



# PROSOLV<sup>®</sup>

Silicified Microcrystalline Cellulose



**PROSOLV<sup>®</sup> - The Proven Innovation  
Accelerating Product Excellence**

**JRS PHARMA**



**LEADING  
THE WORLD  
IN EXCIPIENTS**  
A Member of the JRS Group



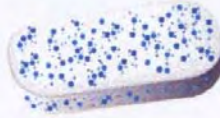
**PT SIGNA HUSADA**

# PROSOLV<sup>®</sup> TECHNOLOGY

PROSOLV<sup>®</sup> provides tremendous benefits throughout the product lifecycle in **Formulation, Manufacturing and Marketing**

## PROSOLV<sup>®</sup> TECHNOLOGY

### Formulation Benefits



#### Enhanced Mixing Characteristics

Optimize content uniformity



#### Enhanced Flow

Increase production speed



#### Less Excipients Needed

Direct cost savings

### Manufacturing Benefits



#### Enable Direct Compression

Avoid costly wet granulation



#### Increase Production Capacity

With existing equipment



#### Improve Compactibility

More robust tablets

### Marketing Benefits



#### Rapid Formulation Development

Shorten time to market



#### Smaller Tablets

Market advantage



**TRUE MULTIFUNCTIONAL EXCIPIENT**

**T E C H N O L O G Y**

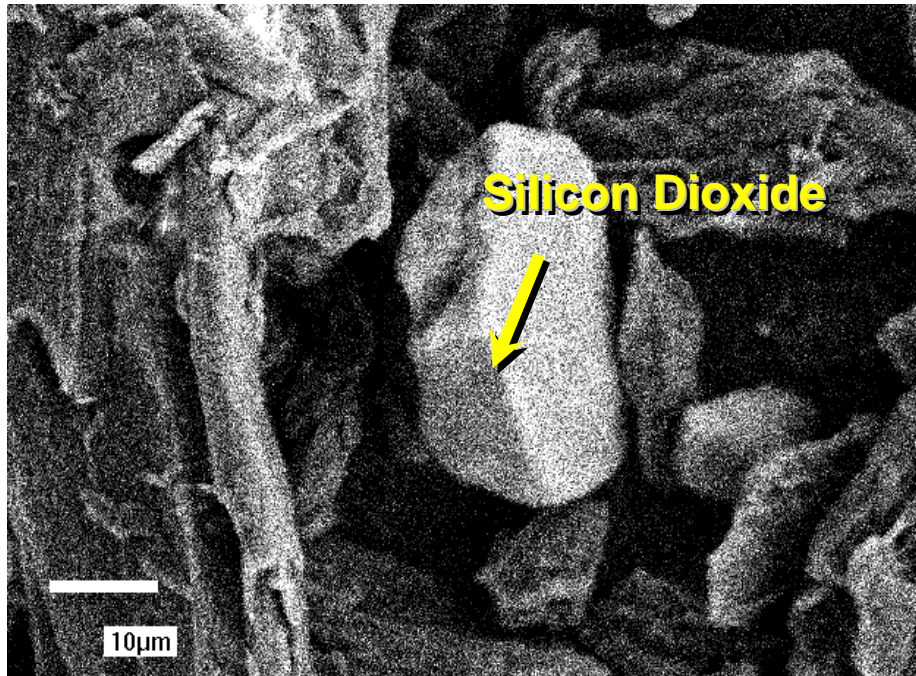


	Process	MCC	MCC HD	DCP	PROSOLV
Flow	xxx	x	xx	xxx	xxx
Compaction	xxx	xx	x	--	xxx
Content Uniformity	xxx	--	x	--	xxx

