

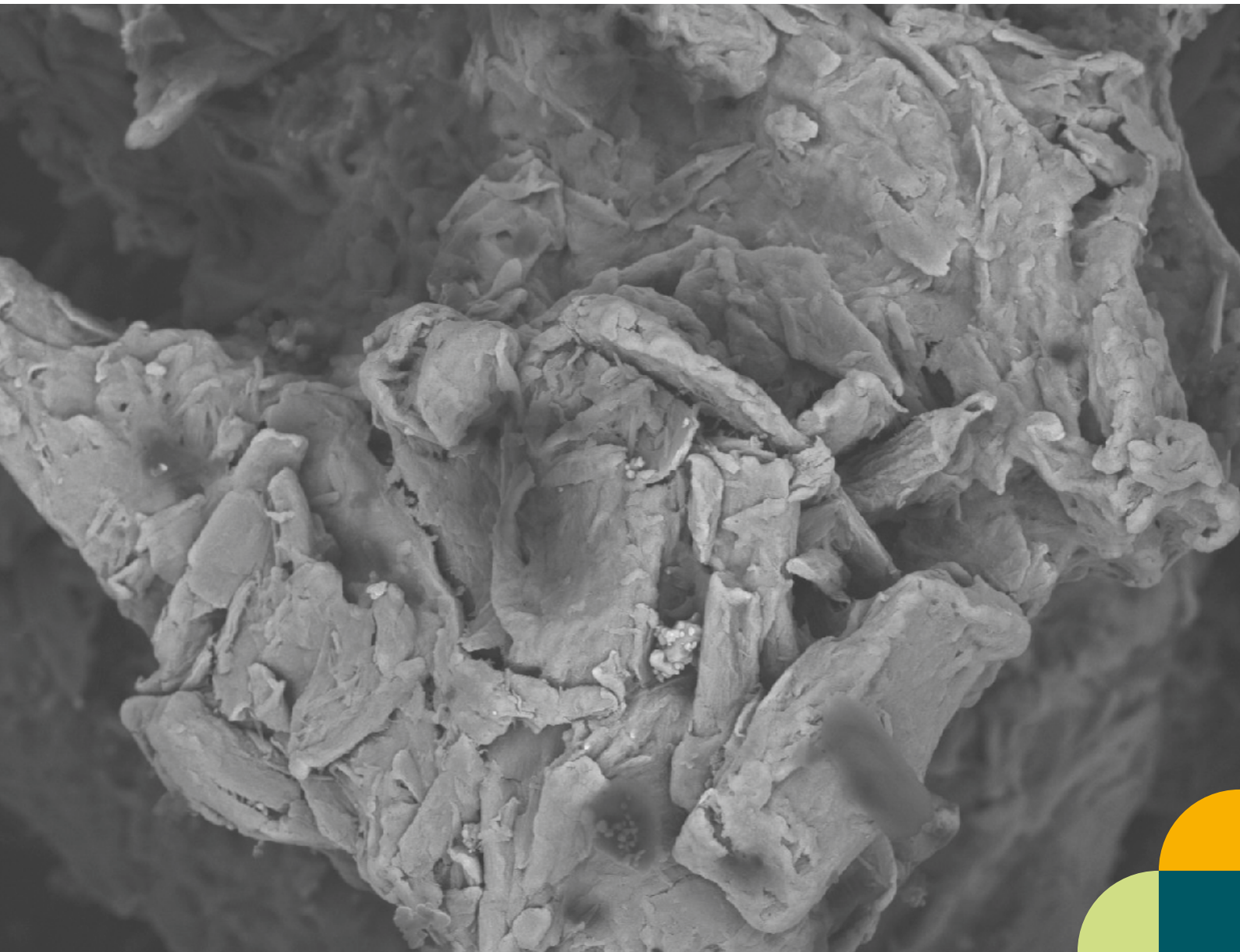


Fibers for Life.

