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ORIGINAL ARTICLE

A study of the compaction process and the properties of tablets made of a new co-processed starch excipient

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Abstract

This article deals with the study of the energetic relationships during compaction and the properties of tablets produced from a co-processed excipient based on starch and called StarCap1500®. This article compares it with the substance Starch1500®. The study also includes the mixtures of StarCap 1500® and the granulated directly compressible lactose Pharmatose DCL®15. The tablet properties tested included tensile strength and disintegration time, examined in dependence on compression force, and also a 0.4% addition of magnesium stearate. The results show a better compressibility of StarCap 1500 in comparison with Starch 1500 and a lower elastic component of energy. The tablets were stronger and disintegrated more rapidly, but the substance possessed a higher sensitivity to an addition of a lubricant than Starch 1500. Increasing portions of StarCap 1500 in the mixtures with Pharmatose DCL 15 increased the tensile strength of tablets, disintegration period as well as the sensitivity to an addition of a lubricant. From the energetic viewpoint, energy for friction was decreasing, while the energy accumulated by the tablet during compaction and the elastic component of energy were increased.

Keywords: StarCap 1500; Starch 1500; tensile strength of tablets; disintegration time; force-displacement profile

Introduction

Starches are important excipients in tablet manufacture. They are used as disintegrating agents, fillers, and binders in the form of a starch paste during moist granulation. Natural starches possess good compacting properties, but due to bad flowability and high lubricant sensitivity they are not suitable to serve as dry binders during direct compression (Jivraj et al., 2000). Compressibility of starches depends on a balanced content of humidity, which is dependent on the relative humidity of the air in which starch is stored. The maximal strength of tablets is found at the relative air humidity of 60–70%, which corresponds to the content of moisture in the powder of about 10% (Boss et al., 1987). Water absorbed inside the starch particles influences the properties of compacts by changing the degree of viscoelasticity (Rees & Tsardaka, 1994). High lubricant sensitivity of starches is due to the mechanism of compaction, which is a plastic deformation (Jarosz & Parrot, 1984).

In order to improve the tableting properties of starches, various modified starches have been prepared, for example by pregelatinization or granulation. Granulation with a 2.5% starch paste improves flow properties, but the compacting properties are improved as well only in the case of rice starch. In addition, with improved flowability also the sensitivity to added lubricants is increased (Boss et al., 1987). Pregelatinization increases the densification of starches during the filling of the matrix and at low compression pressures. It also facilitates a quicker onset of plastic deformation of starches, but it decreases its extent during the compression process (Alebiowu & Itiola, 2002).

Modified starches include, for example the agglomerated form of the modified rice starch Era-Tab, which possesses a better flowability, a higher strength, and a lower abrasion of tablets compared with Starch 1500 (Hsu et al., 1997). Another one is modified agglomerated maize starch, otherwise referred to as granulated starch (Sepistab

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ST 200®), the compressibility of which is similar to that of Starch 1500®, but which possesses better disintegrating properties (Bolhuis & Chowhan, 1996). The Preflo® maize starches produce stronger compacts than the Preflo® potato starches and Starch 1500®. But they have very bad disintegrating properties, which can be used in sustained release formulations (Sanghvi, 1993). In acetylated starches, due to acetylation, the content of water is much decreased and the production of solid molecular bonds is increased severalfold, which improves the tableting properties, above all the strength of tablets (Raatikainen, 2002). Also the spray-dried form of rice starch flows and compresses well (Mitrevej, 1996). In spite of all modifications of starches, the most widely used starch for direct compression is the directly compressible starch Starch 1500®, which is a pregelatinized maize starch composed of both intact starch grains and disrupted starch grains, which are partially hydrolyzed and agglomerated (Carlin, 2008). The product contains 5% of free amylose, 15% of free amylopectin, and 80% of unmodified starch. Free amylopectin is soluble in cold water and is responsible for binding properties. Free amylose and unmodified starch are important for disintegrating properties (Bolhuis & Chowhan, 1996). Starch 1500® is easy to compress, but the strength of compacts is low. It is because plastic deformation is too slow to produce sufficient interparticular connections during quick compression, and in addition, a great share in the final deformation is elastic (Rees & Rue, 1978). Starch 1500® itself possesses lubricating properties, but in the case of an addition of a lubricant a great decrease in the strength of compacts takes place due to the mechanism of compression by plastic deformation (Jarosz & Parrot, 1984). The dilution potential of the substance is also small, and therefore in direct compression it is not used as a filler-binder, but as a filler-disintegrant. The principal advantage of the substance is that it maintains its disintegrating properties without decreasing the flowability and compressibility of tableting formulations in contrast to natural starches (Carlin, 2008).