**C O S T**

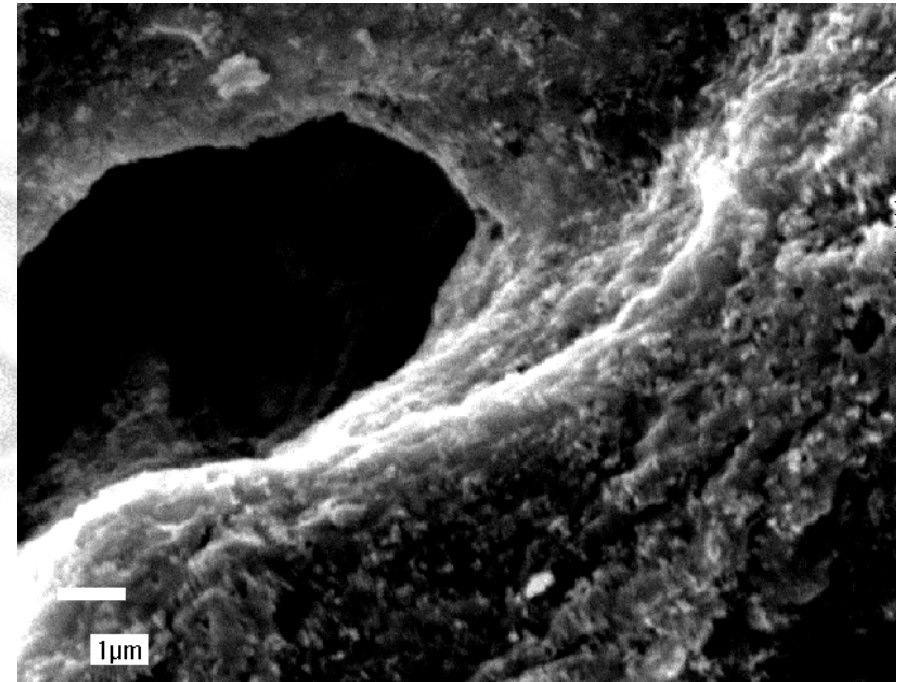


# Blends of MCC & CSD do not show the same Uniform Dispersion



MCC (98%) / CSD  
(2%) blend

Magnification x 1,000

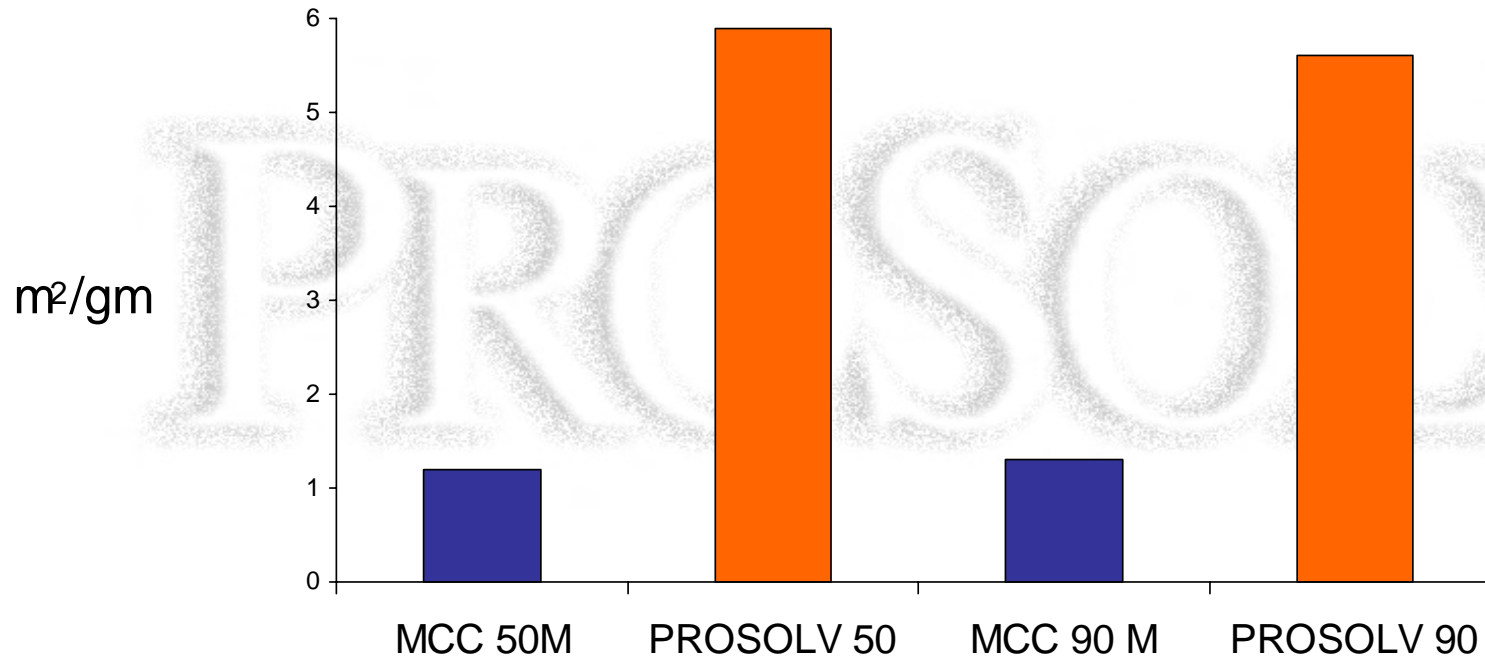


PROSOLV SMCC 90

Magnification x 10,000



## Silicification Increases Surface Area Imparting Superior Flow and Compaction by Dispersing & Distributing All Ingredients in the Formulation



- PROSOLV has Five times the surface area of MCC



