Taste Masking Hydrocodone by Controlling Release in Simulated Saliva Using Ion Exchange Excipients

Amie S. Gehris¹, Jon R. Fisher¹, Martin Deetz¹, Jeanine Hurry¹, Daniel Nugent²
¹The Dow Chemical Company, Advanced Materials Division, USA
²Kelly Scientific Resources, USA
agehris@dow.com

Abstract Summary
In this study it was demonstrated that ion exchange resins could provide up to 92% taste masking efficacy and control the release of a bitter drug in saliva during the residence time in the buccal cavity. Depending on the resin chemistry and coating strategy used, modified release in GI fluids in vivo can be achieved as well.

Introduction
Taste masking of drugs has become important in the pharmaceutical industry with the large variety of orally disintegrating tablet (ODT) technologies that have been developed. Increasing patient compliance, especially in the pediatric and geriatric populations, has driven the direction of drug delivery towards ease of administration and reduced adverse taste. This study demonstrates that loading an active pharmaceutical ingredient (API) onto ion exchange resins inhibits or delays release of the API in the buccal cavity. Varying product and processing parameters can improve the taste masking ability of the excipients.

Experimental Methods
The resinates, drug resin complexes, were synthesized using aqueous solutions of drugs at room temperature. Ion exchange resins were added to the drug solutions and shaken for a period of time to allow the reaction to come to completion. Isolation was achieved by Buchner filtration. The wet cakes were washed and dried in either a fluid bed dryer or vacuum oven at 50°C to a percent loss on drying (%LOD) less than ten. Coating was done in a fluid bed dryer using Wurster coating technology at ten percent by weight. The resinates were assayed using a dynamic assay test and compared to calculated figures created with a loading calculator. Both the dynamic assay and loading calculator were developed at The Dow Chemical Company. The assay test involves pumping an aqueous organic solution with a high ionic concentration, typically 0.5N HCl: 0.5N NaCl + 20% Methanol to displace the drug from the resinate. A 100mg sample is placed in an Omnifit™ column with an adjustable end fitting. Flow rate was 0.5mL/min and 150mLs were collected. A sample of solution was analyzed for drug concentration. Buccal dissolution experiments were run using a novel patented flow-through buccal dissolution test. In this study, resinates were introduced into the buccal cell of the instrument by way of a sampling port. The residence time in the cell was determined by the flow rate and volume of the cell. The flow stream was split 2:1 to allow solids to be removed from the cell via a dip tube and to be analyzed either by flow through UV or fractions for HPLC. The results were reported as a time concentration curve.

GI Dissolution experiments were run using a patented flow through GI dissolution test apparatus, FloVitro™ Technology. The residence time of the drug in each of the three cells, the gastric cell, the intestinal cell and systemic system cell, were based on the in vivo data that was used in a starting point algorithm.

Results and Discussion
Simulated saliva was used as the dissolution medium to show the taste masking efficacy of loading a bitter drug onto an ion exchange resin. As shown in Figure 1, using drug concentration in simulated saliva as the proxy for taste, both the Polacrilin potassium and sodium polystyrene sulfonate resins did an efficient job of controlling the release of drug in the buccal cavity. The methacrylate resin gave 76% taste masking and the polystyrene sulfonate resin gave 92% taste masking efficacy. Coating the resinate improved the taste masking of the drug to 94%. When these resinates were introduced into simulated GI fluids, Figure 2, the drug released and was available for therapeutic effect.
Conclusions

- Loading hydrocodone onto a sodium polystyrene sulfonate or polacrilin potassium resin without coating taste masks the drug.
- Loading hydrocodone onto a sodium polystyrene sulfonate resin and then coating it improves the taste masking of the drug in this study.
- Improved patient compliance can be achieved by reducing bitter drug taste by loading it onto an ion exchange resin.
- Ion exchange resins taste mask bitter drugs in the buccal cavity but release the drug in GI fluids.

References