TECHNICAL INFORMATION

Formulation Effects on Tablet Surface Properties and Film Coating Adhesion

Introduction

The aim of this study was to investigate the influence of different commonly applied lubricants and disintegrants on tablet surface and film coating adhesion. In addition, a commercially available co-processed excipient for direct compression (**PROSOLV® EASYtab**) containing silicified microcrystalline cellulose (SMCC), lubricant and disintegrant was part of the study. The influence of two lubricants, magnesium stearate (MgSt) and sodium stearyl fumarate (SSF) and three disintegrants, croscarmellose sodium (CCS), crospovidone (PVPP) and sodium starch glycolate (SSG) were investigated. Tablets of **PROSOLV® EASYtab**, pure microcrystalline cellulose (MCC) and five physical mixtures containing MCC and either disintegrant or lubricant were prepared. The tensile strength and surface roughness of the tablets as well as the film coating adhesion of aqueous HPMC coatings on these tablets were studied.

Material and Methods

Materials:
Microcrystalline cellulose **VIVAPUR® 12** (MCC), sodium stearyl fumarate **PRUV®** (SSF), croscarmellose sodium **VIVASOL®** (CCS), crospovidone **VIVAPHARM® PVPP XL** (PVPP), sodium starch glycolate **EXPLOTAB®** (SSG), **PROSOLV® EASYtab SP**, and Magnesium stearate LIGAMED MF-2-V (MgSt) , were used as tablet core excipients. The tablets were coated with ready-to-use HPMC coating **VIVACOAT® A** (JRS PHARMA, Germany). Except for MgSt which came from Peter Greven, Germany, all ingredients were JRS PHARMA GmbH + Co KG, Germany.

Methods:
Compaction and coating
Seven different core formulations (Table 1) were compacted with a pressure of 125 MPa using a compaction simulator (STYL'One Evolution, MEDEL'Pharm) equipped with bi-planar round punches with a diameter of 11.28 mm. The coating of the tablet cores was conducted in a perforated drum coater (Solidlab2, Bosch Hüttlin) with a tablet bed temperature of 38 ± 2 °C.
Tablet characterization
The tensile strength of the tablets was measured with a hardness tester (MultiTest 50, Sotax AG). The surface roughness was measured by profilometry (DektakXT Stylus Profiler, Bruker). Scanning Electron Micrographs (Tabletop Microscope TM1000, Hitachi) of the tablet surfaces were evaluated in terms of texture, morphology and quality. The adhesion between film coating and tablet surface was measured with a material testing machine (Retroline BZ2, Zwick Roell) by applying double-sided adhesive tape to fix the tablet to even punches. Prior to adhesion measurement, the coating was carefully detached at the edge of the tablets using a scalpel.

Formulation	Lubricant	Disintegrant	MCC
MCC	–	–	100 %
MCC + MgSt	1 % MgSt	–	99 %
MCC + SSF	1 % SSF	–	99 %
MCC + CCS	–	5 % CCS	95 %
MCC + PVPP	–	5 % PVPP	95 %
MCC + SSG	–	5 % SSG	95 %
PROSOLV® EASYtab	SSF	SSG	SMCC

Tab. 1 Excipient Composition of the Investigated Tablet Cores

Results

Tensile Strength
A high tensile strength of a tablet indicates good compaction behavior and is important for withstanding the coating process [1]. Pure MCC shows the highest tensile strength (Table 2). It is well known that lubricants decrease the tensile strength of tablets [2]. The formulation containing MgSt. displays the largest reduction in tensile strength! **PROSOLV® EASYtab**, containing SSF, shows a higher tensile strength than the physical mixture of MCC with SSF. Hence, despite the good lubrication properties, compactibility is higher for the coprocessed product.
Disintegrants show less impact on tensile strength of tablets than lubricants. There is only a slight decrease of tensile strength which is nearly the same for CCS, PVPP and SSG. This can be attributed to their high capability to form hydrogen bonds, which is crucial for their disintegration properties and enables strong interactions with the MCC particles.

Formulation	Tensile Strength (MPa)
MCC	6.62
MCC + MgSt	1.16
MCC + SSF	3.27
PROSOLV® EASYtab	4.90
MCC + CCS	6.08
MCC + PVPP	5.98
MCC + SSG	5.80

Tab. 2 Tensile Strength of Tablets Compressed with 125 MPa Compaction Pressure

Surface Roughness

In surface roughness measurements, tablets containing MgSt exhibit higher surface roughness than pure MCC tablets (Figure 1). Tablets containing SSF possess a smoother tablet surface than pure MCC tablets. **PROSOLV® EASYtab** provides the smoothest tablet surface of all formulations tested. Disintegrants increase the surface roughness compared to pure MCC.
The corresponding micrographs are shown in Figure 2.

