TECHNICAL INFORMATION

The Influence of Matrix Plasticity on Lubricant Effects

Abstract

Blends of three different filler/binders (MCC, SMCC, and dextrates) with two different lubricants (magnesium stearate and sodium stearyl fumarate) were prepared applying regular (3 minutes) and prolonged (60 minutes) blending times. Compactability curves were recorded for all blends. The combination of MCC with magnesium stearate showed significant hardness loss after prolonged blending, whereas SSF showed this effect to a much lesser extent. SMCC in combination with SSF was completely unaffected by blending time. **EMDEX®** Dextrates, too, showed low lubrication time sensitivity, although it did not reach the same hardness values as the corresponding SMCC blend.

Introduction

During the compaction of tablets, the tablet mass undergoes various steps. At first a rearrangement of the loose powder occurs during which air is expelled and the powder particles assume a denser packing. Beyond this stage, particle deformation takes place. There are three principal forms of deformation:
Plastic deformation, brittle fragmentation and elastic deformation. The elastic deformation may either be immediately reversible or occur in a form, where the stored energy is only released at a later point in time, triggered by factors such as temperature or humidity.
Lubricants are added to tableting blends in order to reduce the friction between tablet and die wall upon ejection. Also, they help to reduce the adhesion of the tablet mass to the punches.
As a negative side effect, lubricants may also affect the bonding between powder particles and thereby the mechanical strength of the tablets.
The susceptibility of tablet masses to lubricants strongly depends on the deformation mechanism of the main ingredients. While brittle material forms new, unlubricated surfaces during tableting, plastic material will remain layered with lubricants after deformation. Consequently the tablet hardness of plastic masses will decrease significantly the more coherently the particles are covered by lubricant.
Apart from the quantity of lubricant, the blending time plays an important role in the degree of lubricant layering. In this study, dextrates NF (**EMDEX®**), as a brittle material and DC-grade Microcrystalline Cellulose (**VIVAPUR® 102**) as a plastically deforming excipient were compared. Their tableting behaviour was examined after regular and prolonged blending with magnesium stearate and sodium stearyl fumarate (**PRUV®**) respectively. In addition, the same was tested using silicified MCC (**PROSOLV® SMCC**) as filler/binder.

Material & Methods

Figure 1 shows the design of the study. The masses obtained after 3 and 60 minutes of blending were compressed at three different compaction forces.

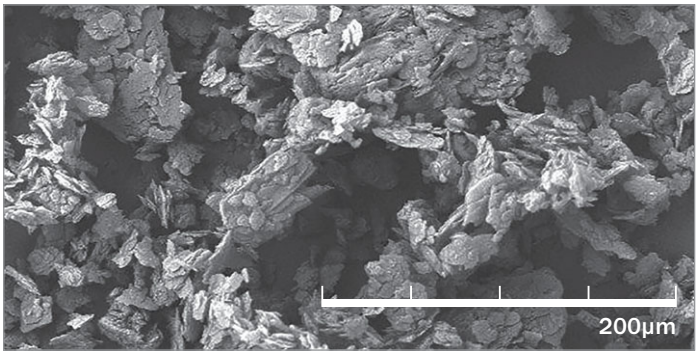
In order to demonstrate the effects of matrix plasticiy and lubricant film formation, the following formulations were studied.

Blending times were 3 minutes and 60 minutes for each blend.

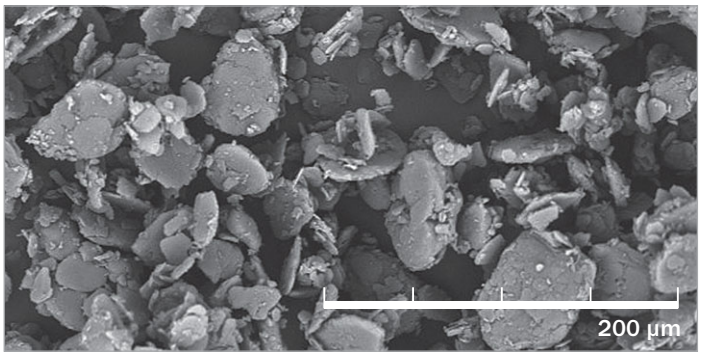
Filler/Binder:		Lubricant:
VIVAPUR® MCC (plastic) Microcrystalline Cellulose **EMDEX® Dextrates** (brittle) **PROSOLV® SMCC** (intermediate) Silicified Microcrystalline Cellulose	+	Magnesium Stearate **PRUV® SSF**

