Starch based excipients for direct compression

JACQUES MICHAUD

Cerestar
Application Centre Pharma & Chemical
Vilvoorde, Belgium

Wet and dry granulation, are frequently used methods for the manufacturing of tablets. But with the availability of specific developed excipients, the pharmaceutical industry has the opportunity to choose for a more efficient and economical process: direct compression. The choice of the excipient is extremely critical in formulating direct compression tablets. Therefore Cerestar, a longstanding supplier of pharmaceutical excipients, is pro-actively active in the research and development of new forms of excipient that are suitable for direct compression.

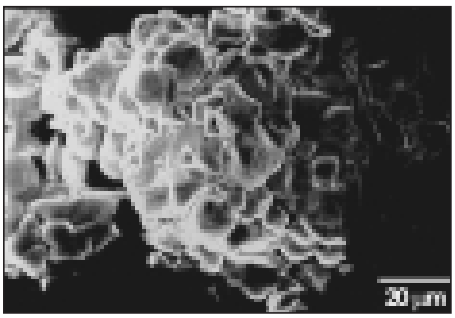

Figure 1 - Scanning electron micrograph of C☆Pharm 93000 at 773 magnifications

To be considered as an excipient for direct compression, certain requirements must be fulfilled especially in terms of flowability and compressibility. Additionally, particle size distribution must be suitable to provide favourable mixing conditions. Compatibility with other excipients or drugs is essential as well as the ability to carry a high amount of active ingredients. Many actives can have a negative influence on the tabletting behaviour, since they are not compressible in either their crystalline or their amorphous form. Therefore a direct compression excipient must possess a high capacity, expressed in dilution potential, without deterioration of the tablet quality. Meeting these requirements is exactly what Cerestar's products for the pharmaceutical industry embody. All Cerestar's products presented in this article comply with the quality standards of the three main pharmacopoeias (European, American and Japanese).

STARCH

Starch is one of the most traditional excipients used for pharmaceutical solid dosage forms. Depending on the application, Cerestar has developed different grades that can be used as a binder, diluent and/or disintegrant. Cerestar is supplying two grades of native maize starch: C☆Pharm 03406 and extra white maize starch, C☆Pharm 03302. Both are used in capsule and tablet formulations as a diluent. Due to swelling properties of the starch granules, native maize starches act as an excellent disintegrant. When wet granulation is applied, native starches can be used as a binder when heated in an aqueous environment in a concentration of 5 to 25% w/w.

In comparison with native starches, the pregelatinised starch, C☆Pharm 12012, is characterised by an enhanced flow and compressibility, such that it can be used as a

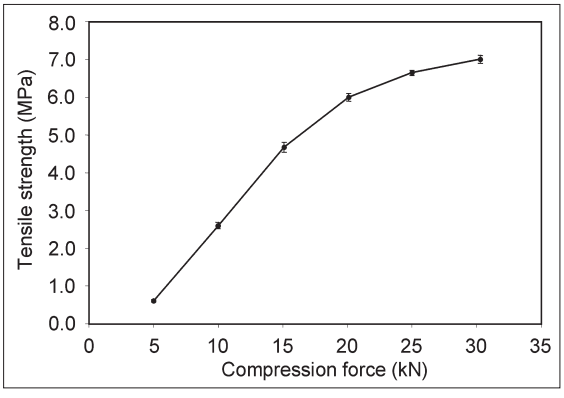

Figure 2 - Compression profile of C☆Pharm 93000. Lubricated with 0.5% magnesium stearate and with the addition of 0.25% SiO_2

Table I - Physical characteristics of C☆Pharm 93000

Appearance		White coloured, odourless
Moisture content	(%)	10-12
Mass median diameter	(m)	100
Loose density	(g/l)	530
Tapped density	(g/l)	660
Carr Index	(%)	19.7
Hausner ratio		1.24

binder in direct compression as well as in wet and dry granulation. Pregelatinised starch offers also the advantage of being soluble in water without heating.

To meet the demand of the pharmaceutical industry for high-quality direct compressible excipients, Cerestar has recently launched a direct compressible starch (patent pending) meeting the requirement of the monographs of pregelatinised starch. The spherical shape (Figure 1) and the favourable particle size distribution of the C☆Pharm 93000 result in good flow properties as demonstrated in Table I by the Hausner ratio of 1.24 and a Carr Index of 19.7.

The compression profile of C☆Pharm 93000, lubricated with 0.5% magnesium stearate, is shown on Figure 2. It demonstrates the ability of this new excipient to produce tablets of a very high hardness. Even at very high compression forces, up to 30 kN, an increase in hardness can still be observed without sign of capping or laminating. Due to its specific structure C☆Pharm 93000 possesses a strong binding capacity and at the same time fast disintegration (Figure 3). With its high compressibility and compatibility, C☆Pharm 93000 can be considered as a versatile high-quality multi-functional excipient. In wet and dry granulation as well as in direct compression C☆Pharm 93000 can be used as a diluent, binder and disintegrant.

