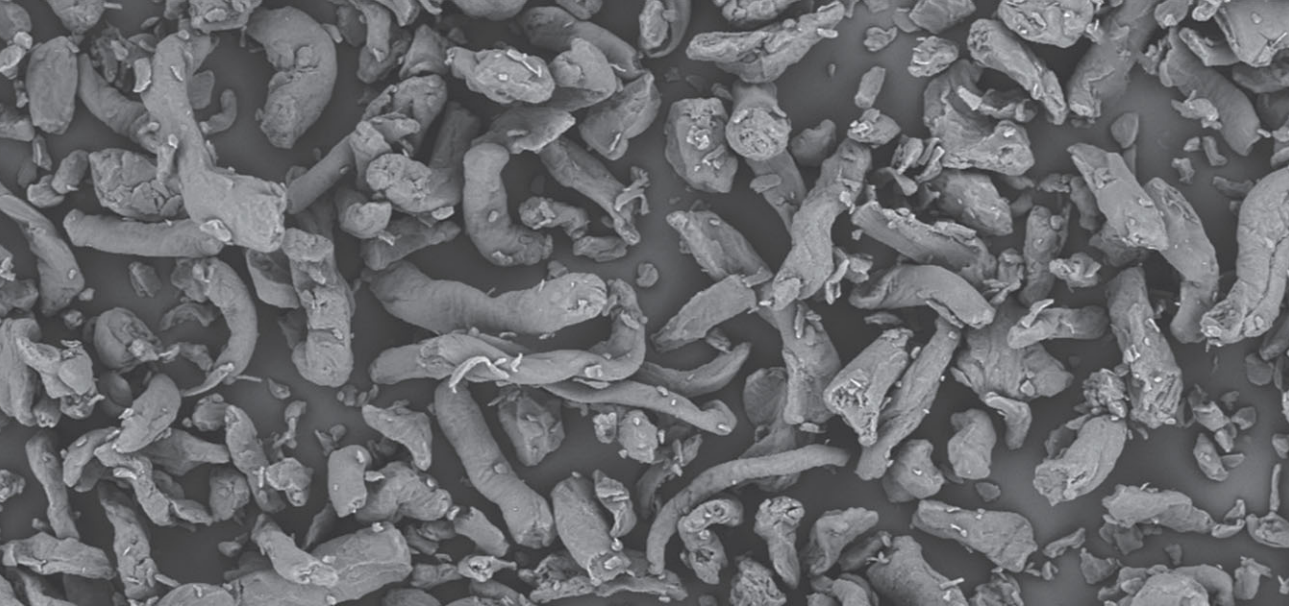


VIVASOL®

Croscarmellose Sodium
Ph.Eur., NF, JP



back-up security:
**2 Production
Plants**

**The Efficient Superdisintegrant
for Pharma and Food Applications**

Non GMO Grade Available
From Renewable Sources
Secure Supply Chain

JRS PHARMA
The Global Excipient Maker



FAMILY
A Member of the JRS Group

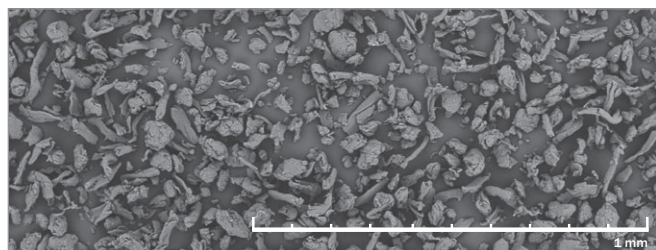
What is **VIVASOL®** ?

