EVALUATION OF ENGINEERED SPHERICAL LACTOSE PARTICLES FOR DIRECT COMPRESSION USING THE STYLCAM 100R

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INTRODUCTION

Direct compression is the most economical method of tablet production in terms of time, personnel and resources. Lack of drug compactibility and/or fluidity can be compensated for by the use of suitable direct compression excipients. The attributes of an ideal direct compression excipient are not embodied in a single material and in practice it is desirable to mix two or more excipients together to optimise tableting characteristics. Thus, it would be highly desirable to encompass most of the desired properties required for tablet direct compression in a single material. This would facilitate the formulation and reduce the cost of manufacturing, whilst achieving a good quality product.

The shape of drug or excipient particles can play an important role in improving powder characteristics. Many studies have shown that powder flowability, compressibility and compactibility were improved when spherical shaped particles were used (Kawashima et al, 1989 &1994). Different crystallisation techniques have been used to produce spherical particles (Kawashima et al, 2001; Bhadra et al, 2004). However, the term 'spherical crystallization' is misleading, because ideal spherical particles were not obtained. The resulting particles were an agglomeration of needle shaped, rod or plate-like microcrystallites.

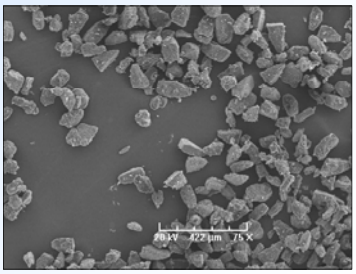
Fig. 1. The Stylcam 100R rotary press simulator

The Stylcam 100R (Medel'Pharm, France) is a single punch, rotary tablet press simulator built upon a modifiable mechanical cam and a programmable electronic cam (www.medelco.fr/medelpharm).

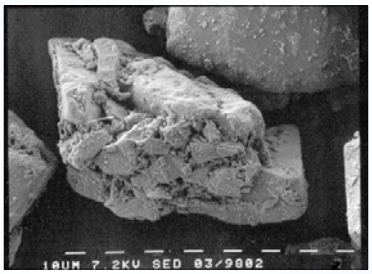
The aim was to produce spherical lactose particles (EL) using a novel crystallization technique and to compare their compaction properties with commercial lactose (CL) and microcrystalline cellulose (Avicel® PH102).

EXPERIMENTAL

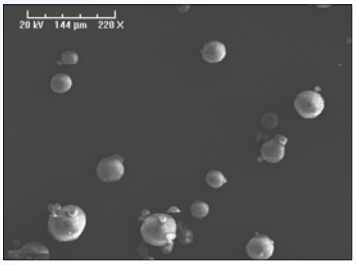
Spherical lactose was engineered by a novel recrystallization technique. Blends of lactose, either EL or CL (Pharmatose®, DMV International, Netherlands) Microcrystalline cellulose (Avicel® PH102, FMC Corp, Belgium), and 0.5% w/w Magnesium stearate (BDH Chemicals, UK) were mixed for 2 min (2C turbula mixer, WAB, Switzerland). Tablets were compressed using a Stylcam® 100R rotary press simulator (Medel'Pharm, France) fitted with 12.75 mm flat punches. 6 tablets (350 mg) were compressed at 5, 10, 15 or 20 kN and speeds of 10 or 30 Tab min^{-1}. Crushing strength was assessed 24h after ejection (Schleuniger, Model 6D, Germany). Ejection forces were monitored throughout the compaction runs via the Analis® software associated with the Stylcam®. Scanning electron microscope images of particles were obtained (Jeol, JSM-U3, Japan).



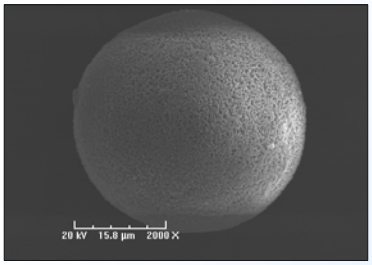
a) CL General view



b) CL Close view



c) EL General view



d) EL Close view

Figure 1: Scanning electron micrographs for CL (a,b) and EL (c,d) particles.

