The Influence Dissolution Media pH on Drug Release from Ethylcellulose Coated Multipurplicates

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Abstract Summary

The influence of dissolution media pH on drug release from ETHOCEL™ coated multiparticulates was investigated. Drug release was found to be independent of dissolution medium pH.

Introduction

In order to achieve a consistent extended drug release, it may be necessary to maintain similar drug release while dosage form travels across the physiological pH range. This objective was to carry out a comparative evaluation of drug release from ethylcellulose coated multiparticulates in both gastric and intestinal media for tonic or non-tonic drugs.

Experimental Methods

Ethylcellulose Coating of Drug Layered Sugar Spheres

Four model drugs; chlorpheniramine maleate (CPM), guaifenesin (GUA), acetaminophen (APAP) and amlodipine besylate (AMD) were used in this study. The four model drugs are characterized below (Table 1).

The model drugs coated were 16/20 mesh (50 - 100 µm) sugar spheres (SUGLETS™, Colorcon), in a Pam-Glatt GPCG-1 fluidized bed coater (Pam-Glatt Pharma Technologies, India) equipped with a Wärtsilä (200mm length) using Hypromellose 2910 (ETHOCEL™) as binder. Process parameters employed in the drug layering are listed in Table 2. Two groups of soluble drugs (APAP and AMD) required a higher proportion of binder to assist with the adherence of the suspended drug particles onto the coating substrate. The poorly water soluble drugs did not contribute to the viscosity of the drug layering dispersion thus allowing for higher fluid delivery rates. Lower fluid delivery rates were used for a more uniform application of the poorly soluble drug.

Drug release across a barrier membrane is expected to occur via diffusion through the polymer network, dissociation or some form in the coating. A partitioning of drug in a polymeric film coat is generally dependent on the state of ionization of the drug molecule, molecular affinity (determined by solubility parameter) and its aqueous solubility. The degree of ionization of a drug depends on its pKa and the pH of the aqueous solution in which it is dissolved. Amlodipine, a weak organic base (pKa=9.3) is expected to be essentially non-ionized at physiological pH (both at 0.1 M HCl and pH 7.4 buffer). Amlodipine solubility does not vary with pH from 1.2-8.0 corresponding to the in vivo range in the GIT. As expected, a pH independent behavior was observed in the case of amlodipine (Figure 1).

Guaifenesin, a neutral molecule, with absence of any ionizable groups in the molecule also showed pH independent drug release (Figure 2). Guaifenesin is less soluble in a more acidic environment, while in a higher pH environment, guaifenesin is readily soluble. Chlorpheniramine maleate (pKa=2.6), salt of the weak base chlorpheniramine maleate (APM) is reported to have similar solubility, in both 0.1 M HCl and pH 7.4 phosphate buffer at 25°C also showed pH independent release behavior (Figure 3).

The poorly water soluble ethylcellulose coated pellets has also been reported previously by other researchers.

Experimental Results

Drug release from ETHOCEL™ coated pellets was found to be independent of the dissolution medium for a range of actives with varying solubility.

Drug release rate independent of the dissolution medium may indicate that the diffusion was the dominant mechanism of drug release. It has been reported that, pH independent drug release at higher pH could represent a diffusion-controlled mechanism. A pH independent dissolution form may offer some advantage over the barrier membrane film technology, in the barrier membrane film technology, or increased complexity of the film by inclusion of a porogen such as hypromellose.

References


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