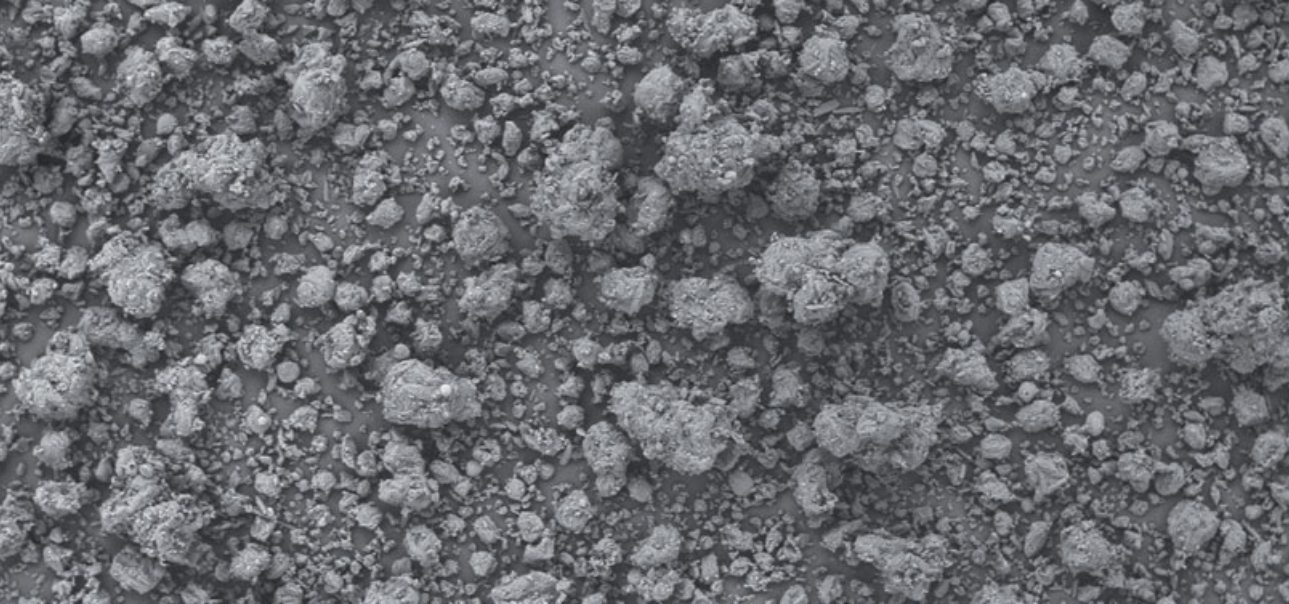


VIVAPUR® MCG

Microcrystalline Cellulose (MCC) and
Carboxymethylcellulose Sodium (Na-CMC), NF, Ph.Eur., E460(i)&E466



Dispersible Cellulose

High Performance Stabilizing Agent
for Suspensions, Reconstitutable Powders,
Creams, Lotions and Sprays



VIVAPUR® MCG

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VIVAPUR® MCG – A Powerful Tool For Liquid Dosage Forms

Introduction

Liquid dosage forms are a common and popular approach to overcoming the many obstacles of administering medicines to children, the elderly, and animals. However, instabilities such as sedimentation, flocculation, or caking – especially in suspensions – are major challenges in the development of new formulations. **VIVAPUR® MCG** addresses those challenges and allows a custom balance of rheological properties to guarantee high content uniformity and excellent long-term stability in suspensions, without the need for an excessive increase in viscosity.

What is VIVAPUR® MCG ?

VIVAPUR® MCG is a free-flowing powder consisting of microcrystalline cellulose (MCC) and sodium carboxymethyl cellulose (Na-CMC). It is more than just a physical blend; the Na-CMC is interwoven with the microcrystalline cellulose, resulting in unique synergistic properties. The Na-CMC acts as a protective colloid to prevent the re-aggregation of the microcrystalline cellulose and ensures easy dispersibility.

