

Influence of Various DC-Lactose Types on Tableting and Colour Stability of Ascorbic Acid

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Introduction

In solid dosage forms, drug and excipient have an intimate contact, which can affect drug stability. Excipients can initiate, accelerate or participate in chemical or physical interactions with the drug (1).

Lactose is one of the most used excipient in tablets. In many cases moisture is involved in different reaction types of drugs (2,3)

In our investigation we focused on direct compressible lactose qualities, to compare the influence of agglomerated, spray dried lactose-monohydrate and anhydrous lactose on tableting properties and the discolouration of ascorbic acid formulations.

Material & Methods

Agglomerated lactose (AG) from Meggle, Germany (Tablettose™ 80), spray dried lactose(SD) from Foremost, USA (Fast Flo™) & Meggle, Germany (Flowlac™), lactose anhydrous (LA) from DMV, Netherlands (Pharmatose™ DCL 21), Mg-stearate and ascorbic acid (AA) from Merck, Germany were used.

Tablets were produced on a instrumented single punch press (Korsch EK 0, 8mm punches, 240 mg, flat faceted), using a mixture of 79.5% excipient, 20% AA and 0.5% Mg-stearate. Powders and tablets were stored at 25°C, 60% r.H. and 40°C, 75% r.H.

Analytical equipment

UV Spectrometer – Kontron Uvikon 939; tablet hardness – Erweka, type TBH 30; disintegration – Erweka, type ZT 3-2.

Colour was measured by UV-absorption at 400 nm. Flowability, tablet hardness and disintegration were tested according to standard pharmacopoeial methods.

Results:

The two spray dried products showed very good flow, followed by the agglomerated lactose, which can be explained by the spherical shape of the granules. On the other hand the flow for the anhydrous lactose was poor. Due to the high portion of fine AA the flow of the formulation decreased significantly (see fig. 1)

Best hardness yield was obtained by using the spray dried types followed by the anhydrous lactose (see fig.2). In all formulations a friability under 1% can be achieved. The ranking for placebo tablets was the same, but on a higher level.

Disintegration varied between 89 sec and 389 sec at approx. 65 N tablet hardness (friability < 1%). (see fig.3). It has to be noted, that anhydrous lactose tablets disintegrate even at a low tablet hardness very slowly and reached a plateau.

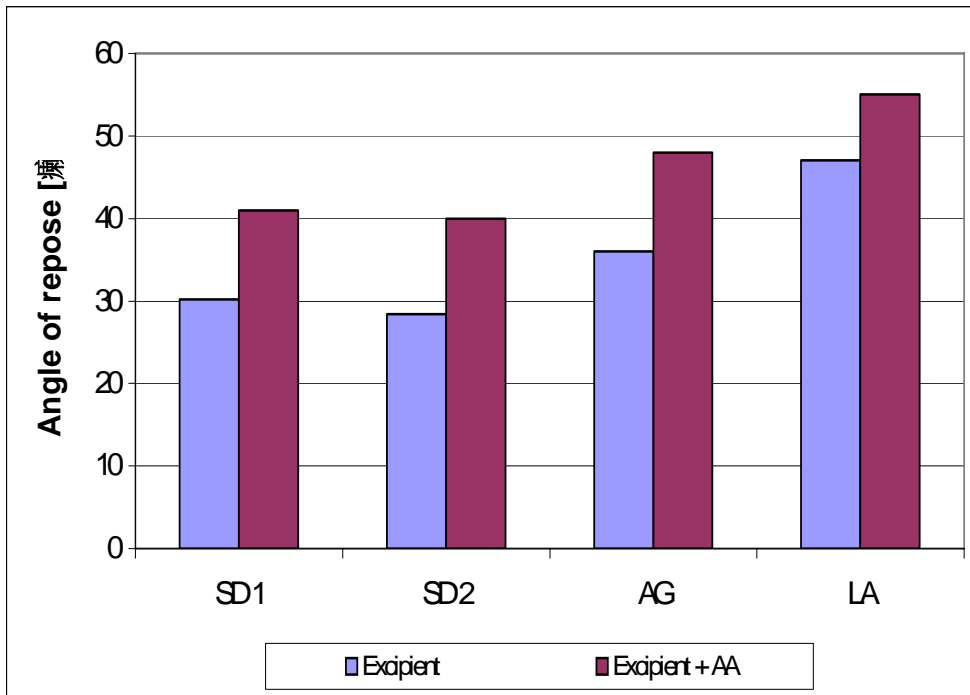


Figure 1: Angle of repose of the various lactose types and in a formulation with 20% ascorbic acid

