INFLUENCING THE DISSOLUTION BEHAVIOUR OF SUSTAINED RELEASE FORMULATIONS PRODUCED BY DRY POWDER COATING

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INTRODUCTION

Dry powder coating is a technique to coat substrates without the use of any organic solvent or water. The polymer powder is applied to the cores without any preparation like dissolving or suspending leading to reduced preparation and process time. Previous studies investigating the suitability of ethylcellulose powder for dry coating processes demonstrated the impact of liquid plasticisers on film formation and coating efficiency. However, films containing pure ethylcellulose reveal a strong sustained release effect which requires the use of pore forming excipients.

The aim of this study was to investigate the influence of combining ethylcellulose with a water permeable polymer, Ammonio Methacrylate Copolymer Type A (Eudragit® RL), in powdered form on the dissolution behaviour of coated theophylline pellets. Several mixtures, coating levels and particle sizes were evaluated.

MATERIALS AND METHODS

Materials

Micronized ethylcellulose powder (Ethocel® Standard FP 10, d_{50}=4µm)) was provided by DOW Chemical (Midland, USA). Theophylline pellets were donated by Temmler Ireland Ltd. (Killorglin, Ireland). Eudragit® RL PO (Evonik, Darmstadt, Germany) was used as received (d_{50}=47µm) and in micronized form (d_{50}=7µm). Isopropyl myristate was received from Cognis (Duesseldorf, Germany) and dibutyl sebacate from Sigma Aldrich (Seelze, Germany).

Coating

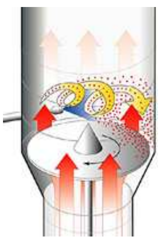
Dry powder coating was performed in a rotary fluid bed (GPCG 1.1, Glatt, Binzen, Germany). Ethylcellulose powder and ethylcellulose/Eudragit® RL powder mixtures (Table 1) were fed to the cores via a three way nozzle using a gravimetric powder feeder (K-tron, Gelnhausen, Germany). A mixture of dibutyl sebacate and isopropyl myristate (75/25 w/w) was fed to the cores by the same nozzle to plasticise the polymer powder and to enhance the polymer adhesion on the cores.

Tab. 1 *Mixtures of ethylcellulose/Eudragit® RL*

Ethylcellulose [%]	100	90	80	75
Eudragit® RL [%]	0	10	20	25

Process parameters

process parameters	coating phase
inlet air temperature	50-53°C
product temperature	40-42°C
outlet air temperature	39-41°C
air flow rate	70 m³/h
atomizing air pressure	1.5 bar
spray rate	3.3 g/min
powder feed rate	11.1 g/min
rotor speed	230 rpm



Rotor-GPCG 1.1, Glatt

Curing

Curing of coated pellets was conducted in an oven at 80 C for 24 hours.

Dissolution studies

Dissolution testing was performed in a paddle apparatus (Erweka DT6, Heusenstamm, Germany). Samples were analysed every 3 min. Drug release of theophylline was determined by UV spectroscopy at 242 nm.

RESULTS AND DISCUSSION

Coating of theophylline pellets with ethylcellulose and different amounts of Eudragit® RL resulted in a variety of dissolution profiles. Figure 1 shows the drug release of pellets with a coating level of 20% polymer. Ethylcellulose films without Eudragit® RL revealed a strong sustained release effect with a drug release of approximately 10% after 12 hours. Addition of 10% Eudragit® RL resulted in a slightly higher release of 28% after 12 hours. 20% Eudragit® RL amount increased the drug release to 85% after 12 hours. Pellets coated with a 75/25 mixture of ethylcellulose/Eudragit RL® released 100% after 8 hours.

Figure 2 demonstrates the influence of different coating levels on dissolution behaviour on the mixture ethylcellulose:Eudragit® RL 80/20. Expectedly, the higher the coating level the slower the drug release obtained. Consequently, dissolution behaviour can be modified by varying the amount of Eudragit® RL as well as by modifying the coating thickness.

Figure 3 presents the dissolution of pellets coated with non micronized Eudragit® RL (d_{50}=47µm). It was possible to modify the drug release and to obtain film formation despite the larger particle size.

Figure 4 shows scanning electron microscopy images of pellets cured at 80°C for 24 hours and uncured ones. Curing of pellets led to coalescence of polymer and thus to film formation whereas uncured pellets showed a rough surface with visible single polymer particles.

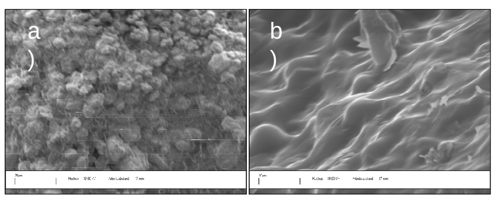


Fig. 4 *SEM images of a) cured and b) uncured pellets (80 C/24h)*

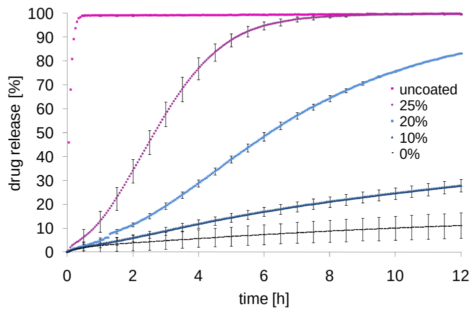


Fig. 1 *Dissolution profiles of theophylline pellets, uncoated and coated with pure ethylcellulose and different ratios of Eudragit® RL, coating level 20%. Aqua dem., 50 rpm, n=3, mean ± SD*

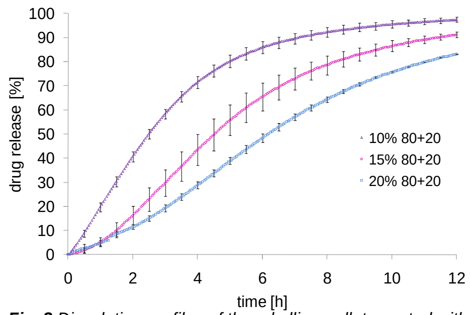


Fig. 2 *Dissolution profiles of theophylline pellets coated with different coating levels of a mixture of ethylcellulose (80%) and Eudragit® RL (20%). Aqua dem., 50 rpm, n=3, mean ± SD*

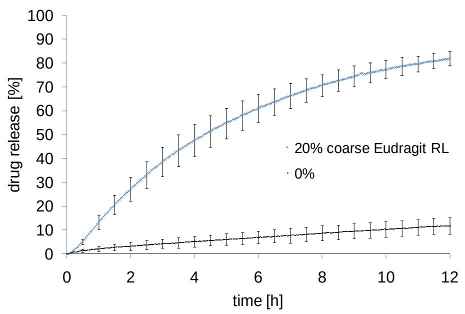


Fig. 3 *Dissolution profiles of theophylline pellets coated with pure ethylcellulose and with a mixture of ethylcellulose and 20% coarse Eudragit® RL. Aqua dem., 50 rpm, n=3, mean SD*

CONCLUSION

It is possible to coat pellets with ethylcellulose/Eudragit® RL powder mixtures without using any organic solvent or water. Combining ethylcellulose with the water permeable polymer Eudragit® RL offers the possibility to vary dissolution profiles in a wide range by applying formulations containing different amounts of Eudragit® RL as well as by varying the coating level. Dissolution behaviour can be modified with micronized and with coarse Eudragit® RL powder showing the robustness of the process regarding particle sizes.

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