The Influence of Drug Release on Release from Ethylcellulose Barrier Membrane Coated Multicarriers

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Abstract Summary

The influence of drug solubility on release from ETHOCEL™ Premium (EC) coated multiparticulates was investigated. Drug release was retarded with decreasing drug solubility. Apart from drug solubility, other factors such as API particle size, membrane thickness or the degree of saturation of the drug may also influence drug release rates. Similar trends in drug release were observed for solvent and aqueous coated EC. The addition of a pore former yielded a faster drug release. Poorly soluble drugs exhibit significantly slower release when coated with EC using an organic solvent.

Introduction

A previous study investigated the relationship between drug release and aqueous ethylcellulose coating (Surelease®, Coloron, Harleysville, PA) and the objectives of the study was to carry out a comparative evaluation of drug release from solvent-coated ethylcellulose multiparticulates using the same model drugs.

Experimental Methods

Drug Layering of Sugar Spheres

Four model drugs; chlorpheniramine maleate (CPM), guaifenesin (GUA), acetaminophen (APAP) and amlodipine besylate (AMD) of different solubility levels were used in this study. The four model drugs were coated with aqueous dispersions of ETHOCEL™ 10cP (10% w/w) and ETHOCEL™ 10 Std Premium (EC) (The Dow Chemical Company, USA) with and without HPMC 2910 (METHOCEL™ 6cP) as pore-formers, at a 75:25 ratio in the presence of sodium bicarbonate, incorporating and water (90:10). Debit® spheric (DBS, USA) was added as a plastisizer. Drug coated multiparticulates and coated glass beads were evaluated using GPCG 1.1 fluid-bed apparatus. Ethylcellulose barrier membrane coating process parameters are shown in Tables 3 and 4.

Results and Discussion

The rank order of aqueous solubility is CPM > GUA > APAP > AMD. Drug release rates followed the rank order of GUA > APAP > CPM > AMD (Figures 1, 2 and 3), regardless of coating solvent. Drug release rate was found to be slower for poorly soluble drugs (CPM, GUA). An increased solute concentration gradient over the membrane lead to slower drug release than when coated with aqueous dispersion. Drug release rate increased with the addition of methacrylic acid and solubility of the drug. This may be related to different partition coefficients of drugs into the ethylcellulose membranes. Similar trends in drug release were observed for solute as well as aqueous coated EC.

Conclusions

Multicarriers coated with ethylcellulose barrier membrane lead to slower drug release than when coated with aqueous dispersion. Drug release rate increased with addition of methacrylic acid as a pore former. The addition of a pore former did not result in any increase in the drug release rate for amlodipine. Guaifenesin, a neutral molecule and water soluble drug, showed faster drug release than CPM. For a slightly soluble drug (amlodipine), a very slow drug release was obtained when EC was applied using an organic solvent. The addition of a pore former did not result in any increase in the drug release rate for amlodipine.

References

2. USP 33/ NF 28, Access online, October 21, 2010

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Figure 1. Coated with ETHOCEL™ 10cP (10% w/w)

A deviation from the trend was observed for CPM, a freely soluble drug in water, for CPM as compared to APAP (sparingly water soluble) for as well as aqueous coated EC.

Figure 2. Coated with Surelease® (8% w/w)

Table 1. Drug Characteristics

Table 2. Drug Layering Process Parameters

Table 3. Coating Parameters used for EC Coating (with pore former)

Table 4. Coating Parameters used for EC Coating (without pore former)

Table 5. Dissolution Testing

Table 6. Experimental Methods

Table 7. Results and Discussion

Table 8. References

Figure 3. Coated with SURELEASE™ 30cP with and without pore-former

Figure 4. Coated at 100°C with ETHOCEL™ 8cP with and without pore-former

Figure 5. Coated with METHOCEL™ ES 100cP (10% w/w)