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COMPARISON OF PROPERTIES OF TABLETS AND ENERGY PROFILE OF COMPACTION OF TWO SPRAY-DRIED LACTOSES

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Abstract: The paper compared two spray-dried lactoses Flowlac® 100 and SuperTab® 14SD from the standpoint of tensile strength and disintegration time of tablets, the effect of an addition of the lubricant magnesium stearate and silicified microcrystalline cellulose on these properties, and also from the standpoint of the energy profile of compression. The comparison of the values was performed at the compression force of 15 kN. The strength of tablets was higher in the case of SuperTab 14SD, an increase in the concentration of magnesium stearate did not decrease tablet strength. Prosolv SMCC 90 increased the strength of tablets and made it equal for both lactoses, but it also increased the sensitivity to the added lubricant. The disintegration time of tablets was shorter in the case of SuperTab 14SD, an increased concentration of magnesium stearate prolonged it, and an addition of Prosolv SMCC 90 shortened it and made it equal for both lactoses. From the energy standpoint, the maximal energy was higher in the case of SuperTab 14SD, an addition of Prosolv SMCC 90 increased it and again made it equal for both lactoses. The differences in the values of the maximal energy were primarily due to the values of the energy for friction and the energy accumulated by the tablet after compression, and there was no marked difference in the values of the energy of decompression. SuperTab 14SD showed a higher plasticity than Flowlac 100.

Keywords: spray-dried lactose, silicified microcrystalline cellulose, tensile strength of tablets, disintegration time of tablets, force – displacement profile

Spray-dried lactose was the first dry binder that started the technology of direct compression of tablets. Though half a century has passed since, spray-dried lactose has been still used in the form of several company products. The first products had better binding and flow properties than α-lactose monohydrate, but they had also some disadvantages. These disadvantages included a loss of the original color due to the presence of impurities in the basic solution (mainly 5-(hydroxymethyl)-2-furaldehyde) and a reaction with primary amines, during which the tablets get brown on storage. Another problem which had to be solved was low compressibility. Impurities were later removed from the parent solution before spray-drying, but primary amines are incompatible with lactose. More perfect products have been prepared since the 1970s, when concentrated suspensions of smaller crystals in water began to be spray-dried. The result of spray-drying is spherical particles, which contain microcrystals of α-lactose monohydrate glued together with amorphous lactose, which positively influences compressibility. An increased share of amorphous lactose increases compressibility of products. Commercially available products contain approximately 15–20% of amorphous lactose and 80–85% of α-lactose monohydrate (1). The presence of amorphous lactose in spray-dried lactose may be problematic if it is stored in open containers at relative humidities over 50%. In that case, the amorphous part slowly crystallizes to α-lactose monohydrate (2). On the whole, spray-dried lactose in comparison with other dry binders possesses bad compressibility and a relatively low dilution potential. On the other hand, it possesses excellent flow properties, best of all directly compressible fillers, which is due to a larger size of particles and sphericity of spray-dried aggregates. Spray-dried lactose is compressed by fragmentation particles, but also plastically. Above a particle size of 45 μm, fragmentation takes place, smaller particles undergo plastic deformation, as well as the amorphous share of the product, and therefore, there is certain sensitivity to the presence of lubricants. There exist a number of products of spray-dried lac-

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tose from different companies, which, of course, have the conditions and procedures of production adjusted in a different way, and that is why it gives rise to products with different properties (2, 3). The aim of this paper results from this fact; it aims to compare the company spray-dried lactose products Flowlac® 100 and SuperTab® 14SD from the standpoint of tensile strength and disintegration time of tablets, effect of an addition of the lubricant magnesium stearate and silicified microcrystalline cellulose on these properties and further from the standpoint of the energy profile of compaction.