JRS PHARMA

# PROSOLV<sup>®</sup> RX 90

Ready-to-Use, High Functionality Excipient Composite  
for Direct Compression and Continuous Manufacturing



# Streamline Your R&D and Production

## Introduction

The health science industry faces a wide variety of challenges including increased pressure to:

- › Reduce costs
- › Accelerate time to market
- › Improve product performance
- › Cope with high demands and tight capacities
- › Utilize modern technology

These challenges drive health science companies to find new solutions for improving time – and cost– efficiency in oral dosage form development and production. Formulation scientists developing direct compression formulations generally require several conventional excipients – often at high levels – to obtain good material flow, compaction, blending properties, content uniformity, carrying capacity, stability, lubricity, and disintegration. Finding the proper excipient combinations and concentrations to achieve adequate solid dosage formulas is a time-consuming, and often expensive process, that varies with active pharmaceutical ingredient (API) characteristics.

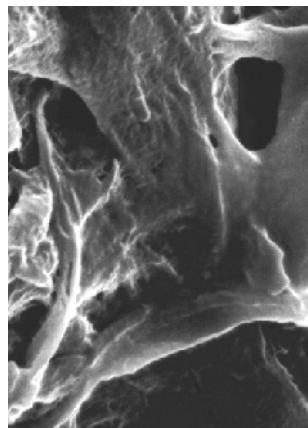
PROSOLV® RX 90 was developed to provide an innovative solution to meet these challenges.

Beyond its benefits in conventional batch production, PROSOLV® RX 90 presents a set of properties that make it well-suited for continuous manufacturing (see page 9). Because it acts multifunctionally as a filler/binder, flow aid, disintegrant, and lubricant at

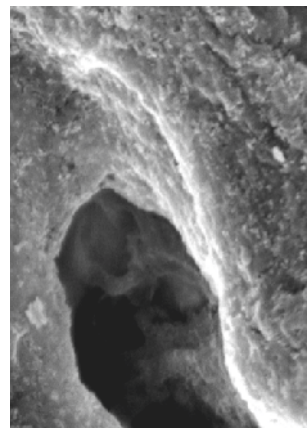
the same time, production requires only two feeders. This not only leads to space saving, but also helps to simplify control of the production process.

The unique surface structure and good flowability of PROSOLV® RX 90 enable fast and segregation-free blending with APIs.

## PROSOLV® technology



Pic. 1 Regular MCC with smooth surface areas.



Pic. 2 Micro-rugosity introduced by PROSOLV® technology.

Compounding with the PROSOLV® Technology leads to a homogeneous distribution of the individual components throughout the particle and on its surface. The synergistic effects achieved by this technology include better compactability, flowability, and content uniformity, due to a significantly increased surface area.



Furthermore, its all-in-one structure provides outstanding robustness in terms of blending times:

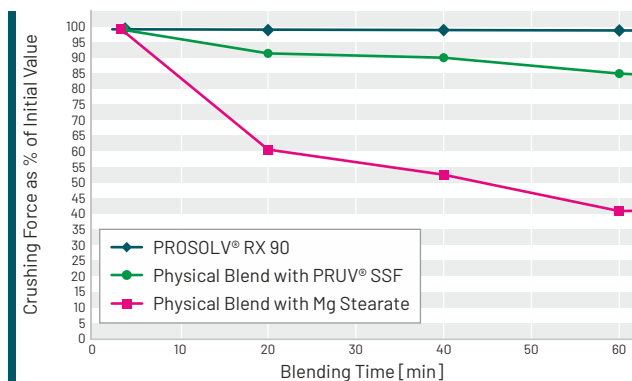


Fig. 1 Effect of blending time on tablet hardness. PROSOLV® RX 90 in comparison with physical mixtures of microcrystalline cellulose (MCC), colloidal anhydrous silica (CSD), sodium starch glycolate (SSG) and sodium stearyl fumarate (SSF) or magnesium stearate, respectively, as a lubricant.

