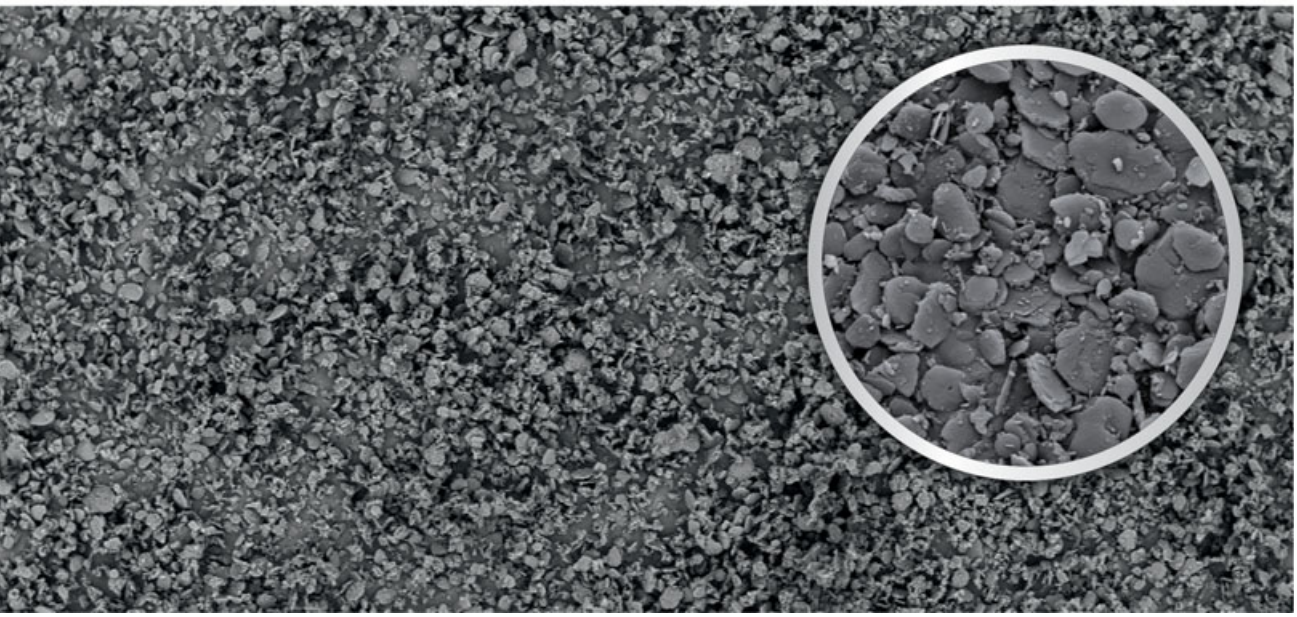
PRUV®

Sodium Stearyl Fumarate, Ph. Eur., NF, JPE



Beyond Tablet Lubrication

Improved API Stability
Superior Blending Properties
Faster Disintegration
Faster Dissolution Times

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

PRUV®

Sodium Stearyl Fumarate,
Ph. Eur., NF, JPE

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:

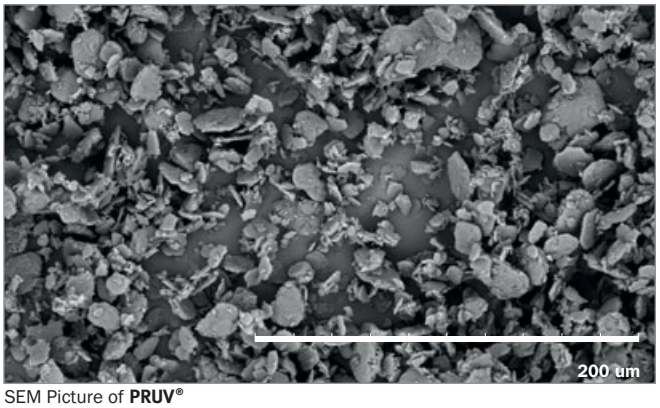
1. No adverse effect on dissolution
2. Robustness to over-lubrication
3. Improved appearance of effervescent solutions
4. High degree of API compatibility (see page 3)

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

Due to its high melting point, **PRUV®** is also an ideal lubricant for hot melt extrusion.