General Information

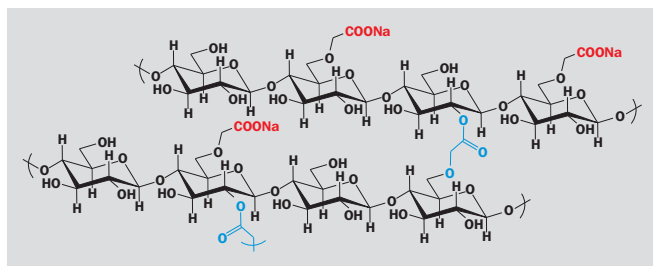
VIVASOL®, croscarmellose sodium (croscarmellose), is a well recognized superdisintegrant specifically used for tablets as well as capsules. Its unique performance establishes **VIVASOL®** as a globally accepted product used in the pharmaceutical and nutritional industries.

Manufacturing Process and Structure

JRS PHARMA produces four croscarmellose grades: **VIVASOL®**, **VIVASOL® SF**, **VIVASOL® GF** and **VIVASOL® GF LM**. The specifications and functional performance of **VIVASOL®** and **VIVASOL® GF** are similar.



Pic 1 **VIVASOL®**



Croscarmellose Sodium **VIVASOL®**

VIVASOL® and **VIVASOL® SF** are derived from cotton linters, while **VIVASOL® GF** and **VIVASOL® GF LM** are produced from wood cellulose. For all types, the cellulose chains are substituted with carboxymethyl-groups which introduce the hydrophilicity and the rapid water uptake of **VIVASOL®** products. In a second step the cellulose chains are crosslinked to obtain optimal disintegration properties.

Microscopy shows the fibrous nature of the cellulose based materials. These fibers possess a wicking effect, the water is distributed quickly through the entire tablet structure, facilitating rapid disintegration.

Your Benefits from **VIVASOL®**

VIVASOL® Business Benefits

- Cost effective superdisintegrant compared to Crospovidone.
- Supply chain security guaranteed through two production facilities on two continents.
- Cost competitive sourcing available.
- JRS PHARMA's broad excipient product line offers one-stop-shopping, saving administration and logistic costs.
- Formulation and process advice available from JRS PHARMA's formulation scientists.

Formulation and Manufacturing Benefits

- Short tablet disintegration times.
- Excellent dissolution results.
- Combination with **VIVASOL®** (sodium stearyl fumarate) and/or **VIVASOL® SMCC** (silicified microcrystalline cellulose) facilitates faster disintegration.
- **VIVASOL®** performs well in direct compression and granulation processes.
- Good mixing properties.
- High brightness degree and limited visible specks are advantageous for uncoated tablets.
- No UV interference.
- Relatively inert because all **VIVASOL®** grades are derived from natural celluloses.
- Excellent API stability. Used in pharma and food applications.
- All FRCs from Ph.Eur. are tested and monitored by JRS PHARMA guaranteeing **VIVASOL®**'s high performance.
- Allowed in most countries for health supplements too.

VIVASOL® – First in its Class

JRS Monitores all FRCs

The Ph.Eur. describes Functional Related Characteristics (FRCs) of excipients. These characteristics are recognized as being relevant control parameters for the functions of the substance.¹

JRS PHARMA monitors the FRCs for croscarmellose sodium and guarantees the high performance of **VIVASOL®**.

¹ Ph.Eur.6.5 – Croscarmellose sodium

FRCs for croscarmellose according Ph. Eur. are :

- Settling Volume
- Degree of Substitution
- Particle Size Distribution
- Hausner Ratio

Settling Volume

The settling volume is the measurement of 1.5 g croscarmellose in 100 ml water after 4 hours.

JRS PHARMA specifies the settling volume of **VIVASOL®** as 10.0 – 30.0 ml.

➔ The lower the settling volume, the better the capillary effect of croscarmellose sodium.

Degree of Substitution

The degree of substitution is calculated as the milliequivalent of sodium hydroxide required to neutralize 1 g of material.

JRS PHARMA specifies the degree of substitution of **VIVASOL®** as 0.60 – 0.85.

Croscarmellose with a lower degree of substitution act as thickeners.

➔ The higher the substitution the better the disintegration properties.