A new product of the firm Colorcon is the substance StarCap 1500®, which is a co-processed excipient of maize starch and pregelatinized starch. It is a freely flowable substance which can be used as the filler in the manufacture of capsules and tablets. The disintegrating and dissolution properties are independent of media pH (Colorcon, 2010). This article aims to study the energetic profile of compression, strength, and disintegration period of the tablets made of this substance. It also included a comparison with the substance Starch 1500®. The mixtures of StarCap 1500® with the directly compressible lactose Pharmatose DCL® 15 in the ratios of 1:3, 1:1, and 3:1 were examined as well.

Experimental

Materials

StarCap 1500® (Colorcon, USA) is a co-processed mixture of corn starch and pregelatinized starch. Its particle size was 18.9% > 125 μm, 39.9% > 75 μm, 41.3% < 75 μm, humidity content 8.9%, bulk density 0.4855 g/cm^3, and tape density 0.5807 g/cm^3.

Starch 1500® (Colorcon, USA) is pregelatinized starch of a particle size of 90% < 150 μm, 25% < 53 μm, humidity content 14%, bulk density 0.6741 g/cm^3, and tape density 0.8240 g/cm^3.

Pharmatose DCL®15 (DMV International, Netherlands) is granulated directly compressible lactose with a particle size of 90% < 274.55 μm, 50% < 137.07 μm, 10% < 48.33 μm, humidity content 4.52%, bulk density 0.5686 g/cm^3, and tape density 0.6438 g/cm^3.

Magnesium stearate (Acros Organics, New Jersey, USA) was used as the lubricant.

Particle size and humidity content were stated in the certificates of analysis. Densities were determined following the method Apparent Volume described in the chapter *Pharmaceutical Technical Procedures* in the European Pharmacopoeia, 6th Edition.

Preparation of tableting compositions

The tests included the tableting compositions made of the pure substances StarCap 1500, Starch 1500, mixtures of StarCap + Pharmatose DCL 15 in the ratios of 1:3, 1:1, and 3:1, and also all these tableting compositions with an addition of 0.4% of magnesium stearate, and Pharmatose DCL 15 with 0.4% magnesium stearate, altogether 11 tableting compositions. Mixtures of dry binders were prepared by mixing in a stainless steel cube KB 15S (Erweka GmbH, Hausenstamm, Germany) for a period of 5 min. Dry binders with a lubricant were also mixed for 5 min, in the case of the mixtures of dry binders the lubricant was added at the end and mixing lasted again 5 min. The rotation rate of the mixing cube was always 17 revolutions/minute. The amount of prepared tableting compositions was 30 g.

Preparation of tablets and energy evaluation of the process of compaction

All tableting materials were used to produce 16 tablets compressed with the use of a special die with an upper and a lower punch on a material testing equipment T1-FRO 50 TH.A1K Zwick/Roell (Zwick GmbH&Co, Ulm, Germany). Proper compaction took place by applying the pressure on the upper punch. The tablets were of a cylindrical shape without facets with a diameter of 13 mm and weight of 500 ± 1 mg. Compression velocity was 40 mm/min and compression forces 11, 13, and 15 kN, in the case of Starch 1500, 15 kN. In 10 tablets from each group, the 'force-displacement' plot was drawn by means of a computer program testXpert V 9.01 and the compression process was evaluated as far as energy was concerned, that is the energies E1, E2, and E3 were expressed numerically. Energy E1 is the energy consumed by friction, energy E2 is the energy accumulated by the tablet in the course of compression, and energy E3 is the energy released during decompression (Figure 1) (Ragnarsson, 1996).

