Comparison of three novel lubrication compositions to some commonly used lubricants

G. Stobbe, M. Lachmann
Biogrund GmbH, Neukirchner Str. 5, 65510 Hünstetten, mlachmann@biogrund.com

Introduction

Lubricants are important excipients used in manufacturing of tablets. The main function of a lubricant is to reduce the friction between the die wall and tablets during ejection. Secondary aims of lubricant use can be the prevention of sticking and the increase of bulk density. While their main function does not aim at a glidant-effect, some lubricants might also improve powder flow. Hydrophobic lubricants (e.g. Magnesium Stearate or Talc) are commonly used in concentrations between 0.25% and 5% w/w[1]. Identifying the ideal lubricant candidate and an appropriate concentration is a challenge due to the impact of the lubricants on the mechanical properties of tablets. Moreover, the lubrication efficiency is affected by the mixing time as well as the particle size grade, surface area and the morphology of the chosen lubricant. In this study, the performance of three novel lubricants, CompactCel LUB (pharma grade, food grade and a bio-vegan grade) was investigated in comparison to nine commonly used lubricant materials.

Materials

All materials were used as provided by the manufacturers: Microcrystalline Cellulose MCC 200 (MCC), DC grade Anhydrous Dibasic Calcium Phosphate (DCPA), Croscarmellose Sodium (CCS), Sodium Carboxymethyl Cellulose (CMC), pregelatinized Starch (ST), granular Vitamin-C (VC), super fine HPC powder (HPC). Five types of Mg-Stearate (MgSt A - E), Calcium stearate (CaSt), Zinc stearate (ZnSt), Glyceryl behenate (GlyBe), Stearic acid (StAc), were used as delivered by the manufacturers. The novel lubricants were of the CompactCel® range of BIOGRUND. Two coconut milk based lubricants: CompactCel® LUB Food (CC FOOD), CompactCel® LUB Bio-Vegan (CC BIO-VEGAN) and a carrier based system containing medium chain triglycerides CompactCel® LUB Pharma (CC PHARM).

Table 1: **Composition of tableting mixtures in %**

	MCC	DCPA	CCS	CMC	ST	VC	Mg-St-A	HPC
M1	62,6	27,9	2,0	7,5	–	–	–	–
M2	20,0	77,9	2,0	–	–	–	0,1	–
M3	15,6	–	2,0	–	60,4	20,0	–	2,0

Methods

Tableting Mixtures

The components were blended for 10 minutes in a 10l drum blender at batch sizes of 5 kg. Pre-lubrication was required for M2 by admixing 0,1 % of Mg-St-A for 30 minutes after mixing the other components as mentioned above. All mixtures were designed to yield moderate to high ejection forces as shown in Figure 1. Lubrication was achieved by admixing the lubricants in a Turbula Blender for 3 minutes. For the evaluation of mixing time effects on the tensile strength of lubricants the blending times were prolonged to 9 and 15 minutes. Lubricant concentrations were as follows: MgSt A-E, GlyBe, StAc, CaSt 1 % in M1, M2 and 0,5 % in M3. CC FOOD: in M1=2,5 %, M2=3 %, M3=1 %; CC BIO-VEGAN: M1+M2=3 %, M3=1 %; CC PHARM: M1=2,5 % , M2=3 %; M3=0,6 %.

Tableting

Mixtures were compressed on a RoTab T rotary press using flat-faced 11.28-mm punches. Compaction forces fixed for each mixture individually (M1=10 kN; M2=12, 5 kN; M3=15 kN). Breaking force values were converted to the corresponding tensile strengths (TS) and the lubricant sensitive ratio was calculated using equation 1 where σu is the TS of the unlubricated tablet and σl that of the lubricated compact. Tablet tooling was cleaned and polished after each experimental run. Ejection forces were measured fore each produced tablet (n ≈150–250) with the recording being started after the values reached plateau level with no further observable drifts.

$$LSR = 100 * \frac{\sigma_u - \sigma_l}{\sigma_u} \qquad \text{Equation 1}$$

Results

Lubricant sensitivity ratio did not vary significantly after compression at different compaction forces. However, ejection forces mostly increased with increasing force (data not shown here averages for a compression force range from 10 kN–15 kN, equivalent to 100 MPa–150 MPa). For all lubricants, the ejection forces were reduced sufficiently to enable a smooth production process of defectless tablets.
Figure 1 shows all obtained LSR values for a mixing time of 3 minutes. Especially mixture M3, a composition containing a high quantity of elastically deforming starch, suffers from severe loss of tensile strength after lubricant addition.