Physical Properties of **PRUV®**

- White, fine powder
- Less hydrophobic than magnesium stearate
- Anti-adherent properties
- High melting point
- Controlled particle size
- Well defined specific surface area
- Lamellar structure



SEM Picture of **PRUV®**

pH	about 8.5 (10 % aqueous solution at 90 °C)
Saponification Value	142.2 – 146.0
Moisture	< 5.0 %
Solubility	0.5 mg/100 mL at 25 °C
	10 g/100 mL at 80 °C
	20 g/100 mL at 90 °C
Melting point	224 - 245 °C (dec.)

Tab. 1 Typical Properties **PRUV®**

Benefits of **PRUV®**

- Improved drug stability
- Shorter disintegration times
- Faster dissolution rates
- Enhanced lubrication efficiency
- Less sensitivity to blending time
- Reduced probability of overblending
- Harder tablets in comparison to tablets produced with magnesium stearate
- Excellent batch-to-batch consistency
- Faster formulation development and scale-up

Applications

- Wet granulation
- Dry granulation
- Capsules
- Direct compression
- Continuous manufacturing
- Hot melt extrusion

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 (Mg^{2+}) 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.

PRUV® is preferred for better taste

Miconazole
Triamcinolone

PRUV® is preferred for sulfogroups

Almotriptan malate
Azathioprine
Omeprazole
Sulfasalazine

PRUV® is preferred for organic salts

Albuterol sulfate
Clopidogrel acetate
Fosinopril sodium
Fluroxamine maleate
Metoprolol succinate
Metoprolol tartrate
Pravastatin sodium

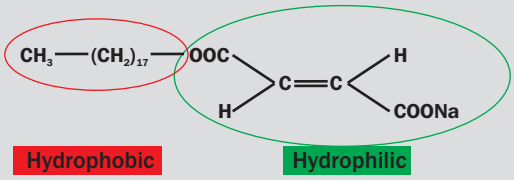
PRUV® is preferred for other APIs

Fluvoxamine
Isosorbidmononitrate
Roxithromycin
Zolpidem
Tramadol
Vitamin B_{12}
Buprenorphine

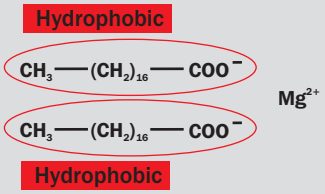
PRUV® is preferred for APIs with carbonyl and/or carboxyl groups

Trandolapril
Levofloxacin
Felodipine
Clarithromycin
Salicylic acid
Ramipril
Ketorolac
Doxazosin
Cilazapril
Fosinopril
Nifedipine
Ibuprofen
Donepezil-HCl
Cefaclor
Fenofibrate
Metaxalone
Fexofenadine
Diclofenac
Amlodipine
Ibandronic acid

PRUV® Sodium Stearyl Fumarate



Magnesium Stearate



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 compatability, and better taste.

	PRUV®	Magnesium Stearate
Lubricant Concentration	Ejection Force [N]	
0.25 %	320	325
0.50 %	225	160
1 %	110	125

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.