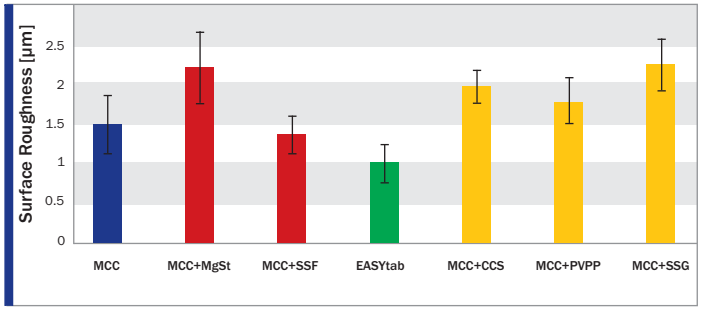

Fig. 1 Surface Roughness of Tablet Cores

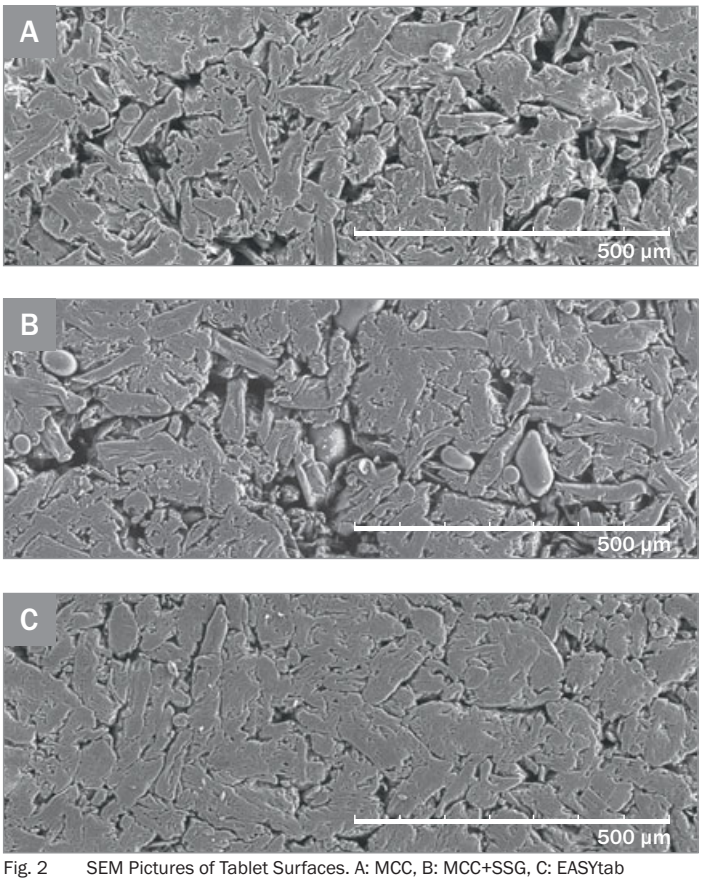

Fig. 2 SEM Pictures of Tablet Surfaces. A: MCC, B: MCC+SSG, C: EASYtab

Film Coating Adhesion

The investigation of film coating adhesion (measured as stress of failure) showed that lubricants strongly decrease the adhesion of aqueous HPMC coatings (Figure3). MgSt showed a stronger effect than SSF. Disintegrants also lead to a decrease of film coating adhesion, but to a lesser extent than lubricants (Figure 4).

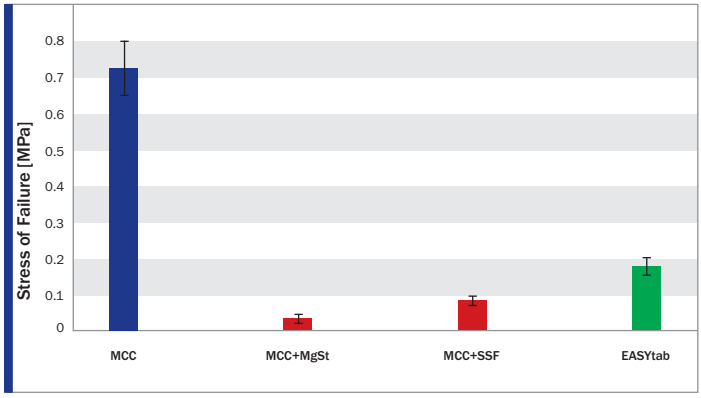

Fig. 3 Stress of Failure of Tablet Cores Containing Lubricants Compared to Pure MCC