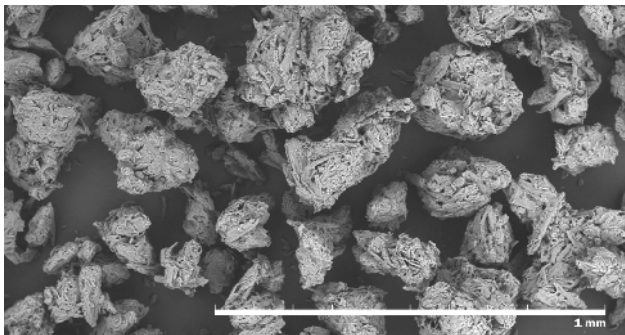
### What is PROSOLV® RX 90?

PROSOLV® RX 90 was developed using JRS PHARMA's proven PROSOLV® Technology and was the first lubricated high functionality excipient (HFE) on the market. PROSOLV® RX 90 is an all-in-one, ready-to-use excipient composite. It effectively combines all functionalities required for tableting in a single excipient composite.

PROSOLV® RX 90 is more than a simple physical blend. It is a homogeneous, lubricated high functionality excipient composite. Each component of the composite maintains its chemical identity while synergistically providing increased functional performance.

# 6 Elements of Success

Powder flow, blend homogeneity and good compactability are prerequisites for successful tableting. Mechanical robustness of tablets enables dust-free coating and packaging. Fast disintegration is essential for in-vivo performance of the tablet. PROSOLV® RX 90 combines these 6 elements of success in one excipient:



Pic. 4 SEM of PROSOLV® RX 90 particle size and morphology of the composite material enable good powder flow and high content uniformity.

## 1. Excellent powder flow

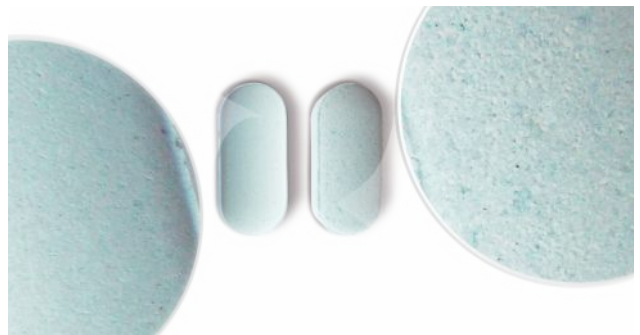
Due to its favorable particle morphology, PROSOLV® RX 90 shows significantly better powder flow properties than the corresponding physical mixture of its individual ingredients. PROSOLV® RX 90 is therefore perfectly suited for direct compression processing, even on high speed tablet presses.



Pic. 5 Excellent flowability of members of the PROSOLV® Family as shown by the angle of repose.

## 2. Superb blend homogeneity

The composite nature of PROSOLV® RX 90 prevents segregation of the individual excipient components. Moreover, the porous surface structure promotes adhesion of low-dose, micronized active ingredients, thus improving the content uniformity in the powder blend and the finished product (see page 6).



Pic. 6 The surface structure promotes interactive blending and, thus, homogeneous distribution of fine-particle APIs in the tablet matrix. The tablet on the left was formulated with PROSOLV® RX 90 and a blue dye as a model API. The formulation based on regular MCC (right) shows a spotty appearance indicating non homogeneous distribution of the model API.

## 3. Outstanding compactability performance

The excellent compaction and lubrication of PROSOLV® RX 90 result in less capping and breakage, increasing yields and improving profitability. With PROSOLV® RX 90, mechanically robust tablets can be produced at a low compaction force. This leads to prolonged equipment and tooling life.

Due to a smaller excipient amount needed and the possibility of high active ingredient loads, smaller tablet sizes and lower tablet weight can be reached, which results in high patient compliance.

