Abstract Summary

A study was conducted to evaluate the ability of ion exchange resins to control the release rate of opiate drugs in GI fluids with and without the presence of 40% alcohol. It was found that the release profile of a schedule II 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.

The reason for the study was to see if using an ion exchange resin in the presence of alcohol would maintain abuse deterrent properties of the formulation. It was found that release rate of drug from an ion exchange resin in the presence of 40% ethanol was slightly increased but did not allow for immediate release of the entire dose maintaining an abuse deterrent property.

Introduction

Whether intentional or unintentional, the abuse of schedule II drugs can be life threatening. One of the best known types of abuse is that of the opiates, such as hydrocodone, which can be linked to serious life threatening overdose. Loading a schedule II drug onto an ion exchange resin to create a resinate can slow the release of the drug sufficiently to reduce the potential for a large dose of drug to be available in the body at one time. This technology can be employed to reduce the high risk associated with abuse thus reducing the likelihood of overdose and making extraction more difficult and less efficient.

Experimental Methods

The resinate complexes, 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 cake was isolated, washed, and dried. Coating was performed in a fluid bed dryer using Wurster coating technology. The resinate complexes were assayed using a dynamic assay test that was developed at The Dow Chemical Company. Dynamic dissolution experiments were run using a patented flow-through GI dissolution test apparatus, FloVitro™ Technology that ran for 24 hours while using in line UV spectrophotometry. A batch dissolution test method was run using a standard FDA static dissolution test where samples were prepared in 100 mls of simulated gastric fluid (SGF) with and without 40% ethanol, gently shaken overnight and analyzed with a UV spectrophotometer @ 265nm.

Results and Discussion

Extended release of hydrocodone was observed using polystyrene sulfonate uncoated resinate. Coated resinate showed additional modified release characteristics. In five hours only 37% percent of the drug was available from the resinate and 33% available from the coated resinate compared to 55% seen with the standard in standard GI fluids. These results demonstrate a 40% reduction of available drug in a short period of time thus extending the release of a dose in the efficacious range.
The addition of 40% alcohol in the gastric fluid did not increase the drug available from the resinate at five hours, as only 37% was available. The coated resinate result did increase by 10% to 37% drug available but maintained an abuse deterrent drug profile. The 40% alcohol results from FloVitro™ dissolution testing are maintaining a 40% reduction of available drug suggesting the prevention of dose dumping of dangerous levels of a schedule II drug.

The FDA batch test results show a slightly higher result of drug being removed from the resinate from both the uncoated and coated versions but still do not allow immediate release of the API.

Conclusions

- Based on dissolution results, ion exchange resins modify the release of hydrocodone to aid in abuse deterrent formulations of a tablet, suspension or ODT formulation.
- Coating a resinate allows formulators to modify drug release from a dosage form to the desired plasma profile.
- Creating an opiate resinate reduces the chance of dose dumping in 40% ethanol.

References