TECHNICAL INFORMATION

Influence of Different Lubricants on Tableting Characteristics and Dissolution Behavior

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Abstract

Apart from their desired effect of reducing the ejection force and punch adhesion, lubricants also have a considerable influence on the tablet hardness, disintegration, and dissolution times due to their inherent hydrophobicity. This study aimed to investigate the influence of the lubricant molecular structure on the aforementioned characteristics. For this purpose, active pharmaceutical ingredients (APIs) with high and low water solubility have been evaluated in combination with 4 different, stearyl-based lubricants. The study showed that the molecular structure of the lubricant had a significant influence on all of the above mentioned tablet characteristics. A good molecular balance between hydrophobic and slightly hydrophilic moieties - as obtained for sodium stearyl fumarate (**PRUV®**) - resulted in the best overall outcome.

Introduction

Lubricants are a very important part of the tablet formulation. During the tableting process, powder particles are forced to rearrange under the increasing compression force. Lubricants influence this rearrangement and bonding process depending on their molecular structure. After compression, the tablet has to be ejected by the lower punch of the tablet press. The lubricant is also important in this step of the process because it inhibits sticking between the tablet and the punch, which can lead to damage and stop the machines. Finally, the lubricant influences the dissolution and disintegration times and, thus, the quality attributes of the tablets. Due to their importance in formulating tablets, there are a lot of lubricants on the market. Most of them are characterized by a long fatty acid chain which imparts hydrophobicity to the lubricant. Examples for such commonly used lubricants are magnesium stearate, sodium stearate, stearic acid, and sodium stearyl fumarate. These lubricants were utilized in this study about the influence of lubricants on tableting characteristics.

Study Design

Different commonly used lubricants were evaluated for their influence on tableting features and dissolution behavior. To avoid any influences of disintegrant variability and detect even minor differences between the lubricants, no disintegrants were used for this study. Furthermore, the lubricant level was set to 2 % for all formulations, instead of the common use level of about 1 %. Different Active Pharmaceutical Ingredients (API) covering a wide range of solubilities were selected for this study. These APIs were blended with an inert carrier, **PROSOLV® SMCC HD 90** (silicified microcrystalline cellulose) - and were then compacted on a rotary tablet press. For the dissolution studies, water was chosen as the dissolution medium to avoid any influences of salts or pH on the dissolution properties of the resulting tablets.

Materials and Methods

All powder blends were prepared using a free fall blender. First, the API was blended with **PROSOLV® SMCC HD 90** for 15 minutes. Afterwards, the sieved lubricant was added and the mixture was blended for another 3 minutes. This blend was then transferred to the tablet press and compressed immediately. Compression profiles for the different blends have been recorded. Tablet hardness was tested directly after compression, while disintegration as well as dissolution time was tested after one day.
For the dissolution testing, the medium water was tempered to 37 °C. Detection of the different APIs was performed with a UV-Vis spectrophotometer using 1 mm cuvettes. Acetaminophen was detected at λ = 271 nm and ranitidine hydrochloride at λ = 290 nm. Tablets of the same tensile strength have been used for the comparisons of the dissolution profiles.

Ingredient	Solubility	Trade Name
Silicified Microcrystalline Cellulose (SMCC)		**PROSOLV® SMCC HD 90**
Sodium Stearyl Fumarate (SSF)		**PRUV®**
Magnesium Stearate (animal source)		
Stearic Acid		
Sodium Stearate		
Acetaminophen	12.8 g/L	
Ranitidine Hydrochloride	1.8 g/L	
Ibuprofen	0.37 g/L	

Tab. 1 List of Ingredients

Free Fall Blender	Brunitec Suisse, Brunimat Type Porta
Analytical Balance	Sartorius M-PROVE
Tablet Press	IMA Kilian Pressima 13EU-D
Tablet Hardness Tester	Erweka TBH 425 TD
Disintegration Tester	Sotax Dt2
Dissolution Tester	Pharma Test, Pharma Test PTWS 100

Tab. 2 Equipment List

Influence of Different Lubricants on Tableting Characteristics and Dissolution Behavior

Acetaminophen	62.5 %	500 mg
PROSOLV® SMCC HD 90	35.5 %	248 mg
Lubricant	2.0 %	16 mg
Total	**100.0 %**	800 mg