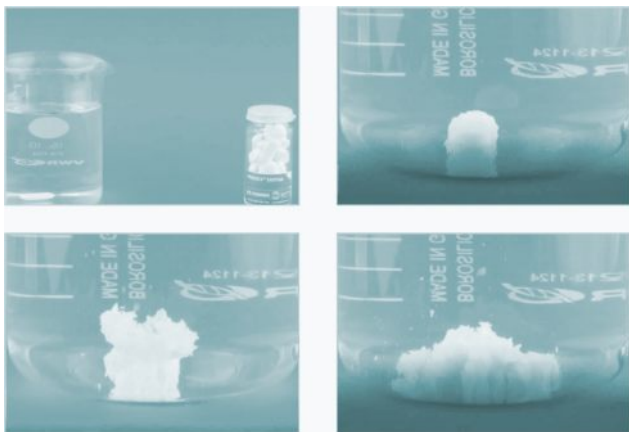


#### 4. Ultimate robustness, improved tablet handling

PROSOLV® RX 90 tablets are mechanically robust and have a low friability, even in the case of demanding tablet shapes. Tablet robustness enables all packaging and coating options. PROSOLV® RX 90 tablet production generates less dust. Tableting with PROSOLV® RX 90 can reduce cleaning and change - overtimes (see pages 7 and 8).

#### 5. Rapid disintegration

The built-in superdisintegrant enables rapid disintegration with minimum variation from tablet to tablet.



Pic. 7 Disintegration of a PROSOLV® RX 90 tablet.

#### 6. Ideal for film coating

Due to its unique surface structure, the PROSOLV® RX 90 line is ideally suited for film-coated tablets. It enables crisp logo definition and excellent film adhesion to the core.

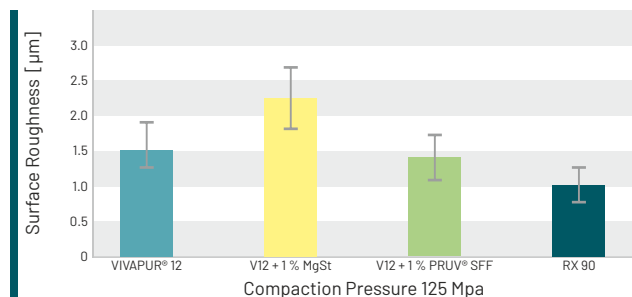
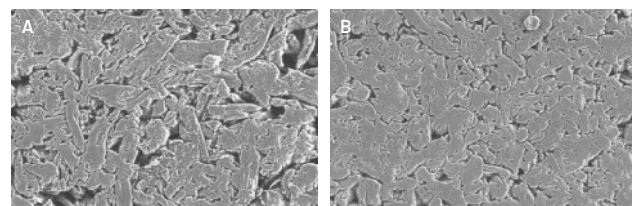


Fig. 2 Surface roughness of tablet cores. (V12 = VIVAPUR® 12 MCC)



