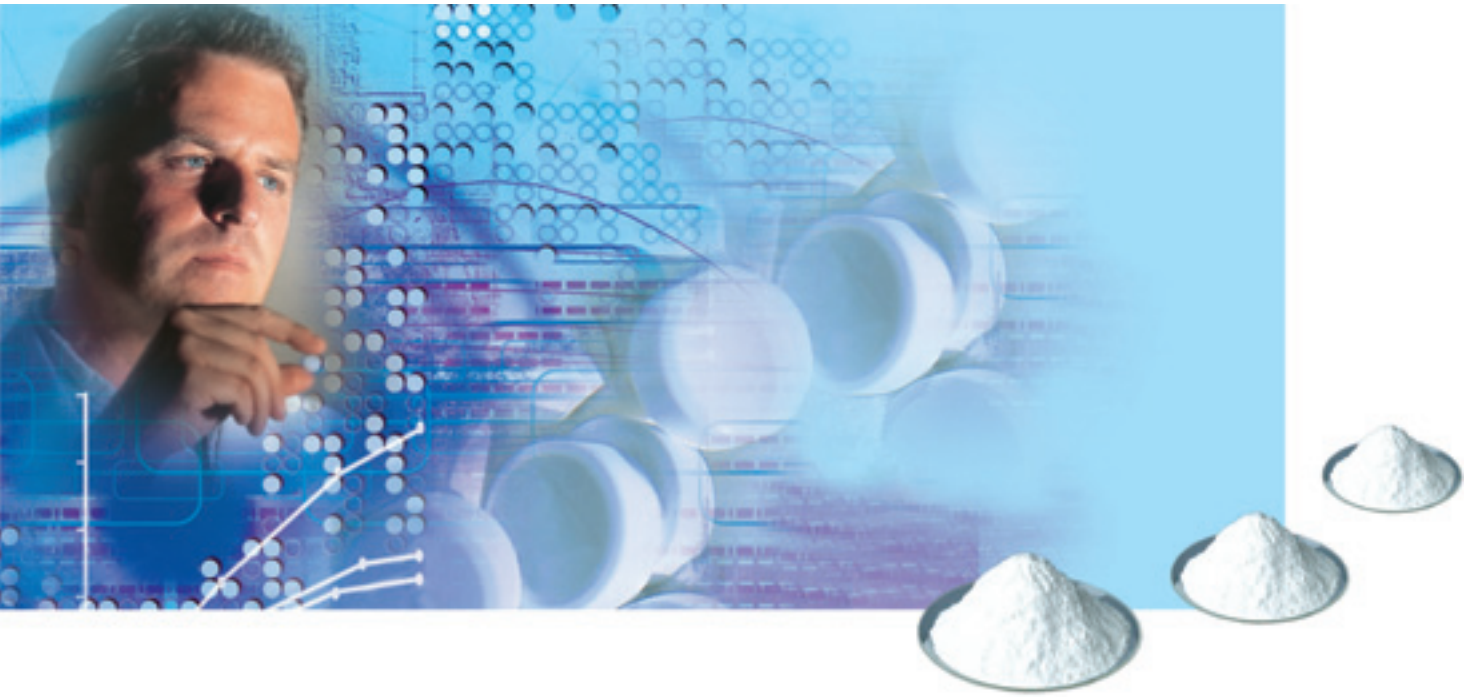
PROSOLV® SMCC

Silicified Microcrystalline Cellulose



The Original Silicified MCC

Tremendous Benefits for Solid Dosage Forms in

- **Formulation**
- **Manufacturing**
- **Marketing**

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• Excipients • Coatings
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Silicified Microcrystalline Cellulose

Introduction

Excipients play a major role in the development of tablets and capsules for the health science industry. As APIs and manufacturing processes evolve, the need for excipients with greater functionality increases.