Particle Size Distribution

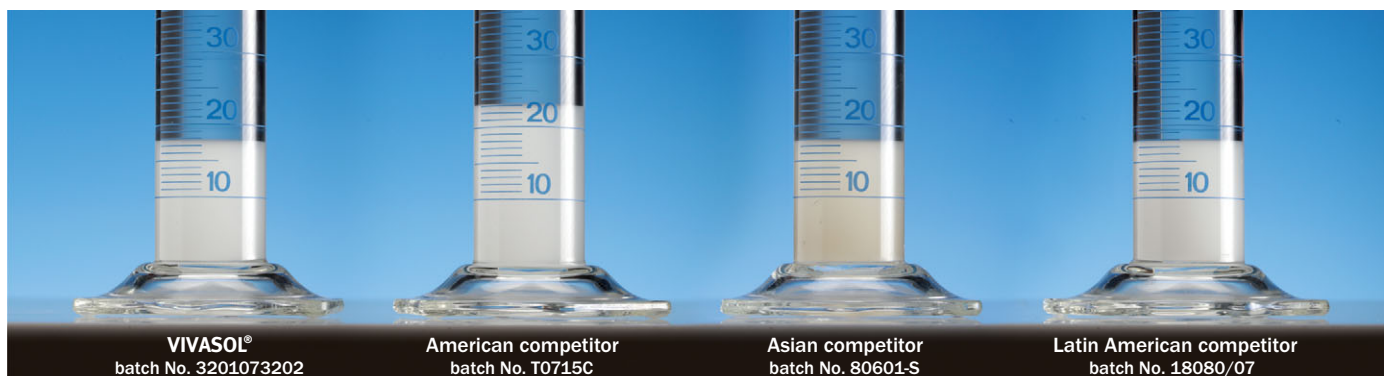
Particle size distribution can be measured by sieve analysis or laser diffraction. JRS PHARMA specifies the results of the air jet sieve analysis on the certificate of analysis as follows.: max. 2 % retained on a 75 µm sieve and max. 10 % retained on a 45 µm sieve.

➔ Only the optimal particle size distribution gives good disintegration results.

Hausner Ratio

The Hausner ratio provides an indication on flowability of a powder. It is the quotient of tapped density divided by bulk density.

➔ The lower the Hausner ratio, the better the flowability of the powder mix.



Pic 4 Settling volume



VIVASOL®
Croscarmellose Sodium

VIVASOL® for Visibly High Quality Tablets

VIVASOL® Croscarmelloses are produced under highly controlled manufacturing conditions, resulting in an ingredient with exceptional brightness and a low visible speck count.

VIVASOL® Croscarmelloses are produced using organic solvents, which are removed during drying. The solvent residue is an important parameter for finished dosage form with solvent limitations.

VIVASOL® GF LM (solvent ethanol) loss on drying max. 6 % for food application E 468.

JRS PHARMA continually monitors **VIVASOL®** 's brightness and visible speck count.

Typical results:

Colored particles: 4 – 5 / 25 cm²

VIVASOL® Grades

Grade	Raw Material	GMO free	Loss on drying	Solvent Content	
VIVASOL®	cotton floc		max. 10 %	max. 1.0 % MeOH	A cellulose-based superdisintegrant, providing excellent results in tablet disintegration. Used at a level of 1 - 2 % only, it is one of the most efficient superdisintegrants in the pharmaceutical technology. VIVASOL® can be used in all tableting processes. Especially good for medium soluble actives.
VIVASOL® GF	wood pulp	✓	max. 10 %	max. 3.0 % EtOH	
VIVASOL® GF LM	wood pulp	✓	max. 6 %	max. 0.5 % EtOH	Grade with less than 6 % of moisture for food applications (E468).
VIVASOL® SF	cotton floc		max. 6 %	max. 0.3 % MeOH	Special grade with very low methanol content. Especially suited for alcohol and moisture sensitive actives, no interaction with antibiotics known.