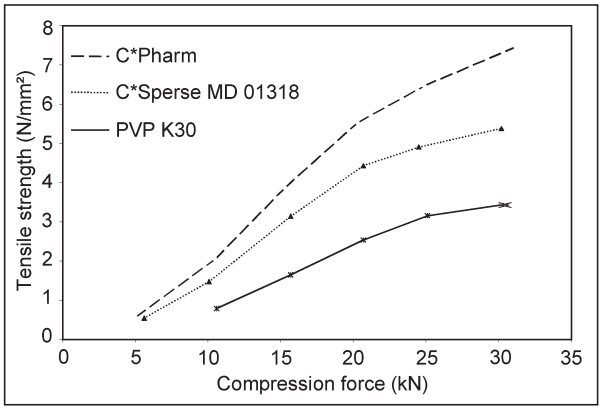

Figure 4 - Compression profile of different maltodextrin grades in comparison with PVP K30 (0.5% magnesium stearate and 0.25% SiO_2)

MALTODEXTRINS

Maltodextrins are obtained by partial hydrolysis of starch whereby the basic polymeric structure is obtained. Maltodextrin is a versatile binder used as a 3 to 15% solution in water or added dry to powder blends. Different grades of maltodextrins and Spray-dried Glucose are developed according the application. These different grades differ from each other by their degree of hydrolysis characterised by the "Dextrose Equivalent" or DE (C☆Pharm 01980, C☆Pharm 01982, C☆Pharm 01983, C☆Pharm 01984) and by their particle in the case of agglomerated grades C☆Sperse 01314 and C☆Sperse 01318. They all show excellent compressibility (Figure 4) and tablet properties, with regard to tablet hardness and uniformity of weight. Very often maltodextrins are considered as a good replacement for polyvinylpyrrolidone.

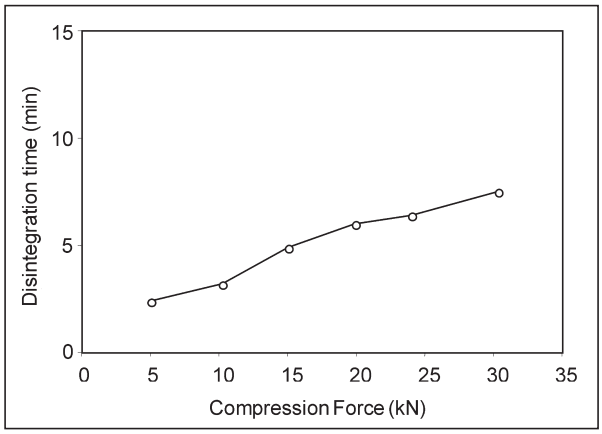

Figure 3 - Disintegration profile of C☆Pharm 93000. Lubricated with 0.5% magnesium stearate and with the addition of 0.25% SiO_2

SORBITOL

Sorbitol is a widely used excipient in the pharmaceutical industry. Its pleasant, sweet, cooling taste, non-cariogenic properties and excellent compatibility with actives make sorbitol a unique excipient for the manufacturing of lozenges and chewable tablets. Sorbitol is a versatile excipient that can be used as a diluent to impart sweetness and as a binder to impart hardness to tablets. Therefore Cerestar has developed a wide range of sorbitol grades with respect to particle size distribution, flowability and minimisation of compression force needed for direct compression. C☆Sorbidex P 16656 and C☆Sorbidex P 16616, both sorbitol grades specially designed for direct compression, show due to their stable crystalline structure high compressibility (Figure 5) and good flowability. Additionally the workability at high speed is excellent. With regard to the softer chewable tablets, a special sorbitol grade is designed, C☆Sorbidex S 16603.

MANNITOL

Mannitol is a desired diluent for tablet formulation. Comparable with sorbitol, also mannitol has a pleasant, slightly sweet taste with a cool, melt-down mouth feel, which makes mannitol an excellent excipient for chewable tablets. Mannitol additionally exhibits a very low hygroscopicity and is therefore very stable in presence of moisture (Figure 6).

DEXTROSE

Last but not least, monohydrate dextrose is a well known diluent in tabletting. It is widely used where a sweet taste is desired, as in chewable tablets.. The trend for the development of direct compressible excipient is going on. It is likely that in the future new physical forms of existing products will have to be developed. The products presented in this article are already a strong asset for the starch derivatives and one can rely on the fact that many other specialties are in the pipe for the next years.

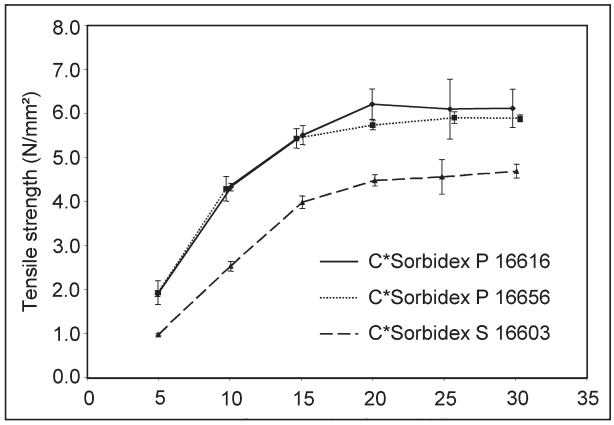

Figure 5 - Compression profile of sorbitol. Lubricated with 1% magnesium stearate

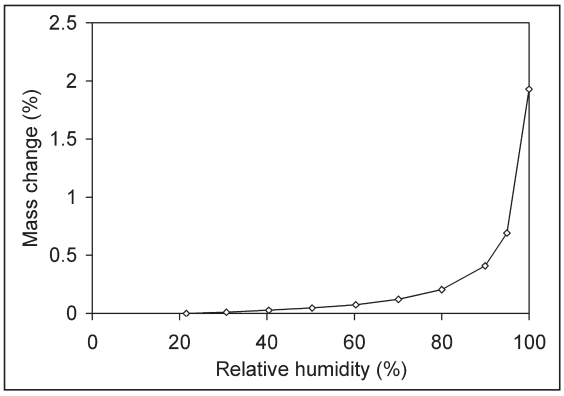

Figure 6 - Absorption isotherm of mannitol