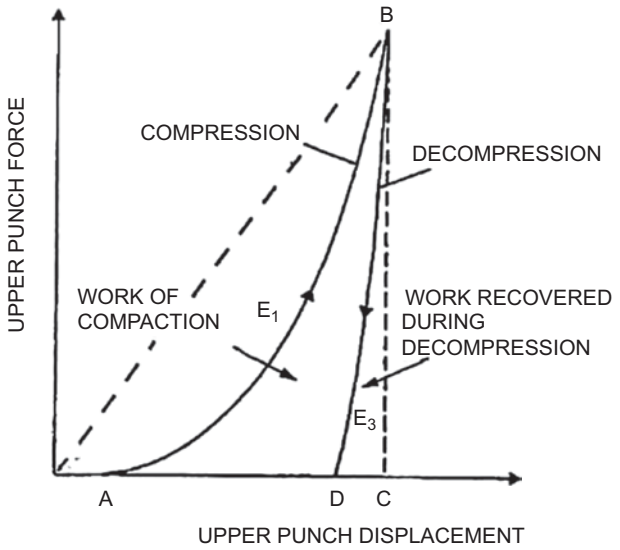

Figure 1. Plot of upper punch force versus upper punch displacement during compression and decompression.

Measurement of tensile strength of tablets and evaluation of the lubricant sensitivity of tableting materials

Tensile strength was always evaluated in 10 tablets, first no sooner than 24 h after compaction. Measurements were performed on a Schleuniger apparatus (Dr. Schleuniger Pharmatron AG, Solothurn, Switzerland), which measured tablet sizes accurate to 0.01 mm and crushing force in N. Tensile strength of tablets was calculated according to Eq. (1):

$$P = \frac{2F}{\pi.\mathrm{d.h}}, \quad (1)$$

where P is the tensile strength of tablets [MPa], F is the crushing force [N], d is the tablet diameter [mm], and h is the thickness of the tablet [mm] (Fell & Newton, 1970).

Lubricant sensitivity ratio (LSR) values, which make it possible to quantify and mutually compare the lubricant sensitivity of tableting materials, were calculated according to Eq. (2):

$$\mathrm{LSR} = \frac{(Csu - Csl)}{Csu}, \quad (2)$$

where *Csu* is the crushing strength of tablets without an added lubricant and *Csl* is the crushing strength with a lubricant. The more this value approaches 1, the more the dry binder is sensitive to an added lubricant from the viewpoint of decreased strength of tablets (Bos et al., 1987). In this paper, the values of tensile strength, not those of crushing strength, are used in the equation.

Measurement of disintegration time of tablets

Disintegration times of tablets were evaluated earliest 24 h after compaction always in six tablets. Measurements were performed on an apparatus for the determination of disintegration time of tablets Erweka ZT 301 (Erweka GmbH, Hausenstamm, Germany) following the method described in the chapter *Pharmaceutical Technical Procedures* in the European Pharmacopoeia, 6th Edition. The test was carried out without discs in the medium of purified water tempered to 37°C ± 1°C. The tablet was considered disintegrated at the moment when there was no remainder on the net.

The results of strengths and disintegration times were statistically processed by means of the computer programs Excel and Qcexpert. Elementary data analysis yielded the mean values with standard deviations, which were plotted into dependences on compression force. In the cases of unclear significance of differences in the values, unpaired *t*-test at a level of significance of 0.05 was used.

