High Performance Pediatric Oral Suspensions

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INTRODUCTION

Oral suspensions

- Alternative dosage form to tablets and capsules with benefits in dosing flexibility and ease of swallowing
- Oral suspensions challenges include particle growth, sedimentation, caking and adhesion of particles to the container, which affect dispersion uniformity, even upon vigorous shaking, potentially leading to dosing errors
- Selection of excipients, especially the suspending agent, is critical.

Carbopol® polymers are crosslinked polyacrylic acid polymer excipients that are efficient rheology modifiers at low inclusion levels. They exhibit high yield value, being effective suspending agents enabling stable and permanent suspensions (Figure 1).[1] Carbopol® polymers have mucoadhesive properties[2] which can bring additional benefits such as protective tissue coating and improve drug bioavailability.

Oral Suspensions Formulation Challenges	Carbopol® Polymer Feature
Difficulty suspending particles	High yield value for permanent suspension
Poor stability/shelf life	
Inefficient, high-energy process	Simplified cold processing
Concern about microorganisms	Does not support mold or bacterial growth
Bitter API	Taste masking via granulation

Figure 1. Addressing oral suspension formulation challenges with Carbopol ® polymers - (API: Active Pharmaceutical Ingredient)

OBJECTIVE

The research was focused on using the multifunctionality of Carbopol® polymers to develop a cold-processed, sugar-free, no-spill "permanent suspension" (no need for shaking) formulation with improved sensorial properties.

MATERIALS

Acetaminophen, Carbopol® 971P NF polymer; sorbitol 70%; sucralose; flavors; methyl paraben sodium; polysorbate 80; sodium hydroxide; disodium hydrogen phosphate.

Two commercial suspensions were used as benchmarks.

METHODS

Preparation

Suspensions were prepared at a target dose strength of 250 mg Acetaminophen/5 mL by the process shown in Figure 2.

Formulation Ingredients
Acetaminophen
Carbopol® polymer
Sorbitol 70%
Sucralose
Flavor
Methyl paraben sodium
Propylparaben sodium
Tween 80
NaOH (10%)/Na_2HPO_4
Purified water

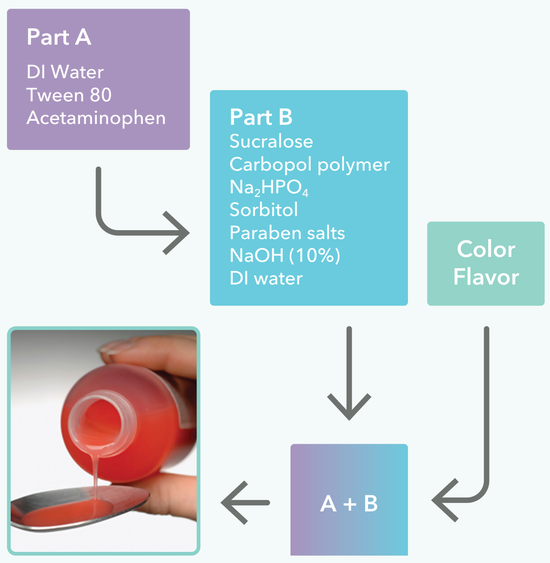


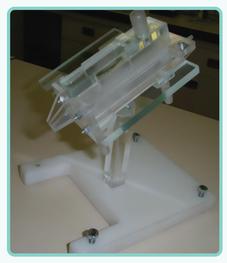
Figure 2. Suspension preparation via cold process

Formulation variables

- Carbopol polymer inclusion level: 0.5% - 1%
- Concentration of electrolytes in the formulation (Na_2HPO_4): 0% -1%
- Formulation pH: 5.5-6.5

Formulation characterization

- Viscosity - measured using Brookfield viscometer (20 rpm; room temperature)
- Mucoadhesive properties - Lubrizol internally developed method (Figure 3)[2]
- "No-spill" property - qualitatively estimated by placing the formulations in a spoon and shaking/rotating the spoon



In vitro Oesophageal Retention Model (IVOR)

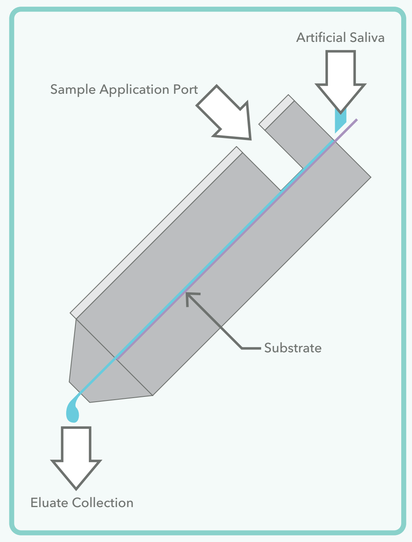


Figure 3: In vitro Oesophageal Retention Model (IVOR) for mucoadhesion testing

RESULTS

The acetaminophen suspension preparation containing Carbopol® polymers as suspending agents was achieved using a cold process, which allowed for ease of scalability and manufacturing. The viscosity of the formulations was controlled by adjusting the level and the degree of neutralization of Carbopol polymers and the level of electrolytes in the formulations. The viscosity values ranged from 2000 cP to 13000 cP.

