

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

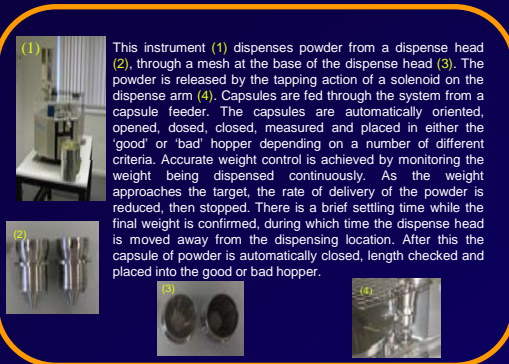
C.Andrès<sup>1</sup>, V. Bérard<sup>1</sup>, M. Savill<sup>2</sup>

- 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
- GB Innomech Ltd, Cambridge Research Centre, Building 4, Granta Park, Great Abington, Cambridgeshire, United Kingdom

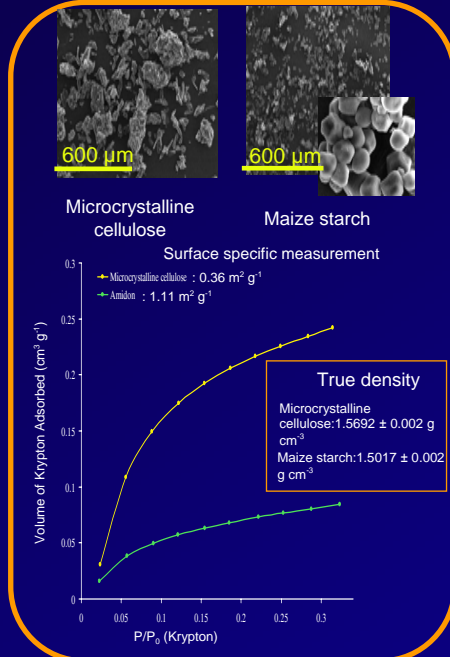
## • Purpose:

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

### • What is the Xcelodose® system ?



## • Powders characterization:



## • 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.

11 binary mixes of these materials were produced containing 0% to 100% w/w of microcrystalline cellulose by steps of 10%.

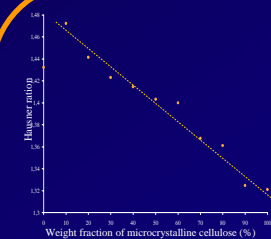
Each material was characterized in terms of particle shape, size, material density and powder bed packing properties.

Tests were carried out on an eccentric tablet press (EKO, Korsch) 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 of constructor specification, type of head are not adapted for each binary mixes and remains constant throughout the test. Weight uniformity and fill times for each capsule were also recorded.

## • Results:

### • Mixes characterization:

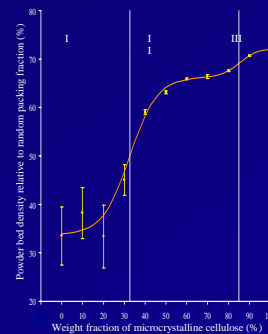


Rheological properties of each mixes are first assessed with Stampfvolumenometer (STAV 2003). The bulk density is calculated from the volume of powder after turning over the cylinder, and the tap density is obtained from the volume after 1250 taps. From these data, Hausner ratio is calculated.

The value of Hausner ratio decreases with the increase of the weight fraction of microcrystalline cellulose in the mixes. Inversely, it points out that the flowability of the mixes should decrease with the proportion of starch.

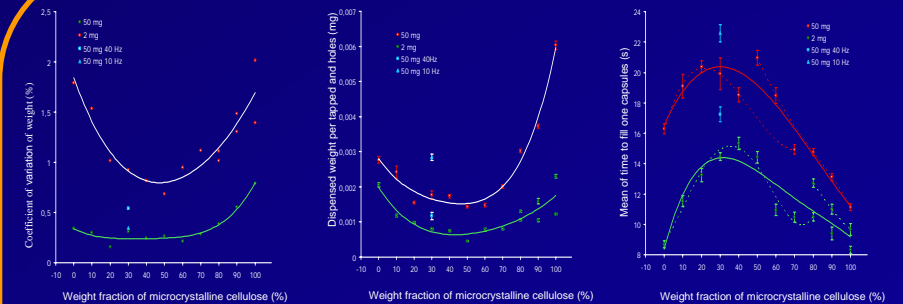
Tests on eccentric tablet press consist for each mix to product 30 tablets with an aim of evaluating their capability to fill the matrix in a reproducible way. The powder bed density relative to random packing fraction is estimated from the average bed powder density and packed density. Its evolution according to the weight fraction of microcrystalline cellulose shows:

- 1- a strong reduction of its value when the quantity of starch increases. That indicates a clear reduction in the flowability. In parallel, one observes a progressive increase of the coefficient of variation of the tablet weights from 0,5% to 50%.
- 2- the shape structure indicates the existence of three different structures of the powder beds (essentially similar with that (I) of the starch, (II) of the cellulose, (III) new powder bed structure).



The mixes containing more than 60% of starch (I) prohibited any automatic tablet production.

### • Xcelodose® system study:



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 achieved the weight specifications irrespective of powder flow properties. Indeed, the coefficient of variation of weight remains below 1% for 50 mg capsules and below 2% for 2 mg, even for the mixes containing more than 60% of starch.

There is no common point between the parameters 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, a minimal value at the middle of the powder blend range (40% - 50% cellulose). These minimal values are respectively 0.3 % for 50 mg capsule and 0.7% for 2 mg.

To better including the existence of this minimum, the quantity of delivered powder is considered in terms of weight powder delivered by solenoid tap and by hole present in the dispense head.

It appears that there is also a minimal value for the dispensed quantity: it thus seems obvious that, for the mix containing 50% of cellulose, the coefficient of variation of the weight is minimal because the elementary quantity distributed by the system is also minimal. In parallel, the time require for the capsule filling should be a maximum value because, in all logic, it needs more tapping action to reach the target mass. In fact, the graph of the average time appears more complex: the optimum is moved towards the large proportion of starch and several distinct parts of functions are visible. However, it must be considered that the problem of time required for a capsule filling is complex since it is necessary to take into account the time required by the system to carry out a weighing.

Independently of any other consideration, it is clear that the process of filling implemented by the Xcelodose® system is very different from the traditional processes of filling. This system, finally which acts like a salt box, will require probably new conceptual tools to understand its dynamic behaviour. In particular, it seems essential to define new relevant parameters of characterization of the powder technology according to the principle of powder distribution.

## • Conclusion:

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.