Pic. 8 SEM pictures of tablet surfaces. A: MCC, B: PROSOLV® RX 90

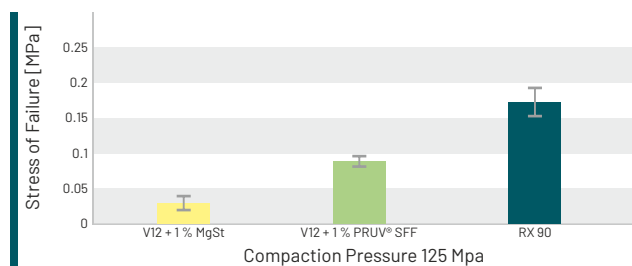
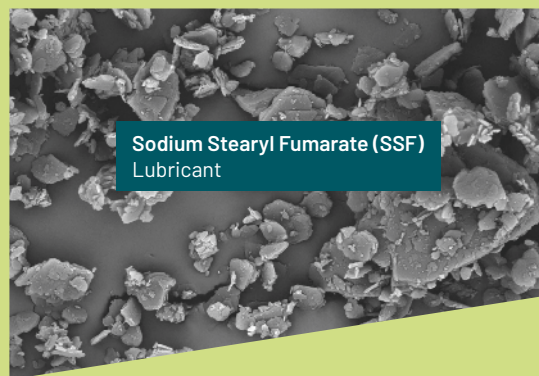
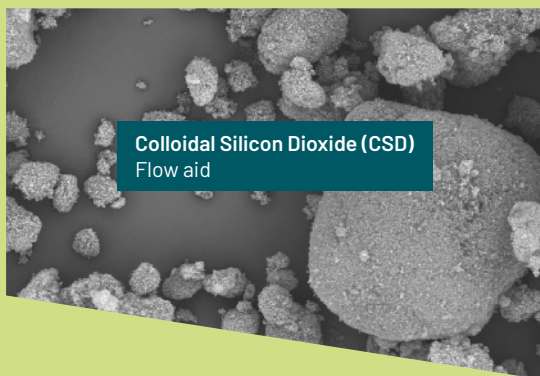
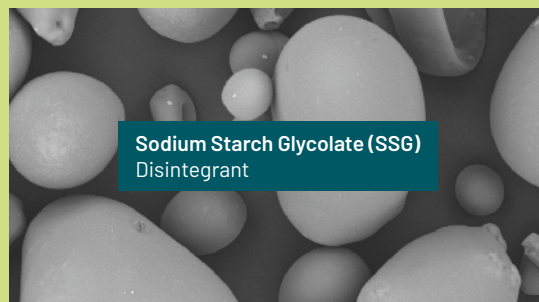
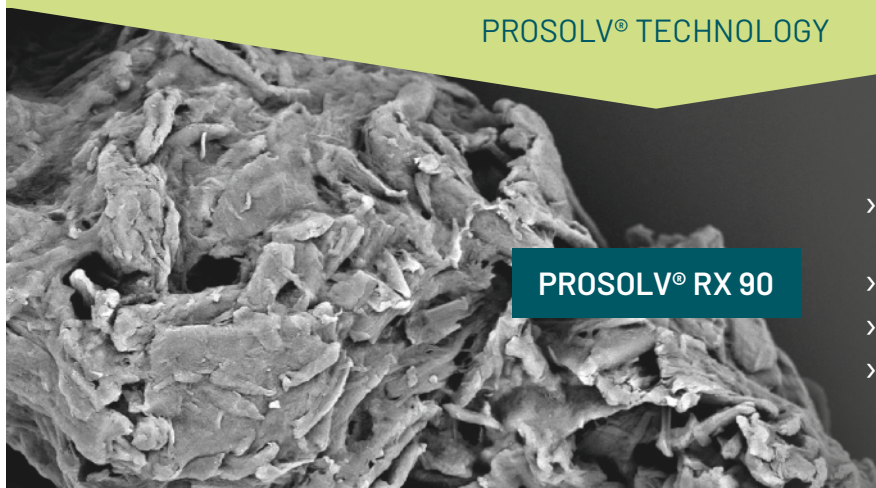


Fig. 3 Adhesion of VIVACOAT® films to tablet cores.

# PROSOLV<sup>®</sup> RX 90 Composition



## PROSOLV<sup>®</sup> TECHNOLOGY



- > Homogeneous, monoparticulate composite
- > High functionality excipient
- > Enhanced flowability
- > Increased surface area

## Case Study

# Improving Content Uniformity in Low-Dose DC Formulations

### Introduction

Direct compression of low dosage APIs often leads to content uniformity issues. The unique PROSOLV® Technology used to produce PROSOLV® RX 90 creates a significant increase of the specific surface area compared to the physical blend. This, along with its micro-rugosity, promotes high content uniformity when using low dosage APIs.