Results and discussion

StarCap 1500 is a new co-processed excipient containing maize and pregelatinized starch, suitable as a filler for capsules as well as for tablets. The aim of this paper was to evaluate the strength and disintegration time of tablets made of this substance, the mixtures with Pharmatose DCL 15 in the ratios of 1:3, 1:1, and 3:1, and to compare these properties with the directly compressible starch Starch 1500. The energetic profile of compression was evaluated as well. Compression forces were selected in such a way as to make the strength of tablets made of pure StarCap oscillate in the optimal range of strength of 0.56–1.11 MPa (Belousov, 1976). The compression forces of 11, 13, and 15 kN were selected. Starch 1500 was compressed using only the force of 15 kN, as the first two compression forces were too low. The tableting materials with 0.4% magnesium stearate were also evaluated. The mixtures with Pharmatose DCL 15 were tested because of the combination of plastically deformable starch with fragmenting lactose monohydrate with the assumption of decreased sensitivity to the added lubricant and possibly improved compressibility.

The values in the figures and tables are the mean values with standard deviations calculated from 10 measured values in the case of the tests of tensile strength of tablets and the energetic profile of compaction, and from 6 values in the case of the tests of disintegration time of tablets.

Figure 2 represents the dependence of tensile strength of tablets on compression force for StarCap 1500, StarCap 1500 with 0.4% of magnesium stearate, and Pharmatose DCL 15 with 0.4% of magnesium stearate. At the compression force of 15 kN, the value of strength for Starch 1500 and Starch 1500 with 0.4% magnesium stearate is also shown. The dependence increases and the highest strength is achieved in the tablets made of StarCap 1500, followed by Pharmatose DCL 15 with magnesium stearate. The softening effect of 0.4% addition of magnesium stearate on the strength of tablets made of StarCap 1500 is very high. The strength of tablets made of StarCap 1500 at the compression force of 15 kN is 2-fold compared with

the tablets made of the substance Starch 1500, in which the softening effect of magnesium stearate is lower.

The same dependence for the mixtures of StarCap 1500 and Pharmatose DCL 15 in the ratios of 1:3, 1:1, and 3:1 is shown in Figure 3. Strength grows again with compression force and increases with growing portions of StarCap 1500. With increasing portions of this substance in the mixture, the sensitivity to the addition of the lubricant magnesium stearate is also increased. In another article investigating the same mixtures, but with the substance Starch 1500, the strength was increased, on the other hand, due to increasing portions of Pharmatose DCL 15 (Mužíková & Moučková, 2006).

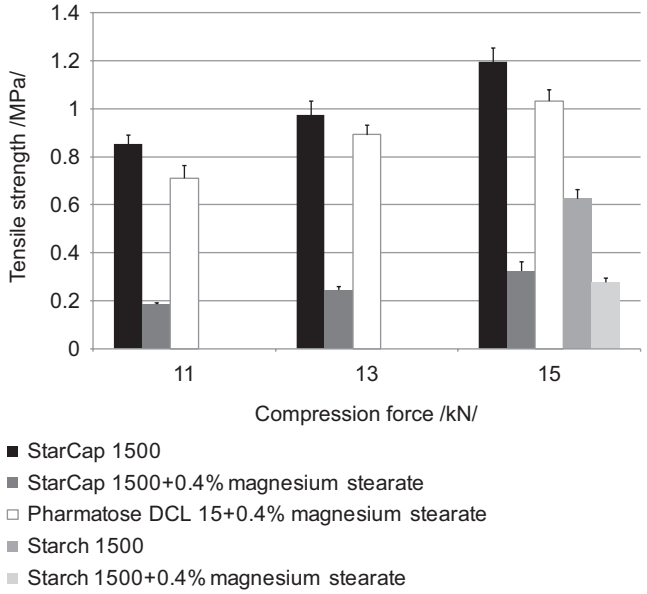

Figure 2. Tensile strength of tablets in function of compression force.

