Objectives

• Develop an ethylcellulose (EC)-based coating formulation for glipizide and verapamil HCl osmotic pump tablets equivalent to commercially available drug products.
• Compare film properties, tablet stability, and in-vitro and in-vivo drug release of osmotic pump tablets coated with EC-based formulations to those coated with cellulose acetate (CA)-based formulations.
• Develop an application technology package to provide best practice guidelines to customers.

Introduction

The superior properties of osmotic pump technology make it possible to achieve zero-order drug release in a controlled release dosage form. Interest in osmotic pump technology continues to grow as many of the main patents for this technology have expired, making it more accessible to formulators. POLYOX™ (ethoxylate block (EO)) and METHOCEL™ (hydroxypropyl methylcellulose) are key functional polymers commonly used in osmotic pump formulations, which are then typically coated using cellulose acetate. The purpose of this project was to develop a coating for the osmotic pump tablet based on ETHOCEL™ ethylcellulose with equivalent in-vitro and in-vivo performance to commonly used cellulose acetate coated tablets.

Materials

Active pharmaceutical ingredients (APIs) were glipizide (Beijing Hengxin Pharmaceutical, Inc., 11 mg, and verapamil HCl (Tianjin Central Pharma Co., Ltd.), 11 mg, and verapamil HCl (Tianjin Central Pharma Co., Ltd.), 11 mg, and verapamil HCl (Tianjin Central Pharma Co., Ltd.), 11 mg), NaCl (China National Pharmaceutical Group Corp.), magnesium stearate (China National Pharmaceutical Group Corp.), POLYOX N750 (glipizide tablets only, The Dow Chemical Company, NaCl (China National Pharmaceutical Group Corp.), and Fe3O4 (China National Pharmaceutical Group Corp.). The push layer included POLYOX Coagulant (The Dow Chemical Company, NaCl (China National Pharmaceutical Group Corp.), and Fe3O4 (China National Pharmaceutical Group Corp.)). The push layer included POLYOX Coagulant (The Dow Chemical Company, NaCl (China National Pharmaceutical Group Corp.), and Fe3O4 (China National Pharmaceutical Group Corp.)).

Results and Discussion

Glipizide

Acceptable similarity in glipizide release was demonstrated for the tablets coated with the optimum EC-based coating and the equivalent commercial product (Figure 2). In-vitro drug release for tablets containing glipizide, comparing tablets coated with an EC-based coating and commercial product. (Figure 2).

Verapamil HCl

Acceptable similarity in verapamil HCl release was demonstrated for the optimum tablets coated with an EC-based coating and commercial product under different media pH conditions. (Figure 6). Conditions included C, E, and F, as described earlier.

Table 1. Pharmacokinetic parameters for beagle dogs treated with verapamil HCl with test and reference coating formulations (n=6).

Conclusions

Ethylcellulose-based coatings on glipizide osmotic pump tablets had equivalent drug release performance as a commercial product under standard conditions, emulsified GI tract conditions, and simulated stomach. Ethylcellulose-based coatings on verapamil HCl osmotic pump tablets had acceptable similarity to the equivalent commercial product under standard conditions and in simulated GI tract conditions. In addition, in-vitro testing of the verapamil HCl tablets showed equivalence between the test (EC-based coating) and the reference (CA-based coating). A stability study indicated that the verapamil HCl tablets coated with the EC-based coating were stable for at least 6 months under accelerated conditions.