Fig. 1

In spite of being a very efficient lubricant, **PRUV®** is known to be less prone to formation of coherent films as a result of its different morphology compared to magnesium stearate. (Picture 1 and 2)



Pic. 1 Magnesium Stearate



Pic. 2 **PRUV®**

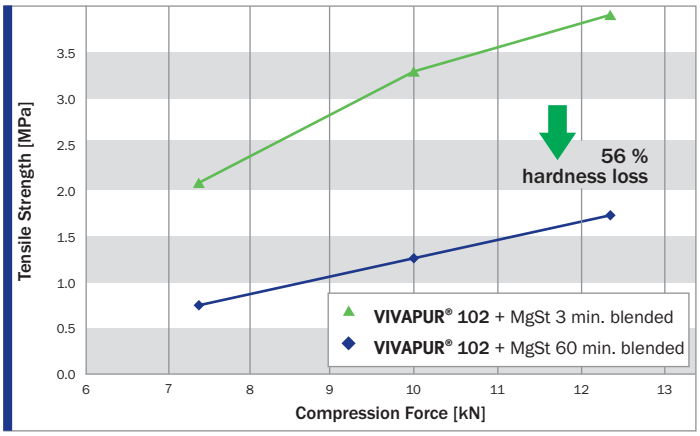
Results

Graph 1 shows the profiles for MCC and magnesium stearate after 3 and 60 minutes. A marked decrease of the tablet hardness was observed with increased blending time.
By contrast, the fragmenting excipient **EMDEX®** was less affected by the blending time (Graph 2).

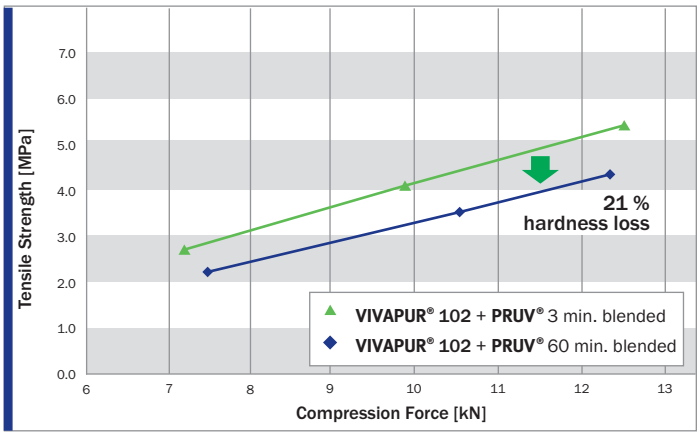
Apparently, the prolonged blending time has led to a coherent film formation of magnesium stearate. Due to its plastic deformation mechanism, MCC was more affected by this than **EMDEX®**.

The reduction of tensile strength after excessive blending of **PRUV®** with MCC is far less pronounced than in the case of magnesium stearate (Graph 3).

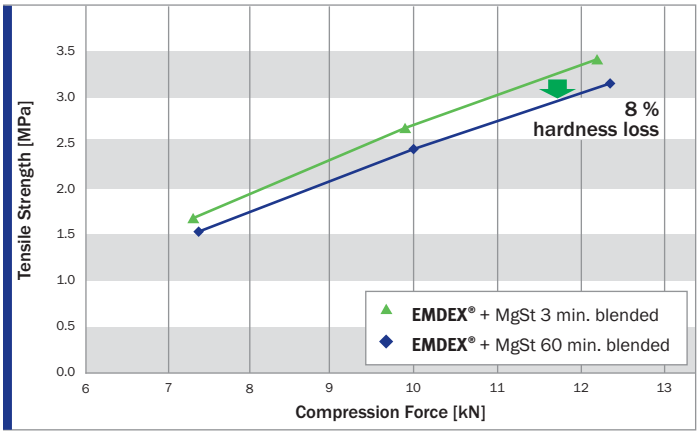
For **EMDEX®**, however, the effect is completely eliminated. (Graph 4)