Over 20 years ago, JRS PHARMA developed a new and innovative excipient, **PROSOLV® SMCC** (silicified microcrystalline cellulose), to alleviate some of the known deficiencies of conventional binders including: low bulk density, poor flow, loss of compatibility, stickiness issues, and sensitivity to lubricants. **PROSOLV® SMCC** not only addresses these challenges, but also offers enhanced performance.

Physical Properties of PROSOLV® SMCC

- White, free flowing powder
- High degree of brightness
- Practically insoluble in water, acetone, and anhydrous ethanol
- Chemically inert
- Excellent compactibility
- High intrinsic flow
- Enhanced lubrication efficiency
- Improved blending properties
- Exhibits both brittle fracture and plastic deformation, leading to superior binding properties
- Five times greater specific surface area than MCC alone

Effects of Silicification

The specific production process of **PROSOLV® SMCC** leads to a homogenous distribution of the colloidal silicon dioxide particles throughout the product and on the particle surfaces.

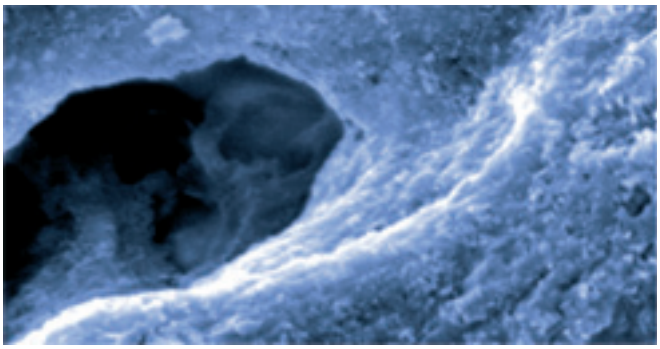
At low magnification, traditional and silicified MCC look very similar in terms of their particle size and shape. At high magnification, however, electron microscopy reveals the differentiation in the microstructures of silicified MCC and traditional MCC.

Silicification reduces the cohesiveness of the powder bed. Consequently, **PROSOLV® SMCC** shows much better powder flowability than traditional MCC grades of the same particle size.

Compared to traditional MCC, the unique surface structure of **PROSOLV® SMCC** enables excellent blend homogeneity and content uniformity, even for low-dosed, micronized active ingredients.

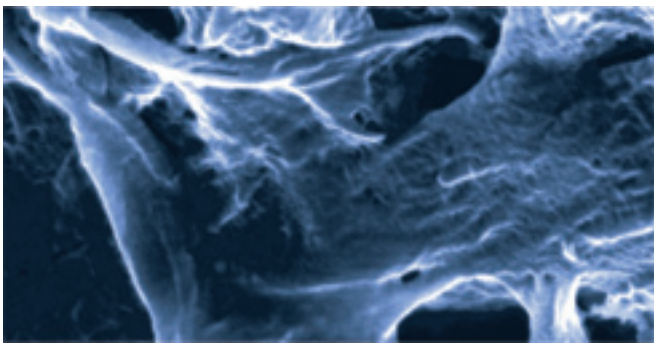
Lastly, silicification further increases the surface area by a factor of five thus improving the outstanding binding properties of microcrystalline cellulose. This makes **PROSOLV® SMCC** an ideal choice for high dose, direct compression formulations.

PROSOLV® SMCC 90



Silicified Microcrystalline Cellulose

Traditional MCC



Traditional Microcrystalline Cellulose

High magnification SEMs show CSD particles on the SMCC surface and in the SMCC pores.

Benefits

JRS PHARMA has been producing **PROSOLV® SMCC** for over 20 years. With this experience comes proven batch-to-batch consistency. Manufacturing sites located in the USA, Germany, and Finland guarantee high supply security.

