PROSOLV® SMCC

High Functionality Excipient

Problem Solving for over 25 years.

Smaller Tablets
Harder Tablets
Faster Output

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

PROSOLV® SMCC

Silicified Microcrystalline Cellulose, NF

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 25 years ago JRS PHARMA developed a new high functionality excipient, **PROSOLV® SMCC**, with enhanced properties for modern, high-speed tableting processes.

PROSOLV® SMCC provides solutions to problems formulators often encounter with conventional binders in terms of low bulk density, poor flow, loss of compactability, stickiness issues and sensitivity to lubricants.

PROSOLV® SMCC addresses these challenges and offers additional benefits.

Physical Properties of **PROSOLV® SMCC**

- White, free flowing powder
- High degree of brightness
- Practically insoluble in water, acetone, and anhydrous ethanol
- Chemically inert
- Excellent compactability
- High intrinsic flow
- Enhanced lubrication efficiency
- Improved blending properties
- Five times greater specific surface area than Microcrystalline Cellulose (MCC) alone
- Dust free Colloidal Anhydrous Silica (CSD) handling

Effects of **PROSOLV®** Technology

Co-processing of MCC with CSD using the **PROSOLV®** technology leads to a homogenous distribution of CSD particles throughout the product and on the particle surfaces.

At low magnification, traditional MCC and SMCC look very similar in terms of their particle size and shape. At high magnification, however, electron microscopy reveals the differences in the microstructures of the silicified MCC **PROSOLV® SMCC** (Picture 1) and traditional MCC (Picture 2).

Silicification reduces the cohesiveness of the powder bed. Consequently, it has much better powder flowability than traditional MCC grades of the same particle size leading to more manufacturing output, via high-speed tableting.

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

Lastly, **PROSOLV® SMCC** exhibits a 5 times increased surface area thus improving the outstanding binding properties of MCC (Figure 1). This makes **PROSOLV® SMCC** an ideal choice for high dose, direct compression formulations and roller compaction processes*

*Technical information available

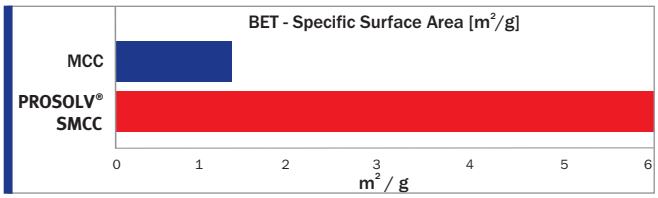
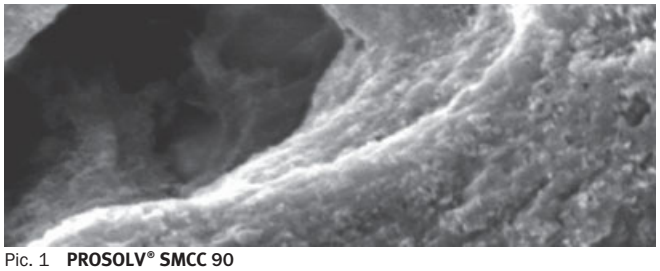
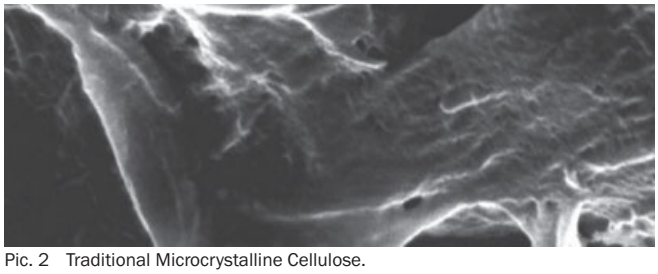


Fig. 1 5 Fold Increase in Specific Surface Area.



Pic. 1 **PROSOLV® SMCC 90**

High Magnification SEMs Show CSD Particles Tightly Bound to the MCC Surfaces and Pores.



Pic. 2 Traditional Microcrystalline Cellulose.

Performance of Various Grades of **PROSOLV® SMCC**

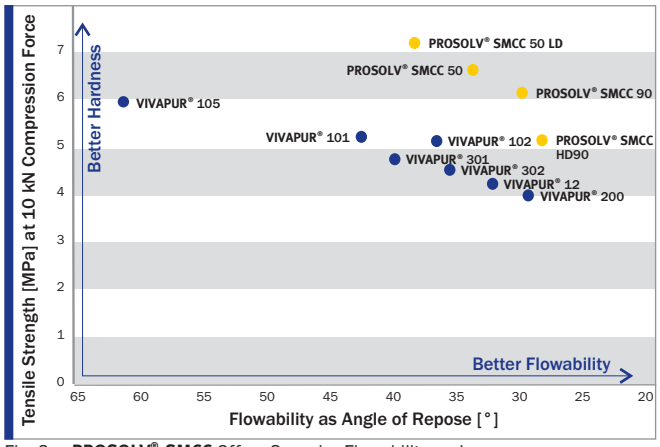


Fig. 2 **PROSOLV® SMCC** Offers Superior Flowability and Tablet Strength Compared to MCC **VIVAPUR®**.