Benefits

Convenience

- Easy handling of the dry powder:
 - Excellent flow
 - Long shelf-life stability
- Hassle-free handling of the activated gel:
 - Easy cleaning of the equipment
 - Ideal pumpability
 - Full functionality in hot and cold water
- Robust versatile stabilizer:
 - Stable over a wide pH range
 - Sterilizable and freeze / thaw stable
 - Compatible with a wide range of ingredients
 - Combinable and synergistic with other stabilizers

High Acceptance

- Negligible caloric value
- Excellent sensory properties:
 - Odorless & tasteless
 - Smooth texture
 - Easy to swallow
 - Not sticky
- Non-laxative
- Accurate Dosage:
 - Ideal sprayability
 - Easy pumpability
 - Drop-by-drop dosing

Applications

VIVAPUR® MCG can be used with a variety of active pharmaceutical ingredients (APIs), offering the opportunity for new applications and line extensions for existing products. **VIVAPUR® MCG** is used as a suspending agent, emulsifier, opacifier, and thickener for:

- Oral suspensions
- Veterinary drenches
- Sprays (nasal, oral, or topical sprays)
- Reconstitutable powders
- Creams, gels, and lotions

Regulatory Benefits

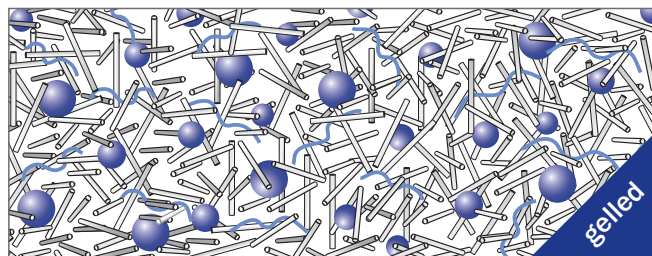
- Halal / Kosher
- Conforms with Ph.Eur./USP
- GMO/BSE/TSE free
- cGMP production standards
- Non-animal origin
- Conforms to the residual solvents requirement of USP <467>
- Allowable for animal health products, pediatric suspensions, and nutraceuticals



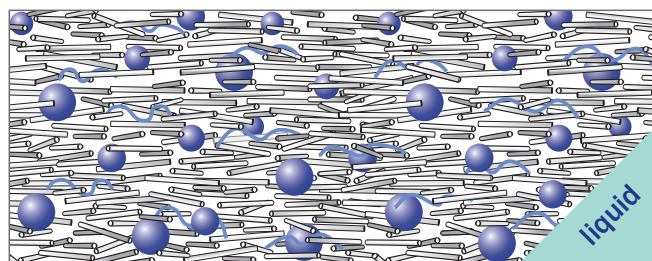
VIVAPUR® MCG – More than a Thickener

Mechanism of Stabilization

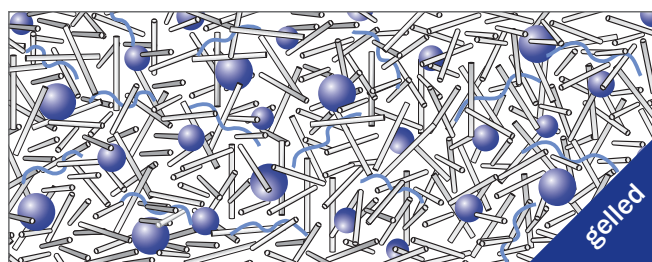
Reliable stabilization of particles in a suspension cannot be guaranteed solely by high viscosity because this only slows down settlement. **VIVAPUR® MCG** is more than just a thickener. After activation in water, **VIVAPUR® MCG** forms a three-dimensional elastic gel-network of insoluble cellulose fibrils, building a yield point. The yield point is the minimum shear stress required to initiate flow. The suspension is stable if the force of gravity operating on the particle mass does not exceed the liquid's yield point. All particles can be kept homogeneously within the sustaining network and are prevented from settling.



Agitation



Storage



- Microcrystalline Cellulose
- Carboxymethylcellulose Sodium
- API

Upon agitation, such as shaking of a medicine bottle, the cellulose fibrils arrange themselves in the direction of the movement. Thereby, the network loosens up and viscosity decreases. Thus, the dosage form becomes liquid and can be easily poured out of the bottle and measured. Soon after the movement ceases, the cellulose fibrils entangle again and form a three-dimensional network. The dispersions regain their full stabilizing ability, resulting in long-term stability and content uniformity.