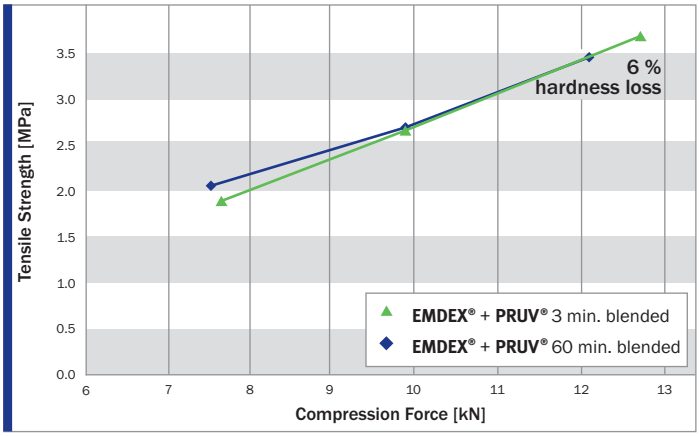
Graph 1



Graph 3



Graph 2

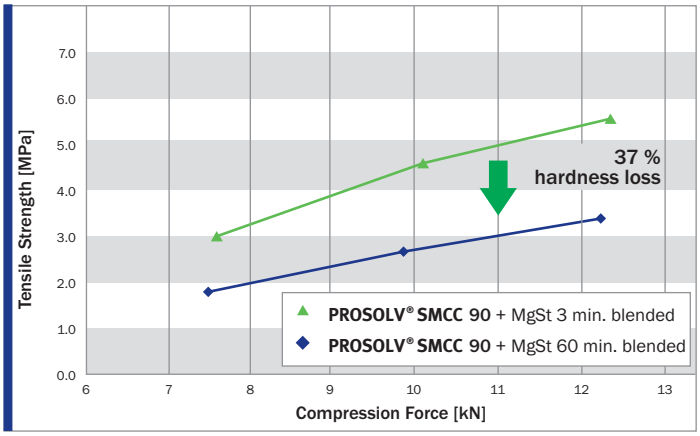


Graph 4

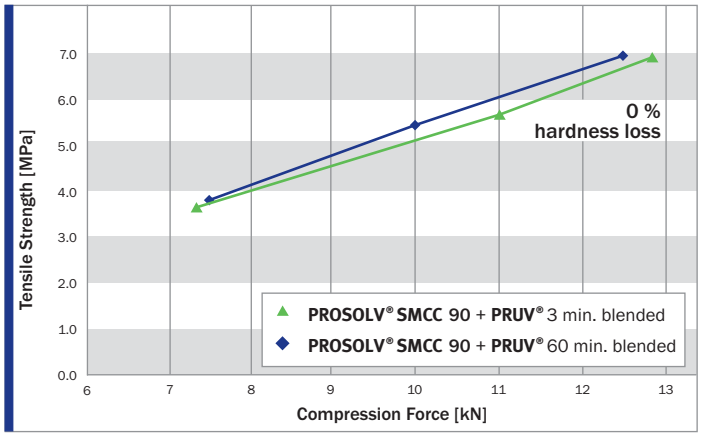
Blending with **PROSOLV® SMCC**:

PROSOLV® SMCC is obtained by co-processing MCC with colloidal silicon dioxide (CSD). Compared to regular MCC, SMCC exhibits a higher compactability and flowability as well as an increase of the specific surface area by a factor of five. The combination of larger surface area with higher compactability may be expected to mitigate the effect of over-lubrication.

Graph 5 and 6 show the comparison of **PROSOLV® SMCC** with magnesium stearate and SSF respectively. While magnesium stearate still causes a loss in hardness, this drop is significantly reduced compared to plain MCC. For the combination of SMCC and SSF no drop was observed at all.



