The Influence of Film Coatings on Performance of Hypromellose Matrices

INTRODUCTION

Hypromellose (hydroxypropylmethylcellulose, HPMC) has been widely used in oral slow drug release matrix systems.[1] Formulation development is simple and reproducible release profiles are well documented. The majority of reported studies in literature are based on uncoated matrices. Here, the influence of three film coating systems on the performance of hypromellose SR matrices, stored under different conditions up to 12 months, is investigated.

EXPERIMENTAL METHODS

A model formulation containing only 20% hypromellose (METHOCEL™ premium cellulose ethers, K4M Premium), 30% model drug, 49.25% microcrystalline cellulose (Avicel PH102, FMC), 0.5% fumed silica (Aerosil 200, Degussa AG) and 0.25% magnesium stearate (Peter Greven) was used. Chlorpheniramine maleate (CPM), which is freely water-soluble, and theophylline (TP), which is water-soluble, were used as model drugs.

All ingredients, with the exception of magnesium stearate, were blended in a Turbular mixer (Type T2A, Pleuger, Basel, Switzerland) for 10 minutes. Then magnesium stearate was added and mixed for an additional five minutes. Tablets (333 mg) containing 100 mg drug were directly compressed using an instrumented Piccola rotary 10-station tablet press with 9 mm concave tooling at 10 kN and 30 rpm. Tablets were coated with four different film coating systems (Table 1) in a 38-cm side vented pan (Labcoat II-X, O'Hara) using a Schlick spray gun.

Table 1 – Coating Systems

	Polymer used in the system	Weight gain (%w/w)
Opadry® II	HPMC	4
Opadry® II	PVA[1]	4
Opadry® amb	PVA	4

[1] Polyvinyl alcohol

Uncoated and coated tablets were stored in Securitainer polypropylene jars (Jaycare, Ltd) at 25ºC/60% RH, 30°C/60% RH and 40°C/75% RH for up to 12 months. Tablets were tested initially and after 1, 2, 3 and 6 months storage. Drug release from the matrices was determined using a Caleva ST7 dissolution tester, USP apparatus II (paddle) and sinkers, in 37±1ºC water at 100 rpm. Tablet mechanical strength was also measured.

RESULTS AND DISCUSSION

Table 2 shows properties of powder mixtures and uncoated tablets. All coated and uncoated tablets with both drugs had low weight variation and good mechanical strength both initially and after 12 months storage. Application of film coatings generally resulted in an increase in tablet breaking force. Good stability results were produced at all storage conditions after 1, 2, 3, 6 and 12 months. No changes were observed in tablet appearance.

Table 2 - Properties of Powder Mixtures and Uncoated Tablets

	CPM	TP
Powder bulk density (g/cm^3)	0.449 ± 0.001	0.423 ± 0.003
Powder tapped density (g/cm^3)	0.542 ± 0.002	0.526 ± 0.002
Compressibility Index	17	20
Tablet weight (mg)	333 ± 3	333 ± 4
Tablet diameter (mm)	9.24 ± 0.006	9.022 ± 0.005
Tablet thickness (mm)	5.053 ± 0.018	4.939 ± 0.029
Tablet breaking force (kp)	18.6 ± 0.5	23.6 ± 1.3
Tablet friability (%)	< 0.001	< 0.001

No significant decrease in tablet mechanical strength was recorded. Drug release did not change after storage at all four storage conditions. Figures 1-4 show drug release profiles at 0 and 12 months time points. For both CPM and TP, there are no differences between the drug release from coated or uncoated matrices. In addition, drug release from these matrices remained the same after 12 months stability at 40ºC/75%RH.