EXPERIMENTAL

Materials

The study used two types of spray-dried lactose, SuperTab® 14SD (DMV – Fonterra Excipients, Germany) and FlowLac®100 (Meggle – Pharma, Germany), and silicified microcrystalline cellulose Prosolv® SMCC 90 (JRS PHARMA GmbH+ Co.KG, Germany). The lubricant was magnesium stearate (Acros Organics, New Jersey, USA).

Preparation of tableting compositions:

Altogether 10 tableting compositions were prepared:

- SuperTab 14SD or Flowlac 100 with 0.5% of magnesium stearate,
- SuperTab 14SD or Flowlac 100 with 1% of magnesium stearate,
- SuperTab 14SD or Flowlac 100 + Prosolv SMCC 90 in a ratio of 3 : 1,
- SuperTab 14SD or Flowlac 100 + Prosolv SMCC 90 in a ratio of 3 : 1 with 0.5% of magnesium stearate,
- SuperTab 14SD or Flowlac 100 + Prosolv SMCC 90 in a ratio of 3 : 1 with 1% magnesium stearate.

Mixtures were prepared by mixing in a mixing cube KB 15S (Erweka GmbH, Hausenstamm, Germany). Spray-dried lactoses were mixed with magnesium stearate for 5 min, with silicified microcrystalline cellulose in a ratio of 3 : 1 for 7 min. If the lubricant was contained in the mixtures of lactoses and silicified microcrystalline cellulose, it was added at the end for a period of 5 min. The rate of rotation of the mixing cube was 17 revolutions in one minute and 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 0.5 ± 0.0010 g. Compression velocity was 40 mm/min and compression force 15 kN. In 10 tablets from each tableting composition, the "force-displacement" plot was drawn by means of a computer programme testXpert V 9.01 and the compaction process was evaluated as far as energy was concerned, i.e., the energies E_1, E_2, and E_3 were expressed numerically. Energy E_1 is the energy consumed by friction, energy E_2 is the energy accumulated by the tablet in the course of compression, and energy E_3 is the energy released during decompression (Fig. 1) (4). The above-mentioned energies were used to calculate also the total energy Emax, which is the sum of all energies and plasticity (PL) according to Eq. [1] (4):

$$Pl = 100\ E_2/E_2 + E_3 \qquad [1]$$

Measurement of tensile strength of tablets

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 destruction force in N. Tensile strength of tablets was calculated according to Eq. [2]:

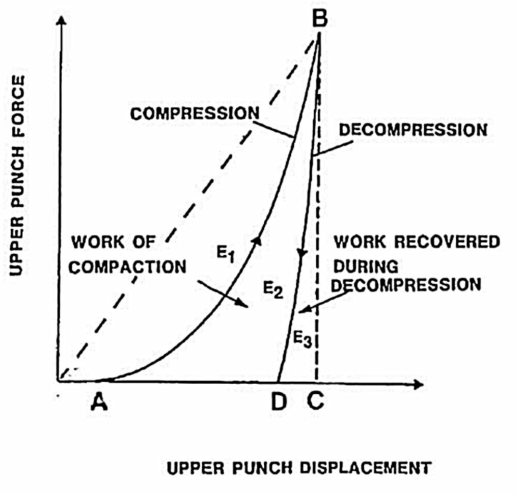

Figure 1. Plot of upper punch force *vs.* upper punch displacement during compression and decompression. E_1 – energy for friction. E_2 – energy accumulated by the tablet after compression. E_3 – energy of decompression

$$P = \frac{2F}{\pi \times d \times h}, \qquad [2]$$

where P is the tensile strength of tablets [MPa], F is the destruction force [N], d is the tablet diameter [mm], and h is the thickness of the tablet [mm] (5).

Measurement of disintegration time of tablets

Disintegration times of tablets were evaluated at earliest 24 h after compaction always in 6 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 7th edition (6). The test was carried out without discs in the medium of purified water tempered to 37 ± 1°C. The tablet was considered disintegrated at the moment when there was no remainder on the net.

