Beyond Tablet Lubrication

Improved API Stability
Superior Blending Properties
Faster Disintegration
Faster Dissolution Times
PRUV® is a tablet lubricant specifically designed for formulations in which other lubricants lead to formulation and/or manufacturing challenges. As opposed to the frequently used lubricant magnesium stearate, PRUV® offers the following advantages:

1. No adverse effect on dissolution
2. Robustness to over-lubrication
3. Improved appearance of effervescent solutions
4. High degree of API compatibility*

*APIs reported to have incompatibility problems with magnesium stearate include: Azathioprin, Cefaclor, Cilazapril, Clopidogrelacetate, Diclofenac, Fosinopril, Ibuprofen, Ketorolac, Levofloxacin, Nifedipine, Omeprazole, Ramipril, and Trandolapril.

PRUV® helps to accelerate product development and is particularly well suited for high-speed direct compression of tablets.

Physical Properties of PRUV®

- White, fine powder
- Hydrophilic
- Anti-adherent properties
- High melting point
- Controlled particle size
- Well defined specific surface area
- Lamellar structure

Benefits of PRUV®

- Improved drug stability
- Faster dissolution rates
- Shorter disintegration times
- Harder tablets
- Less overblending
- Faster formulation development and scale-up
- Enhanced lubrication efficiency
- Acts as boundary lubricant
- Less sensitivity to blending time
- Superior hardness characteristics in comparison to tablets produced with magnesium stearate
- Excellent batch-to-batch consistency in comparison to magnesium stearate

Applications

- Wet granulation
- Dry granulation
- Capsules
- Direct compression
- Continuous manufacturing

Table 1

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>pH</strong></td>
<td>about 8.5 (10% aqueous solution at 90 °C)</td>
</tr>
<tr>
<td><strong>Saponification Value</strong></td>
<td>142.2 - 146.0</td>
</tr>
<tr>
<td><strong>Moisture</strong></td>
<td>&lt; 5.0 %</td>
</tr>
<tr>
<td><strong>Solubility</strong></td>
<td>0.5 mg/100 mL at 25 °C</td>
</tr>
<tr>
<td></td>
<td>10 g/100 mL at 80 °C</td>
</tr>
<tr>
<td></td>
<td>20 g/100 mL at 90 °C</td>
</tr>
</tbody>
</table>

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**PRUV® vs. Magnesium Stearate**

**PRUV® helps to avoid API incompatibilities and enhances API stability.** With a few exceptions, **PRUV®** can be applied to any formulation for lubrication, particularly those in which API stability or tablet taste is compromised due to magnesium stearate.

Because the magnesium cation (Mg²⁺) is electrophilic, it interacts with the free electrons of an API and forms insoluble salts. This is one of the many causes of API incompatibility with magnesium stearate.

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**PRUV® is preferred for better taste**
- Miconazole
- Triamcinolone

**PRUV® is preferred for organic salts**
- Albuterol sulfate
- Clopidogrel acetate
- Fosinopril sodium
- Fluoxetine maleate
- Metoprolol succinate
- Metoprolol tartrate
- Pravastatin sodium

**PRUV® is preferred for sulfogroups**
- Almotriptan malate
- Azathioprine
- Sulfasalazine

**PRUV® is preferred for other APIs**
- Fluvoxamine
- Isosorbide mononitrate
- Roxithromycin
- Zolpidem
- Tramadol
- Vitamin B₁₂
- Buprenorphine

**PRUV® is preferred for APIs with carbonyl and/or carboxyl groups**
- Trandolapril
- Levofoxacin
- Felodipine
- Clarithromycin
- Salicylic acid
- Ramipril
- Ketorolac
- Doxazosin
- Cilazapril
- Fosinopril
- Nifedipine
- Ibuprofen
- Donepezil-HCl
- Cefaclor
- Fenofibrate
- Metaxalone
- Fexofenadine
- Diclofenac
- Amlodipine
- Ibandronic acid

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**Electrostatic Properties**

Magnesium stearate shows higher voltage and retention times than **PRUV®**. Low electric charge and retention improve lubricant dispersion during blending. As a result, **PRUV®**, due to its low voltage and retention, can be considered a superior lubricant with improved lubricant uniformity.
Results

Lubrication Efficiency and Ejection Force

PRUV® demonstrates equivalent lubrication performance to the most widely used tableting lubricant magnesium stearate. Additionally, PRUV® offers faster dissolution, superior API compatibility, and better taste.

<table>
<thead>
<tr>
<th>Lubricant Concentration</th>
<th>PRUV®</th>
<th>Magnesium Stearate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 %</td>
<td>320</td>
<td>325</td>
</tr>
<tr>
<td>0.50 %</td>
<td>225</td>
<td>160</td>
</tr>
<tr>
<td>1 %</td>
<td>110</td>
<td>125</td>
</tr>
</tbody>
</table>

Tab. 2 MCC Placebo Tablets: Ejection Forces after 5 Minutes of Blending Time

Enhanced Mechanical Robustness

Tablets made with PRUV® (vs. magnesium stearate) are mechanically more robust leading to enhanced production yields and shortened formulation and scale-up time.

Superior Blending Robustness

Formulations with magnesium stearate are extremely sensitive to blending times. Even a slight overblending can lead to a dramatic drop in the mechanical strength of the resulting tablets. By contrast, blending time has very little effect on tablet strength in formulations made with PRUV®.

Better Dissolution Rates

The dissolution of poorly soluble active ingredients may be impaired by the presence of highly hydrophobic ingredients (such as magnesium stearate) in a formulation. Due to its partial hydrophilicity, PRUV® enables rapid dissolution of low solubility APIs as demonstrated in the case study outlined below.