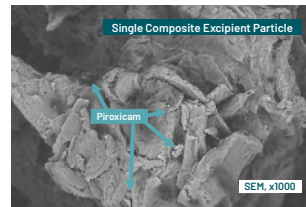
Formulation	PROSOLV® RX 90 [%]	Physical Mixture [%]
Piroxicam	5.0	5.0
PROSOLV® RX 90	95.0	-
VIVAPUR® 102 (MCC)	-	91.5
EXPLOTAB® (SSG)	-	1.0
PRUV® (SSF)	-	0.5
CSD	-	2.0
Total	100.0	100.0
Content Uniformity RSD	1.24	1.24

Tab. 2 Case study: Piroxicam tablets (8 mm, 100 mg) were pressed on a IMA Kilian -Pressima 13EU-D

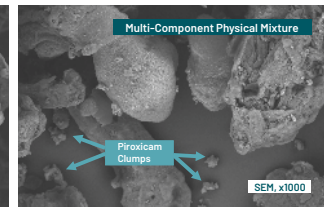
### Piroxicam direct compression tablets

Formulation	PROSOLV® RX 90 [%]	Physical Mixture [%]
Piroxicam	5.0	5.0
PROSOLV® RX 90	95.0	-
VIVAPUR® 102 (MCC)	-	91.68
EXPLOTAB® (SSG)	-	0.95
PRUV® (SSF)	-	0.47
CSD	-	1.90
Total	100.0	100.0
Content Uniformity RSD	1.62	19.56

Tab. 3 Case study: piroxicam tablets (8 mm, 200 mg) were pressed on a IMA kilian -pressima 13EU-D kilian -pressima 13EU-D



Pic. 9 Piroxicam embedded in PROSOLV® RX 90



Pic. 10 Physical mixture plus piroxicam

## Case Study

# Medium-Dosage Paracetamol Formulation

In these formulations, the properties of the API dominate the formulation and compaction properties. A formulation containing 40 % Paracetamol as a poorly compressible model API was evaluated to investigate the compaction properties of PROSOLV® RX 90 in a challenging formulation.

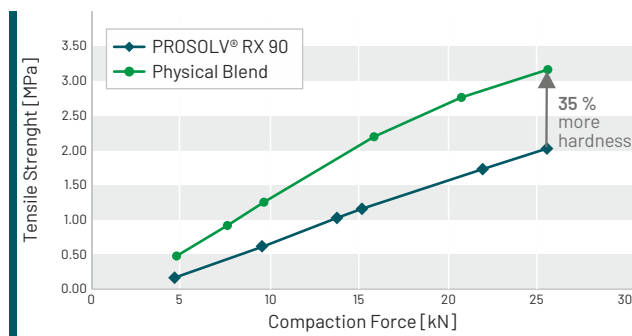


Fig. 4 Compressibility 40 % paracetamol formulation

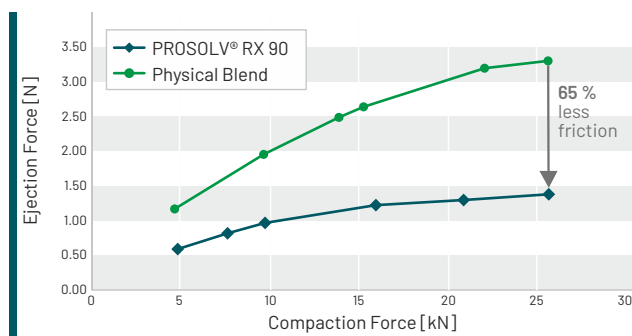


Fig. 5 Ejection force 40 % paracetamol formulation

Case study: poorly compressible API  
PROSOLV® RX 90 + paracetamol tablets (13 mm, 500 mg) were pressed on a IMA Kilian – Pressima 13 EU-D.

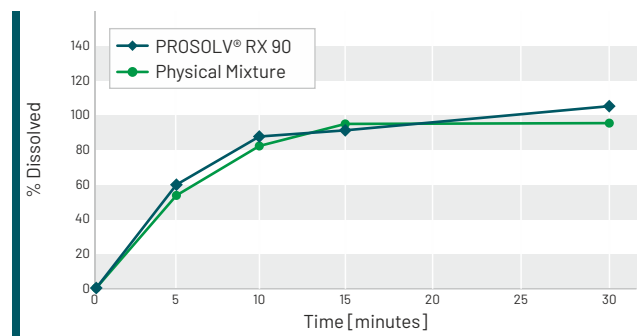


Fig. 6 Dissolution profile 40 % paracetamol formulation

## Conclusion

The analyzed tablets showed significantly improved tablet properties in comparison to the tablets made from the physical blend.