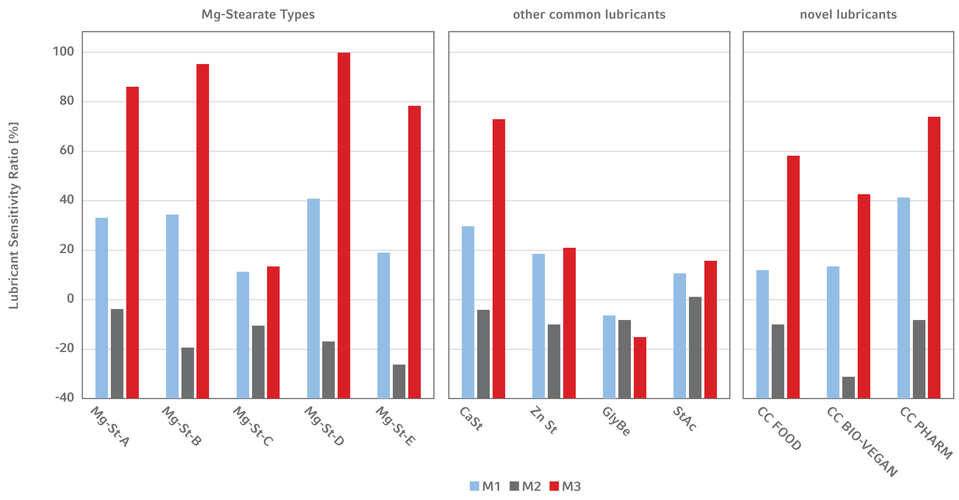

Figure 1: **Lubricant sensitivity ratios for all used lubricants after mixing for 3 minutes**

Using Mg-Stearate types resulted in greater losses of tensile strength than using other common lubricants or the novel compositions from BIOGRUND. Mixtures with M1 showed up to 41 % loss of tensile strength with LSR values ranging from 41 % to −6 %. Remarkably the range of LSR values for the use of Mg-St types lies between 41 and 11 %, indicating that the type of Mg-St can have a severe impact on the outcome of the tableting process. For mixture M2 the lubricants caused an increase of the tensile strength. This phenomenon has been reported in the literature[2], is not that common and is most likely correlated to the deformation behaviour of the tableting excipients used for that formulation.

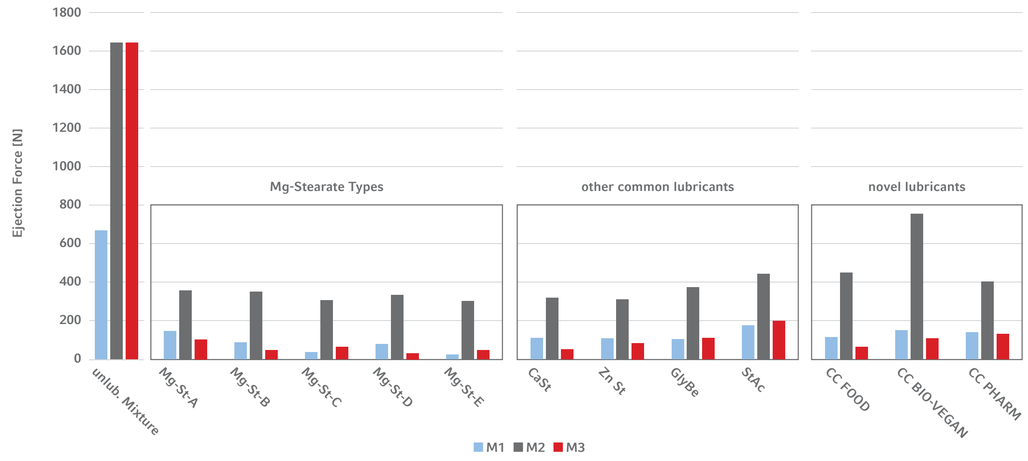

Figure 2: **Ejection forces for all used lubricants after mixing for 3 minutes**

Figure 2 shows the ejection forces as an indicator for the lubricant efficacy. Great variations can be observed regarding the performance of the commonly used lubricants for mixtures M1 and M3. The new BIOGRUND lubricants provide sufficient lubrication in all cases and their performance is within the performance range of the other materials for mixtures M1 and M3 while providing slightly less lubrication for M2. This indicates that slightly higher levels of these lubricants should be used for such a mixture.

