Modified Release Strategies for Ionizable Drugs Using Ion Exchange Resins

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Abstract Summary

A study was conducted to evaluate the ability of ion exchange resins to modify the release rate of drugs. It was found that the release profile of an active pharmaceutical ingredient (API) can be modified to deliver the API at the desired rate by employing the following strategies: a) loading the API onto an ion exchange resin, b) loading the API onto an ion exchange resin and coating the resinate or c) loading the API onto an ion exchange resin and combining the resinate with various ratios of unloaded resin.

Introduction

It is important for pharmaceutical companies to be able to provide modified release formulations allowing patients to easily comply with dosing regiments. The best known example of modified release formulations using ion exchange resins is in the area of cough and cold with the Tussionex® and Delsym® products which are formulated cough suppressant suspensions. In this study it was demonstrated that loading an API onto an ion exchange resin and coating the resinate, can change the release rate of the drugs. Adding unloaded resin in the formulation that contains a resinate can also give the formulator additional flexibility.

Experimental Methods

The resinates, drug-resin complexes, were synthesized using aqueous solutions of drugs at room temperature. Ion exchange resin was added to the drug solution in the desired ratio. The wet resinate was isolated by filtration, rinsed, and dried. The coating was performed in a fluid bed dryer using Wurster coating technology. The resinates were assayed using a dynamic assay test that was developed and patented at The Dow Chemical Company. Dissolution experiments were run using a flow-through patented GI dissolution test apparatus (ref 1). 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

Extended release of dextromethorphan was observed using polystyrene sulfonate uncoated resinate. Coated resinate showed additional modified release characteristics extending the T_max out to 259 minutes compared to 176 minutes seen with the standard. C_max was reduced from 22mg/L to 6mg/L. When adding unloaded resin to a formulation with uncoated resinate, similar modified release was achieved compared to a coating strategy. The C_max in the resin + resinate experiment was 5.7mg/L and the T_max was 236 minutes demonstrating that it is not
necessary to coat the resin for controlled release.

Figure 1: Modified Release with Coating

Figure 2: Modified Release without Coating

Conclusions
With these experiments we have demonstrated the utility of ion exchange resins in modifying the release of drugs. Providing a coating to a resinate or implementing a resin plus resinate strategy, allows formulators to further modify the drug release from a dosage form to the desired plasma profile.

References