Figure 4 shows the dependence of disintegration time on compression force for StarCap 1500, StarCap 1500 with magnesium stearate, and Pharmatose DCL 15 with magnesium stearate. At the compression force of 15 kN, also the values of disintegration times for the tablets made of Starch 1500 and Starch 1500 with magnesium stearate are shown. The longest disintegration period was observed in the tablets made of Starch 1500, as the gel-like layer, which is formed in combination with water decelerates their disintegration. The addition of magnesium stearate in this case causes a shortening of disintegration period due to a marked decrease in tensile strength. Tablets made of StarCap 1500 possess a markedly shorter disintegration period than Starch 1500, though their strength is much higher, the values slightly increasing with compression force. The significantly shorter disintegration time of compacts is caused most probably by the technology of the manufacture of the co-processed dry binder and the tablets made of this substance possess most probably a more efficiently functioning capillary network. An addition of magnesium stearate to StarCap 1500 makes the disintegration period shorter, though not so markedly as in the case of Starch 1500. The tablets made of Pharmatose DCL 15 with magnesium stearate possess a similar disintegration time as those made of StarCap 1500 with magnesium stearate; they disintegrate by means of a passive mechanism in contrast to starch tablets which disintegrate by means of an active mechanism (Ferrari et al., 1996). Disintegration period in dependence on compression force is also represented in Figure 5, showing disintegration periods of

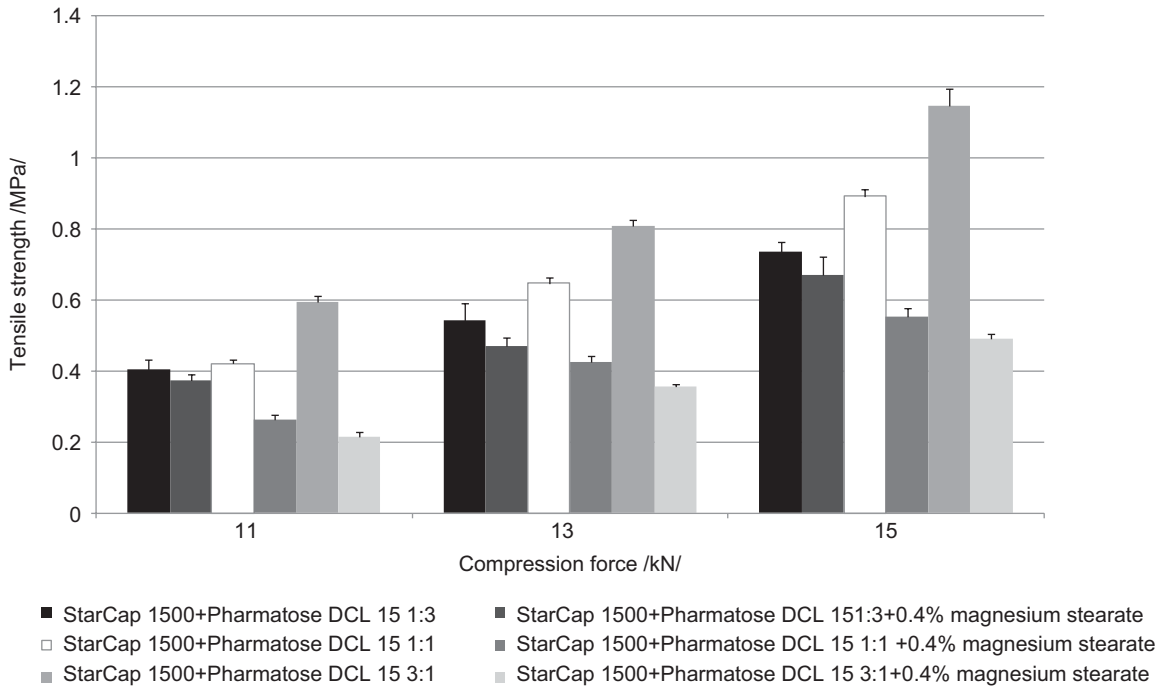

Figure 3. Tensile strength of tablets in function of compression force: Mixtures of StarCap 1500 and Pharmatose DCL 15.