# PROSOLV

## SMCC<sup>™</sup>

*Silicified Microcrystalline Cellulose*  
(Microcrystalline Cellulose, NF, JP, Ph. Eur., BP  
and Colloidal Silicon Dioxide, NF, JP, Ph. Eur., BP)

# PROSOLV<sup>™</sup>

## HD 90

High Density

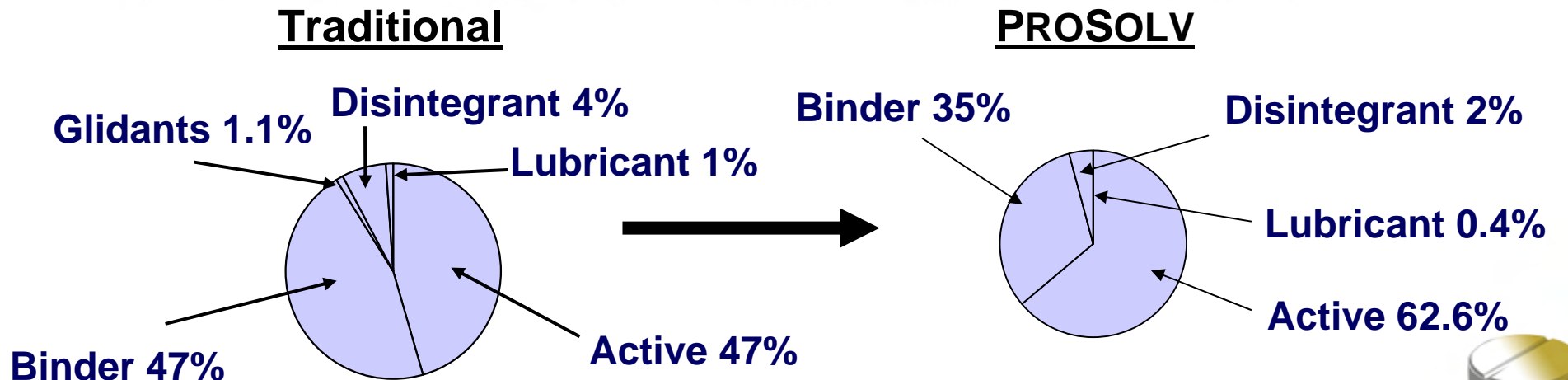
*Silicified Microcrystalline Cellulose*  
(Microcrystalline Cellulose, NF, JP, Ph. Eur., BP  
and Colloidal Silicon Dioxide, NF, JP<sup>®</sup>, Ph. Eur., BP)

