Ethanol-Resistant Polymeric Film Coatings for Controlled Drug Delivery

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ABSTRACT SUMMARY
The aim of this study was to develop a novel type of controlled release film coating, which is ethanol-resistant and the presence of high ethanol concentrations in the surrounding bulk fluid (e.g., up to 40 %) should not affect the resulting drug release kinetics. Interestingly, blends of ethylcellulose and medium or high viscosity guar gums provide such ethanol resistance. Theophylline release from pellets coated with the aqueous ethylcellulose dispersion Aquacoat® ECD containing 10 or 15% medium and high viscosity guar gum was virtually unaffected by the addition of 40 % ethanol to the release medium.

INTRODUCTION
"Dose dumping" is often referred to as "Unintended, rapid drug release in a short period of time of the entire amount or a significant fraction of the drug contained in a modified release dosage form".1 This phenomenon can represent a major risk for the patient, because: (i) toxic drug concentrations might be attained with potentially severe consequences for the patient, and/or (ii) the therapeutic efficiency might no more be assured during the intended time period. Such “dose dumping” can for example be caused by the consumption of alcoholic beverages, leading to high ethanol concentrations in the contents of the stomach.2

The aim of this study was to develop a novel type of polymeric film coatings providing ethanol insensitive drug release patterns. The basic idea was to add small amounts of an ethanol-insoluble polymer to a commonly used polymer used for film coating: ethylcellulose. The presence of this second compound was intended to effectively hinder the potential dissolution of ethylcellulose in aqueous media containing high ethanol concentrations. Also, the presence of ethyl cellulose was intended to effectively hinder the potential dissolution of the ethanol-insoluble polymer in pure aqueous media.

EXPERIMENTAL METHODS
Theophylline matrix cores were coated with different Aquacoat® ECD:guar gum blends (very low η guar gum, 15 cps; low η guar gum, 52 cPs; medium η guar gum, 320 cPs; high η guar gum, 575-625 cPs). Aquacoat ECD was plasticized for 1 d with 25 % DBS. Guar gum was dissolved in purified water. The two liquids were blended and stirred for 30 min prior to use. The coating dispersions were sprayed onto theophylline pellets using a fluidized bed coater (Strea 1, Wurster insert) and cured in an oven. Theophylline release from coated pellets was measured in 0.1 M HCl or 0.1 M HCl: ethanol 60:40, followed by phosphate buffer pH 7.4 (USP 36) using the USP 36 paddle apparatus (900 mL, complete medium change after 2 h; 37 °C, 100 rpm). At pre-determined time points, 3 mL samples were withdrawn and analyzed UV-spectrophotometrically. All apparent viscosities were measured using an AR2000Ex rheometer at a shear rate of 50 s⁻¹ in a 1 % aqueous guar gum solution measured rotationally at 20 °C after 1 min equilibration using a 6 cm acrylic cone (1°), wherein the shear was ramped up linearly from 1 to 50 s⁻¹ in 25 steps over 29 s.

RESULTS AND DISCUSSION
Importantly, the sensitivity of theophylline release from coated pellets significantly decreased with increasing viscosity of the guar gum. As it can be seen in Figure 1c, in the case of pellets coated with Aquacoat®ECD:high η guar gum 90:10 ethanol insensitive drug release was observed.
Thus, the strategy to add practically ethanol-insoluble guar gum to ethylcellulose film coatings in order to minimize undesired film dissolution in media containing significant amounts of ethanol has been successful.

Furthermore, drug release from the proposed coated dosage forms was long term stable, even upon open storage (without packaging material) under stress conditions (Figure 2).

**CONCLUSION**

The addition of small amounts of guar gum to ethylcellulose based film coatings effectively reduces the sensitivity of the resulting drug release kinetics to the presence of significant concentrations of ethanol in the bulk fluid. This is of great practical importance for highly potent drugs, for which dose dumping can be critical.

**REFERENCES**