Investigation of Compression Behavior of a Co-processed Mixture of Corn Starch and Pregelatinized Starch as a Direct Compression Excipient

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Purpose

The use of modified starch products as tablet excipients continues to grow, due to their multifunctional properties, wide regulatory acceptance and availability. The aim of this study was to investigate the compression behavior of a co-processed mixture of corn starch and pregelatinized starch (StarCap 1500®, co-processed starch excipient) under simulated rotary tablet press production conditions.

Methods

Compaction properties of StarCap 1500 alone, or blends of StarCap 1500 with different lubricants; magnesium stearate (MS) or stearic acid (SA), at concentrations of 0.25, 0.5 or 1.0% w/w were evaluated using a Stylcam 100R rotary press compaction simulator (Medel'Pharm, France). The compression cycle followed a generic rotary press profile. Measurements of punch displacement, compaction force (from which compaction pressure was calculated) and ejection force were determined using the Analis software. Heckel plots were constructed and mean yield pressures were determined at low (Py1) and high speed (Py2). The strain rate sensitivity (%SRS) of StarCap 1500 was calculated based on the mean yield pressures according to Equation 1[1]:

Equation 1. $\%SRS = ((Py2 - Py1)/ Py2) \times 100$

Tablets of StarCap 1500 (400 mg) were produced at compaction pressure of 100 MPa or 300 MPa (10 or 30 kN) and speeds of 10 or 30 tablets/min (equivalent to dwell times of 30 and 10 ms respectively) using 11.28 mm flat-faced tooling.

Methods

In order to evaluate the influence of StarCap 1500 on physico-mechanical properties of a formulation, 300 mg tablets of a candidate drug were prepared. The formulation contained famotidine (6.7%, Molekula, UK), StarCap 1500 (46.6%, Colorcon, UK), microcrystalline cellulose (46.5%, Microcel 102, Blanver, Brazil) and magnesium stearate (0.25%).

In all cases, tablet weight, thickness (digital micrometer, Mitutoyo, Japan), crushing strength (Pharmatron 6D, Dr. Schleuniger, Germany), friability (PTFR-A, PharmaTest, Germany) and disintegration time (PTZ, PharmaTest, Germany) were determined.

Results

The mean particle size of StarCap 1500 used in this study was 94 µm with a true density of 1.597 (±0.029 gcm^{-3}). It has been reported that the StarCap 1500 has very good flow (Carr's Index of around 20 and Sotax flow rate of 5.45g/sec)[2].

Tablet physical and mechanical properties of StarCap 1500 in the presence and absence of lubricants prepared using the Stylcam rotary compaction simulator at 300 MPa compaction pressure (30 kN) and 10 tabs/min tableting speed are shown in Table 1.

Table 1. Physical and mechanical properties of StarCap 1500 in the presence and absence of 0.5% lubricants (MS: magnesium stearate, SA: stearic acid). Tablets were prepared using flat-faced tooling at 10 tabs/min and 300 MPa compaction pressure (30 kN) (dwell time of 30 ms ~ 44,000 tablets/hr)

	StarCap 1500	StarCap 1500 + 0.5% MS	StarCap 1500 + 0.5% SA
Tablet hardness (kP)	10.0	2.5	5.0
Ejection force (N)	500	30	30
Friability (%)	0.2	1.4	1.5
Disintegration time (seconds)	350	104	95

Results

The ejection forces of StarCap 1500 were consistently low (< 540 N) at all compaction forces and speeds. Tablet hardness of StarCap 1500 was reduced in the presence of lubricants, but to a lower extent when stearic acid was used.

Table 2 shows the mean yield pressure and % strain rate sensitivity values for StarCap 1500. The mean SRS value of 10.0% may suggest that StarCap 1500 undergoes strain-rate dependent deformation when compacted.

Table 2. True density, mean yield pressure and strain rate sensitivity values

	StarCap 1500
Density (gcm^{-3})	1.597 (±0.029)
Py_1 (MPa)	78.1
Py_2 (MPa)	86.8
%SRS	10.0

Modified starch products are plastically deforming and show compression sensitivity in the presence of lubricant as shown in Table 1. The reduction in tablet strength has been related to self-lubricity of the modified starches and reduction in interparticulate bonding due to lubricant film formation on the surface of the particles. The compaction energy data for StarCap 1500 in the absence or presence of different concentrations of magnesium stearate and stearic acid are shown in Table 3. The data clearly show that StarCap 1500 predominantly undergoes plastic deformation when compressed without or with the lubricants studied here.