PROSOLV® RX 90 tablets exhibited

- > 30 - 50 % higher robustness (tensile strength)
- > 100 % higher lubrication efficiency on average
- > Similar dissolution profiles for both products

## Case Study

# High-speed Tableting of PROSOLV<sup>®</sup> RX 90

## Introduction

The reduction of tablet manufacturing costs has become increasingly important for the pharmaceutical industry. One of the ways to save production costs is to increase the speed of tableting to produce more tablets in the same amount of time. An improvement of the tableting process often requires the need to simplify the formulation through the use of high functionality excipients.

The lubricated high functionality excipient PROSOLV<sup>®</sup> RX 90 provides the necessary robustness and consistency of tablet manufacturing, leading to increased production efficiency and tremendous cost savings.

PROSOLV<sup>®</sup> RX 90 and the corresponding physical blend of the single components were compared in high speed compression on a FETTE 2090i tablet press. Paracetamol was used as a model API in a dose of 40 %. The tablet characteristics, as well as the production costs, were compared.

## Conclusion

- › PROSOLV<sup>®</sup> RX 90 converts technical benefits into commercial success.
- › PROSOLV<sup>®</sup> RX 90 is ideally suited for high-speed tableting equipment.
- › Faster tablet production leads to more efficient output.
- › In this case study a 300 % increase in production speed led to 2/3 cost reduction.
- › PROSOLV<sup>®</sup> RX 90 is a great way to increase capacity without investing in new buildings and machines and adapt to increased market demands quickly without capital risk.

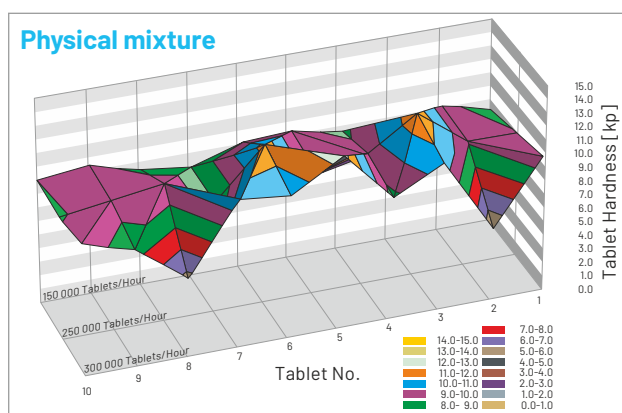


Fig. 9 Tablet hardness uniformity –\* physical mixture with 40 % paracetamol \* as function of tableting speed

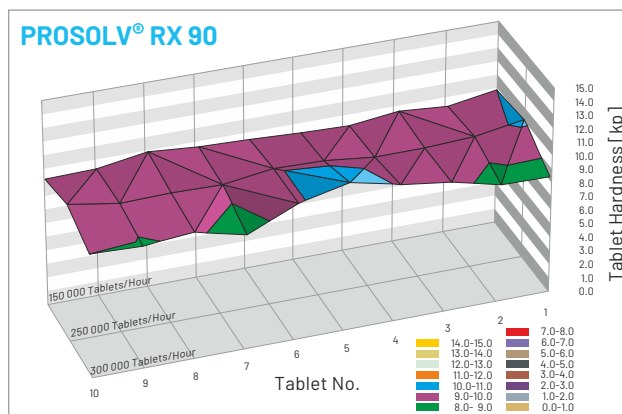


Fig. 9 Tablet hardness uniformity –\* PROSOLV<sup>®</sup> RX 90 with 40 % paracetamol \* as function of tableting speed

	Physical Mixture 100.000 Tablets/h	PROSOLV <sup>®</sup> RX 90 300.000 Tablets/h
Weighing + Sieving	4 h	2 h
Production Time	60 h	20 h
Total	64 h	22 h

Tab. 5 Production time for 6 million tablets  
PROSOLV<sup>®</sup> RX 90 showed consistent high tablet hardness, while the physical mixture has significant variations especially when the tableting speed was increased to 300.000 tablets per hour.



