Tableting of StarLac® Compared to Tableting of Binary Mixtures from Spray-dried Lactose and Maize Starch

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INTRODUCTION

Direct compression is a major formulation process in Pharmaceutical Technology. StarLac® is a new direct compression excipient, produced by spray-drying of α-lactose-monohydrate and maize starch. Powder properties like densities and particle size distribution are useful to characterize the flowability of materials. Pressure-time-profiles, pressureporosity-profiles and compactibility plots help to evaluate the tableting properties.
Aim of this study is to characterize both the pure substances and the physical mixtures of spray-dried lactose and maize starch in comparison to the new direct compression excipient StarLac®.

MATERIALS & METHODS

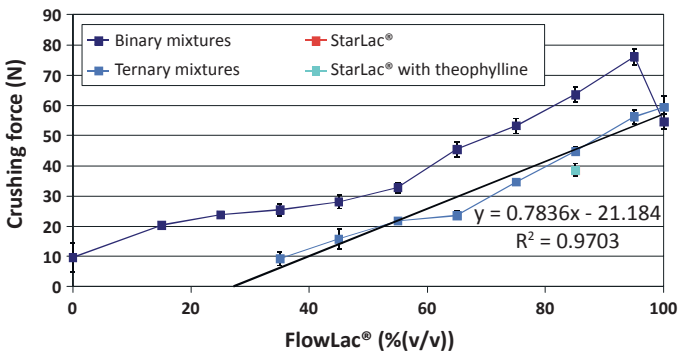
StarLac®, a spray-dried compound of lactose and maize starch, Lot # L 0007 (Roquette Frères, Lestrem, France and Meggle GmbH, Wasserburg, Germany); FlowLac® 100, spray-dried lactose, Lot # L 0043 (Meggle GmbH, Wasserburg, Germany); maize starch, Lot # S 8463 (Roquette Frères, Lestrem, France); theophylline monohydrate Lot # 21835894 (Carl Roth GmbH, Karlsruhe, Germany) and magnesium stearate, Lot # 93810410 (Caelo GmbH, Hilden, Germany).

RESULTS & DISCUSSION

Tablet properties

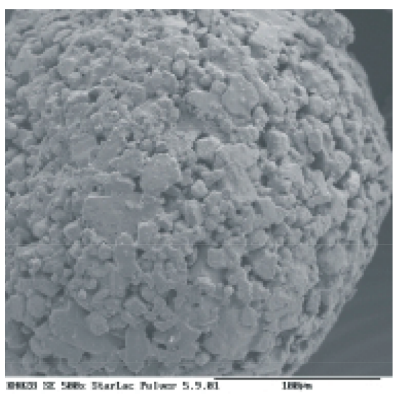
The compactibility of maize starch indicated by radial crushing force is insufficient. FlowLac® and StarLac® have a sufficient compactibility at a maximum relative density of 0.90 (StarLac® : 79 N at 134 MPa; FlowLac®: 113 N at 191 MPa). The crushing force relative to the volume fraction increases lineary in the order ternary mixtures < binary mixtures, but that of StarLac® is significant lower than that both mixtures at 85 % (v/v). FlowLac® and theophylline monohydrate had no influence on the crushing force of StarLac®.

Figure 3. Crushing force of the binary, ternary mixtures, StarLac® and a mixture of StarLac® with 20% theophylline monohydrate.



Powder properties

Figure 6. SEM of particle of StarLac® at 500 magnification.



The mean particle size of StarLac® (**Fig. 6**) and FlowLac®, both the D50-data and the distribution of particle size, differ scarcely. Maize starch consists of smaller particles in comparison to the other materials. The densities and the resulting parameters describe, that the good flowability of StarLac® is similar to that of FlowLac®. Both Hausner ratio and Carr-Index increase in the order FlowLac® < StarLac® << maize starch.

Tableting

Tablets were produced on an instrumented eccentric tableting machine (Korsch EK0, Korsch Maschinenfabrik, Berlin, Germany) with 11 mm flat faced punches (Ritter GmbH, Berlin,Germany).The mass for each tablet was calculated for each maximum relative density used (0.75, 0.80, 0.85, 0.90, 0.95). Each tablet was manually filled in and produced with an accuracy of ±0,001 at maximum relative density. 0,5 % magnesium stearate were used as lubricant. For mathematical analysis of the data the three-dimensonal model [1,2] was primarily used because only this method includes all the three parameters time, porosity and pressure simultaneously. The equation is as follows:

$$z = \ln \frac{1}{1 - D}$$

$$= ((t - t_{max}) * (d + \omega * (P_{max} - P))) + (e * P) + (f + d * t_{max})$$

with t = time, p = pressure, ω = angle of torsion, D = relative density, d = time plasticity, e = pressure plasticity , f = intersection.