PROSOLV® SMCC provides tremendous technical and manufacturing benefits through the product lifecycle including:

- Rapid formulation development
- Dust-free handling during production
- Superior flow
- Improved compactibility, leading to more robust tablets
- Fewer excipients needed at lower use levels
- Smaller tablet size
- Enhanced mixing characteristics
- Optimized content uniformity
- Shorter disintegration time

Typical Reduction of Excipient Usage with PROSOLV® SMCC

Formulations including **PROSOLV® SMCC** typically require lower excipient use levels including:

- 30 - 50 % less MCC/binders
- 25 - 50 % less lubricants
- 25 - 50 % less disintegrants
- No DCP
- No CSD/glidants

Grades of PROSOLV® SMCC

The wide variety of **PROSOLV® SMCC** grades available ensures the perfect solution for a range of different formulation challenges.

Silicified Microcrystalline Cellulose, NF
(Microcrystalline Cellulose, Ph.Eur., NF, JP, E 460(i) and Silica, Colloidal Anhydrous, Ph.Eur., E 551[1])

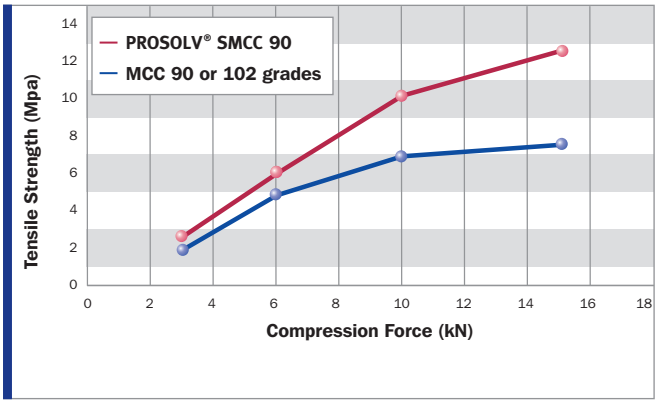
Grade	Average Particle Size by Laser Diffraction (µm)	Bulk Density (g/mL)	Main Application
PROSOLV® SMCC 50	65	0.25 - 0.37	Formulas in which optimal compaction and decent flow are required.
PROSOLV® SMCC 50 LD	50	0.20 - 0.30	Best in class binder.
PROSOLV® SMCC 90	125	0.25 - 0.37	Formulas in which a balance of flow and compaction are required.
PROSOLV® SMCC HD 90	125	0.38 - 0.50	Formulas in which optimal flow and consolidation are required. This grade shows the best disintegration times. **Low moisture grade available on request.*
PROSOLV® SMCC 90 LM	125	0.27 - 0.39	Equivalent to quality of **PROSOLV® SMCC 90**, but with lower moisture content (< 3 %)