VIVAPUR® MCG – The Gel that Exhibits Fluid Properties

Upon agitation, MCG dispersions show a time- and shear-dependent decrease in viscosity and become liquid. A complete, also time-dependent, regeneration of viscosity takes place during a subsequent rest period. This so-called “thixotropic behavior” allows:

- Outstanding sprayability of sprays
- User-friendly dosing via drenches and dispensers
- Accurate dosage of oral suspensions
- Hassle-free handling of the activated gel
- Ideal pumpability
- Smooth and pleasant swallowing
- Excellent content uniformity

VIVAPUR® MCG Grades – Different Solutions for a Variety of Applications

Grades

The available grades, **VIVAPUR® MCG 581**, **591**, **611** and **811 P**, are distinguished by a varying, viscosity, elasticity, and Na-CMC content (Tab. 1). For nutraceutical applications, an additional grade (**VIVAPUR® MCG 900X F**) is available. **Recommended use levels are 0.5 – 3.0 %** and depend on grade and desired function.

The density of the MCG network depends on the concentration of the applied **VIVAPUR® MCG** (Fig. 1). The higher the concentration, the tighter the network and the better the retention of any particulate matter, such as the API. Thus, the required performance and viscosity can easily be adjusted by the concentration used. The viscosity increases mainly within the first hour and remains constant after 24 hours.

VIVAPUR® MCG 811 P – Your First Choice

VIVAPUR® MCG 811 P is JRS PHARMA's newest MCC / NaCMC composite for ready-to-use suspensions, nasal sprays, gels, and emulsions.

Benefits include:

- Superior particle stabilizing performance
- Lower susceptibility to acids and salts compared to 591 and 581 types

- Lower levels needed due to highest viscosity (Fig. 1), elasticity (Fig. 2), and yield point
- Fastest particle stabilization due to rapid gelling (Fig. 2, Tab. 1)

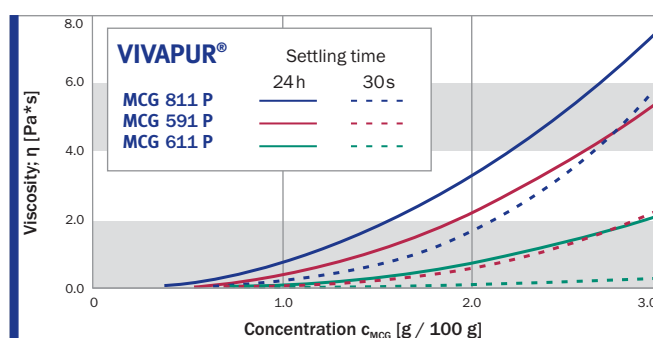


Fig. 1 Effect of the Concentration of Different **VIVAPUR® MCG** Types on the Resulting Viscosity Directly after Activation (30 s) and after 24 h Settling Time.

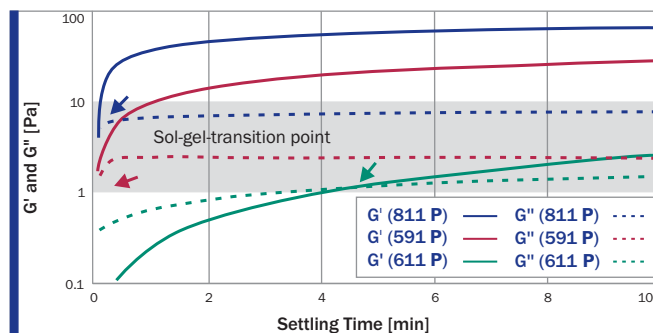


Fig. 2 The Gel-Point Occurs after a Few Seconds to Minutes of Settling Time and Ensures a Rapid Stabilization of Particles. The Gel Point (Sol-Gel Transition) is Defined as the Intersection of the Modulus of Viscosity (G'' , Dotted Line) and Elasticity (G' , solid line). Different Types of **VIVAPUR® MCG** were Measured by Oscillation Rheometry at a 3 % w / v Level

VIVAPUR® MCG	581 P	591 P	611 P	811 P
Viscosity after 30s	72 – 168 mPa s (1.2 %)	39 – 91 mPa s (1.2 %)	50 – 118 mPa s (2.6 %)	2400 – 5600 mPa s (2.6 %)
Elasticity G'_{360s} (3 %)	22 Pa	24 Pa	2 Pa	60 Pa
Gel-Point (3 %)	5 s	5 s	184 s	2 s
CMC-Na Content	8.3 – 13.8 %	8.3 – 13.8 %	11.3 – 18.8 %	11.3 – 18.8 %
Particle Size	> 250 μ m max. 0.1 % > 75 μ m max. 35 %	> 250 μ m max. 0.1 % > 45 μ m max. 45 %	> 250 μ m max. 0.1 % > 45 μ m max. 50 %	> 250 μ m max. 3 %
Applications	Oral Suspensions, Sprays, Drenches, Gels, Emulsions	Oral Suspensions, Sprays, Drenches, Gels, Emulsions	Reconstitutable Powders	Oral Suspensions, Sprays, Drenches, Gels, Emulsions

Tab. 1 Characteristics of Different Grades of **VIVAPUR® MCG**

a G' =Modulus of Elasticity is an Indicator for the Stabilizing Performance of the Gel Network. Measured by Oscillation Rheometry. The Higher G' , the Better the Stability.