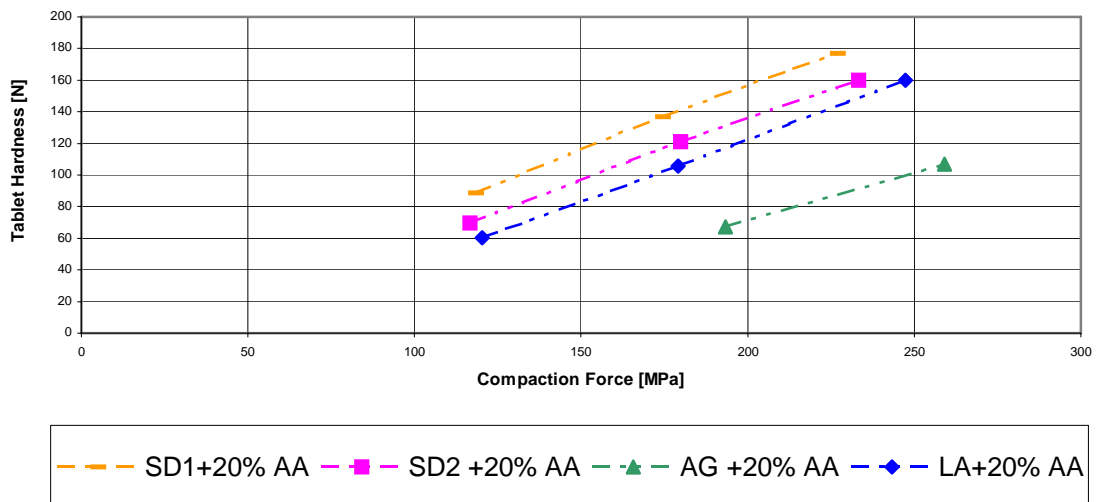


Figure 2: Compaction profile of various DC-lactose-types in a formulation with 20% ascorbic acid (lubricant: 0,5% Mg-stearate)

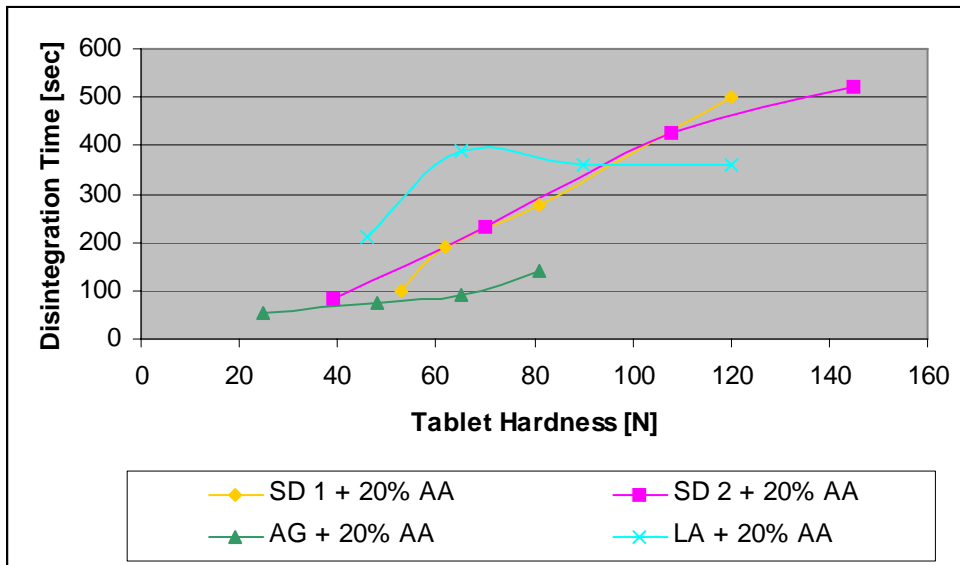


Figure 3: Disintegration profile of various DC-lactose types in a formulation with 20% ascorbic acid (lubricant: 0,5% Mg-stearate)

At 40° C, 75% r. H. discolouration occurs in all formulations and varied from yellowish to yellow for the powder and from off white to yellow for the tablets. The UV-absorption is presented in figure 4 & 5 (powder & tablets resp.). Only a moderate discolouration was found at 25°C. The most was obtained with anhydrous lactose.