The results of tensile strengths and disintegration times were statistically processed by means of the computer programmes Excel and Qcexpert. The values of the energies and plasticity were statistically processed by the computer programme testXpert V 9.01 directly during compaction. Elementary data analysis yielded the mean values with standard deviations, which were graphically processed. In the cases of unclear significance of differences in the values, unpaired *t*-test at a level of significance of 0.05 was employed.

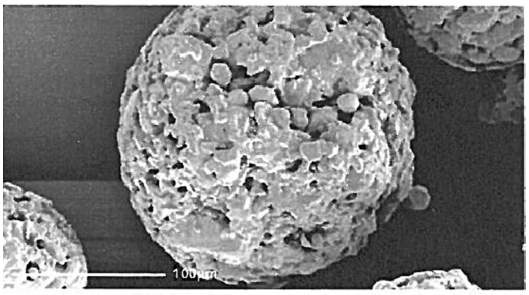

Figure 2. Particles of SuperTab 14SD

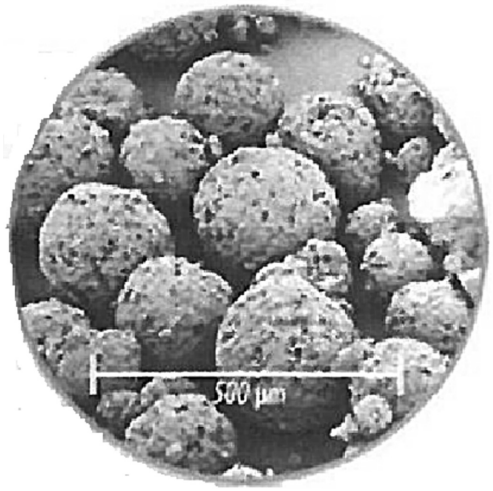

Figure 3. Particles of Flowlac 100

RESULTS AND DISCUSSION

The spray-dried lactoses studied were SuperTab® 14SD and Flowlac®100. Their microscopic characteristics are presented in Figs. 2 and 3 (7, 8). Silicified microcrystalline cellulose was Prosolv® SMCC 90 and its share in the mixtures with lactoses was 25%. The use of mixtures of lactoses and microcrystalline cellulose is very frequent and this concentration was selected because a ratio of 1 : 3 of the components cellulose and lactose is optimal, improving their compressibility as well as disintegration capacity (2). In this percentages cellulose and lactose are represented also e.g., in the co-processed dry binders MicroceLac®100 (9) and Cellactose®80 (10). Prosolv SMCC 90 contains, besides microcrystalline cellulose, 2% of colloidal silicon dioxide, which improves the flowability and compressibility, and decreases the sensitivity to an addition of lubricants (9), and that is why it was selected instead of pure microcrystalline cellulose. Concentrations of magnesium stearate were 0.5 and 1%. Besides the properties of tablets, the evaluations included also the energy balance of compression (4). For the evaluation of all parameters under study, the compression force of 15 kN was selected, as at this compression force the values of tensile strength of tablets from spray-dried lactoses with the lubricants without silicified microcrystalline cellulose oscillated about the upper limit of the optimal range of strength (0.56-1.11 MPa) (11).

Tensile strength of tablets from both spray-dried lactoses with two concentrations of magnesium stearate and silicified microcrystalline cellulose is presented in Fig. 4. Tablets containing only spray-dried lactose with a lubricant were stronger in the case of SuperTab 14SD. An increase in the concentration of the lubricant did not exert a negative effect on the strength of both spray-dried lactoses. An addition of 25% of Prosolv SMCC 90 increased and equalled the strength of tablets from both lactoses, but after the addition of the lubricant there was a decrease in the strength of tablets, more marked in the mixture with Flowlac 100. A decrease