Table 3. Percent elastic and plastic energies of StarCap 1500 **with** magnesium stearate (MS) **or** stearic acid (SA) at 10 tabs/min and 300 MPa compaction pressure (30 kN) (dwell time of 30 ms)

	% Elastic Energy	% Plastic Energy
StarCap 1500	10.0	90.0
StarCap 1500 + 0.25% MS	11.4	88.6
StarCap 1500 + 0.50% MS	6.7	93.6
StarCap 1500 + 0.25% SA	8.4	91.6
StarCap 1500 + 0.50% SA	6.4	93.6

StarCap 1500 tablets exhibited low percentage friability at all compaction conditions, with only a slight increase at the higher compression speed. StarCap 1500 tablets disintegrated in less than 90 seconds when produced at a low compression force and less than 6 minutes when produced at the higher compaction force, due to the increase in tablet strengths.

The friability data of StarCap 1500 in the presence of lubricant were in accordance with the trends observed in tablet crushing strengths. Tablets were more friable when produced at low compaction forces and/or high compaction speeds. Lowest tablet friability was achieved when using stearic acid and tablets were produced at a high compaction force. It should be noted that the tablets were flat-faced and, therefore, friability was inevitably increased.

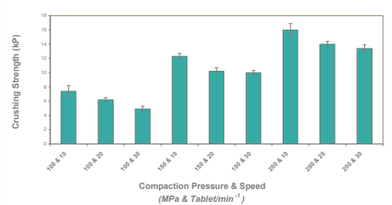
All tablets with lubricants disintegrated in less than 2 minutes. Higher lubricant levels generally decreased disintegration times due to a reduction in tablet breaking force and higher compaction forces generally increased disintegration times.

Active formulation

The ejection forces recorded during production of famotidine tablets (comprising 0.25 % w/w magnesium stearate as lubricant) were consistently low (<290 N) at all compaction conditions. The weights of famotidine tablets were consistent throughout production at different compaction conditions. Coefficient of variation values were below 2% for every batch indicating reproducible die filling representative of good flow properties of the formulation.

Robust tablets were produced at all compaction conditions suggesting that the model formulation comprising of 46.6 % w/w StarCap 1500 possessed good compressibility. Despite the strain-rate dependent deformation of StarCap 1500, only slight reductions were seen in the strength of famotidine tablets when produced at higher speeds and lower dwell times of 10 ms (equivalent to high production speed on a rotary tablet press), as shown in Figure 1.

Figure 1. The effect of compaction force and speed on tablet crushing strength of famotidine tablets (mean values ± s.d. n = 10)



The friability values of famotidine tablets were below 0.2% at all compaction conditions, indicating the robust nature of the tablets and good compressibility of the formulation. Famotidine tablets disintegrated in less than 60 seconds when produced at 100 or 150 MPa (10 or 15 kN) and in less than 90 seconds when produced at 200 or 250 MPa (20 or 25 kN). Despite the high strength of the tablets, particularly at the high compaction forces, the model formulation comprising StarCap 1500 produced rapidly disintegrating tablets thus aiding drug release. All tablets meet the dissolution requirements of USP 32.

Conclusions

The compaction simulation results of this study showed that StarCap 1500 predominantly undergoes plastic deformation during compression. Similar to other modified starch products and plastically deforming excipients, StarCap 1500 produced tablets of lower crushing strength in the presence of lubricants. Therefore, addition of lubricant to formulations requires optimization with regards to type and quantity of lubricant used. The good flow and compressibility behavior of StarCap 1500, under simulated rotary tablet press production conditions and in a famotidine model formulation, indicated characteristics of the StarCap 1500 suitable for direct compression applications.

References

1. Roberts, R.J. and Rowe, R.C., *J. Pharm. Pharmacol.* 1985; 37 377-384
2. Colorcon application data, 2008