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Drug release modification by interpolymer interaction between countercharged types of Eudragit® RL 30D and FS 30D in double-layer films

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ABSTRACT

Interpolymer interactions between the countercharged methacrylate copolymers Eudragit® RL 3 (polycation) and Eudragit® FS 30D (polyanion), were investigated in conditions mimicking the gastro testinal environment. The formation of inter-macromolecular ionic bonds between Eudragit® RL 30D a Eudragit® FS 30D was investigated using FT-IR spectroscopy and modulated DSC. The FT-IR spectra of tested polymeric matrices are characterized by visible changes in the observed IR region indicating interaction between chains of two oppositely charged copolymers. A new band at 1570 cm^{-1} appea which was assigned to the absorption of the carboxylate groups that form the ionic bonds with the q ternary ammonium groups. Moreover, while increasing the pH values from pH 5.8 to 7.4, a decrease the intensity of the band at 960 cm^{-1} (quaternary ammonium group vibration) was observed. All bin mixtures were characterized by the presence of only one and narrow *Tg*, pointing to sample homogene because of the compatibility of components. As a result of electrostatic interaction between the copo mer chains during swelling, the resulting *Tg* is decreased significantly and was dependent on the quant of copolymers present in the structure of polycomplexes formed. Overall, the interaction between cou tercharged copolymers during passage in gastrointestinal tract can strongly modify the release profile the model drug diclofenac sodium.

1. Introduction

The combination of countercharged types of (meth)acrylate copolymers, including their blends, in order to control the site and time of drug release from oral drug delivery systems (DDS) was discussed in previously published reviews (Gallardo et al., 2008; Siepmann et al., 2008). A comprehensive analysis of the physicochemical principles behind the intermacromolecular interactions that govern the mechanism for regulating the drug release rate from oral DDS based on chemically complementary Eudragit® grades was recently published by our research group (Mustafin, 2011).

One of the first attempts to study the influence of the combination of two countercharged Eudragit® types was focused on the development of oral colon-specific DDS under the trade name EUDRACOL®, registered by Evonik/Degussa Röhm GmbH (Gupta et al., 2001a, 2001b; Rudolph et al., 2001; Skalsky and Petereit, 2008). The delivery system consists of drug-layered pellets coat with an inner layer of a combination of two pH-independent po mers, Eudragit RL and Eudragit RS (2:8), and an outer layer o pH-dependent polymer, Eudragit FS (Fig. 1). These grades we combined in the oral DDS because it was thought that the ou coating would provide localized release into the colon (FS). A consequence, the combination of two pH-independent copolym RL/RS, the required permeability of which was set by their rat would enable the drug release rate to be controlled.

However, testing of the system using the release of aminosalicylic acid (5-ASA) showed that the release profiles we characterized by an unexpected decrease of the drug release ra The researchers took into account the opposite charges of the us copolymers and hypothesized that there may have been intern cromolecular interactions of reactive groups on portions of t polymer chains located at the boundary of each layer. They model the conditions for preparing the formulation by preparing bila systems and layering a preliminary dried coating onto another the same sequence that was used to prepare the pellets. Howev interpolymer interactions were not observed by physicochemi analysis of the prepared bilayer films using FT-IR, ^{13}C NMR sp troscopy and DSC. Despite the negative results, the research

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