Evaluation of Xcelodose® Micro-dosing Technology to Overcome Variations in Powder Flowability

C. Andrés1, V. Bérard1, M. Savill2

1. Laboratoire de Recherches sur la Réactivité des Solides (CNRS UMR 5613), Université de Bourgogne, UFR Pharmacie, 7 Bd Jeanne d’Arc, F-21033 Dijon Cedex, France
2. GB Innovem Ltd, Cambridge Research Centre, Building 4, Granita Park, Great Abington, Cambridgeshire, United Kingdom

• Purpose:
To assess the capability of the Xcelodose® system for precision filling of powders with varying flowability.

• What is the Xcelodose® system?
This instrument (1) dispenses powder from a dispense head (2), through a mesh of the base of the dispense head (3). The powder is released by the lapping action of a sintered on the dispense arm (4). Capsules are fed through the system from a capsule feeder. The capsules are automatically oriented, opened, dusted, measured, and placed in either the 'good' or 'bad' hopper depending on a number of different criteria. Accurate weight control is achieved by monitoring the weight being dispensed continuously. As the weight approaches the target, the rate of delivery of the powder is reduced, then stopped. There is a brief settling time while the final weight is confirmed, during which time the dispense head is moved away from the dispensing location. After this the capsule of powder is automatically closed, length checked and placed into the good or bad hopper.

• Methodology:
To generate a wide range of flowability characteristics, two powders with extreme rheological characteristics were chosen: microcrystalline cellulose with good flowability and maize starch with very poor flowability.

1. Binary mixes of these materials were produced containing 0% to 100% w/w of microcrystalline cellulose by steps of 10%.
2. Each material was characterized in terms of particle size, shape, surface area, and powder bed packing properties.

• Results:
Tests were carried out on an eccentric tablet press (EKO, Kocho) to evaluate the industrial flowability characteristics of each mix.

100 capsules containing 2 mg or 50 mg of powder of each mix were then filled using an Xcelodose® 600 system, respectively with FP dispense head (41 holes of 400 µm diameter) and JY dispense head (123 holes of 600 µm diameter). Contrary to constructor specification, type of head was adapted for each binary mixes and remains constant throughout the test. Weight uniformity and fill times for each capsule were also recorded.

• Conclusions:
The method of filling used by the Xcelodose® system is very original compared to the traditional methods and this study shows that it is not sensitive to the flow properties of the powders. Poor flowability is a common characteristic of drug powders at the early stages of their development. The Xcelodose® system is an efficient method for micro-dosing of drugs exhibiting poor flowability and it offers a convenient way for precision dosing of such powders into capsules.

• powdered characterization:
Rheological properties of each mix are first assessed with Stampfvolumeter (STAV 2003). The bulk density is calculated from the volume of powder after pouring into the cylinder, and the tap density is obtained from the volume after 1250 taps. From these data, Hausner ratio is calculated.

With the Xcelodose® system, the situation is very different: contrary to the traditional techniques of gravimetric filling, the weight uniformity do not deteriorate with the decrease in powder flowability and an accurate and repeatable flow of powder properties. Indeed, the coefficient of variation of weight remains below 1% for 50 mg capsules and below 2% for 2 mg, even for the mix containing more than 60% of starch.

There is no common point between the percentages used usually to evaluate the flow properties of a powder and the response obtained by the Xcelodose® system. In particular, it appears on the curve of the evolution of weight coefficient of variation, according to the weight fraction of microcrystalline cellulose in the mix, that there is a progressive increase of the coefficient of variation of the target weights from 0.5% to 55%.

The mixes containing more than 60% of starch prohibited any automatic tablet press.