Graph 5



Graph 6

	Magnesium Stearate			PRUV®		
	3 min. [MPa]	60 min. [MPa]	hardness loss [%]	3 min. [MPa]	60 min. [MPa]	hardness loss [%]
MCC	3.9	1.7	56 %	5.4	4.3	21 %
EMDEX®	3.4	3.1	8 %	3.6	3.4	6 %
SMCC	5.5	3.5	37 %	6.9	7.0	0 %

Tab. 1 Summary of the Findings of the Six Experiments

Summary

- Comparing the 3 and 60 minute results, MCC showed a 60 % loss of tensile strength with magnesium stearate but only 20 % with **PRUV®**.
- **EMDEX®**, due to its brittleness displayed minus 8 % hardness for magnesium stearate and none for SSF.
- **PROSOLV® SMCC** lost 40 % of tensile strength when over-blended with magnesium stearate but none in combination with **PRUV®**.
- In terms of absolute tensile strength after 3 minutes, **PROSOLV® SMCC** + **PRUV®** gave the strongest tablets with 6.9 MPa, followed by **VIVAPUR® MCC** + **PRUV®** (5.4 MPa) and **EMDEX®** + **PRUV®** (3.6 MPa)

Conclusion

Keeping blending times to a minimum to reduce the risk of over-lubrication is well established practice in pharmaceutical production. It has to be considered, though, that powder handling and extended dwell-time in the feed frame may contribute to the effective overall blending time beyond the actual time in the blender. In order to create more robustness in this sense, the use of **PROSOLV® SMCC** instead of MCC for more overall tablet hardness is recommended.
PRUV® considerably reduces the effect of blending time and over-lubrication, especially in combination with **EMDEX®** or **PROSOLV®**.

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- JRS Sales Companies (Additionally, dedicated representatives in almost every country.)
- Technical Competence Centers
- Application Labs

HIGH FUNCTIONALITY EXCIPIENTS

PROSOLV® SMCC
Silicified Microcrystalline Cellulose

PROSOLV® EASYtab SP
Microcrystalline Cellulose, Colloidal Silicon Dioxide, Sodium Starch Glycolate, Sodium Stearyl Fumarate

PROSOLV® EASYtab NUTRA
All-in-one Composite for Nutraceutical Applications

PROSOLV® ODT G2
Microcrystalline Cellulose, Colloidal Silicon Dioxide, Mannitol, Fructose, Crospovidone

DISINTEGRANTS

VIVASTAR®, EXPLOTAB®
Sodium Starch Glycolate, Sodium Carboxymethyl Starch

VIVASOL®
Croscarmellose Sodium

EMCOSOY®
Soy Polysaccharides

VIVAPHARM® Crospovidone
Polyvinylpyrrolidone, crosslinked

COATINGS

VIVACOAT®
Ready-to-Use Coating System

VIVACOAT® protect
Ready-to-Use High Functional Coating System

VIVAPHARM® HPMC
Hypromellose

VIVAPHARM® PVA
Polyvinyl Alcohol

BINDERS

VIVAPUR®, EMCOCEL®
Microcrystalline Cellulose

EMDEX®
Dextrates

VIVAPHARM® Povidones
Povidone and Copovidone

LUBRICANTS

PRUV®
Sodium Stearyl Fumarate

LUBRITAB®
Hydrogenated Vegetable Oil, Hydrogenated Oil

LUBRI-PREZ™
Magnesium Stearate

CARRIERS

VIVAPUR® MCC SPHERES
Microcrystalline Cellulose Pellets

VIVAPHARM® Sugar Spheres
Sugar Pellets, Non-GMO

FUNCTIONAL FILLERS

ARBOCEL®
Powdered Cellulose

EMCOMPRESS®
Calcium Phosphates

COMPACTROL®
Calcium Sulfate Dihydrate

THICKENERS • STABILIZERS • GELLING AGENTS

VIVAPUR® MCG
Microcrystalline Cellulose and Carboxymethylcellulose Sodium

VIVAPHARM® Alginates
Calcium Alginate

VIVAPHARM® Alginates
Sodium Alginate

VIVAPHARM® Alginates
Alginic Acid

VIVAPHARM® Pectins

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www.jrspharma.com

JRS PHARMA GMBH & CO. KG
Business Unit Excipients
73494 Rosenberg (Germany)
Phone: +49 7967 152-312
ExcipientsService@JRSPharma.de

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