the mixtures StarCap 1500 and Pharmatose DCL 15 in the ratios of 1:3, 1:1, and 3:1. Disintegration time increases with compression force and the increasing portions of StarCap 1500. The presence of magnesium stearate intervenes into the disintegration time of tablets in a more significant manner only in the case of the mixture of StarCap 1500 and Pharmatose DCL 15 1:1 at the compression force of 11kN and further in all compression forces in the case of the mixtures with the prevalence of StarCap 1500. In these cases, its softening effect on the tablets causes a shortening of the disintegration time of tablets.

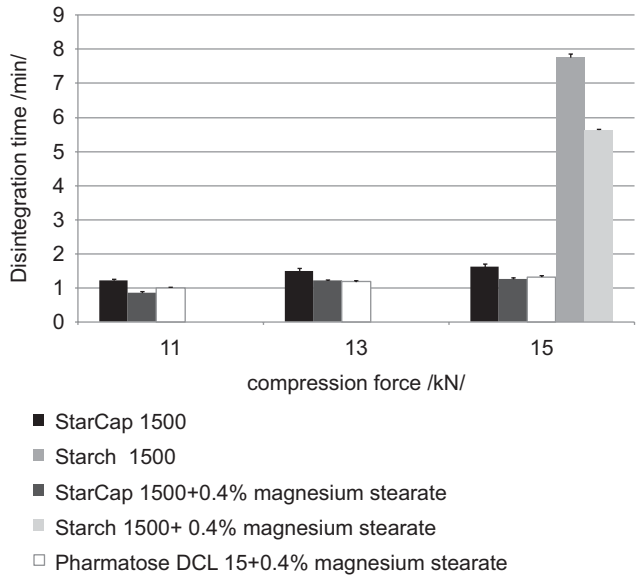

Figure 4. Disintegration time in function of compression force.

Furthermore, an energetic evaluation of the compression process was performed during which the individual types of energies needed for the compression of all types of the tableting materials under evaluation were quantified. The total energy E_{max} is the sum of the energies of E_1, E_2, and E_3, the energy E_1 being the energy consumed by friction, E_2 the energy accumulated by the tablet during compression, and E_3 the elastic component of energy (Ragnarsson, 1996). The values of energies at the compression force of 15 kN are presented in Table 1. The highest total energy is observed in the substance StarCap 1500, whose value is markedly higher than that in the case of Starch 1500. Magnesium stearate decreases the total energy in the case of both StarCap 1500 and Starch 1500, above all due to a decrease in the energy consumed for friction (E_1). In the case of the mixtures of StarCap 1500 and Pharmatose DCL 15, there are no significant differences in the values of the energy E_{max}, the values with magnesium stearate being always lower. The total energy for StarCap 1500 is the highest due to the high values of the energy for friction (E_1) and the energy accumulated by the tablet during compression (E_2). The energy for friction is higher in the case of Pharmatose DCL 15 with magnesium stearate than in the case of starches. An addition of magnesium stearate to starches again decreases this energy. In the case of the mixtures, the energy for friction decreases with the increasing portions of StarCap 1500 and magnesium stearate again decreases it. The energy accumulated by the tablet during compression is the highest in the case of StarCap 1500, and the lowest in the case of Pharmatose DCL 15 with magnesium stearate. In the mixtures of dry binders, its value increases with the increasing portion of StarCap 1500 in the mixture. In this