- PROSOLV SMCC 50** - Most compactible grade, for WG and DC
- PROSOLV SMCC 90** - High Compactibility and excellent flow for DC
- PROSOLV HD<sup>®</sup> 90** - Higher density for optimum flow and increased batch size, excellent disintegration



## Less Excipients, Fewer Excipients

- PROSOLV reduces binder required
- PROSOLV's superior flow reduces the need for glidants and anti-adherants
- Less disintegrant is required
- Lower lubricant levels are required



## Reduce Tablet Size

# PROSOLV: Fewer and Less Excipients

- Typical Reduction\* In Excipients With PROSOLV



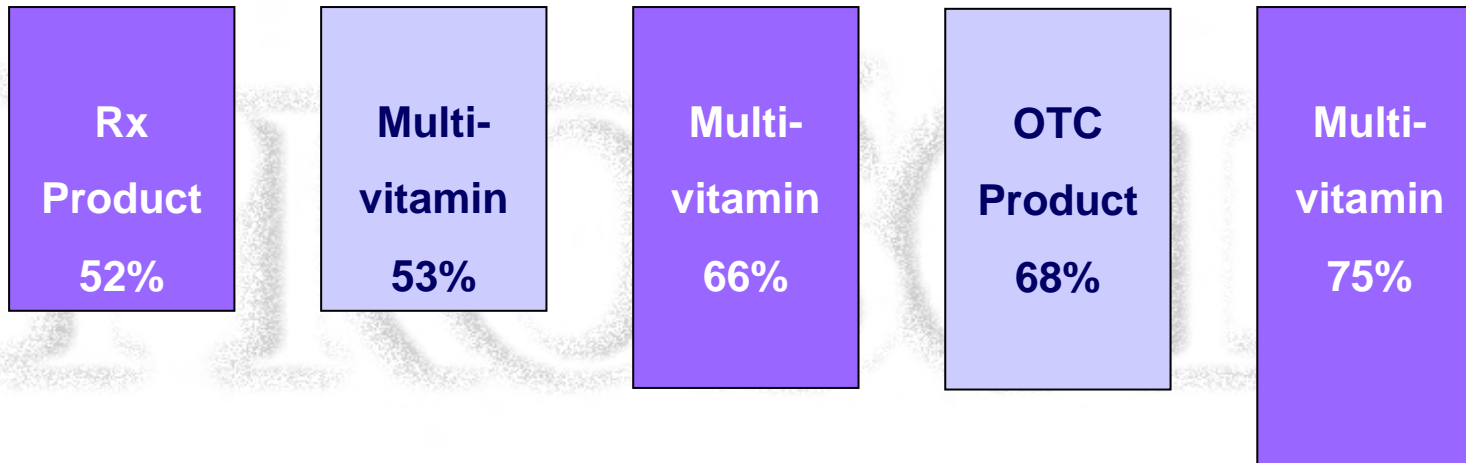
\* Actual usage level is formulation and active dependent.



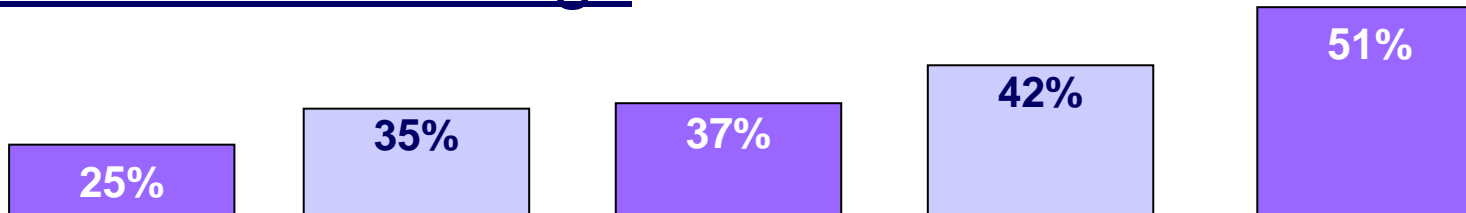
**Reduce Tablet Size**

**PROSOLV Technology Reduces Excipient Use/Cost**

% Binder Reduction in PROSOLV Formulations





Ingredient Cost Savings



## Reduce Tablet Size

Ginseng is a difficult extract that has severe problems with flow and hygroscopicity. **RediRun DC** was able to deliver the necessary flow while reducing non-actives significantly.