Tab. 3 Acetaminophen Formulation

Ranitidine Hydrochloride	48.0 %	336 mg
PROSOLV® SMCC HD 90	50.0 %	350 mg
Lubricant	2.0 %	14 mg
Total	**100.0 %**	**700 mg**

Tab. 4 Ranitidine Formulation

Ibuprofen	50.0 %	200 mg
PROSOLV® SMCC HD 90	48.0 %	192 mg
Lubricant	2.0 %	8 mg
Total	**100.0 %**	**400 mg**

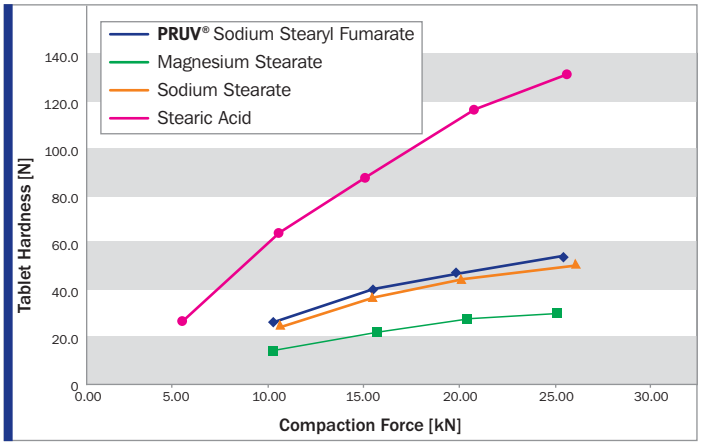
Tab. 5 Ibuprofen Formulation

Results

a.) The Effect of Lubricants on the Performance of a Acetaminophen Formulation

Compactability

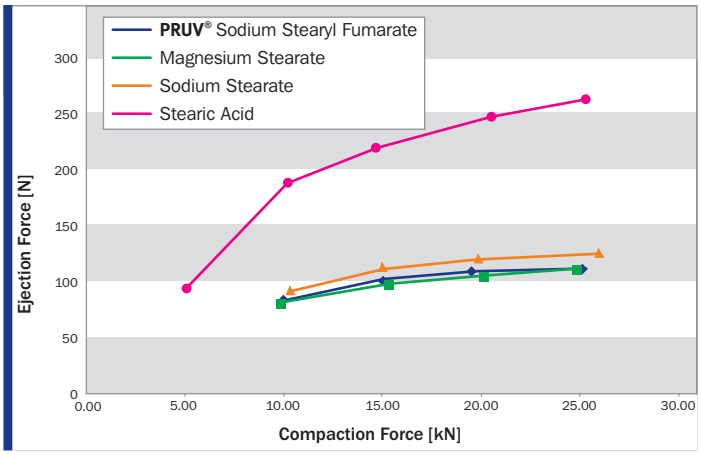
The kind of lubricant used had a significant influence on the hardness of the tablets. While tablets lubricated with stearic acid resulted in the highest tablet hardness, those made from magnesium stearate exhibited the lowest hardness. Tablets lubricated with different sodium compounds (sodium stearyl fumarate, sodium stearate) showed intermediate hardness (Graph 1).



Graph 1. Hardness of Acetaminophen Tablets Lubricated with 4 Different Lubricants

Lubrication Efficiency

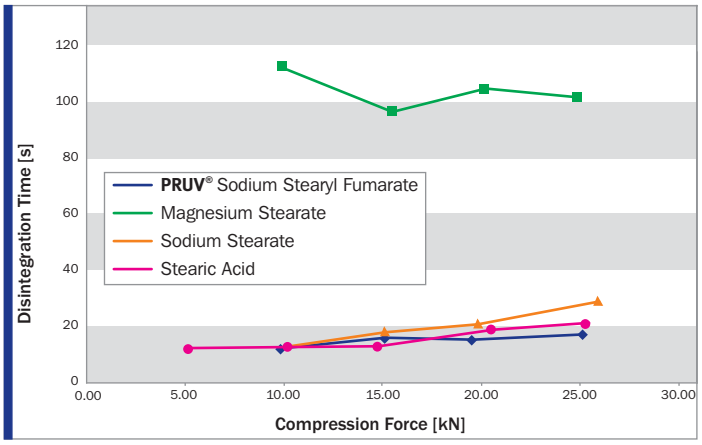
As for compactibility, a similar trend could be observed in the ejection forces. The tablets lubricated with stearic acid showed the highest ejection forces, while magnesium stearate was found on the lower end of the ejection force spectrum. In spite of their higher tablet hardness, tablets made with sodium stearyl fumarate (**PRUV®**) exhibited the same low ejection forces as their magnesium stearate counterparts. Slightly higher ejection forces were found for sodium stearate (Graph 2).