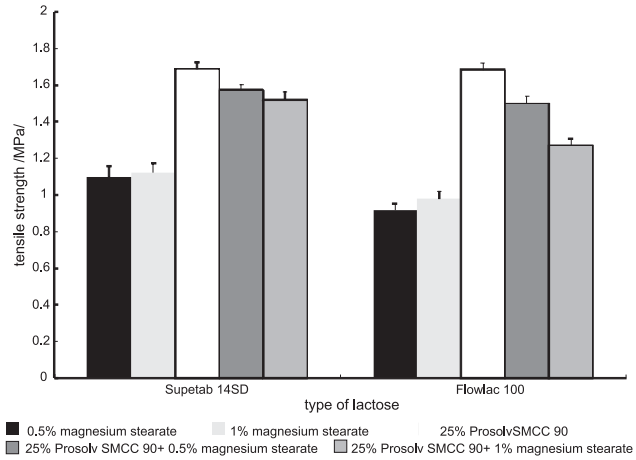

Figure 4. Tensile strength of tablets at the compression force of 15 kN

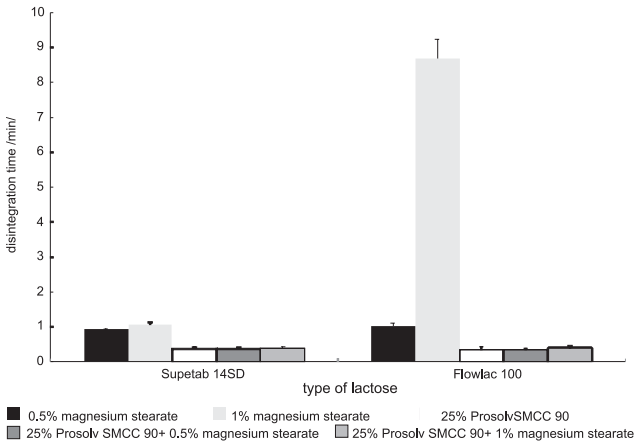

Figure 5. Disintegration time of tablets at the compression force of 15 kN

in strength was expected, because silicified microcrystalline cellulose is compacted plastically (1, 12). A higher decrease in strength in the case of the mixture with Flowlac 100 seems to suggest its higher plasticity, but it is not confirmed by the result with an increased concentration of magnesium stearate in the case of Flowlac 100 alone, where no negative effect on strength was demonstrated. Figure 5 shows disintegration time again at a compression force of 15 kN. The Figure clearly shows that a longer disintegration time in the case of the mixtures of lactoses only with stearate was observed in the tablets made from Flowlac 100. An increased concentration of the lubricant prolonged the disintegration period, in the case of Flowlac 100 in a very marked manner. After an addition of Prosolv SMCC 90, which also acts as a disintegrating agent, there occurred a shortening of disintegration time and equalization of the values in both spray-dried lactoses. No statistically significant difference was shown even after an addition of the lubricant in both concentrations, so the hydrophobicity of magnesium stearate did not prolong disintegration time.

Other Figures summarize the energy balance on compaction. Energy balance was evaluated using the "force-displacement" profiles. The "force-displacement" profiles are useful as a material characteristic in preformulation work or for detecting batch-to-batch variations in the compression properties of materials (4). Figure 6 presents the values of the maximal energy Emax, which is the sum of the energy for friction, the energy accumulated by the tablet