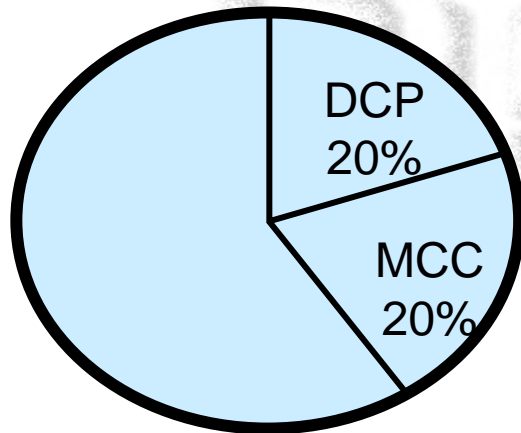
	<i>Actual Size</i>	<i>Weight Per Tab/Cap</i>	<i>Dose Per Tab/Cap</i>
<b>RediRun DC™ Herbal Formulation</b>		752 mg	500 mg
<b>Granulation (A commercial product)</b>		780 mg each	100 mg Each



## Case Study - Marketed Multivitamin

PROSOLV enables customers to reduce tablet size by 33% and decrease production and binder costs by 37%.

The Challenge: Excessive Tablet Size 1800 mg



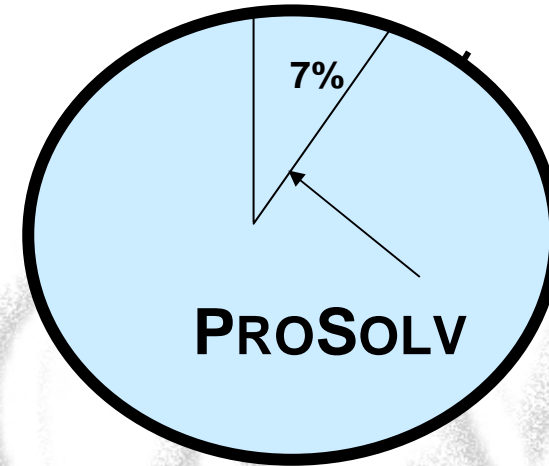
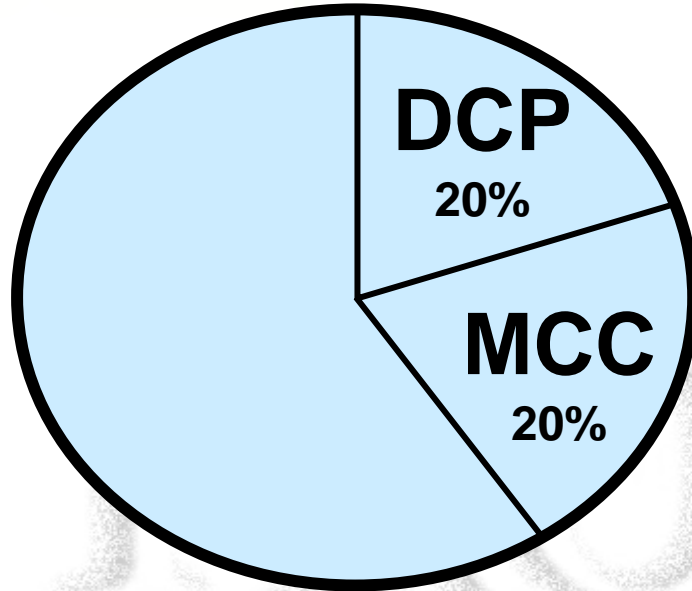
=Excessive tablet size  
due to 720 mg of binder

- Significant segregation of active (consist of 19 API including herbal constituent)
- Low content uniformity, poor flow
- PROSOLV must impart flow and compaction