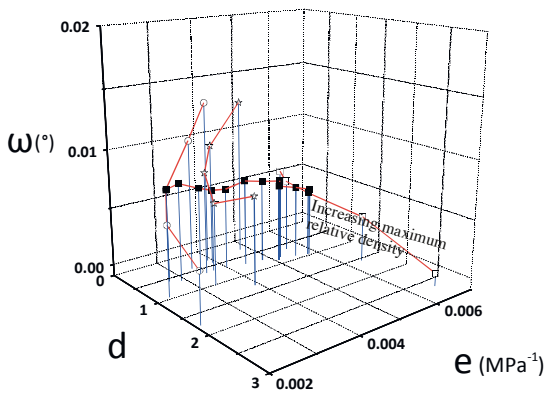


Figure 1. 3D parameter plot of StarLac® (♂), FlowLac® (○), maize starch (□) and binary mixtures (■).

Pressure plasticity e correlates with the micro-hardness of the final tablets, the angle of torsion with the Young's modul and time plasticity d is influenced by tableting speed [2].

Analysis by three-dimensional modeling indicates that the tableting behavior of StarLac® at a maximum relative density from 0.75 to 0.90 is similar to that of FlowLac® (**Fig.1**). StarLac® and FlowLac® deformed plastically, whereby the plasticity decreased with higher relative density. The same was the case for the slope of the Heckel function of both substances. The influence of maize starch becomes visible at a maximum relative density from 0.90 to 0.95 as well by the pressure plasticity of the 3D-Model as by the slope of the Heckel function. Maize starch shows a higher percentry of elastic deformation in comparison to StarLac® and FlowLac® (**Fig.1**). Time plasticity increases in the order FlowLac® < StarLac® << maize starch . The time plasticity of maize starch, FlowLac® and StarLac® correlates exponentially to the maximum relative density. The pressure plasticity of StarLac® and FlowLac® decreases linearily with higher maximum relative density. Only maize starch shows variation, but the pressure plasticity of maize starch is much higher than that of StarLac® (FlowLac® < StarLac®). The angle of torsion increases in the order maize starch << FlowLac® < StarLac®, which indicates, that the Young's modul of maize starch is much lower than that of FlowLac® and StarLac®.

Figure 4. SEM of powder of StarLac® at 15000 magnification.

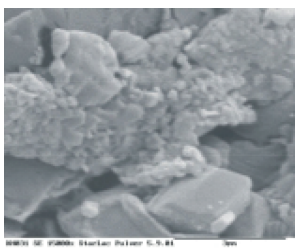
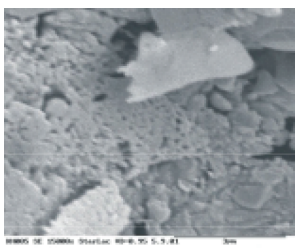


Figure 5. SEM of tablets of StarLac® at 0.95 maximum relative density at 15000 magnification.



The SEMs show the difference before (**Fig.4**) and after (**Fig.5**) tabletting of StarLac®. The powder of StarLac® has regular crystals of lactose (A), embedding crystals of lactose in the amorphous lactose (B) and a starch particle (C). After deformation the crystals are smaller and the particle of starch create a fine net work. A reason of this phenomenom can be the viscoelastic flow of starch at high pressure, because only at a maximum relative density of 0.95 this can be detected.

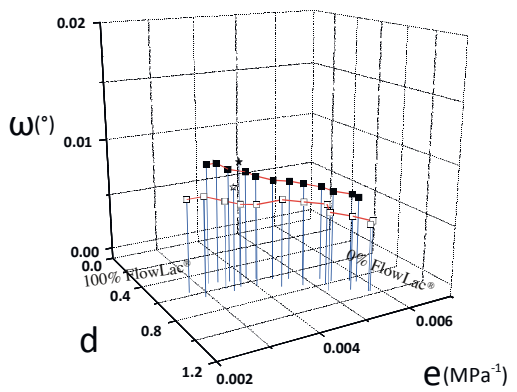


Figure 2. 3D parameter plot of binary [□] and ternary [■] mixtures, supplementary StarLac® [♂] and the mixture of StarLac® with theophylline monohydrate [♂].

The binary mixtures deform plastically. The relationship between volume fraction and the parameters of the 3D- model (**Fig.2**) is linear as the slope of the Heckel function. The data from the mixture with 95 % maize starch can be interpreted by the percolation theory of Leuenberger [3]. The data of the volume fraction of 30 % and 90 % deviate from linearity. The deformation of StarLac®, a spray-dried product of lactose and starch, is significantly more plastically than the physical mixture. This result applies to the ternary mixture with the active substance theophylline monohydrate as well.

CONCLUSION

Flowability and tableting properties indicate, that StarLac® is a useful new excipient for direct compression. Its advantage compared to FlowLac® is the higher plastic deformability. The better compactibility and the flowability are superior to maize starch. The improvement compared to the physical mixtures can be derived from the deformation properties.

ACKNOWLEDGEMENTS

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