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

PROSOLV® SMCC 50 LD
Best in class binder.

PROSOLV® SMCC 50
Formulas in which optimal compaction and decent flow are required.

PROSOLV® SMCC 90
Formulas in which a balance of flow and compaction are required.

PROSOLV® SMCC HD 90*
Formulas in which optimal flow and consolidation are required. This grade shows the best disintegration time.

PROSOLV® SMCC 90 LM
Equivalent to quality of **PROSOLV® SMCC 90**, with lower moisture content (< 3 %).

*For **PROSOLV® SMCC HD 90** low moisture grade is available upon request.

Benefits

PROSOLV® SMCC provides unique technical and manufacturing benefits throughout the product lifecycle including:

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

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 Dibasic Calcium Phospate (DCP) needed
- No additional CSD/glidants needed

Functional Benefits

Direct Compression

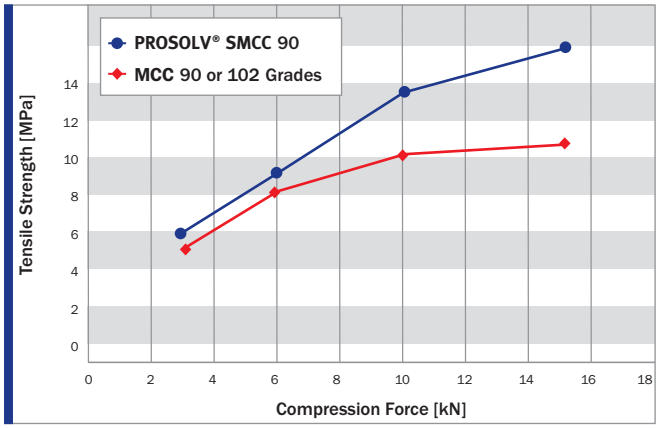


Fig. 3 Comparison of the Compression Profiles of **PROSOLV® SMCC 90** and a Conventional MCC of the Same Particle Size.

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

Volume Flow

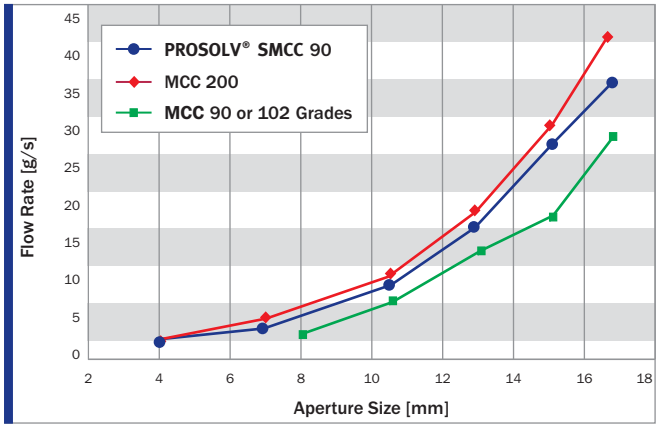
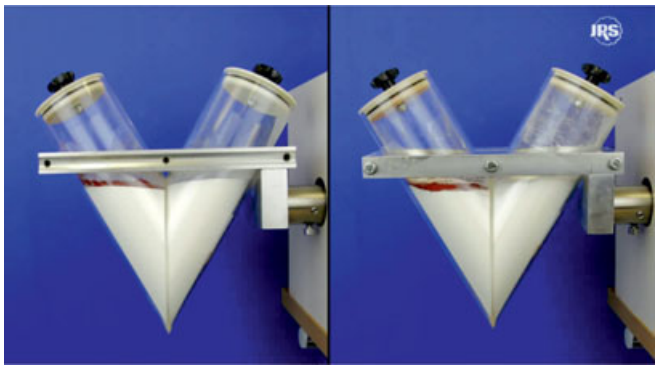


Fig. 4 Comparison of the Flow Properties of **PROSOLV® SMCC** and Different Conventional MCCs.

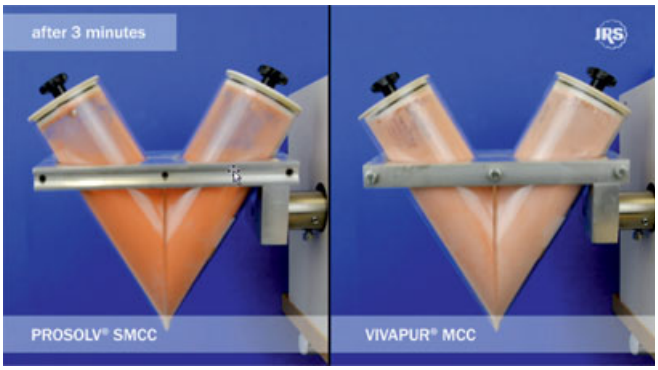
PROSOLV® SMCC offers a balance of best in class compaction and flow for tablet formulations. Silicification provides flow that is comparable to doubling the particle size of MCC in addition to superior compaction (Figure 4).