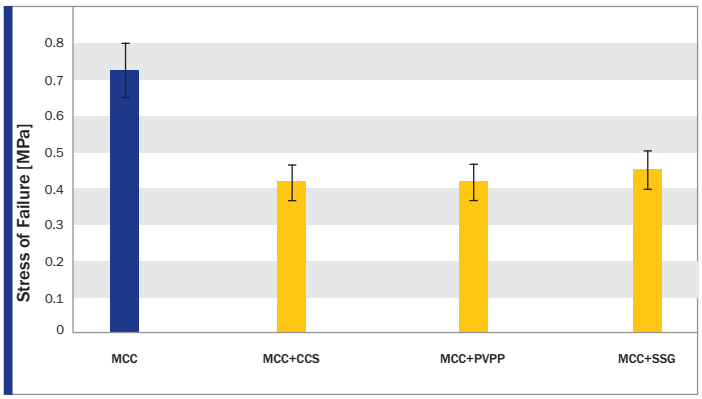

Fig. 4 Stress of Failure of Lubricant Free Tablet Cores

Discussion

Magnesium stearate has a layering effect [3] which leads to a lower overall bondability and therefore lower tensile strength, higher friability (data not shown) and higher surface roughness. Surface roughness, in combination with the hydrophobicity of MgSt, leads to reduced film coating adhesion. The layering effect occurs to a lesser extent for SSF [4] or can even be reversed [5]. Therefore, higher tensile strength was observed for SSF compared to MgSt. Furthermore, the lubricating effect of SSF decreases the punch adhesion which, together with higher tensile strength, leads to smoother tablet surfaces compared to pure MCC cores and cores containing MgSt. Since SSF is less hydrophobic than MgSt, higher film coating adhesion values were observed for SSF. The best results within the group of tablets containing lubricants were found for **PROSOLV® EASYtab** cores. Their high tensile strength and smooth surface led to the highest film coating adhesion values.

Conclusion

Any addition of further compounds reduced MCC tablet performance. Lubricants showed a strong negative effect on film coating adhesion. Disintegrants also exhibited an adverse effect, nonetheless, less distinct and less diverse compared to lubricants. Surface roughness and hydrophobicity play a vital role in this context. Higher tensile strength, smooth tablet surface as well as higher film coating adhesion were achieved with coprocessed **PROSOLV® EASYtab** compared to physical mixtures of excipients.

Acknowledgements:

This study is based on the master thesis "Investigation of the influence of functional excipients for tablet cores on the quality of applied coatings" of Martin Wewers (under the direction of Dr. Jan Henrik Finke) at the Technical University in Braunschweig. The study was conducted at the iPAT of the TU Braunschweig and in part at JRS PHARMA, in Rosenberg, Germany.

References:

1 Carlin, B. A. C., Direct Compression and the Role of Filler-binders. In Augsburger, L. L. and Hoag, S. W. (Eds.) Pharmaceutical Dosage Forms: Tablets: Volume 2: Rational Design and Formulation, 3rd edn. Informa Healthcare USA, New York, pp 173–216 (2008)

2 Strickland, W. A., Nelson, E. and Busse, L. W., Higuchi, T., The Physics of Tablet Compression IX: Fundamental Aspects of Tablet Lubrication. J. Am. Pharm. Assoc. 45(1): 51–55 (1956)

3 Hussain, M. S. H., York, P. and Timmins, P., A Study of the Formation of Magnesium Stearate Film on Sodium Chloride Using Energy-Dispersive X-ray Analysis. Int. J. Pharm. 42(1-3): 89–95 (1988)

4 Hölzer, A. W. and Sjögren, J., Evaluation of Sodium Stearyl Fumarate as a Tablet Lubricant. Int. J. Pharm. 2(3-4): 145–153 (1979)

5 Louw, R., Evaluation and Comparison of Magnesium Stearate and Sodium Stearyl Fumarate (Pruv) as Lubricants in Directly Compressible Tablet Formulations: Their Effect on Tablet Properties and Drug Dissolution (2003)

JRS PHARMA

The Global Excipient Maker

Products and Services

Excipients

Family of High Functionality Excipients
Binders
Functional Fillers
Lubricants
Thickeners+Stabilizers
Carriers
Superdisintegrants
Calcium Supplements

Coatings

Biopharma Services

ProJect Pharmaceutics www.project-pharmaceutics.com

CELONIC www.celonic.com

First Class Manufacturer of Excipients and Coatings for

Global Network

- Excipients
- Coatings
- Biopharma Services
- JRS Sales Companies
- Technical Competence Centers
- Application Lab's

Additionally, dedicated representatives in almost every country.

JRS PHARMA The Global Excipient Maker JRS FAMILY A Member of the JRS Group

www.jrspharma.com

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

5268_GB_V1_3.01809KE