PROSOLV® SMCC
High Functionality Excipient

Problem Solving for over 25 years.

Smaller Tablets
Harder Tablets
Faster Output
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

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 Phosphate (DCP) needed
- No additional CSD/glidants needed
**Functional Benefits**

**Direct Compression**

![Graph showing Compression Force vs. Tensile Strength](image)

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**

![Graph showing Flow Rate vs. Aperture Size](image)

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.

![Images of blend uniformity before and after blending](image)

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

<table>
<thead>
<tr>
<th>MCC/DCP Formulation</th>
<th>PROSOLV® SMCC Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 % MCC</td>
<td>7 % PROSOLV® SMCC 90 No DCP required</td>
</tr>
<tr>
<td>20 % DCP</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Low compactibility</th>
<th>Exceptional tablet compaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Hardness 90 - 120 N</td>
</tr>
<tr>
<td></td>
<td>• Friability 0.08 %</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Excessive tablet weight &gt; 1800 mg</th>
<th>Target weight achieved &lt; 1300 mg</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Low bulk density</th>
<th>Consolidated powder blend with excellent flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active with poor flow</td>
<td>• Increased production output</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Significant segregation of active</th>
<th>Non-segregating formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Fine particles seen floating on top of blend</td>
<td>• Separation of fine particles reduced</td>
</tr>
<tr>
<td></td>
<td>• &lt; 2 % Relative Standard Deviation(RSD) in tablet weight</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>RLD</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>API</td>
<td>&lt; 5</td>
<td>&lt; 5</td>
<td>&lt; 5</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>Lactose</td>
<td>~ 65</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microcrystalline Cellulose</td>
<td>~ 20</td>
<td></td>
<td>~56</td>
<td></td>
</tr>
<tr>
<td>PROSOLV® SMCC HD 90</td>
<td>~55</td>
<td>~37</td>
<td>&gt; 95</td>
<td></td>
</tr>
<tr>
<td>PROSOLV® SMCC 50</td>
<td>~36</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colloidal Silicone Dioxide</td>
<td>~ 9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Croscarmellose Sodium</td>
<td>~ 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Talc</td>
<td>&lt; 0.6</td>
<td>&lt; 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium Stearate</td>
<td>&gt; 0.4</td>
<td>&gt; 0.4</td>
<td>&gt; 0.4</td>
<td>&lt; 0.4</td>
</tr>
</tbody>
</table>

Tab. 2 Tested Formulations.

Lesson Learned: The final formulation exhibited excellent content uniformity throughout the tabletting run.

Formulation C, Content Uniformity Analysis

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Ø - Recovery [%] (n=10)</th>
<th>RSD [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beginning</td>
<td>98.6</td>
<td>0.5</td>
</tr>
<tr>
<td>Mid</td>
<td>97.1</td>
<td>0.5</td>
</tr>
<tr>
<td>End</td>
<td>98.7</td>
<td>1.2</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>State</th>
<th>Regulatory Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>Silicified Microcrystalline Cellulose, NF Microcrystalline Cellulose, Ph.Eur. Microcrystalline Cellulose and Silicon Dioxide are listed in the positive list for Food</td>
</tr>
<tr>
<td>Canada</td>
<td>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</td>
</tr>
<tr>
<td>China</td>
<td>Silicified Microcrystalline Cellulose, ChP IDL available now. Chinese DMF will be submitted in end of 2018.</td>
</tr>
<tr>
<td>Europe</td>
<td>Microcrystalline Cellulose, Ph.Eur. Silica, Colloidal Anhydrous, Ph.Eur. Upcoming monograph for co-processed excipients Microcrystalline Cellulose, E 460 Silicon Dioxide, E 551</td>
</tr>
<tr>
<td>Japan</td>
<td>Silicified Microcrystalline Cellulose, JPE</td>
</tr>
<tr>
<td>USA</td>
<td>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</td>
</tr>
</tbody>
</table>

| 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.

Disclaimer:
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.
The Global Excipient Maker

Products and Services

Excipients
Family of High Functionality Excipients
Binders
Functional Fillers
Lubricants
Thickeners + Stabilizers
Carriers
Superdisintegrants
Calcium Supplements

Coatings

Biopharma Services

Global Network

- Excipients
- Coatings
- Biopharma Services
- JRS Sales Companies
- Technical Competence Centers
- Application Lab's

Additionally, dedicated representatives in almost every country.

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