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RESULTS & DISCUSSION

Figure 1 shows a general and close view for both commercial (CL) and spherical lactose (EL). CL has a tomahawk shape and rough surface (Fig 1a,b), whereas, EL has a spherical shape with smooth surface (Fig 1c,d) which can facilitate the flow properties of the powder.

EL tablets displayed higher crushing strengths than CL tablets (Figure 2). Increasing compression rate had no effect on crushing strengths of either EL or CL, suggesting that fragmentation is the dominant mechanism of compaction for both materials. The differences in crushing strengths of EL and CL tablets could be attributed to differences in the extent of fragmentation between both materials as revealed from scanning electron micrographs of the compressed tablets (not shown). Microcrystalline cellulose (Avicel® PH102) is known to be the most compressible excipient, however, this study has shown that EL formed tablets of higher crushing strength than Avicel® PH102. For example, EL tablets compressed at 15kN exhibited similar or higher crushing strength values than Avicel® PH102 tablets made at 20kN. Thus, a low compression force could be used to produce tablets with high crushing strength, consequently reducing wear and tear on tablet tooling. Microcrystalline cellulose deforms plastically and increasing compression speed reduces the crushing strength of its tablets due to the reduction in dwell time, whereas, increasing compression speed has no effect on the crushing strength of EL, suggesting that faster production speeds could be used without compromising tablet strength.

Ejection forces increased with increasing compression force for both CL and EL, whereas, increasing compression force has less effect on Avicel® PH102 (Table 1). CL tablets showed higher ejection forces than EL and Avicel® PH102 tablets, at higher compression forces. CL fragmented extensively at high forces, resulting in more particulate contact with the die wall, disruption of the magnesium stearate film and subsequently, increased friction. Avicel® deforms plastically and increasing compression force has little effect on the ejection force.

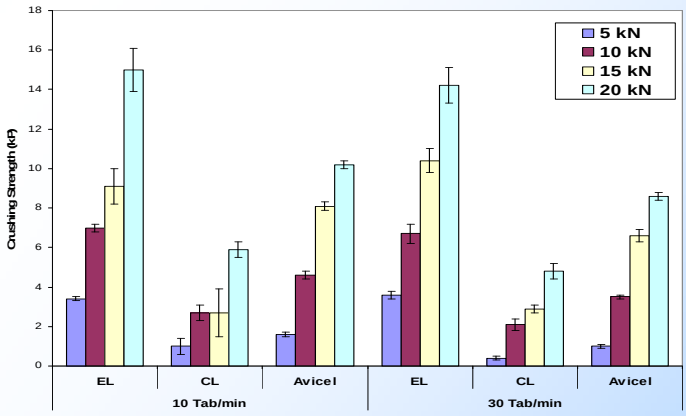

Figure 2. The effect of compression force on the crushing strength of engineered spherical lactose, commercial lactose and Avicel® PH102 tablets at production speeds of 10 and 30 tablet min^{-1} (mean values ± s.d. n =10).

Compression Force [kN]	10 Tab min^{-1}			30 Tab min^{-1}		
	EL	CL	Avicel PH102	EL	CL	Avicel PH102
5	16 ± 0.7	14 ± 0.3	21 ± 0.7	18 ± 0.1	18 ± 2.1	19 ± 0.3
10	21 ± 0.5	24 ± 0.6	19 ± 0.2	24 ± 0.6	24 ± 2.1	19 ± 0.4
15	25 ± 0.7	24 ± 0.5	19 ± 0.2	27 ± 1.0	29 ± 0.7	20 ± 0.3
20	28 ± 0.8	35 ± 0.9	19 ± 0.3	31 ± 1.2	39 ± 0.9	20 ± 0.4

Table 1. The effect of compression force on the ejection force (daN) of engineered spherical lactose, commercial lactose and Avicel® PH102 tablets at production speeds of 10 and 30 tablet min^{-1} (mean values ± s.d. n =30)

CONCLUSIONS

Lactose was chosen as a model material and through a novel crystallization technique, spherical particles were produced which displayed excellent compaction properties.

Through particle engineering, it is possible to embrace most of the desired properties required for tablet direct compression in a single material as shown in this study.

The Stylcam 100R is useful research tool for characterizing and assessing the compaction properties of new materials.