Formulations containing Carbopol® polymer exhibited higher retention (up to 30 minutes) on the mucoadhesive membrane (better mucoadhesion) than the benchmark formulations (less than 2 minutes retention; Figures 4 and 5).

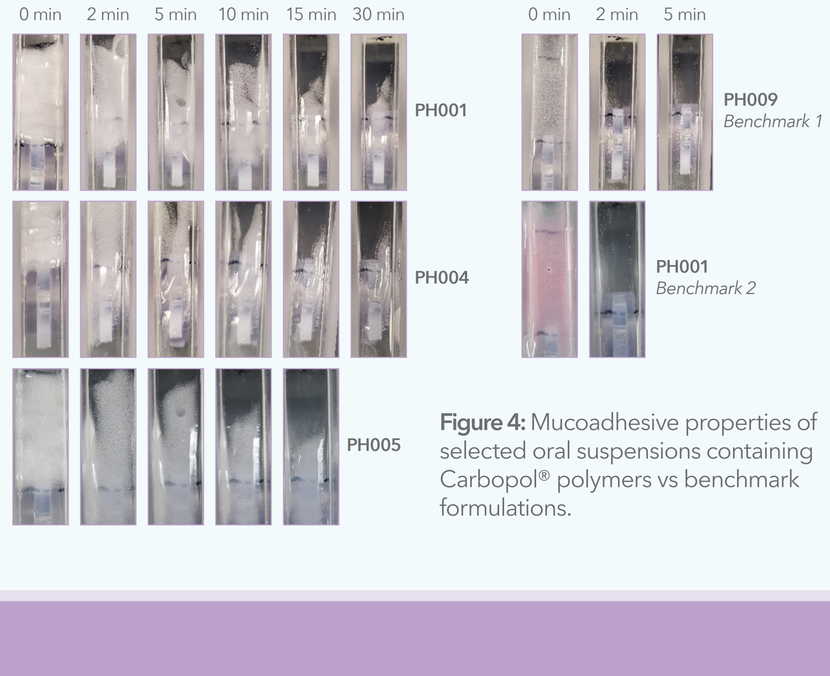


Figure 4: Mucoadhesive properties of selected oral suspensions containing Carbopol® polymers vs benchmark formulations.

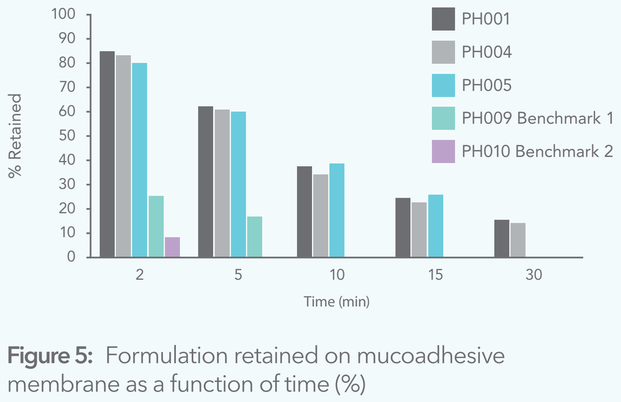


Figure 5: Formulation retained on mucoadhesive membrane as a function of time (%)

CONCLUSION

Carbopol® polymers enabled a sugar-free, no-spill "permanent suspension" (no need for shaking) formulation with mucoadhesive properties. Mucoadhesion with Carbopol® polymers offers a new opportunity for differentiation in oral liquid formulations by providing coating and protecting of the irritated or damaged mucosal tissue.

The model drug used was acetaminophen, however the formulation is expected to be applicable to a broad range of drugs. The suspension preparation was achieved using a cold process, which allows for time and energy savings and ease of scalability and manufacturing.

References: [1] *Lubrizol webpage Oral-Drug-Delivery--Excipients-for-oral-solids-solutions-and-suspensions.pdf (lubrizol.com)*
[2] *Lubrizol webpage Mucoadhesive-Polymers-in-Pharmaceutical-Formulations.pdf (lubrizol.com)*

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