Tab. 1



Pic 5 a **VIVASOL®** 91.3 % vs. BaSO₄
Batch No. 3201073202



Pic 5 b American Competitor 90.2 % vs. BaSO₄
Batch No. T0715C



Pic 5 c Asian Competitor 77.8 % vs. BaSO₄
Batch No. 80601-S



Pic 5 d Latin American Competitor 88.6 % vs. BaSO₄
Batch No. 18080/07

Technical Data and Application

VIVASOL® Disintegration Mechanism

VIVASOL® scanning electron microscopy: SEM shows that the powder possesses a fibrous nature. This provides **VIVASOL®**'s "wicking effects", which is responsible for rapid capillary water transport into the tablet matrix. As a result, **VIVASOL®** use level remains low while providing superior tablet disintegration properties.

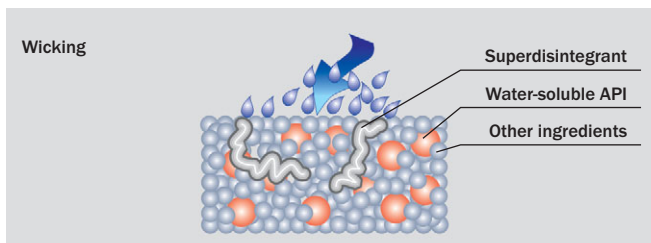


Fig. 1 a

The fibers rapidly transport water into the tablet matrix, which dissolves soluble tablet ingredients and causes tablet disintegration.

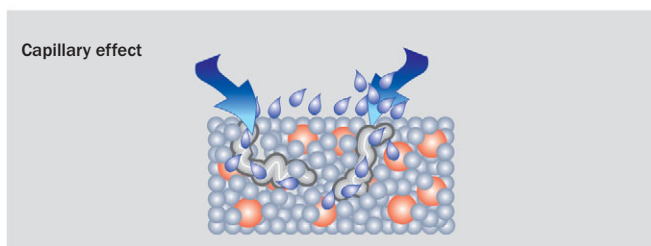


Fig. 1 b

Because **VIVASOL®** also exhibits swelling character, upon wetting with tablets produced with insoluble ingredients, it swells causing disruption of the tablet matrix resulting in rapid tablet disintegration.

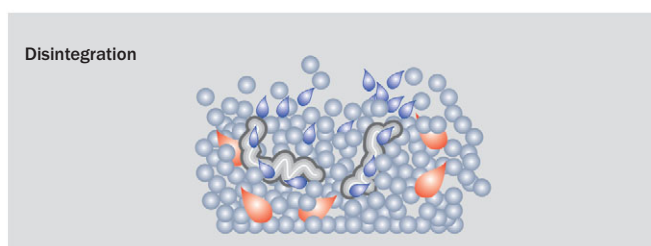
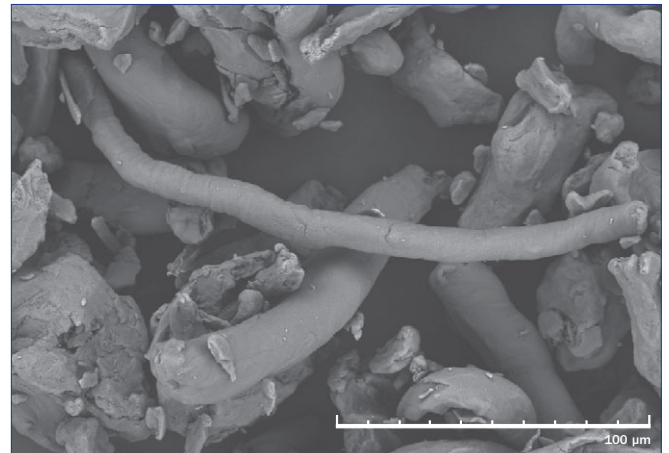