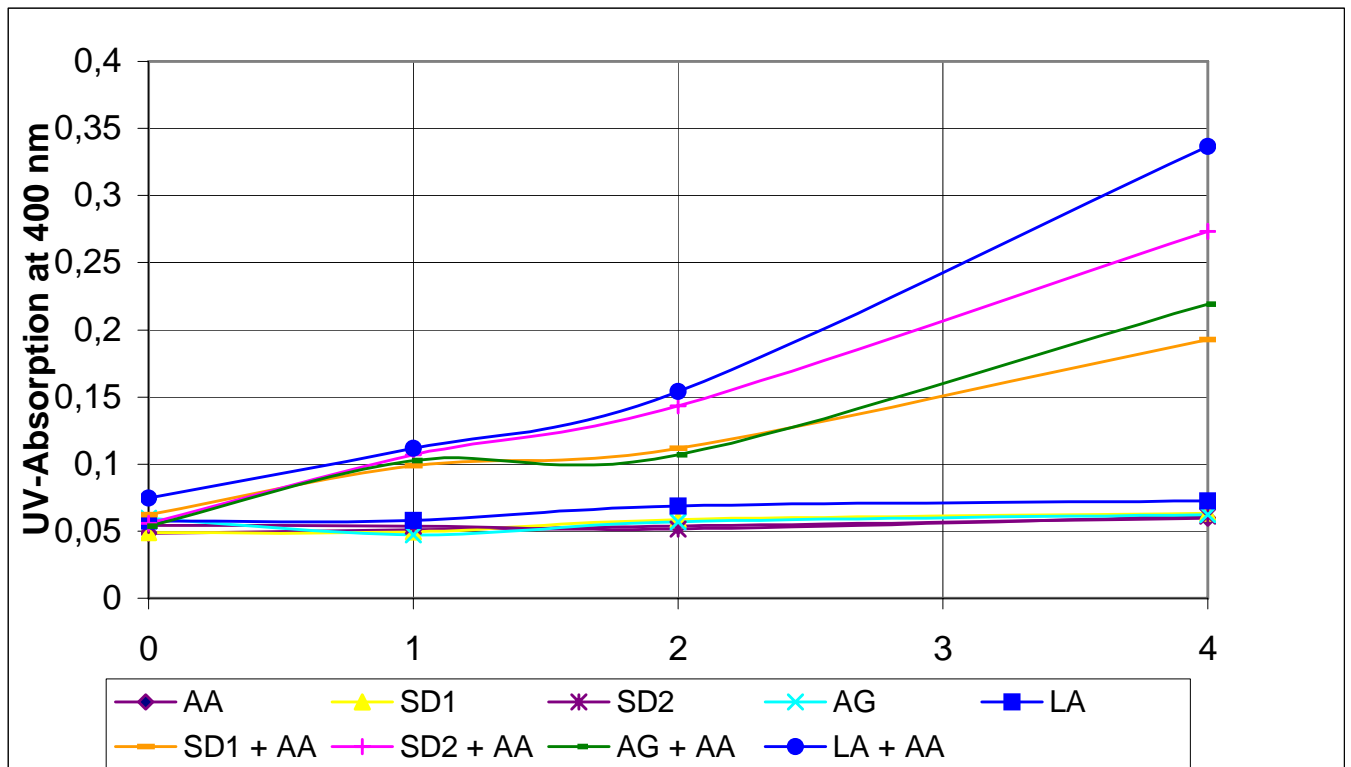


Figure 4: UV-Absorption of the powder formulation (stored at 40°C, 75% r.H.)

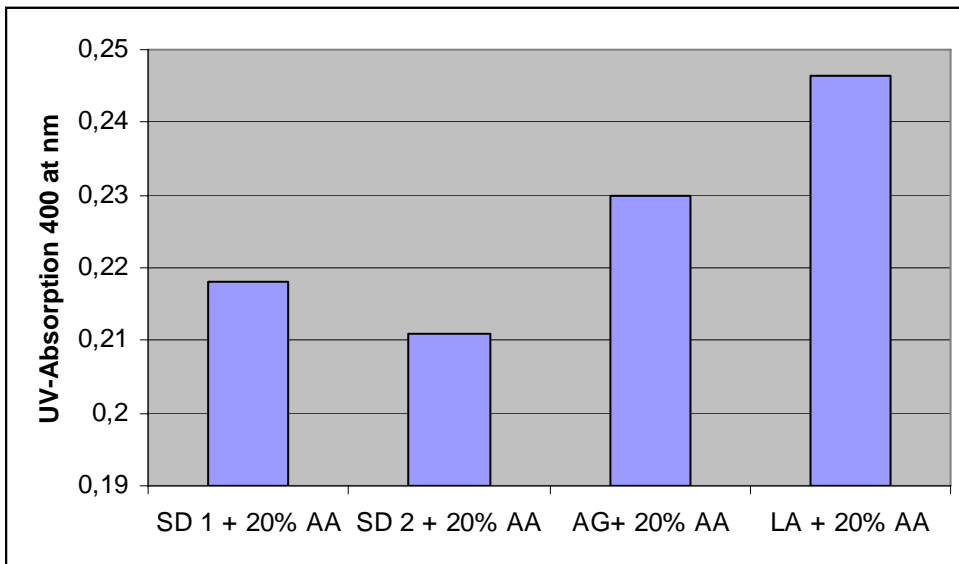


Figure 5: UV-Absorption of the tablets (stored at 40°C, 75% r.H.)

Conclusion

Agglomerated, spray dried lactose monohydrate and anhydrous lactose show some considerable differences concerning tableting properties and discolouration of ascorbic acid formulations.

Spray dried lactose showed the best properties for direct compression application. Best compressibility and flow, whereas anhydrous lactose was less compressible, but still better than agglomerated lactose. On the other hand anhydrous lactose shows poor flow.

Most discolouration was observed in the formulation with anhydrous lactose. Above 60% r.H. anhydrous lactose take much more water up than spray dried or agglomerated lactose. It can be assumed, that the crystal water in lactose monohydrate has less influence on the colour stability of ascorbic acid than the parameter of water uptake caused by the excipient itself.

References:

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- 3) J. Du and S. Hoag (2001) The influence of excipients on the stability of the moisture sensitive drugs aspirin and niacinamide: Comparison of tablets containing lactose-monohydrate with tablets containing anhydrous lactose
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