# Advantages of PROSOLV® RX 90 in Continuous Tablet Manufacturing

Continuous Manufacturing Technology continues to gain importance in pharmaceutical manufacturing. Multifunctional excipients, such as PROSOLV® RX 90, may be particularly well-suited for continuous processes because of three of their unique features:

## 1. All-in-one composite

A typical tablet formulation consists of at least one API, a filler/binder, a disintegrant, and a lubricant. Thus, even a simple formulation consists of at least four ingredients to be accurately fed into the continuous manufacturing system. The use of multifunctional excipients will therefore, be advantageous. PROSOLV® RX 90 especially stands out in terms of combining all the required blend functionalities into a single co-processed excipient. Using PROSOLV® RX 90 reduces the number of necessary feeder units to just two, one for the active ingredient and one for the excipient composite.

## 2. Blend uniformity

Achieving high blend uniformity is essential for any tableting manufacturing process, be it batch or continuous. In continuous processes, blending is particularly demanding, because in comparison to batch processes, dwell times in the blender are limited. The blending advantages of PROSOLV® products are outstanding, due to their unique surface structure, enabling good homogeneity even for low dose APIs via interactive blending.

## 3. Blending robustness

Another critical aspect of blending is the risk of over-lubrication resulting from excessive blending. Therefore, it is advantageous to select lubricants for continuous manufacturing, which are less sensitive to blending times and conditions or to choose all-in-one excipient. Composites, such as PROSOLV® RX 90 contain the particle lubricant within their unique structure and are less sensitive towards overlubrication.

## Benefits

- › The PROSOLV® RX 90 line is especially well suited for continuous manufacturing
- › Only 2 feeders are needed
  - one for the API
  - one for the PROSOLV® RX 90 composite which acts as filler/binder, flow aid, disintegrant and lubricant at the same time
- › Unique surface structure enables fast and segregation-free blending with API's
- › Outstanding robustness in terms of blending time, especially for the SSF containing PROSOLV® RX 90.

# Benefits of PROSOLV® RX 90

## Simplify tableting



Fig. 10 Comparison of the number of production steps for different ways of manufacturing tablets

Traditional tablet production methods include dry granulation, wet granulation, and direct compression. Granulation processes are typically complex, requiring a great deal of equipment, human resources, and time. The lengthy, multi-stage process leaves room for error, and thus, batch losses. Direct compression is a shorter, and often preferred, production process. It requires fewer resources than wet granulation and leaves less room for error and batch loss (Figure 3). The PROSOLV® RX 90 line includes all the necessary excipients for direct compression in an all-in-one-composite. Simply add the APIs, blend and compress into tablets. This easy method of tableting allows for

shorter development times and lower R&D costs, leading to faster time to market. The outstanding compaction properties enable smaller tablet sizes, faster production and may boost profitability due to prolonged tooling life. With PROSOLV® RX 90, buy, analyse and store only one excipient instead of five, thus reducing storage and quality control costs.

## Conclusion

- > GMO-Free
- > Allergen-Free
- > BSE/TSE-Free
- > Complies with general chapters for residual solvents (USP <467>, Ph. Eur. 5.4)
- > Re-evaluation date: 3 years
- > US DMF available
- > Full regulatory package available
- > Regulatory information available for registration in all major markets.

### Packaging

20 kg carton box with MDPE liner bag

### Packaging

16 carton boxes (320 kg) on Euro pallet (800 x 1200 mm)

20 carton boxes (400 kg) on container pallet (975 x 1175 mm)

### Sample Sizes

400 g or 2 kg in aluminium bag



**Fibers for Life.**

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