Fig. 1 c



Pic 6 **VIVASOL®**

Formulation Advice

- The recommended use level for all **VIVASOL®** types is between 1.0 – 4.0 %
- In granulation processes, intra- and extra-granular addition is recommended. Extra-granular **VIVASOL®** addition facilitates tablet disintegration, while intra-granular addition promotes granule disintegration.
- In addition to the disintegrant, tablet disintegration time may be affected by lubricant type and use level. Care should be taken to optimize ejection without compromising tablet disintegration.
- Better disintegration results may be achieved by combining **VIVASOL®** with **PRUV®** Sodium Stearyl Fumarate (lubricant) and/or **PROSOLV®** Silicified Microcrystalline Cellulose (high functionality excipient).
- In some formulation applications, **VIVASOL®** and **EXPLOTAB®**, Sodium Starch Glycolate, are used in a synergistic combination to promote rapid tablet wicking and hydration, which compliments **EXPLOTAB®**'s rapid swelling.

More information may be obtained from the JRS brochure "Disintegration Mechanisms".



VIVASOL®

Croscarmellose Sodium

Model Formulations with VIVASOL®

High Dosage Formulation

Glucosamine 500 mg, Chondroitin 400 mg

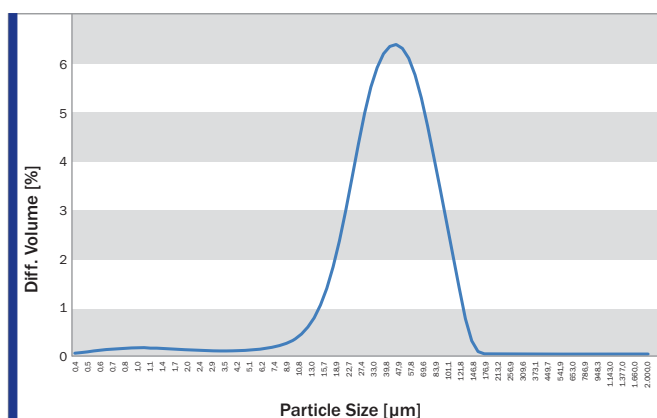
Formulation	
Glucosamine HCl	581.7 mg
Chondroitin Sulfate	465.6 mg
VIVASOL® (Croscarmellose Sodium)	20.5 mg
PROSOLV® SMCC 90 (Silicified Microcrystalline Cellulose)	199.2 mg
Talcum	20.0 mg
Blending Time 15 minutes.	
PRUV® (Sodium Stearyl Fumarate)	13.0 mg
Lubrication Time 3 minutes.	

Tab. 2

Parameter	
Diameter	16 mm
Tablet Weight	1300 mg
Compaction Force	18 – 20 kN
Crushing Strength	80 N
Disintegration Time	60 seconds

Tab. 3

VIVASOL® Particle Size Distribution



For Oral Disintegrating Tablet (ODT) formulations, we recommend **PROSOLV® ODT**.
More under www.jrspharma.com

Metformin Formulation

Metformin in direct compression

Formulation		
Metformin	70.8 %	850 mg
PROSOLV® SMCC 50 (Silicified Microcrystalline Cellulose)	26.6 %	319 mg
VIVASOL® (Croscarmellose Sodium)	2.1 %	25 mg
Blending Time 15 minutes.		
PRUV® (Sodium Stearyl Fumarate)	0.5 %	6 mg
Lubrication Time 3 minutes.		