VIVAPUR® MCG – Practical Advice & Exemplary Formulations

Basic Preparation of Ready-to-Use Suspensions and Spray Applications

1. Disperse **VIVAPUR® MCG** in de-ionized water with low shear force (max. 5 % w/w). Do not add any other ingredients at this stage.
2. Apply high shear (Pic. 1) (colloidal mill at max. rpm. 3 – 10 min; homogenizer min. 150 bar). After activation, the suspension must have a rest period of at least 15 minutes.
3. Dissolve the remaining soluble ingredients in the remaining water/liquid phase. Mix the liquids and remaining ingredients under medium stirring.
4. Adjust to final volume and pH and/or sterilize as required. Avoid air intake, particularly in steps 2 and 3.



Pic. 1 Preparation of **VIVAPUR® MCG** dispersion

Paracetamol (Acetaminophen) Oral Suspension

Ingredients	[g/ 100 mL]
Paracetamol	3.20
VIVAPUR® MCG 811 P	0.70
Water (Deionized) for MCG Activation	30.0
Xanthan	0.20
Sucrose	40.0
Glycerol	5.00
Citric acid (Anhydrous)	0.22
Sodium Citrate Dihydrate	0.25
Polysorbate 80	0.10
Sodium Benzoate	0.20
Butylparaben	0.03
Sodium Saccharin	q.s.
Colorant / Flavor ad. lib.	q.s.
Water (Deionized) for Volume Adjustment	q.s.

Tab. 2

Acyclovir Oral Suspension

Ingredients	[g/ 100 mL]
Acyclovir	4.0
VIVAPUR® MCG 811 P	1.4
Water (Deionized) for MCG Activation	40.0
Sorbitol	
Glycerin	31.5
Methylparaben	15
Propylparaben	0.1
Flavor	0.02
Water (Deionized) for Volume Adjustment	q.s.

Tab. 3

VIVAPUR® MCG – Practical Advice & Exemplary Formulations

Nasal Sprays

Dispersible cellulose is a multifunctional and commonly used stabilizer for nasal sprays containing APIs such as Fluticasone, Budesonide, Beclometasone, Triamcinolone Acetonide or Oxymetazoline Hydrochloride.

The **VIVAPUR® MCG** gel network keeps the drug particles suspended in the main reservoir of the delivery device. During pumping, the gel becomes fluid in the delivery device and enables eased spraying and efficient, standardized atomization. After administration, the fluid regains its viscosity. Dripping from the nose or outflow into the throat area are prevented and retention time of the API in the nasal cavity is prolonged.

Mometasone Nasal Spray

Ingredients	[g/ 100 mL]
Mometasone furoate hydrate	0.05
VIVAPUR® MCG 811 P	1.80
Water (deionized) for MCG activation	80.0
Polysorbate 80	0.01
Benzalkonium chloride	0.02
Citric acid monohydrate	0.20
Sodium citrate	0.28
Glycerol	2.10
Water (deionized) for volume adjustment	q.s.

Tab. 4



Reconstitutable Powders for Preparation of an Oral Suspension

Many antibiotics are prone to degradation in aqueous environments and thus expire quickly in liquid form. In order to obtain a long shelf-life, it is advisable to package the medicine without water and reconstitute just before the first intake.

VIVAPUR® MCG 611 P is the recommended grade for reconstitution and provides the following advantages:

- Easy to activate by manual shaking
- Reliable functionality irrespective of the grades of water hardness used
- Maintains content uniformity of the API
- Reliable prevention of particle sedimentation
- Accurate dosage
- Long-term stability
- Enhanced pH, salt, and temperature tolerance
- Highly thixotropic

Cefpodoxime Reconstitutable Powder

Ingredients	[g/ 100 mL*]
Cefpodoxime proxetil	0.80
VIVAPUR® MCG 611 P	2.50
Xanthan	0.20
Colloidal silicon dioxide	0.50
Sucrose	50.0
Citric acid (anhydrous)	0.15
Sodium benzoate	0.20
Aspartame	q.s.
Colorant/ Flavor ad. lib.	q.s.

