Superior Lubrication Performance of Sodium Stearyl Fumarate
in Direct Compression and Continuous Manufacturing

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PURPOSE

For the last many decades, the process of lubrication is considered sensitive to overmixing leading to low hardness, increase in disintegration time and ultimately impacting tablet quality. Therefore, the most commonly used lubricant i.e. magnesium stearate (MgSt) is added to other ingredients just before tableting for minimum mixing time possible. This means there are at least a minimum of two steps required for tablet powder mixing. An alternative to MgSt is sodium stearyl fumarate (SSF). In continuous manufacturing (CM), the direct compression blending processes is typically conducted by two consecutive continuous dry powder blenders which separate the blending process into two distinct stages.

OBJECTIVE(S)

To provide more flexibility and reduce blending sensitivity associated with lubricants, this work investigates the effects of addition of sodium stearyl fumarate (SSF) compared to Magnesium Stearate (MgSt) in different blending stages.

METHODS

Model formulation

Tablets were composed of 500 mg Metformin, 196 mg MCC (Avicel® PH-102) or 200 mg co-processed MCC/SiO_2 (containing 2% SiO2, Avicel® SMCC 90), 14 mg croscarmellose (AcDiSol®) and variable contents of lubricant (MgSt or SSF (Alubra®)) and colloidal silica (Aerosil® 200).

Blending

2-step addition: The components (except the lubricant) were blended for 10 min., followed by addition of lubricant and further 3 min. blending.

1-step addition: As in the 2-step addition, except the lubricant was added from the beginning.

METHODS CONTD.

Tableting

Tablets were pressed on a manual single punch hydraulic press to produce 13 mm round, flat-facet tablets at a compaction pressure of 147 MPa. Tablet hardness and disintegration time were analyzed (n=3).

RESULTS

- While a reduced lubricant effect on tensile strength was observed using SSF in 2-step and 1-step blending procedures with formulations containing PH-102 and no added SiO2 (Fig.1), the effect was even more pronounced when co-processed SMCC was used (2% SiO2 related to MCC, 0.56% related to the formulation, Fig.2).
- Further addition of 1% SiO2 to the PH-102 / SSF formulation nearly eliminated the lubricant effect on tablet hardness using the conventional 2-step blending (Fig. 3), while significant advantages where found at high lubricant levels (1-2%) in 1-step addition.
- At higher SiO2 content (2%), advantages in tablet hardness for lubricant SSF were found at higher lubricant levels, 1% and above for the 2-step procedure and 2% in case of the 1-step procedure (Fig. 4).
- Disintegration times were generally between 10 and 30 seconds, increasing with lubricant level. Despite significant differences in tensile strength, dissolution times were comparable using either MgSt or SSF (e.g. Fig. 5 compare Fig. 1 for corresponding tensile strength). However, the co-processed SMCC appears to have a consistently lower disintegration time (Fig. 6 – compare Fig. 2 for corresponding tensile strength)