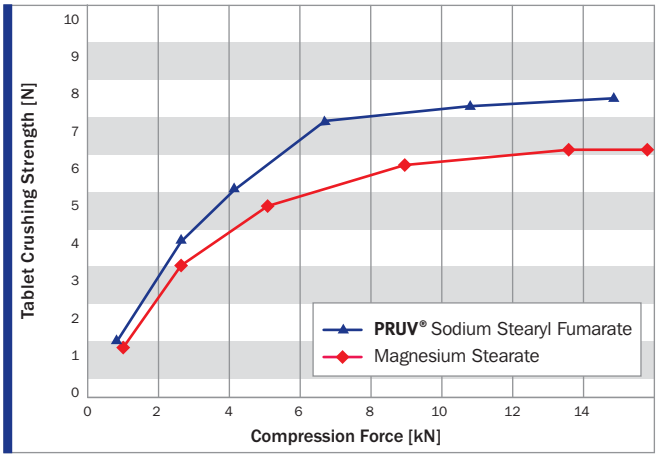


Fig. 2 Effect of Lubricant Choice on the Tablet Crushing Strength of Placebo Tablets

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®**.

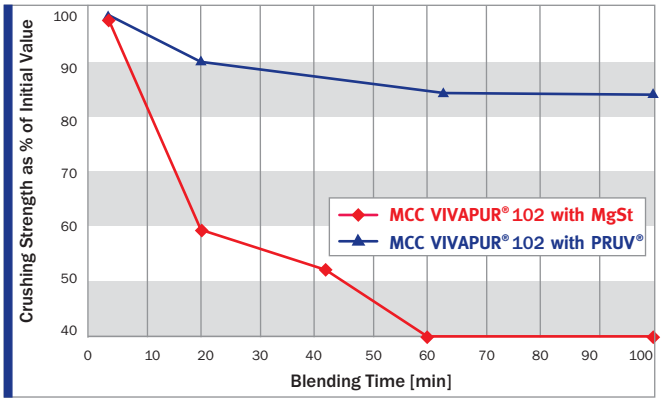


Fig. 3 Relation between Tablet Crushing Strength, Blending Time and Lubricant Choice

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.

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

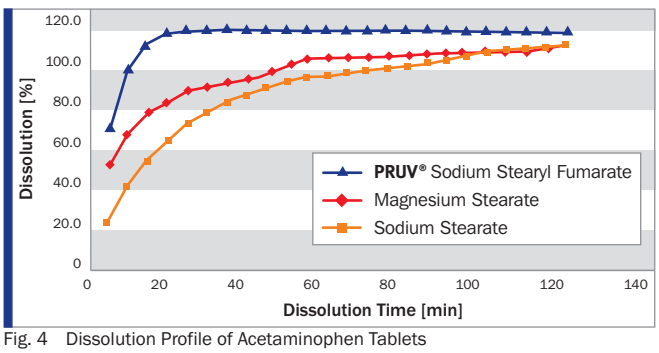


Fig. 4 Dissolution Profile of Acetaminophen Tablets

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).

	d50	BET
SSF Micronized	7.6	4.2 m^2/g
PRUV®	13.6	1.6 m^2/g
PRUV® Coarse Grade (CG)	20.4	0.6 m^2/g

Tab. 4 Particle Size and Specific Surface Area of Various SSF-Types

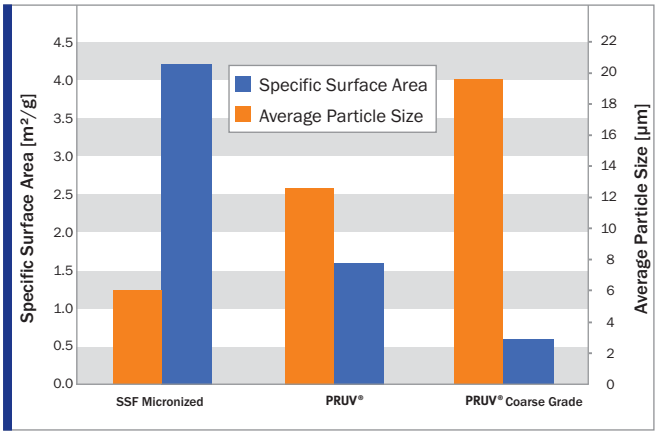


Fig. 5 Specific Surface Area and Average Particle Size of Different Grades of **PRUV®**

A study was carried out to understand the effect of particle size and specific surface area on tableting 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).