<table>
<thead>
<tr>
<th>Acetaminophen</th>
<th>62.5 %</th>
<th>500 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROSOLV® SMCC HD 90</td>
<td>35.5 %</td>
<td>248 mg</td>
</tr>
<tr>
<td>Lubricant</td>
<td>2.0 %</td>
<td>16 mg</td>
</tr>
<tr>
<td>Total</td>
<td>100.0 %</td>
<td>800 mg</td>
</tr>
</tbody>
</table>

Tab. 3 Acetaminophen Formulation
Influence of the Particle Size on the Functionality in a Formulation

The functionality of PRUV® was compared with PRUV® Coarse Grade (CG), a coarser grade of commercially available Sodium Stearyl Fumarate (SSF), and an experimental, micronized type of SSF. Owning to their different particle sizes, the three grades showed significant differences in their specific surface areas (Table 4).

The formulations with PRUV® and PRUV® Coarse Grade (CG) yielded the same tablet hardness. The experimental, micronized grade, by contrast, showed a reduction in tablet hardness. Due to its fine particle size and large surface area, the micronized grade is more likely to form a coherent film on the surface of the filler/binder, thus negatively affecting tablet binding. This effect is similar to the over-blending and overlubrication problems often observed with magnesium stearate.

A study was carried out to understand the effect of particle size and specific surface area on tabletting performance and finished tablet quality. In particular, the compactibility, lubrication efficiency, and disintegration times were compared for placebo tablets consisting of Dibasic Calcium Phosphate, Dihydrate and different grades of SSF (Table 5).

### Effect on Tablet Hardness

![Graph showing the effect of compression force on tablet hardness](www.jrspharma.com)

The formulations with PRUV® and PRUV® Coarse Grade (CG) yielded the same tablet hardness.

The experimental, micronized grade, by contrast, showed a reduction in tablet hardness. Due to its fine particle size and large surface area, the micronized grade is more likely to form a coherent film on the surface of the filler/binder, thus negatively affecting tablet binding. This effect is similar to the over-blending and overlubrication problems often observed with magnesium stearate.

### Formulation

| Emcompress® (Dibasic Calcium Phosphate, Dihydrate) | 99 % |
| Sodium Stearyl Fumarate | 1 % |

Tab. 5
Effect on Lubrication

The effectiveness of lubrication was determined by comparing the ejection forces for the three formulations. **PRUV®** and the micronized grade were equally efficient in terms of reducing the ejection force. **PRUV® Coarse Grade (CG)**, on the other hand, had a reduced lubrication effect as indicated by the increased ejection force. As shown in Figure 7, **PRUV® Coarse Grade (CG)** has a smaller specific surface area than **PRUV®**. Consequently, the surface coverage of the tableting blend is reduced, thus causing higher friction between the tablet and the die wall.

Effect on Disintegration Time

**PRUV®** and **PRUV® Coarse Grade (CG)** had a negligible effect on the final tablet disintegration time at all compaction forces/tablet tensile strengths tested. The experimental, micronized grade of SSF showed significantly higher disintegration times than the other two grades. The formation of a coherent fine particle film (mentioned previously in discussion of tablet hardness) is likely to also have a negative effect on tablet disintegration, as it may be expected to hinder the entry of water into the tablet core.

Summary of Findings

<table>
<thead>
<tr>
<th></th>
<th>PRUV®</th>
<th>PRUV® Coarse Grade</th>
<th>SSF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet Hardness</td>
<td>+</td>
<td>equivalent</td>
<td>reduced</td>
</tr>
<tr>
<td>Lubrication</td>
<td>+</td>
<td>reduced</td>
<td>equivalent</td>
</tr>
<tr>
<td>Disintegration Time</td>
<td>+</td>
<td>equivalent</td>
<td>slower</td>
</tr>
</tbody>
</table>

While **PRUV® Coarse Grade (CG)** is equivalent to **PRUV®** in terms of tablet hardness and disintegration time, it does not show the same outstanding lubrication efficiency.

The experimental, micronized grade, on the other hand, was comparable with **PRUV®** regarding lubrication performance, but showed reduced tablet hardness and increased disintegration times.

**PRUV®** has been shown to have the ideal particle size and specific surface area to offer a perfect balance between all functionality aspects.

Particle size and specific surface area have been defined as Functionality Related Characteristics (FRCs) by the leading pharmacopoeias. The specifications for **PRUV®** have been set correspondingly tightly to ensure consistent performance. In addition, QbD data packages are available upon request.
Regulatory and Packaging

Regulatory Information

- Ph. Eur., NF, JPE, GRAS Status
- RO-CEP 2006-313-Rev 00 - letter of authorization is available upon request
- Non-Animal Origin
- BSE/TSE-Free
- GMO-Free
- OVI-Free (USP<467>) and conforms to the Residual Solvents requirement of Ph. Eur. (5.4) and USP <467>
- CoFA with IR spectrum and TLC analysis
- CEP available

Packaging, Samples and Storage

Storage
Store in original, well-closed container protected from excessive heat and moisture.

Packaging
1 kg plastic container; 5 kg drum or 25 kg drum

Pallet
150 kg (6 x 25 kg drums), stackable
180 kg (36 x 5 kg drums), not stackable

Sample Sizes
100 g aluminium bag

Case Studies
Case studies and formulation examples are available upon request. Please contact your sales rep for more information or visit www.jrspharma.com.

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- Functional Fillers
- Lubricants
- Thickeners + Stabilizers
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Coatings

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- Capsules Fillings
- Suspension Stabilization
- Emulsion Stabilization
- Granules

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