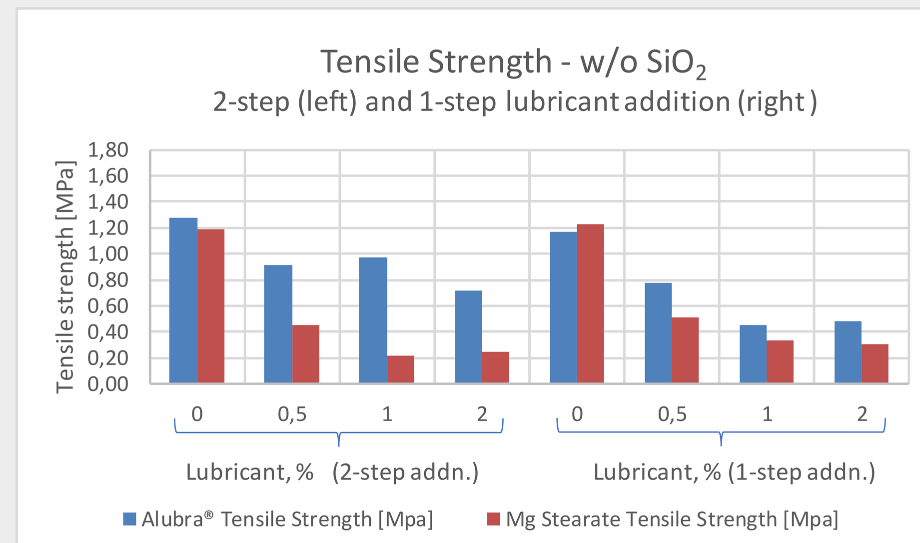

Fig. 1. Tensile strength of PH-102 tablets depending on lubricant addition

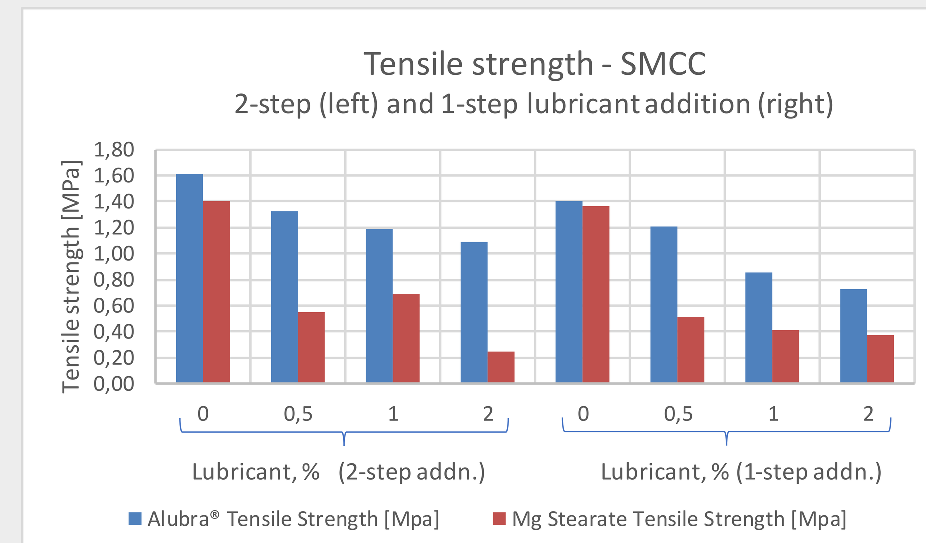

Fig. 2. Tensile strength of SMCC 90 tablets depending on lubricant addition

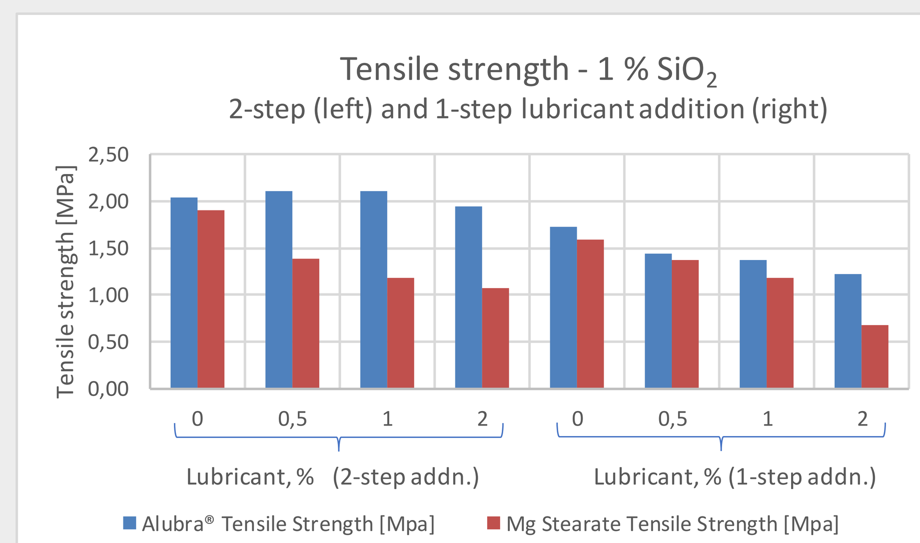

Fig. 3. Tensile strength of PH-102 tablets depending on lubricant addition with 1% SiO_2 added

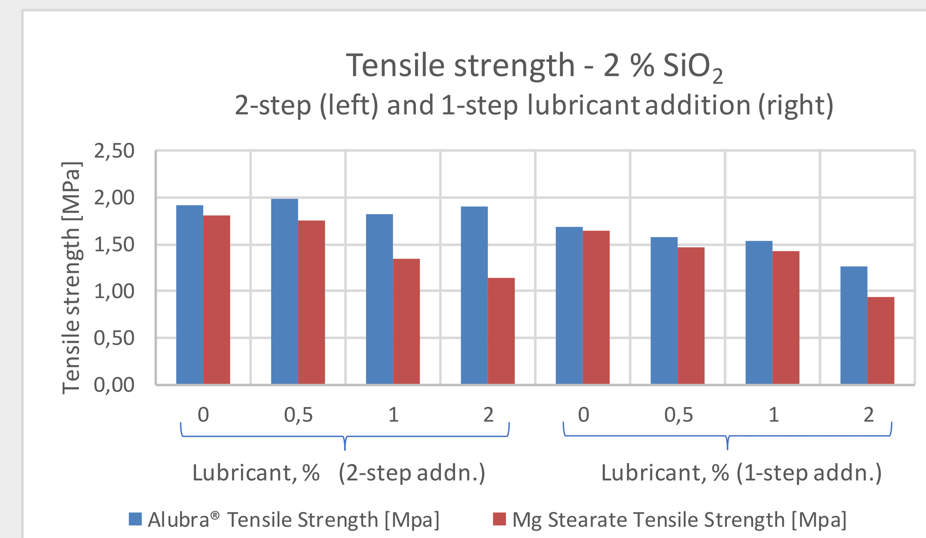

Fig. 4. Tensile strength of PH-102 tablets depending on lubricant addition with 2% SiO_2 added