Formulation

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

Tab. 5 Placebo Formulation for Comparing the Different Grades of **PRUV®**

Effect on Tablet Hardness

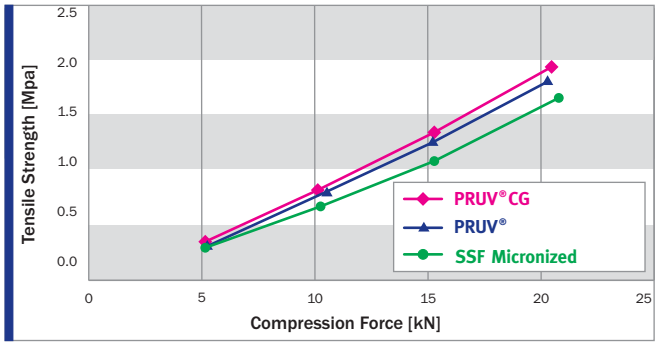


Fig. 6 Tensile Strength of Tablets Made with Different Grades of **PRUV®**

The formulations with **PRUV®** and **PRUV® Coarse Grade (CG)** yielded equivalent 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.

Effect on Lubrication

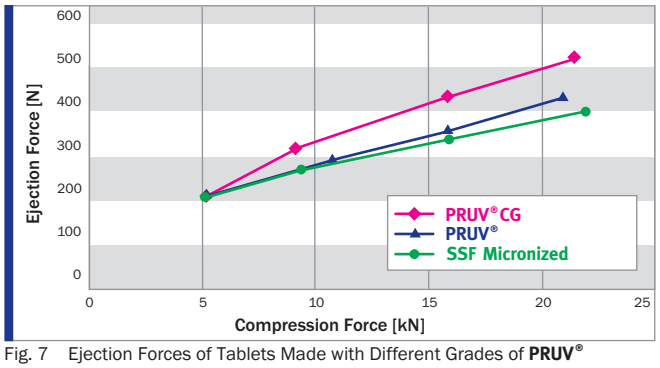


Fig. 7 Ejection Forces of Tablets Made with Different Grades of **PRUV®**

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

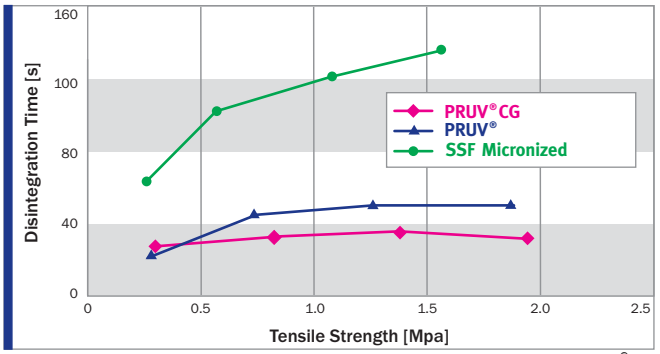


Fig. 8 Disintegration Times of Tablets Made with Different Grades of **PRUV®**

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

	PRUV®	PRUV® CG	SSF Micronized
Tablet Hardness	+	equivalent	reduced
Lubrication	+	reduced	equivalent
Disintegration Time	+	equivalent	slower

Tab. 6 Summary of Findings for the Different Grades of **PRUV®**

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
- RI-CEP 2006-313-Rev 01 - 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
- QbD Dossier available
- Elemental Impurity Statement 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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The information provided in this brochure is based on thorough research and is believed to be completely reliable. Application suggestions are given to assist our customers, but are for guidance only. Circumstances in which our material is used vary and are beyond our control. Therefore, we cannot assume any responsibility for risks or liabilities, which may result from the use of this technical advice.

1 kg Plastic Container

5 kg Drum


25 kg Drum

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