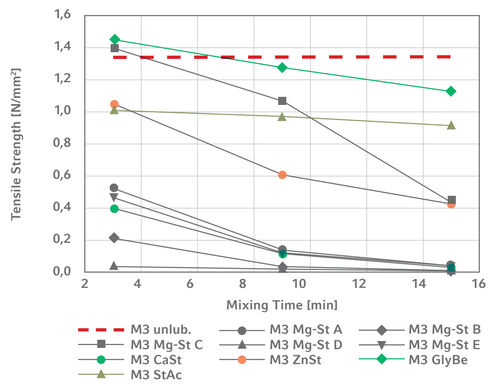

Figure 3: **Tensile strength over mixing time for commonly used lubricants with M3**

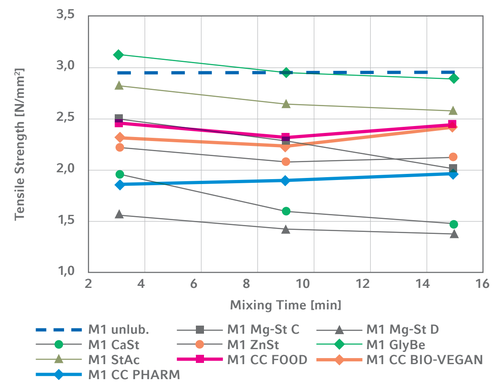

Figure 4: **Tensile strength over mixing time for some commonly used and novel lubricants with M1**

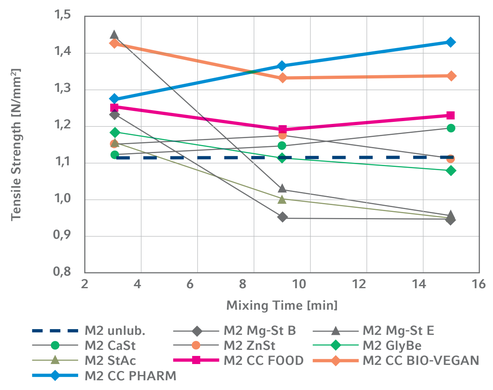

Figure 5: **Tensile strength over mixing time for some commonly used and novel lubricants with M2**

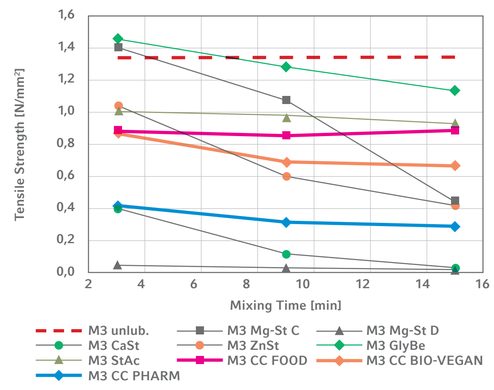

Figure 6: **Tensile strength over mixing time for some commonly used and novel lubricants with M3**

Figure 3 outlines the performance differences of commonly used lubricants and the critically of the mixing time for some of these materials, especially for Mg-Stearate types. In contrast to that Figures 4–6 depict that the novel CompactCel® LUB products suffer from little or no negative mixing time effects. For M1, a plastically deforming mixture, the performance of the novel lubricants is higher than that of any type of Mg-Stearate (best and worst cases shown in Fig. 4–6). For M2 the CompactCel® LUB types show superior performance regarding the tablet tensile strength. In a mixture of soft, elastic materials (M3) especially the CompactCel® products for food application yield harder tablets than those prepared with magnesium salts of stearic acid while showing very little mixing time effects.

Conclusion

Choosing the ideal lubricant candidate, its optimal concentration and an appropriate blending time is a challenging task. It is often disregarded that many tableting formulations are prone to over-lubrication at extended mixing times. The novel CompactCel® LUB compositions from BIOGRUND provide good lubrication properties while their performance does not suffer from mixing time effects.

References:

[1] Li, J., Wu, Y., 2014. Lubricants in Pharmaceutical Solid Dosage Forms. Lubricants. 2(1), 21–43.
[2] Bolhuis, G.K., 1995. Lubricant Sensitivity, in: Alderborn, G., Nyström, C. (Eds.), Pharmaceutical Powder Compaction Technology; CRC Press. Boca Raton, pp. 517–553

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