Tab. 4

Parameter	
Diameter	16 mm
Tablet Weight	1200 mg
Compaction Force	20 – 22 kN
Crushing Strength	55 - 60 N
Disintegration Time	20 seconds

Tab. 5

More formulations may be obtained from the **JRS PHARMA Formulation Handbook** (www.jrspharma.com)



VIVASOL® – Secure Supply

VIVASOL® meets the following requirements:

CAS- No. 74811-65-7

- ✓ Ph. Eur., NF, JP
- ✓ Plant origin
- ✓ BSE/ TSE free
- ✓ Allergen free
- ✓ Gluten free
- ✓ Croscarmellose sodium is listed in the Inactive Ingredients List published by the FDA



Packaging:
25 kg Boxes with PE Inliner



Sample Size:
Aluminum Bags 100 g or 400 g

Stability data:

Batch no.	Tested	LOD	Settling Volume
Specification		max. 10.0 %	10.0-30.0 ml
3211044167	0 months	5.2	18.0
	24 months	6.0	18.0
	48 months	6.8	17.0
	60 months	6.9	17.5

Manufacturing

Supply chain security through two independent production facilities on two continents.

Food Status:
USA: GRAS-Status and
EU E468

Manufacturing

High supply security through two independent production plants on two continents.

Plant I, CHP Pirna, Germany
ISO 9001
FDA DMF No. 3479
EIP available



Utilize the benefits offered by production in a lower cost country.



Plant II, GMW, India
ISO 9001
FDA DMF No. 24809

Re-evaluation date:

4 years

All **VIVASOL®** grades are produced in accordance with the IPEC GMP guidelines.

The Global Excipient Maker

Global Network

GMP Manufacturing and Service Sites

- Excipients
- Coatings
- Biopharma Services
- JRS Sales Companies (Additionally, dedicated representatives in almost every country.)
- Technical Competence Centers
- Application Labs



HIGH FUNCTIONALITY EXCIPIENTS

- PROSOLV® SMCC**
Silicified Microcrystalline Cellulose
- PROSOLV® EASYtab SP**
Microcrystalline Cellulose, Colloidal Silicon Dioxide, Sodium Starch Glycolate, Sodium Stearyl Fumarate
- PROSOLV® EASYtab NUTRA**
All-in-one Composite for Nutraceutical Applications
- PROSOLV® ODT G2**
Microcrystalline Cellulose, Colloidal Silicon Dioxide, Mannitol, Fructose, Crospovidone

DISINTEGRANTS

- VIVASTAR®, EXPLOTAB®**
Sodium Starch Glycolate, Sodium Carboxymethyl Starch
- VIVASOL®**
Croscarmellose Sodium
- EMCOSOY®**
Soy Polysaccharides
- VIVAPHARM® Crospovidone**
Polyvinylpyrrolidone, crosslinked

COATINGS

- VIVACOAT®**
Ready-to-Use Coating System
- VIVACOAT® protect**
Ready-to-Use High Functional Coating System
- VIVAPHARM® HPMC**
Hypromellose
- VIVAPHARM® PVA**
Polyvinyl Alcohol

BINDERS

- VIVAPUR®, EMCOCEL®**
Microcrystalline Cellulose
- EMDEX®**
Dextrates
- VIVAPHARM® Povidones**
Povidone and Copovidone

LUBRICANTS

- PRUV®**
Sodium Stearyl Fumarate
- LUBRITAB®**
Hydrogenated Vegetable Oil, Hydrogenated Oil
- LUBRI-PREZ™**
Magnesium Stearate

CARRIERS

- VIVAPUR® MCC SPHERES**
Microcrystalline Cellulose Pellets
- VIVAPHARM® Sugar Spheres**
Sugar Pellets, Non-GMO

FUNCTIONAL FILLERS

- ARBOCEL®**
Powdered Cellulose
- EMCOMPRESS®**
Calcium Phosphates
- COMPACTROL®**
Calcium Sulfate Dihydrate

THICKENERS • STABILIZERS • GELLING AGENTS

- VIVAPUR® MCG**
Microcrystalline Cellulose and Carboxymethylcellulose Sodium
- VIVAPHARM® Alginates**
Calcium Alginate
- VIVAPHARM® Alginates**
Sodium Alginate
- VIVAPHARM® Alginates**
Alginate Acid
- VIVAPHARM® Pectins**

BIOPHARMA SERVICES

Members of the JRS PHARMA Family