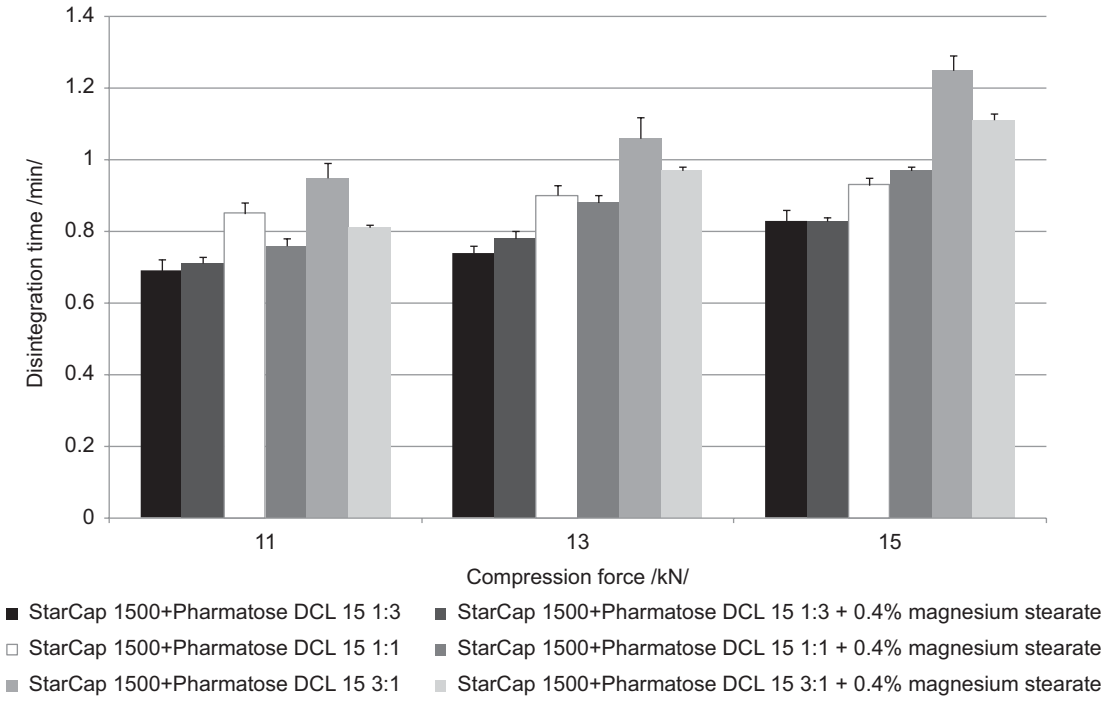

Figure 5. Disintegration time in function of compression force: Mixtures of StarCap 1500 and Pharmatose DCL 15.

Table 1. Values of energies of compression and the value of plasticity at the compression force of 15 kN.

Tableting material	E_{max}/J/(s_d/J/)	E_1/J/(s_d/J/)	E_2/J/(s_d/J/)	E_3/J/(s_d/J/)	Pl/%/(s_d/%/)
SC	33.83 (0.44)	17.593 (0.387)	12.231 (0.106)	4.009 (0.029)	75.31 (0.15)
SC + Mg st	28.82 (0.38)	13.825 (0.349)	10.837 (0.072)	4.162 (0.021)	72.25 (0.12)
S 1500	21.15 (0.50)	9.147 (0.475)	7.853 (0.095)	4.149 (0.053)	65.43 (0.26)
S 1500 + Mg st	18.22 (0.23)	6.651 (0.145)	7.411 (0.097)	4.161 (0.019)	64.04 (0.28)
PH + Mg st	29.18 (0.45)	18.362 (0.463)	6.864 (0.085)	3.956 (0.017)	63.43 (0.27)
SC + PH 1:3	31.95 (0.60)	19.555 (0.615)	8.510 (0.081)	3.882 (0.030)	68.67 (0.21)
SC + PH 1:3 + Mg st	28.95 (0.40)	16.934 (0.380)	8.135 (0.075)	3.885 (0.053)	67.68 (0.46)
SC + PH 1:1	31.76 (0.37)	18.063 (0.304)	9.727 (0.085)	3.966 (0.031)	71.04 (0.26)
SC + PH 1:1 + Mg st	27.92 (0.29)	14.899 (0.225)	9.000 (0.110)	4.022 (0.021)	69.11 (0.24)
SC + PH 3:1	32.72 (0.32)	17.663 (0.282)	11.039 (0.102)	4.018 (0.016)	73.32 (0.18)
SC + PH 3:1 + Mgst	27.89 (0.31)	13.815 (0.263)	9.997 (0.072)	4.077 (0.010)	71.03 (0.14)