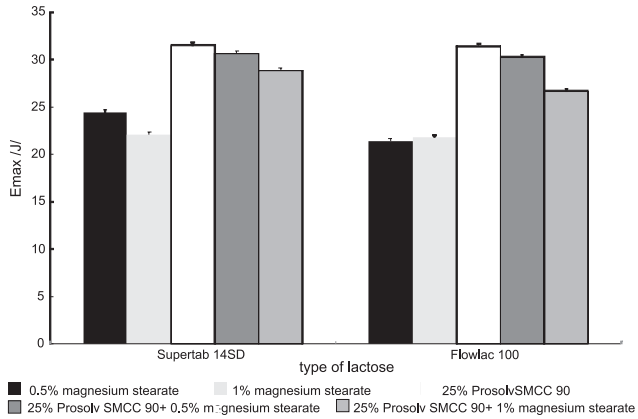

Figure 6. Values of Emax (maximal energy) at the compression force of 15 kN

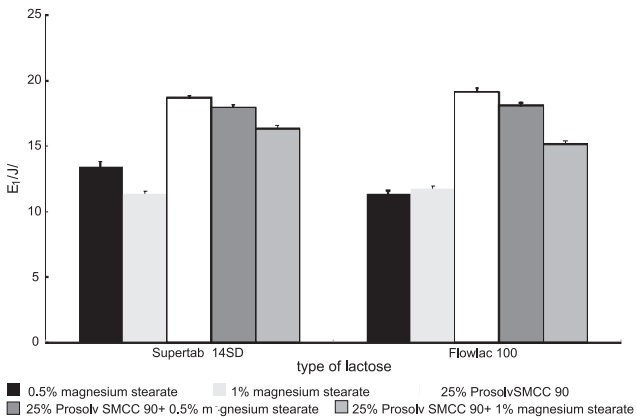

Figure 7. Values of E_1 (energy for friction) at the compression force of 15 kN

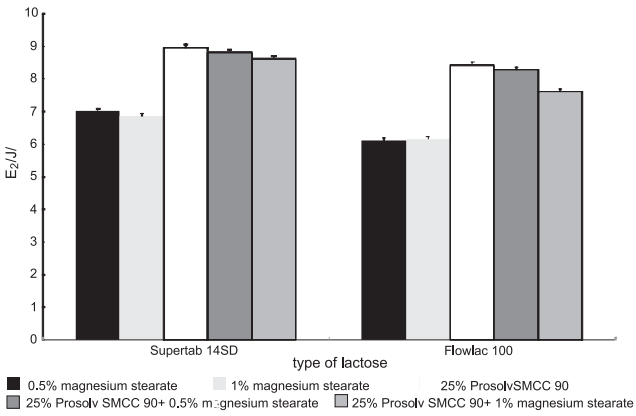

Figure 8. Values of E_2 (energy accumulated by the tablet after compression) at the compression force of 15 kN

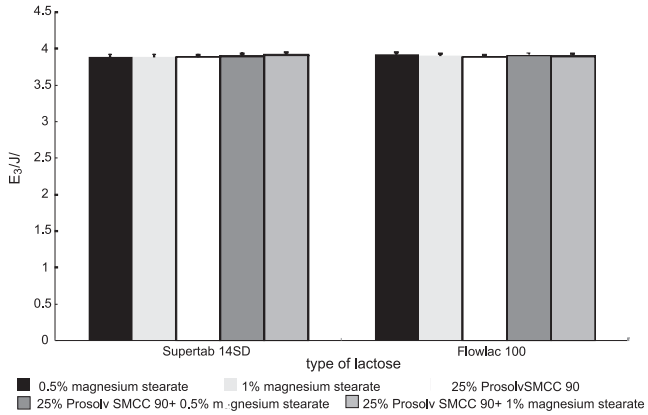

Figure 9. Values of E_3 (energy of decompression) at the compression force of 15 kN

