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Comparative Dissolution Study of Coated Pellets Containing Microcrystalline Cellulose and Lactose As Core Materials

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1. Introduction

A Multiple Unit Pellet System (MUPS) is a solid pharmaceutical dosage form is built up by many pellets. These small particles can be matrix pellets in which the active pharmaceutical ingredient (API) is distributed equally in the whole integrity of the particle (homogeneous) or are of the layered type (heterogeneous) when the API is layered on the surface of spherical inert cores which serve as starting excipients for pharmaceutical pellet manufacturing. Further use may be advantageous for the preparation of modified release preparations (capsules, tablets) [1].

Their application offers a lot of benefits; not only technological but also physiological, and therapeutical points of views. When the route of administration is oral (per os), these systems have a lower chance to irritate the mucosa trough the gastrointestinal tract compared to a single-unit system, such as a non-disintegrant tablet. MUPS can easily reach the duodenum thanks to the small size of the particles, and this is independent of the stomach emptying.

In a MUPS the total dose of the active ingredient is divided over the subunits that make up the system. The odds of a single unit dosage form to fail their modified release is much higher than in the case of a MUPS, thus the chance of dose dumping effect is very low. The number and quality of particles within a MUPS can be easily changed, resulting in numerous benefits to the system. For example, drug load can be easily adjusted. The use of subunits (pellets) with different drug release within a dosage form can provide an initial and sustained dose of the active ingredient. Incompatible drugs within a single dosage form can be administered. The plasma concentration fluctuation can be minimalized. The pharmacokinetic behavior is more reproducible and the intra/inter-subject variability is lower compared to conventional formulations [2].

2. Materials and methods

Lactose (Lactopress® granulated; DFE pharma, Germany) and powder grade microcrystalline cellulose -MCC (Vivapur®101, JRS Pharma GmbH & Co., Germany) were used for the preparation of MCC and MCC/lactose neutral cores.

The different ratios of MCC/lactose blend were wetted with an appropriate amount of purified water; after which the wet masses were extruded using a single screw extruder (Caleva Process Solutions Ltd, United Kingdom). The extrudates were subsequently rounded in a spheronizer (Locost Kft, Hungary), followed by drying at 50 °C in an oven (WTB Binder, Germany) for 24 hours and sieved through a 1100 mm and a 700 mm mesh. Caffeine (Hungaropharma Zrt., Hungary) was layered onto the various inert cores in a fluidised bed coater (Strea I.; Aeromatic-Fielder AG, Switzerland). The drug-layered spheres based on MCC or different types of MCC/lactose cores were coated with an acrylic polymer, Eudragit LR30D (Evonik Industries AG, Darmstadt; Germany) [3, 4].

To evaluate the morphological properties (size and shape) of the samples 4K (Ultra High Definition) definition photos were recorded, using both 2D and 3D measurements, utilizing a Keyence VHX-970 F Digital Light Microscope with 20 – 200× lenses (Osaka, Japan). The dissolution test was carried out using a Hanson SR8-Plus dissolu-

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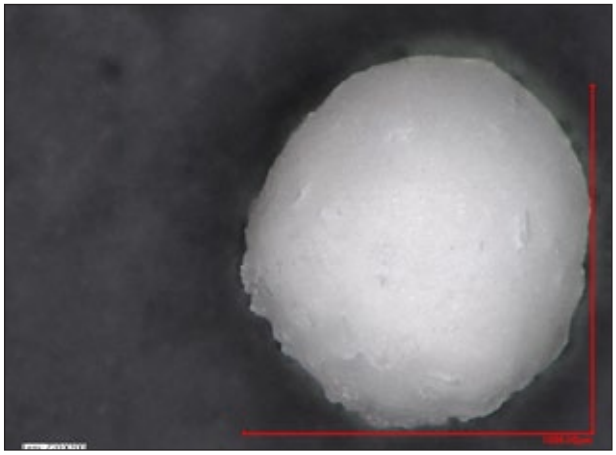

Figure 1 *Microscopic image of inert pellet core of 75% MCC and 25% lactose*

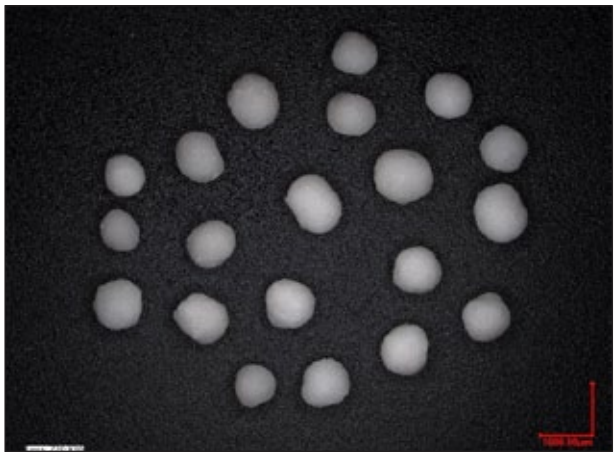

Figure 2 *Microscopic image of inert pellet core based on MCC/lactose according to analysis*

tion test station (Hanson Co., Chatsworth, CA). The drug concentration was measured spectrophotometrically (Agilent 8453 UV–Vis spectrophotometer; Agilent Technologies, Germany).

3. Results

Pellets consisting of various proportions of MCC/lactose were successfully prepared by extrusion-spheronization. The shape parameters of the particulates were appropriate and thus the pellets were suitable for further processes (layering; coating). The pellets based on different types of inert cores resulted in different dissolution profiles.

4. Conclusions

The major objective of this study was to evaluate and compare the effect of the composition of the pellet core on the in vitro drug release profile. Starter cores containing MCC or a blend of MCC and lactose in various ratios were layered with the model drug (caffeine) and were coated with an acrylic polymer. The quality and quantity of excipient used to produce the neutral pellet core are remarkably important from both the production and drug release point of view.

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