E_{max}: total energy ($E_1 + E_2 + E_3$); E_1: energy of friction; E_2: energy of compaction; E_3: energy of decompression; Mg st: magnesium stearate; PH: Pharmatose DCL 15; Pl: plasticity; SC: StarCap 1500; S 1500: Starch 1500; s_d: standard deviation.

case, the presence of magnesium stearate decreases the values of this energy. In the case of the elastic component of the energy (E_3), the value for Pharmatose DCL 15 with magnesium stearate is lower in comparison with that for starches, because the prevailing mechanism of compression is mainly fragmentation (Bolhuis & Chowhan, 1996). The value for StarCap 1500 is markedly lower than that for Starch 1500, the elastic component of the energy is thus markedly lower for this substance, resulting in a higher strength of the compacts. An addition of magnesium stearate increases the elastic energy much more markedly in the case of StarCap 1500, which is connected with its more profound intervention into the strength of the compacts than in the case of the substance Starch 1500. In the case of the mixtures, the elastic portion of energy increases with the increasing proportion of StarCap 1500 and at the same time a higher effect of magnesium stearate on the increase in this energy is increased. The last value shown in Table 1 is plasticity, which is highest in the case of the substance StarCap 1500, and markedly higher compared with the substance Starch 1500. The lowest value is that for Pharmatose DCL 15 with magnesium stearate, which results from the prevailing mechanism of compression, which is fragmentation. In the case of the mixtures of dry binders, plasticity increases with the increasing portions of StarCap 1500 and the effect of magnesium stearate on the decrease in the value of plasticity is also increased. Table 2 presents the LSR values for the compression force of 15 kN, which quantify the sensitivity of the dry binder to the addition of the lubricant (Boss et al., 1987). The table does not present the values for Pharmatose DCL 15, because the pure Pharmatose DCL 15 without a lubricant cannot be compressed due to high friction of the substance. The prevailing mechanism of compression of fragmentation, however, ensures insensitivity to the added lubricant (DMV International, 2000). StarCap 1500 shows a higher LSR value than Starch 1500, and it is therefore more sensitive to added magnesium stearate. Increasing portions of the substance StarCap in the mixture with Pharmatose DCL 15 increase also the LSR values and thus the sensitivity to the addition of the lubricant of magnesium stearate.

Table 2. Values of LSR for tableting materials at the compression force of 15 kN.

Tableting material	LSR	s_d of LSR
SC	0.728	0.034
S 1500	0.554	0.038
SC + PH 1:3	0.089	0.025
SC + PH 1:1	0.379	0.030
SC + PH 3:1	0.572	0.022

LSR: lubricant sensitivity ratio; PH: Pharmatose DCL 15; SC: StarCap 1500; S 1500: Starch 1500; s_d: standard deviation.

Conclusion

It can be concluded that co-processed dry binder StarCap 1500 is better compressible than Starch 1500. The strength of the tablets made of this substance is higher and the elastic share of energy during compaction is markedly lower. A disadvantage is high lubricant sensitivity, which is higher than in the case of Starch 1500. Disintegration time of tablets is markedly shorter than in the case of the substance Starch 1500. With increasing portions of StarCap 1500 in the mixtures with Pharmatose DCL 15, the strength of tablets and the disintegration period are increased, from the energetic viewpoint the energy for friction is decreased, and the energy accumulated by the tablet during compaction and the elastic component of the energy are increased.

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Declaration of interest

The authors report no declarations of interest.

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