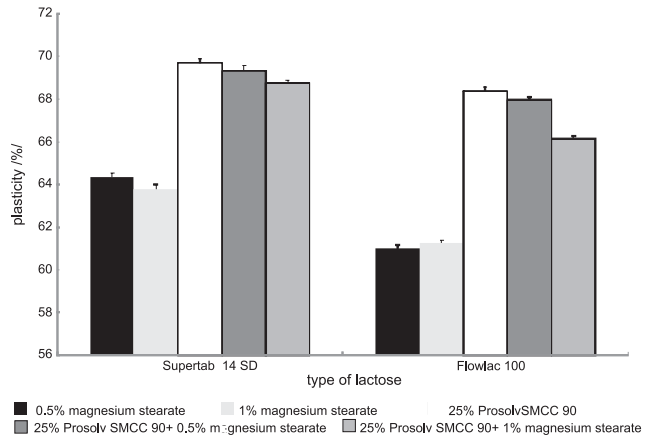

Figure 10. Values of plasticity at the compression force of 15 kN

after compression, and the energy of decompression. In SuperTab 14SD with a lubricant the value of the maximal energy was higher than in Flowlac 100, in addition, the value was decreased here due to the effect of an increased concentration of magnesium stearate, which did not take place in Flowlac 100. An addition of Prosolv SMCC 90 to spray-dried lactose increased the maximal energy and also in the case of strength there was no statistically significant difference between the values of the mixtures without the lubricant, the maximal energy decreased with the concentration of the lubricant, more in the case of the mixture with Flowlac 100 as well as the strength. Figures 7, 8 and 9 show that the differences in the maximal energy determined primarily the values of the energy for friction E_1 (Fig. 7) and the energy accumulated by the tablet after compression E_2 (Fig. 8). There were no marked differences between the values of the energy of decompression E_3 (Fig. 9). The energy for friction was higher in the case of SuperTab 14SD, but it was decreased in it due to an increased concentration of magnesium stearate. This decrease should be theoretically observed also in the case of Flowlac 100 because of decreased friction due to a higher concentration of the lubricant, which did not take place. This may be due to a higher share of larger particles in Flowlac 100, where 1% concentration of magnesium stearate is superfluous and does not decrease friction any more. An addition of Prosolv SMCC 90 increased the values of the energy for friction, but they equalled for both spray-dried lactoses in the mixtures without and with a 0.5%

content of magnesium stearate, which the energies for friction decreased again. The values of the energy accumulated by the tablet after compaction are presented in Figure 8. Higher values in the case of all mixtures were found for SuperTab 14SD. A higher concentration of the lubricant did not markedly influence the value of the energy E_2, an addition of Prosolv SMCC 90 increased the values and subsequently in these mixtures there was a more marked decrease in this energy only after an addition of 1% of magnesium stearate. This held true for both spray-dried lactoses. The last evaluated characteristic was plasticity, whose values are presented in Figure 10. A more plastic behavior of the two spray-dried lactoses was shown by SuperTab 14SD. This can be due to a slightly higher representation of smaller particles and perhaps even due to a higher share of amorphous lactose, which, however, the manufacturers do not state. Generally, SuperTab 14SD is a newer product than Flowlac 100, so certainly there will be an effort to improve its compressibility by increasing the amorphous share by adjusting the conditions of spray-drying during the manufacture of the product. Otherwise, after addition of silicified microcrystalline cellulose to spray-dried lactoses their plasticity would be certainly increased, as this dry binder is compacted plastically, and the addition of magnesium stearate decreased plasticity, more markedly in the case of its 1% concentration.

CONCLUSION

In closing it can be stated that SuperTab 14SD with magnesium stearate at the same compression force yields stronger tablets than Flowlac 100 with magnesium stearate. An increase in the concentration of the lubricant does not produce a decrease in the strength in the cases of both spray-dried lactoses, an addition of Prosolv SMCC 90 increases the strength of tablets and makes it equal for both lactoses, but magnesium stearate decreases the strength of tablets in the case of these mixtures. Disintegration time of tablets is shorter in the case of SuperTab 14SD, an increased concentration of the lubricant prolongs it. An addition of Prosolv SMCC 90 markedly shortens the disintegration time and there is no statistically significant difference between the values for both spray-dried lactoses. From the energy standpoint, the values of the maximal energy are higher in the case of the substance SuperTab 14SD, an addition of Prosolv SMCC 90 equalizes the values for spray-dried lactoses. The resultant differences in the values of the maximal energy are primarily due to the energy for friction and the energy accumulated by the tablet after compaction, as there is no marked difference between the values of the energy of decompression in the tableting materials. The values of plasticity are higher for SuperTab 14SD.

Acknowledgments

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