Blend Uniformity

Pictures 3 a and 3 b show **PROSOLV® SMCC 90** (left) and **VIVAPUR® 102** (right) before and after blending with red iron oxide.
Good blend uniformity is achieved in both cases. However the **PROSOLV®** blend, exhibits a far stronger color intensity than the corresponding MCC blend. This effect can be attributed to the larger specific surface area of SMCC, which promotes blending, and thus content uniformity, for fine-particle APIs.



Pic. 3 a **PROSOLV® SMCC** (left) and **VIVAPUR®** Before Blending with the Model Substance Iron Oxide Red.



Pic. 3b **PROSOLV® SMCC** (left) and **VIVAPUR®102** After 3 Minutes of Blending with the Model Substance Iron Oxide Red.

Case Study: Reducing Tablet Size for a Higher Drug Load

Formulation Challenges

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. The resulting tablet also exceeded target size, due to the multiple components and large amount of excipients.

Formulation Results

After formulating with **PROSOLV® SMCC** the need for DCP was eliminated. Compactability, segregation and content uniformity were improved and tablet weight was reduced by 33 %. Finally, due to the improved flow characteristics and consolidated blending, tableting 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, tablets per batch

Low Bulk Density, Multiple-API Formulation

MCC/DCP Formulation	PROSOLV® SMCC Formulation
20 % MCC 20 % DCP	7 % **PROSOLV® SMCC 90** No DCP required
Low compactibility	Exceptional tablet compaction • Hardness 90 - 120 N • 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 % Relative Standard Deviation(RSD) in tablet weight
 1080 mg API 720 mg Filler / Binder **1800 mg**	 1080 mg API 80 mg **PROSOLV® SMCC** **1160 mg**

Tab. 1 Comparison Between MCC/DCP and **PROSOLV® SMCC** Formulation.

PROSOLV® SMCC
Silicified Microcrystalline Cellulose, NF

Case Study: Simplifying Formulation Development of a Low Dose Cohesive Active

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 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 five to two. The lubricant required was also minimized during scale-up.

Production Benefits and Efficiencies

- Reduced number of excipients used
- Fast and simpler formulation development
- Simplified manufacturing process
- Shortened manufacturing times
- Improved content uniformity

Formulation

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

Tab. 2 Tested Formulations.

RLD = Reference Listed Drug
SMCC = Silicified Microcrystalline Cellulose
RSD = Relative Standard Deviation
API = Active Pharmaceutical Ingredient
A,B = trial formulation
C = final formulation

Formulation C, Content Uniformity Analysis

Time Point	Ø - Recovery [%] (n=10)	RSD [%]
Beginning	98.6	0.5
Mid	97.1	0.5
End	98.7	1.2

Tab. 3 The Final Formulation Exhibited Excellent Content Uniformity Throughout the Tabletting Run.

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, JPE 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, QbD and elemental impurity studies are available.

State	Regulatory Status
Brazil	Silicified Microcrystalline Cellulose, NF Microcrystalline Cellulose, Ph.Eur. Silica, Colloidal Anhydrous, Ph.Eur. Microcrystalline Cellulose and Silicon Dioxide are listed in the positive list for Food
Canada	Silicified Microcrystalline Cellulose, NF Product master file 2006-116 with Health Canada Microcrystalline Cellulose and Silicon Dioxide are permitted as food additive in Health Canada's Food and Drug Regulations
China	Silicified Microcrystalline Cellulose, ChP IDL available now. Chinese DMF will be submitted in end of 2018.
Europe	Microcrystalline Cellulose, Ph.Eur. Silica, Colloidal Anhydrous, Ph.Eur. Upcoming monograph for co-processed excipients Microcrystalline Cellulose, E 460 Silicon Dioxide, E 551
Japan	Silicified Microcrystalline Cellulose, JPE
USA	Silicified Microcrystalline Cellulose, NF SMCC is listed on FDA's Inactive Ingredients Database, Drug master file number 12150 Microcrystalline Cellulose and Silicon Dioxide are considered GRAS and listed on FDA's Food Additive Status List and FDA's Everything Added to Food in the United States (EAFUS) list

Tab. 4 Regulatory Status.

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

High supply security guaranteed by multiple GMP production sites across three different continents.

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

JRS PHARMA

The Global Excipient Maker

Products and Services

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Thickeners+Stabilizers
Carriers
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Calcium Supplements

Coatings

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- Application Lab's

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