## Reduce Tablet Size

New PROSOLV Formulation = Tablet size 1300 mg



- No DCP required, improved flow and compaction
- Non segregating formulation
- Improved content uniformity (<2% RSD)
- 360 mg DCP + 360 MG of MCC = \$1.62 /1000 tabs
- 91 mg of PROSOLV = \$0.63 /1000 tabs
- 37% savings



# Reduce Tablet Size

## Compare the Results

	<b>MCC Formula</b>	<b>ProSolv<sup>®</sup> HD 90</b>	<b>Change</b>
<b>MCC ProSolv<sup>®</sup></b>	<b>285 mg</b>	<b>0</b> <b>74 mg</b> }	<b>-211 mg</b>
<b>DCP</b>	<b>142 mg</b>	<b>0 mg</b>	<b>-142 mg</b>
<b>Tablet Weight</b>	<b>1094 mg</b>	<b>735 mg</b>	<b>-359 mg</b>
<b>Tablet Size</b>	<b>0.313" x 0.750" oblong</b>	<b>0.343" x 0.609" oval</b>	<b>Substantial</b>
<b>Hardness</b>	<b>27 Kp</b>	<b>30 Kp</b>	<b>+3 Kp</b>
<b>Bottle Size (120 count)</b>	<b>200 cc</b>	<b>120 cc</b>	<b>Substantial</b>
<b>Cost/1000 Tablets</b>	<b>\$10.93</b>	<b>\$9.27</b>	<b>-\$1.66</b>



## Case Study of a Low Dose NDA

### Direct Compression Reformulation Solves Content Uniformity and Stability Issues

#### Levothyroxine Challenges

- Low dose formulation (drug active <1%)
- Variation in drug content (5-8%)
- Wet Granulation not satisfactory, in fact, FDA notice on existing formulations



## Enable Direct Compression

# PROSOLV Direct Compression Improves Content Uniformity 10-Fold Over Wet Granulation

Original product	MCC/lactose wet granulation	5-8.0%
MCC blend	DC blend with PH 102	5-8.0%
PROSOLV 50/90	15% pre-blend with PROSOLV 90	0.8-1.0%

**Patented**

... and improves stability by providing a stabilizing matrix.



## Case Study

**Faster Development of Prescription Drugs**

**Fewer Excipients, Simplier Design of Experiments**

### Problems with Original Formula

- **Poor flow due to low bulk density active and loose sticky crystals**
- **15 unsuccessful formulation attempts using conventional excipients to Achieve Flow through 16mm Aperture**



# Formulation Results

## All MCC Formulations Failed Disintegration Target

<u>Formula</u>	<u>MCC X</u>	<u>MCC Y</u>	<u>MCC Z</u>	<u>PROSOLV</u>
No. Ingredients	7	8	6	2
Flow Test (mm)	26.0	22.0	28.0	14.0
Friability %	0.19	0.11	Nil	Nil
Hardness (kP)	26.9	16.6	24.3	16.3
Disintegration (min.)	7.07	3.28	10.22	0.59



# PROSOLV: Significantly Reduces Formulation Development

## Synthroid<sup>®</sup> (Levothyroxine)

Wet granulation  
 Acacia  
 Sugar (containing starch)  
 Lactose  
 Magnesium stearate  
 Povidone  
 Talc

7 Variables

# Experiments = 5,040

## Levo-T<sup>™</sup> (Levothyroxine)

PROSOLV<sup>®</sup>  
 Magnesium stearate  
 Sodium starch glycolate

3 Variables

# Experiments = 6



## Conclusion:

<b>Benefit</b>	<b>Why</b>
Reduces formulation ingredient cost	Less excipients (MCC, disintegrant , lubricant etc)
Enhances productivity	Harder tablets, less friability
Eliminating Processing	Direct compression with excellent content uniformity
Increase patient compliance	Smaller tablet – specially good for elderly and kids or same size with increase API content
Enhance plant capacity	Smaller tablets, enhance production speed
Earlier market entry	Shorter formulation & manufacturing scale up
Extend product life	Prosolv patent can extend product life