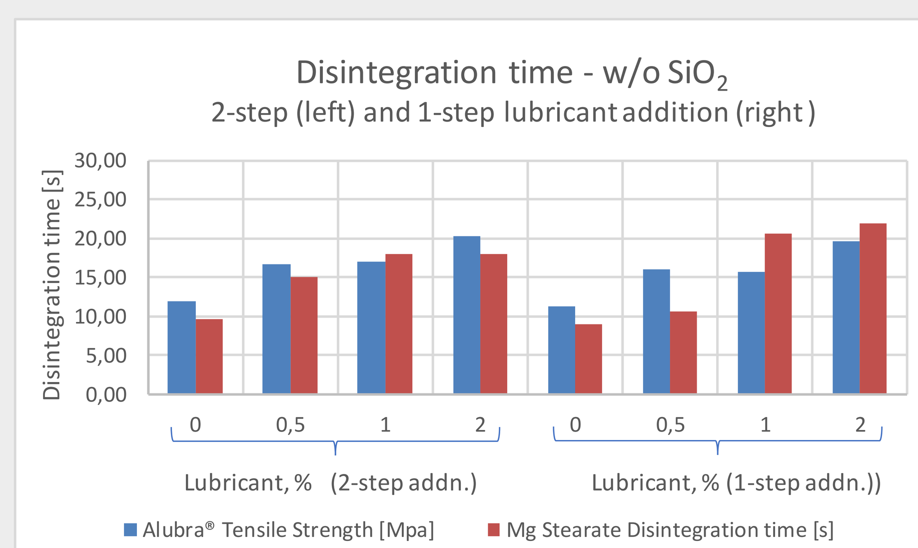

Fig. 5. Disintegration time of PH-102 tablets depending on lubricant addition

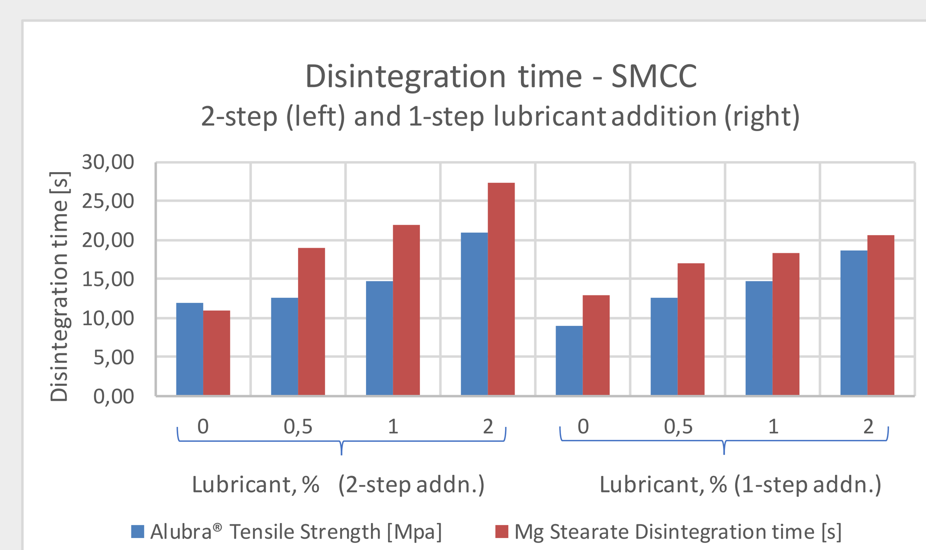

Fig. 6. Disintegration time of SMCC 90 tablets depending on lubricant addition

CONCLUSIONS

It has been demonstrated that SSF (Alubra®) can help to avoid over-lubrication especially at lower mixing time (2-step addition), nearly independently of the amount used and the presence of colloidal silica.

In the case of prolonged mixing in the presence of the lubricant (1-step addition), the benefits of SSF (Alubra®) are seen predominantly in combination with co-processed SMCC or at lubricant addition levels ~2% in case of externally added SiO_2.

The higher tensile strengths observed using formulations containing SSF did not compromise dissolution time, which was similar to or lower than in formulations using MgSt.

REFERENCES

Kleinebudde P, Khinast J, Rantanen J. (editors), Continuous Manufacturing of Pharmaceuticals, John Wiley & Sons, 2017. ISBBN:9781119001348,

Pingali K, Mendez R, Lewis D, Michniak-Kohn B, Cuitino A, Muzzio F., „Mixing order of glidant and lubricant-- influence on powder and tablet properties“, *Int J Pharm.* 409 (2011) 269-277. doi:10.1016/j.ijpharm.2011.02.032

Hölzer AE, Sjögren J, "Evaluation of sodium stearyl fumarate as a tablet lubricant", *Int J Pharm.* 2 (1979) 145-153. doi:10.1016/0378-5173(79)90015-2

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