

Adjustment of Rheological Properties for Veterinary Suspensions

Introduction

Oral suspensions, or drenches, are a popular and common approach to overcoming the many obstacles of administering medicines to animals. Formulating solid dosage forms into suspensions enables line extensions of existing products for various animal species. Suspensions can be administered orally by drench guns or syringes, and can be mixed into feed or metered by dosing pumps into drinking water.

Formulation Objectives

The selection of a suitable stabilizer to adjust the required rheological properties is a major challenge in the development of suspensions. The goal of this study was to develop an oral suspension for animals with optimal stability, administration, and palatability.

Formulation of a Veterinary Oral Suspension (Drench)

Ingredients	Function	[g / 100 mL]
Triclabendazole	API	10.0
VIVAPUR® MCG 811 P	Stabilizer	1.40
Water (deionized)	For MCG activation	45.0
Propylene glycole	Preservative	15.0
Sorbitol	Sweetener	10.0
Polysorbate 80	Surfactant	0.20
Methylparaben	Preservative	0.10
Simethicone emulsion	Antifoam	0.06
Propylparaben	Preservative	0.04
Colorant / Flavor ad lib.	-	q.s.
Water (deionized)	For volume adjustment	q.s.

MCG Activation

VIVAPUR® MCG 811 was chosen as the stabilizer for this formulation. It is a synergistic, co-processed composite consisting of microcrystalline cellulose (MCC) and sodium carboxymethylcellulose (Na-CMC). **VIVAPUR® MCG** is a free flowing powder and becomes a colloidal opaque-white dispersion after activation with water.

- VIVAPUR® MCG** was dispersed in deionized water with low shear force. No other ingredients were added at this stage.
- High shear was applied to activate the MCG. Afterwards, the suspension rested for 15 minutes before other ingredients were added.

MCG Benefits:

- Compatible with a wide range of ingredients commonly used for suspensions such as wetting agents, non-ionic surfactants or preservatives
- Withstands sterilization and long-term heating
- Dispersible in hot and cold water
- Stable in a wide pH range (3.8-10)
- GMO/TSE/BSE free, non-animal origin, cGMP production standard
- Available in Pharma and Food grades

Formulation results

Stability (Fig 1, zone A)

- A use level of 1.4 % **VIVAPUR® MCG 811 P** resulted in a viscosity of 2.7 Pa·s and a yield point of 5 Pa which was sufficient to prevent sedimentation or flocculation of the API.
- The suspension showed an excellent long-term stability.

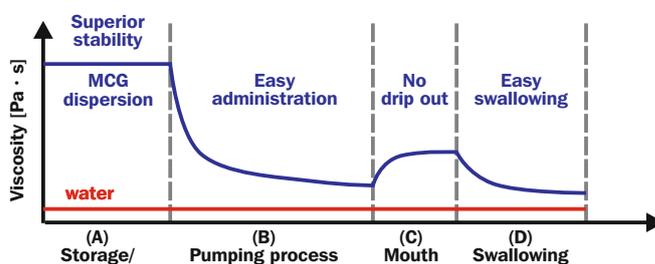
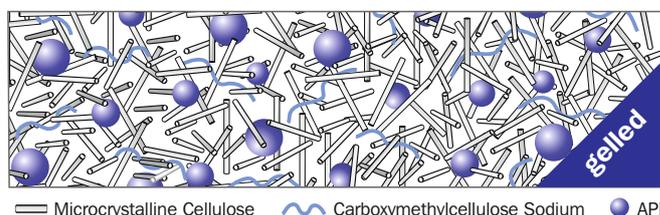


Fig. 1: Schematic representation of the viscosity changes during storage, and administration of an MCG-based suspension.

Mechanism of stabilization

A reliable stabilization of particles in a suspension cannot solely be guaranteed by high viscosity because it only slows down the settlement. **VIVAPUR® MCG** is more than just a viscosifier. It forms a three-dimensional elastic gel-network of insoluble cellulose fibrils in the suspension (Pic. 1), building a yield point. The yield point is the minimum shear stress that is required to initiate the flow. The suspension is stable if the force of gravity operating on the particle mass does not exceed the liquid's yield point.



Pic. 1: Schematic representation of the stabilizing mechanism of an API (blue spheres) in an MCG network.