Graph 2. Ejection Forces of Tablets Made with 4 Different Lubricants

Disintegration Time

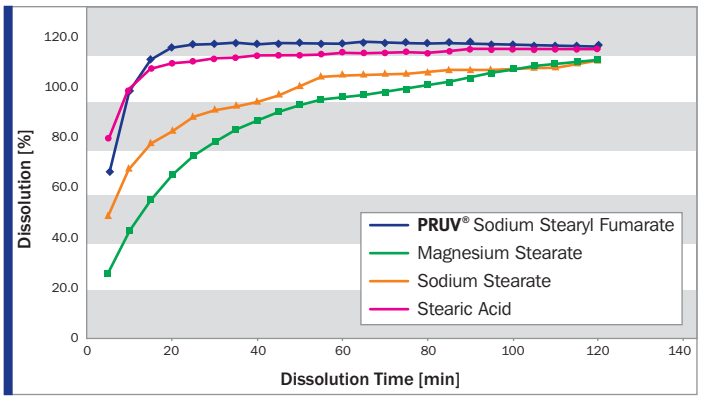
Tablets lubricated with magnesium stearate needed by far the longest time for disintegration. All other tablets were found to have disintegration times in the same range (Graph 3).



Graph 3. Disintegration Time of Acetaminophen Tablets Lubricated with 4 Different Lubricants

Dissolution Behavior

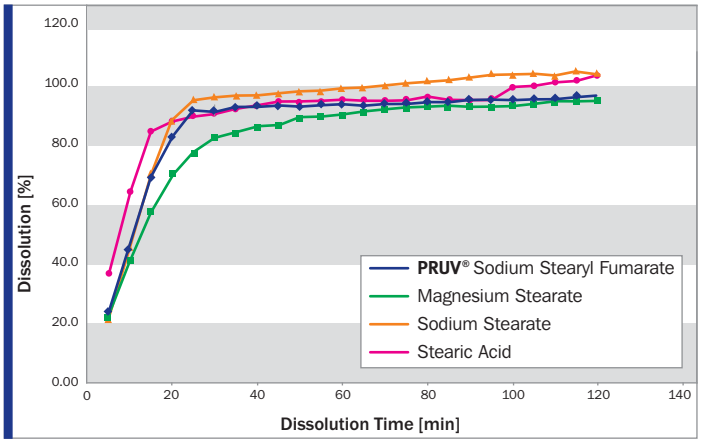
Tablets containing magnesium stearate showed by far the slowest dissolution rates. Sodium stearate and stearic acid lubricated tablets released the API much faster. The fastest drug release was observed for tablets lubricated with **PRUV®** (Graph 4).



Graph 4. Dissolution Profile of Acetaminophen Tablets

b.) The Effect of Different Lubricants on the Dissolution Rates of Ranitidine HCl Tablets.

The second model drug exhibited similar trends in tableting characteristics and disintegration times as the first model drug. In terms of dissolution, tablets lubricated with one of the sodium compounds (sodium stearate and sodium stearyl fumarate) resulted in the fastest and most complete dissolution profiles, while the tablets lubricated with magnesium stearate lagged behind the most (Graph 5).

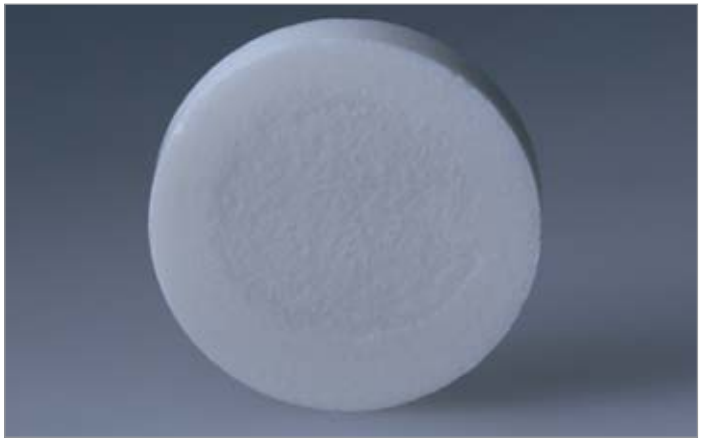


Graph 5. Dissolution Profile of Ranitidine Hydrochloride Tablets

c.) The Effect of Different Lubricants on the Punch Adhesion of an Ibuprofen Formulation

