PVM/MA Copolymer Enhances Antimicrobial Efficacy and Delivery of 4-Isopropyl-3-Methylenophenol in a Model Toothpaste

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The purpose of this study was to evaluate the effect of PVM/MA copolymer (Gantrez™ S-97 polymer) on the in-vitro antimicrobial efficacy and delivery of 4-isopropyl-3-methylenophenol (IPMP) from a model toothpaste using HAP discs. Results showed that Gantrez™ S-97 polymer improved formulation antimicrobial efficacy and increased the retention of IPMP over the non-polymer control. These effects were seen immediately after rinsing the treated HAP discs and after a 1-hour challenge in artificial saliva. These results indicate that Gantrez™ S-97 polymer is potentially a useful functional excipient to help improve the anti-plaque efficacy of IPMP containing toothpastes.

Introduction

Copolymers of methyl vinyl ether and maleic acid (PVM/MA copolymer, Gantrez™ S polymers) are well known to improve the delivery of poorly water soluble active ingredients such as triclosan and botanical oils from toothpaste1.

PVM/MA copolymers (Gantrez™ S polymers) adhere to oral mucosal surfaces for many hours and, by associating with the solubilized active, help retain it in the mouth for improved delivery. The proposed structure of Gantrez™ S polymer association with sodium lauryl sulfate and insoluble actives is shown in stylized form in Figure 1.

Figure 1. Proposed structure of Gantrez™ S polymer interaction with SLS-solubilized active.

α-Cyren-5-ol, also known as 4-isopropyl-3-methylenophenol (IPMP), is an antimicrobial ingredient used in toothpaste for the reduction of plaque2. It is an isomer of thymol and unlike thymol, is tasteless, with much lower water solubility. Because of IPMP’s extremely low water solubility, it is a good candidate to be studied with Gantrez S-97 polymer for delivery in toothpaste.

The objective of this study was to evaluate the effect of PVM/MA copolymer (Gantrez™ S-97 polymer) on the antimicrobial efficacy and chemical retention of IPMP on HAP discs treated with an IPMP containing model toothpaste formulation.

Methods

Treatment of Hydroxyapatite Disks
- Sintered, pellicle coated HAP discs were treated with toothpaste liquid phase for 30 minutes at 37°C, removed from the toothpaste and vortex rinsed 2 times in fresh portions of de-ionized water.
- The rinsed discs were further challenged by vigorously shaking in artificial saliva for one hour and vortex rinsed one time.

Agar Diffusion Assay
- Streptococcus mutans was sub-cultured twice in Todd-Hewitt Yeast Extract (THYE) broth, inoculated into THYE agar (cell density of 10^6 cfu/ml) and poured into Petri dishes. Treated HAP discs were placed on top of the agar (one disc per plate), left overnight in a refrigerator (to allow actives to diffuse into the agar) and then incubated for 48 hours at 37°C and 5% CO2.
- The growth inhibition zones were measured using a caliper.

IPMP Assay
- IPMP was extracted from HAP discs with absolute ethanol and aliquots analyzed using reversed-phase HPLC with UV detection at 279 nm.

Results

Figure 2.
Effect of Gantrez™ S-97 polymer on the zone of inhibition around HAP discs treated with model toothpastes containing 0.1% IPMP (error bars represent ±1 S.D).

Retainion of IPMP

Figure 3.
Effect of Gantrez™ S-97 polymer on the retention of IPMP extracted from HAP discs which were treated with model toothpastes containing 0.1% IPMP (error bars represent ±1 S.D).

Conclusions

PVM/MA copolymer (Gantrez™ S-97 polymer) at 2% in a model toothpaste formula containing 0.1% IPMP significantly improves the retention of IPMP and the antimicrobial efficacy of treated/rinsed HAP discs compared to control without polymer.

References

This work was completed by the Ashland R&D Laboratories. Ashland is the manufacturer of the Gantrez™ S-97 polymer tested herein.

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<tr>
<th>Ingredient</th>
<th>% (w/w)</th>
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<tbody>
<tr>
<td>PVM/MA copolymer (Gantrez™ S-97 polymer)</td>
<td>2.00</td>
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<tr>
<td>IPMP</td>
<td>0.100</td>
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<tr>
<td>Glycerin</td>
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<tr>
<td>Sorbitol 70% Solution</td>
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Abrasive-free Model Toothpaste Formula (pH 6.5)