[1] NF = Colloidal Silicon Dioxide; JP = Light Anhydrous Silicic Acid

PROSOLV® SMCC

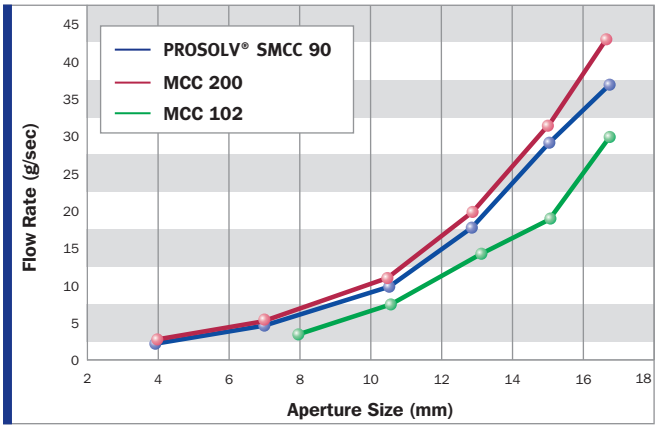
Silicified Microcrystalline Cellulose

Direct Compression



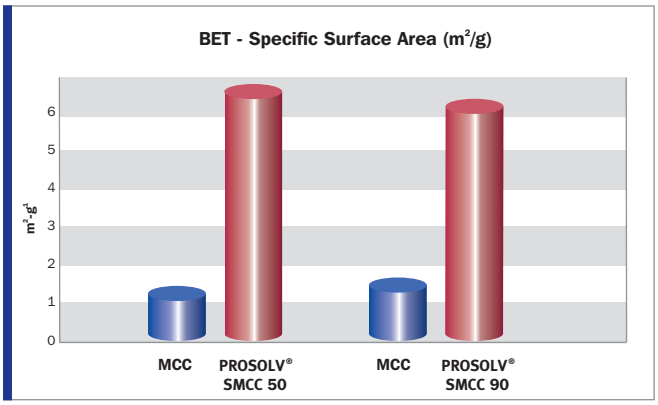
PROSOLV® SMCC is 30-50 % more compactible than MCC. It accommodates poorly compactible APIs, delivers superior compactibility in high drug-loading applications, and excels in roller compaction processes.

Volume Flow



PROSOLV® SMCC offers a balance of best in class compaction and flow for tablet formulations. Silicification provides flow that is comparable to doubling the particle size of MCC in addition to superior compaction.

Surface Area



PROSOLV® SMCC shows a five-fold specific surface area increase compared to MCC. The increased specific surface area enables **PROSOLV® SMCC** to impart enhanced compactibility to formulations.

Case Study: Produce Smaller Tablets for a Multiple, High Dose, Low Bulk Density Actives Formulation

Formulation Characteristics

This **19-active formulation**, including herbal constituents, required large amounts of both MCC and DCP to achieve workable compactibility, yet still exhibited significant segregation, low content uniformity, and poor flow. In addition, due to the multiple components and large amount of excipients, the resulting tablet exceeded target size.

Formulation Results

After formulating with **PROSOLV® SMCC**, the need for DCP was eliminated altogether. Compactibility, segregation, and content uniformity all improved and tablet weight was reduced by 33 %. Finally, due to the improved flow characteristics and consolidated blending, tabletting speed and production efficiency were both increased.

Production Benefits and Efficiencies

- Reduced binder usage significantly
- Eliminated DCP entirely
- Reduced tablet weight by 33 %
- Improved processing characteristics
- Improved tablet content uniformity
- Increased production efficiency

MCC Formulation	PROSOLV® SMCC Formulation
20 % MCC 20 % DCP	7 % **PROSOLV® SMCC 90** No DCP required
Low compactibility	Exceptional tablet compaction • Hardness 9-12 Kp • Friability 0.08 %
Excessive tablet weight > 1800 mg	Target weight achieved < 1300 mg
Low bulk density active with poor flow	Consolidated powder blend with excellent flow • Increased production output
Significant segregation of active • Fine particles seen floating on top of blend	Non-segregating formulation • Separation of fine particles reduced • < 2 % RSD in tablet weight
 1080 mg API 720 mg Filler / Binder **1800 mg**	 1080 mg API 80 mg **PROSOLV® SMCC** **1160 mg**

PROSOLV® SMCC

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Case Study: Simplifying Formulation Development and Manufacture with a Low Dose Cohesive Active

Formulation Objective

Scientists were tasked with developing a single-active, multi-strength, coated tablet to compete with a branded pharmaceutical while reducing cost of goods, limiting ingredient requirements, and compressing development time.

Formulation Results

Through a progressive reformulation strategy, scientists developed a directly compressible low-dose formulation suitable for dose proportional, multi-strength tablet manufacture with excellent content uniformity. The number of excipients was reduced from four to two. The lubricant required was also minimized during scale-up.

Formulation

Ingredient	% w/w			
	RLD	A	B	C
API	< 5	< 5	< 5	< 5
Lactose	~ 65			
Microcrystalline Cellulose	~ 20			
PROSOLV® SMCC HD 90		~ 55	~56	> 95
PROSOLV® SMCC 50		~ 36	~ 37	
Colloidal Silicone Dioxide	~ 9			
Croscarmellose Sodium		~ 2		
Talc	< 0.6	< 5		
Magnesium Stearate	> 0.4	> 0.4	> 0.4	< 0.4

RLD = Reference Listed Drug
MCC = Microcrystalline Celluose
SMCC = Silicified Microcrystalline Cellulose
RSD = Relative Standard Deviation

A,B = trial formulation
C = final formulation

Formulation Challenges

This single active, multi-dose prescription tablet formulation presented issues with API agglomeration that challenged blending and content uniformity. A successful outcome was further challenged by targeting a direct compression tablet manufacturing process.