The third model API was Ibuprofen: a challenging substance due to its tableting characteristics. Tablets were compressed from a very fine, poorly compressible grade of Ibuprofen. During the tableting process, sticking occurred quite frequently. It was most pronounced when the lubricant was sodium stearate. Sticking to the punches, as well as to the tablet press itself, was observed for magnesium stearate, sodium stearate, and stearic acid (Pictures 1 and 2). The tablets did not exhibit any signs of defects related to sticking and no sticking occurred only when **PRUV®** sodium stearyl fumarate was the lubricant.

Pic. 1. Sticking of Powder Mixture with Ibuprofen and Sodium Stearate



Pic. 2. Tablet Defect on Tablet Lubricated with Magnesium Stearate

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Discussion and Conclusion

Discussion

This study investigated the effect of different lubricants on tableting characteristics and dissolution profiles. Four different lubricants with a basic building block of a hydrophobic C18 chain were used. The lubricants included: stearic acid, a non-ionic, very hydrophobic compound that shows slight acidic behavior; metal salts of stearic acid with a metal ion of either magnesium or sodium for magnesium stearate or sodium stearate, respectively, and, sodium stearyl fumarate. Compared to the other three lubricants, the sodium stearyl fumarate molecule is less hydrophobic and, thus, is expected to allow for better wettability of tablets.

In general, all lubricants reduce the hardness of a tablet due to an interaction between microcrystalline cellulose and the lubricant, which weakens the bonding structures within the tablet. In terms of tablet hardness, tablets lubricated with magnesium stearate exhibited the lowest hardness. Thus, this weakening action seemed to be most pronounced for the most hydrophobic molecule.

The tablets lubricated with stearic acid exhibited the highest tablet hardness, but also the highest ejection forces. This may be attributed to insufficient lubrication at the 2 % level. This level was used for all the lubricants in this study, but it may not have been sufficient for the grade of stearic acid used in this study. Although the tablets lubricated with stearic acid exhibited the highest tablet hardness, these tablets may not be suitable for large scale production since the ejection forces are supposed to increase in this scenario, which could possibly lead to microruptures of the tablets and increased gear abrasion.

If either **PRUV®** sodium stearyl fumarate or sodium stearate was used, the tablets exhibited intermediate hardness, ejection forces, and disintegration times. Differences became obvious in the dissolution study. **PRUV®** sodium stearyl fumarate accelerated API release compared to sodium stearate. This was attributed to the molecular structure of **PRUV®** sodium stearyl fumarate which is less hydrophobic than sodium stearate. Tablets made with **PRUV®** exhibited better API release because of the difference in hydrophobicity and the resulting increased wettability of the tablet. This effect was more pronounced for the less water soluble acetaminophen. Here, the influence of the chemical characteristics of **PRUV®** could be seen in the faster and more complete release of acetaminophen. In the case of the well water-soluble ranitidine hydrochloride, API dissolution was markedly reduced for the most hydrophobic lubricant (magnesium stearate) whereas the other lubricants tested showed comparable dissolution rates.

PRUV® is not only suitable to decrease dissolution times, it can also help to cover bad compression characteristics of APIs. This was seen in the case of Ibuprofen: an API known for its bad tableting characteristics. Only **PRUV®** was able to guarantee tableting without problems. All other lubricants led to sticking, resulting in tablet defects.

Conclusion

The choice of lubricant can influence the quality of the tablets as well as the dissolution rates. Since APIs tend to be less water-soluble and difficult to crystallize, choosing the right lubricants continues to become an even more important task.

Most commonly available lubricants are very hydrophobic and, thus, increase dissolution times significantly. In such cases, a less hydrophobic lubricant can help to decrease the dissolution times as well as increase the API release.

PRUV® sodium stearyl fumarate complies with Ph.Eur., NF and JPE. It is the preferred choice over magnesium stearate in terms of improving dissolution times as has been shown in this study.

Furthermore, different particle sizes are available, which help to fine-tune tablet formulations resulting in the desired dissolution profiles.

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