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Administration (Fig. 1, zone B-D)

Upon administration by a syringe or pumping through a drench gun, the viscosity of the suspension declines and the gel is transferred into its liquid state (zone B). This strong shear thinning behavior (Fig. 2) allows for effortless administration. A time-dependent regeneration of the viscosity takes place as soon as the agitation ceases, (thixotropic effect) and prevents dripping out of the mouth (Fig. 1, zone C, Fig. 3). Finally, the shear thinning and thixotropic behavior allows for fast and complete swallowing (zone D).

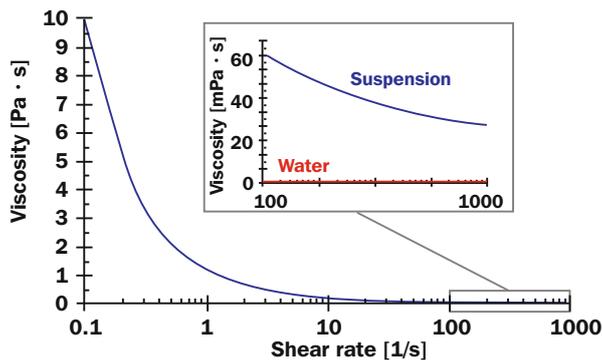


Fig. 2: Shear thinning behavior of the exemplary suspension (without API) allows easy administration and swallowing of the suspension.

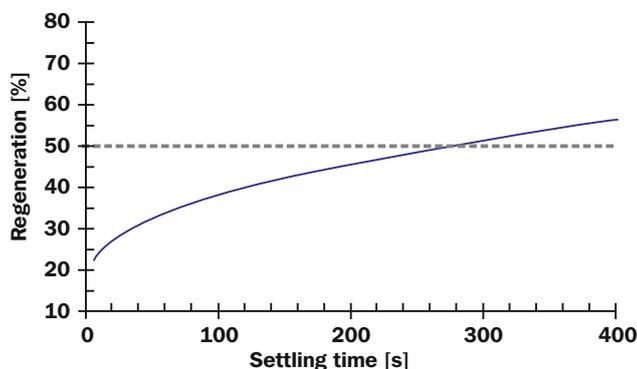
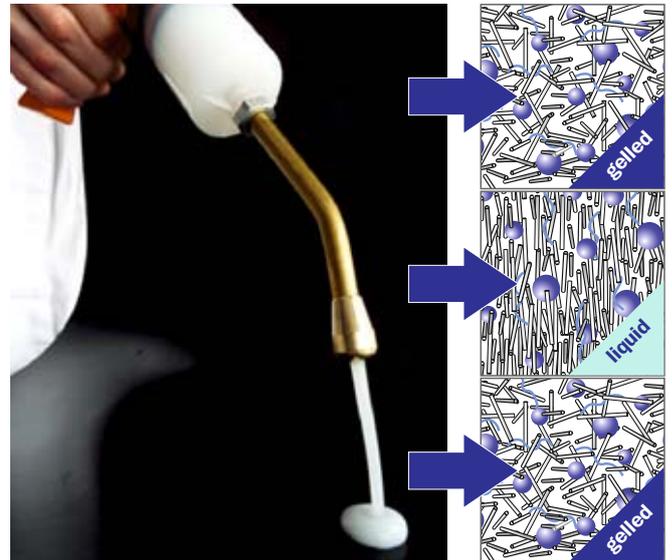


Fig. 3: Regeneration of the viscosity after agitation. 20 % is regained within seconds, 50 % after 260 s. A full regeneration was achieved after 24 h. The sol-gel transition (gel point) occurred after 120 s.



— Microcrystalline Cellulose ~ Carboxymethylcellulose Sodium ● API

Fig. 2: Dosing of an MCG suspension by means of a drench gun

Palatability

Although the palatability is mainly driven by the acceptance of the API and flavors or sweeteners, stabilizers can influence the palatability. The thixotropic gel allows a fast and complete swallowing without the API sticking to the oral mucosa (D) and the tasteless and odorless gel handles flavors well.

Conclusion

The stabilizer chosen for this formulation, **VIVAPUR® MCG 811 P**, allows a tailored balancing of viscosity, shear thinning, yield point and thixotropy of veterinary suspensions. This is mandatory to maintain long-term suspension stability as well as easy administration and swallowing.

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