Formulation C, Content Uniformity Analysis

Time Point	Ave % Recovery (n=10)	% RSD
1	98.6	0.5
2	98.3	0.8
3	97.1	0.5
4	97.5	0.8
5	98.7	1.2

Production Benefits and Efficiencies

- Reduced number of excipients used
- Reduced development timelines
- Simplified manufacturing process
- Shortened manufacturing times
- Decreased excipient levels
- Improved content uniformity

Conclusion

PROSOLV® SMCC HD 90 in formulation C functions as a complete processing system, providing the characteristics required for cost effectively manufacturing a high-quality competitive pharmaceutical product while minimizing the ingredient numbers and levels.

Regulatory Information

PROSOLV® SMCC is an agglomerated composite from Microcrystalline Cellulose Ph.Eur., USP-NF, JP and Colloidal Silicon Dioxide Ph.Eur., USP-NF, JP (Light Anhydrous Silicic Acid JP). It is monographed in the second supplement to NF 27 and is listed in the Inactive Ingredient Database (IID) on the FDA website as an approved ingredient in New Drug Applications (NDA). There are regulatory approvals in all major markets with **PROSOLV® SMCC** including: USA, Europe, Japan, Mexico, Australia, India, and China. TUP studies available.

Packaging, Samples and Storage

Storage
Store in original container. Protected from excessive heat and moisture. Opened containers should be reclosed or stored in a manner which provides the product with protection equal to the original.

Packaging
Available in bags, drums, and supersacks

Sample Sizes
400 g and 2 kg containers available

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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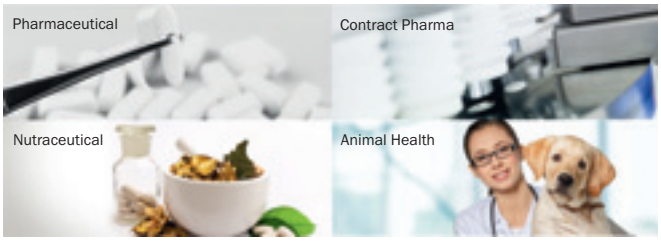

Bringing Health Science to Life

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Lubricants
Thickeners+Stabilizers
Carriers
Superdisintegrants

Coatings

Biopharmaceuticals

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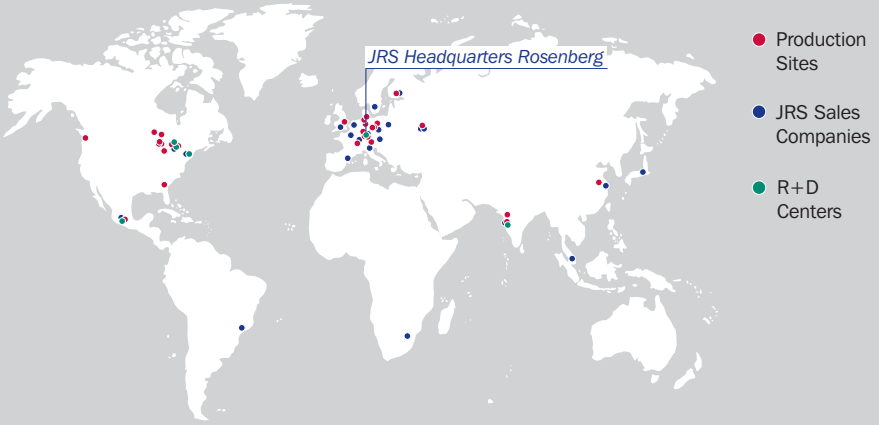
Manufacturing



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