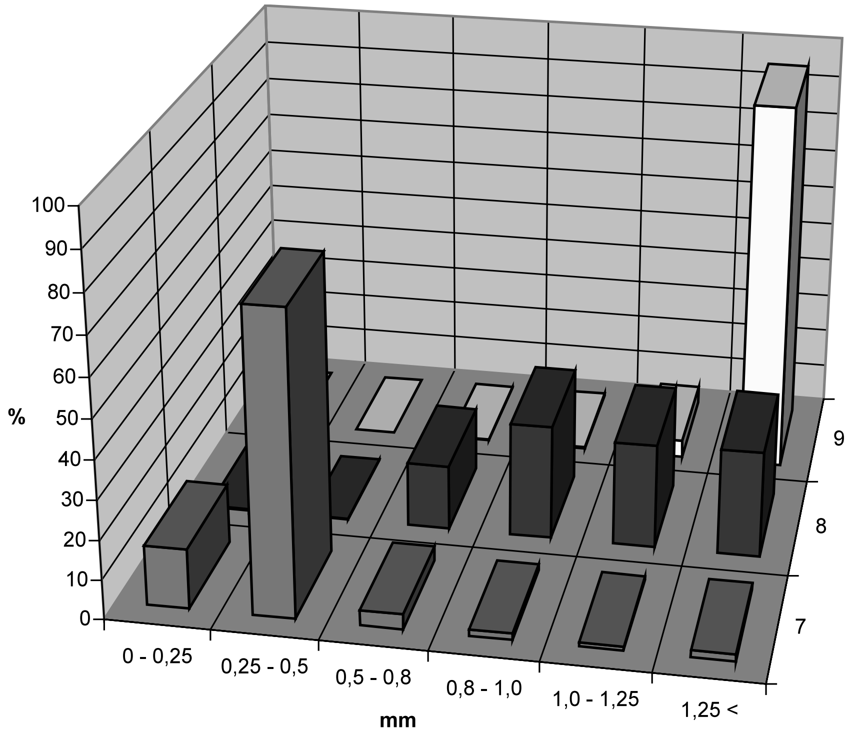

Fig. 3. The influence of the amount of input powder on the pellet size distribution.

Rotoagglomeration process is however sensitive and there are numerous variables influencing the process. The variables, that govern the manufacture of pellets in centrifugal equipment, are including formulation variables (properties of active ingredient and excipients, e.g. particle size, solubility, plasticity, and their formulation ratio) and process variables such as temperature, pressure and air flow at wetting, agglomeration, spheronization and drying stages, speed of wetting, rotor speed in wetting operation and spheronization, load during agglomeration and spheronization and many others (Rabišková, 1998).

The aim of this paper is to describe the influence of water content, spray rate and load on size, size distribution and some other properties of pellets produced in rotary processor by the rotoagglomeration technique.

α-Lactose monohydrate (type 200M), microcrystalline cellulose (Avicel®, type PH-101) were used as starting materials. Demineralized water was used as granulation liquid. All materials were Ph. B. resp. Ph. Eur. quality.

Lactose and microcrystalline cellulose were mixed for 5 min in Stephan mixer (type UMC 5, Stephan and Söhne GmbH and Co, Germany) to homogenize the powder mixture. One kilogram (800, 1200 g) of powder blend was loaded into the

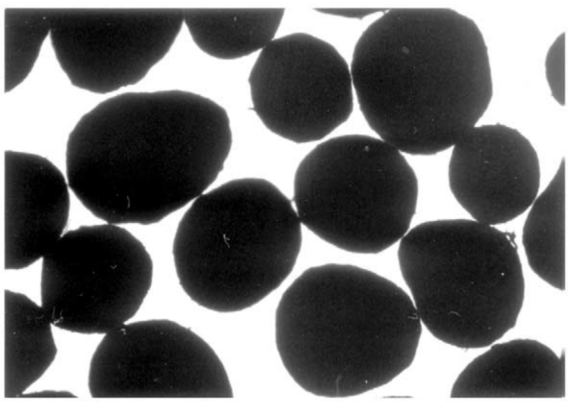

Fig. 4. Pellets of sample 2. Magnification 40 times.

Table 1
Mechanical properties of prepared pellets

Sample (main fraction)	Hardness (kg)	Friability (%)
1[a]	–	1.92
2	0.354	1.65
3	0.369	0.73
4	–	1.86
5	0.354	1.65
6	0.348	1.71
7[a]	–	2.04
8	0.369	0.73
9	1.300	2.41

[a] Samples could not be tested for hardness because of small size.

inner bowl of the rotary processor (MP-1, Aeromatic-Fielder AG, Bubendorf, Switzerland). Water was sprayed into the container at the indicated rate with the aid of a peristaltic pump (type 504 U, Watson–Marlow Ltd., UK) using 0.8×10^5 N/m^2 of atomization pressure. Once all the water was sprayed, spheronization was performed at the specified rotor speed, i.e. 1800 rpm for 2 min. After completion of the pellet formation, the pellets were dried at 50 °C by lifting the inner container of Rotoprocessor.

Size and size distribution of samples were determined by sieve analysis, pellet shape was observed in optical microscope (type DN 45, Lambda Praha, CZ) with ccd camera, the friability was measured in addapted friabilator Erweka (type TAR 10, Erweka, Germany) using glass beads and pellet hardness in tablet hardness tester equipped with C5 load cell (Eng. Systems, Nottingham, UK).

The three series of samples were produced in rotary processor. The amount of water in powder mixture has been changing in series one: samples 1, 2, 3 (29.0%—1, 29.3%—2, 29.6%—3). The spray rate varied in the series two: samples 4, 5, 6 (20 g/min—4, 30 g/min—5, 40 g/min—6). The amount of input powder changed in the series three: samples 7, 8, 9 (800 g—7, 1000 g—8, 1200 g—9). Figs. 1–3 indicate pellet size distribution for each series. The results are showing that the low input powder amount, lower water content and slow spray rate lead to small pellets. On the other hand high input powder amount, higher water content and faster spray rate cause bigger pellet size. The input powder amount 1000 g, water content 29.3% and the spray rate 30 g/min were found optimal for used equipment and the proposed formulation. These values were supported also by the other pellet characteristics: shape (Fig. 4), mechanical properties (Table 1). The spheronizing plate rate during wetting is also very important process parameter and has to be carefully changed within the process.

Acknowledgements

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