COMPARISON OF COMMONLY USED PHARMACEUTICAL SUSPENDING AGENTS

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The Background

Suspensions are appealing to drug manufacturers, due to their highly customizable nature and increased patient compliance. However, they can be a feat to formulate. In a suspension – besides the active pharmaceutical ingredient (API) – multiple excipients are necessary to ensure a uniform, stable drug product with pleasant taste and mouthfeel.

Oftentimes, suspending agents, protective colloids and viscosifiers are applied as critical functional excipients to effectively suspend the API in the formulation. Colloidal microcrystalline cellulose (cMCC) is well-known as an optimal suspending agent – this activated aqueous dispersion forms a strong gel-like network to optimally suspend the API. Similarly, Xanthan and carboxymethylcellulose sodium (NaCMC) are often used but have a lower suspending power than cMCC – thus, they are often used in excipient combinations as protective colloids and to tailor rheological flow.

The Study

In this study, IFF researchers put commonly used excipients – such as cMCC, Xanthan and NaCMC – to the test by evaluating and comparing their suspending capability. In order to assess the suspending capability of these excipients, commercial pharmaceutical grade products were selected to represent each ingredient:

- Avicel® RC-591, Avicel® CL-611
- GRINDSTED® Xanthan 80 PRM Plus, GRINDSTED® Xanthan Clear 80 PRM
- TEXTURECELTM 20,000 PA 07 NaCMC

Researchers prepared liquid model suspensions using these excipients to evaluate their stability and rheological properties.

The Method

Researchers prepared five Paracetamol (acetaminophen) model suspensions (Table 1), preparing the aqueous suspension vehicle for each formulation first. They activated the Avicel® RC-591 water dispersion through an inline high shear mixer at 24,000 rpm, while the Avicel® CL-611 water dispersion was prepared by a low shear overhead/propeller mixer at 900 rpm. The GRINDSTED® Xanthan 80 PRM Plus, GRINDSTED® Xanthan Clear 80 PRM and TEXTURECELTM 20,000 PA 07 were prepared using a Silverson mixer at 4500 rpm.

Researchers then dispersed the paracetamol in lycasin (hydrogenated glucose syrup) and added it into the dissolved sodium benzoate and phenoxyethanol solution, after including polysorbate. They added this dispersion mixture to each aqueous suspension vehicle, with the propeller mixer set at 900 rpm.

Researchers then conducted a microscopy analysis on each suspension to verify uniformity. After resting for 24 hours at room temperature, they measured viscosity using a Brookfield RVT viscometer. Meanwhile, rheological flow was analyzed with a TA-Instrument DHR3 rheometer, using a 50 mm parallel geometry with a 1.8 mm gap size at 20 °C. Using these tools, researchers evaluated the suspensions' performance and stability at specific points within 24 hours – then following one, two and four weeks in room temperature storage.

Table 1. Formulation details

Product	% w/v	% w/v	% w/v	% w/v	% w/v
Paracetamol	2.4	2.4	2.4	2.4	2.4
Avicel® RC-591	1.2				
Avicel® CL-611		2.6			
GRINDSTED® Xanthan 80 PRM Plus			0.5		
GRINSTED® Xanthan Clear 80 PRM				0.5	
TEXTURECEL™ 20,000 PA 07					1.0
Polysorbate 80	0.2	0.2	0.2	0.2	0.2
Lycasin 80/55	20.0	20.0	20.0	20.0	20.0
Sodium benzoate	0.5	0.5	0.5	0.5	0.5
Phenoxyethanol	0.5	0.5	0.5	0.5	0.5
DI water	q.s.	q.s.	q.s.	q.s.	q.s.
Total	100.0	100.0	100.0	100.0	100.0

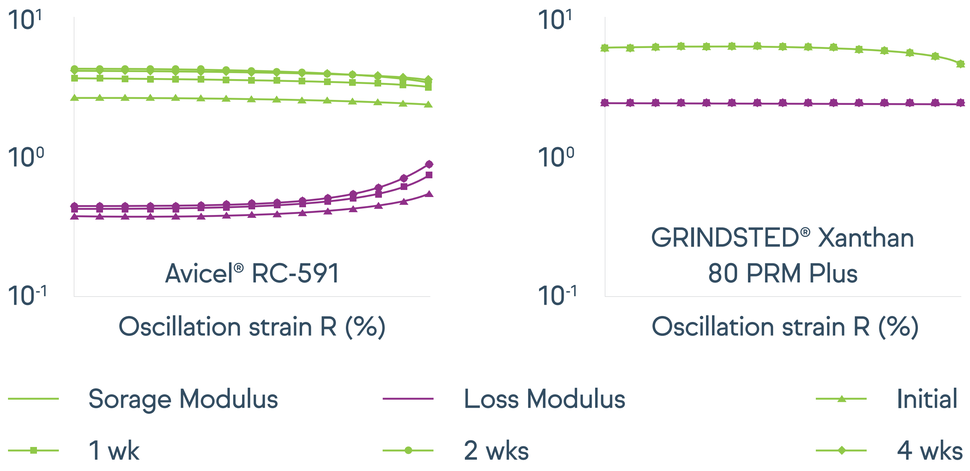
The Results

The paracetamol suspensions containing Avicel® RC-591 or Avicel® CL611 were thixotropic – or had a shear thinning property. The gel-like structure remained stable during the four weeks of storage (Fig. 1). The formulations with GRINDSTED® showed some thixotropic behavior, whereas the formulation with TEXTURE NaCMC did not show any thixotropic properties.

Figure 1. Thixotropy of suspension formulations upon storage

The Avicel® suspensions were the most structured (Fig. 2) followed by those with GRINDSTED®, which showed a weaker gel-like structure. However, the suspension with TEXTURECELTM did not show a gel structure, but demonstrated the highest viscosity over all formulations. In turn, suspensions with GRINDSTED® showed little to no changes in rheological flow, whereas those with TEXTURECELTM saw a slight decrease in viscosity while in storage.

Figure 2. Strain Sweep of suspensions at different storage times



As a result, the Avicel® suspensions were the most stable after four weeks of storage – with the lowest global Turbiscan Stability Index (TSI): a stability ranking of "A" and "B", respectively. The GRINDSTED® formulations resulted in a stability ranking of "C", and those with TEXTURECELTM were determined as unstable solutions.

The Conclusion

As a result, researchers concluded that Avicel® cMCC is the optimal choice as a suspending agent – as it showed stable and strong suspending capabilities. GRINDSTED® Xanthan PRM was found to be an efficient suspending agent, with medium to low suspending capabilities at reduced use. Therefore, when paired with Avicel® cMCC, it can help stabilize the undissolved API and fine-tune the formulation's rheological flow. The TEXTURECELTM NaCMC solution offered a clear suspending vehicle and was an effective viscosifier but provided low suspending capabilities on its own.

To learn more about IFF's suspension solutions, visit **www.iff.com/portfolio/markets/pharmaceutical**