Tab. 5

*related to finished suspension



VIVAPUR® MCG – The Highly Compatible, Robust, and Versatile Stabilizer

Compatibility

VIVAPUR® MCG is compatible with a wide range of ingredients commonly used for suspensions, such as sugars, sugar alcohols, artificial sweeteners, wetting agents, alcohols, nonionic surfactants or preservatives (Fig. 3).

VIVAPUR® MCG:

- Withstands sterilization and long-term heating (Fig. 4)
- Shows excellent freeze thaw stability
- Can be dispersed in hot or cold water
- Stable in a wide pH range (3.8 – 10)

Up to ~2 % w / v (**VIVAPUR® MCG 591 P** and **811 P**) and 5 % w / v (**VIVAPUR® MCG 611 P**) sodium chloride salt is tolerated if it is added after the MCG has been activated in distilled water. If higher amounts of soluble buffer salts, di- or trivalent cations, are part of the suspension, additional protective colloids (8 - 30 % related to the total amount of MCG), such as xanthan, methylcellulose, or HPMC are recommended to prevent a flocculation of the gel network.

The nutraceutical grade **VIVAPUR® MCG 900X F** is coprocessed with Xanthan. It provides maximum pH- and salt tolerance.

Sensory Advantages

Activated MCG builds an opaque-white dispersion which masks insoluble particles, giving the suspension a homogeneous appearance.

The dispersed **VIVAPUR® MCG** is characterized by an odorless and tasteless, smooth but not slimy mouthfeel, and handles flavors well, which is essential for pediatric products.

Would you like to receive a sample?
Please visit www.jrspharma.com

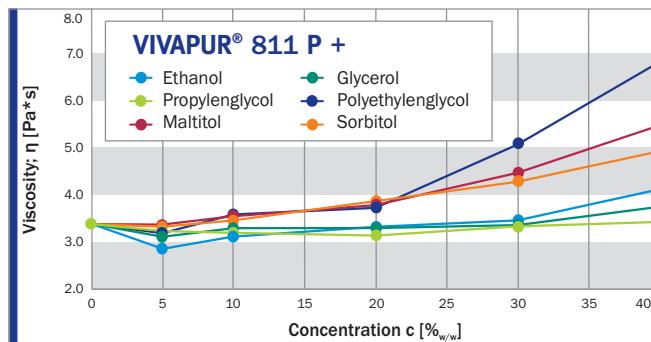


Fig. 3 **VIVAPUR® MCG** is Compatible with a Wide Range of Common Ingredients

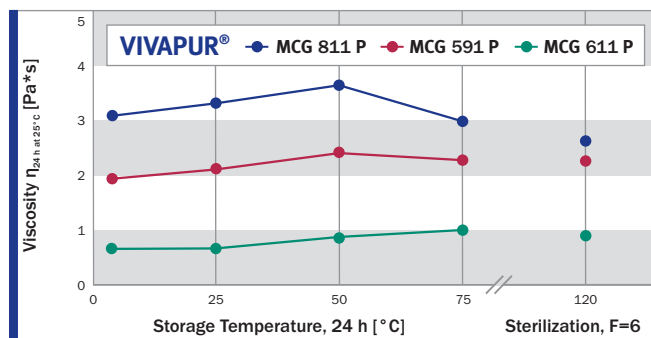


Fig. 4 Effect of Temperature on the Viscosity of a MCG Dispersion (2 % w/v). Viscosity was Measured by a Brookfield Viscometer after Heat Treatment and Subsequent Re-cooling to 25 °C

Packaging, Samples, and Storage

Storage

Protect from excessive heat and moisture

Packaging

25 kg paper bag with polyethylene liner
1 Europallet contains 24 bags 25 kg = 600 kg
Custom tariff '3912 90 90

Sample Sizes

400 g Aluminium pouch
2 kg Aluminium pouch

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.

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First Class Manufacturer of Excipients and Coatings for

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- Emulsion Stabilization
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Customer Benefits

- Convenience
- Total Cost Savings
- Global Services
- Innovation



GMP Manufacturing Sites

- Excipients
- Coatings
- Biopharmaceuticals
- JRS Sales Companies

Additionally, dedicated representatives in almost every country.