Figure 1 – CPM Release at "0" Time Point

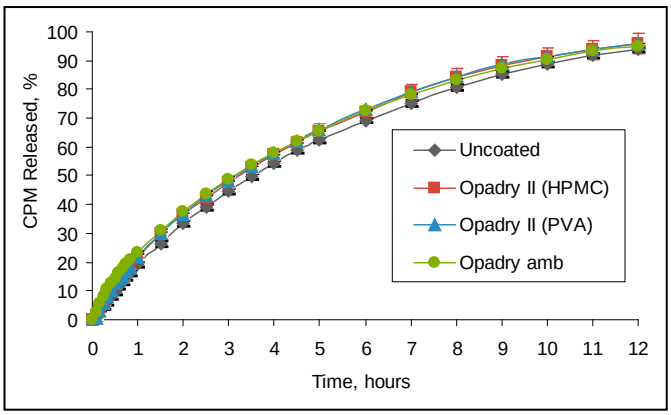


Figure 2 – CPM Release at 12 Months

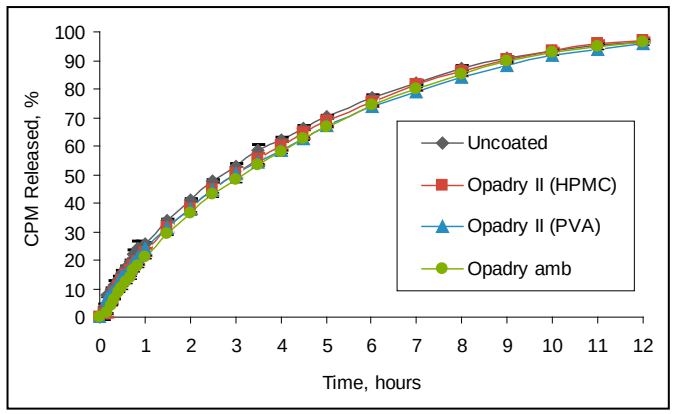


Figure 3 – Theophylline Release at "0" Time Point

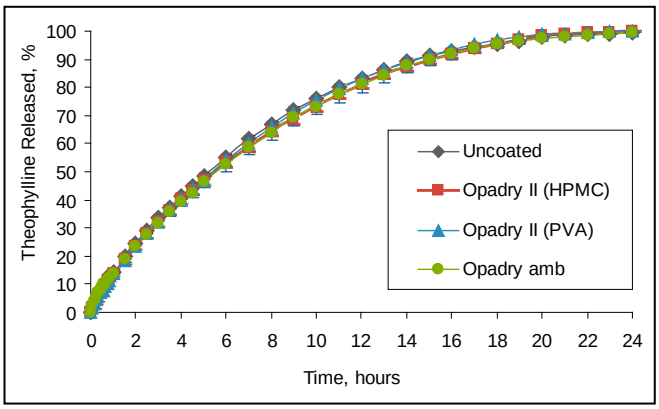
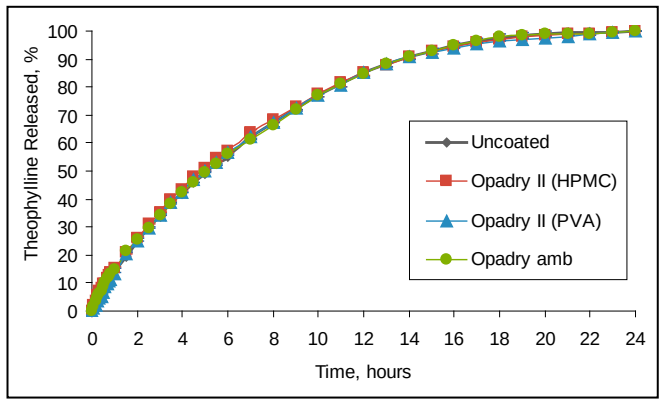


Figure 4 – Theophylline Release after 12 months

Storage at 40ºC/75% RH



CONCLUSIONS

The model chlorpheniramine maleate and theophylline formulations, with METHOCEL™ K4M as the rate controlling polymer, show extended release characteristics with excellent reproducibility after 12 months storage at 25ºC/60%RH, 30ºC/60%RH and 40ºC/75%RH. All the film coating systems used in this study did not influence drug release profiles neither initially nor during 12 months storage under different conditions.

Reprint of poster presented at Controlled Release Society Annual Meeting, 2003, with updates to reflect 12 month vs. six month stability data. Authors, Marina Levina, Peter Wan, Martin Jordan and Ali R. Rajabi-Siahboomi

REFERENCES

1. Rajabi-Siahboomi, A.R. & Jordan M.P. European Pharm. Rev., 5, 4, 21-23 (2000).

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