



Influence of the Particle Size of the Inert Polymer in a Compression Coated Controlled Release Tablet

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Note: The official monograph for
Hydroxypropyl Methylcellulose (HPMC)
has been changed to Hypromellose.

Introduction

Numerous works in the literature have demonstrated the utility of ethylcellulose as a rate controlling polymer in direct compression inert matrix tablet formulations¹⁻³. The drug release rates in these studies were significantly influenced by the ethylcellulose polymer level, its particle size and to a lesser degree, its viscosity grade. A micronized version of ETHOCEL* ethylcellulose, ETHOCEL FP, has been shown to be much more effective than its granular counterpart in these types of applications. In addition to matrix type formulations, reproducible control of drug release can be accomplished by the production of a system containing core tablets surrounded by an inert polymeric coating. The release rates from these systems are affected by the type and amount of polymer used and any defects, i.e., pores, that are intentionally or unintentionally found in the films. These films can be applied by traditional solution techniques or can be formed by the means of compressing dry powder around the core^{4,5}. A recent study⁶ has addressed the physicochemical properties of the porosity modifiers on the compression coating. This work addresses the effect of the particle size of the polymeric film former on the functionality of a compression coating in a model controlled release tablet.

Experimental Methods

Materials:

The following materials were used as received:

- Tramadol HCl, (a gift from Ashbourne Pharmaceuticals, Northampton, GB)
- ETHOCEL Standard 10FP Premium
- ETHOCEL Standard 100FP Premium
- ETHOCEL Standard 10 Premium (The Dow Chemical Company, Midland, MI)
- Dicalcium phosphate anhydrous A-TAB, granular (Rhône-Poulenc, Cranbury, NJ)
- Magnesium stearate, NF, (Mallinckrodt, Inc., St. Louis, MO).

Tablet preparation:

The formulation of the core tablets consisted of 95% Tramadol HCl, 5% ETHOCEL 10FP and 0.05% magnesium stearate. These components were weighed into a small jar and manually mixed with a spatula for 5 minutes. The cores were formed on an automated Carver (model C) laboratory press with 1/4 inch concave tooling. The pump speed and dwell times were held constant at 15% of maximum and at 5 seconds respectively. The applied compression force was 2,000 lbs.

The compression coated tablets were prepared by placing 50% (100 mg) of the coating mix, either pure polymer or binary polymer/dicalcium phosphate blends at various ratios, in a 1/2 inch die containing the bottom concave punch. A core tablet was manually centered on the powder bed and the remaining 50% of the coating mix was applied on top of it. The applied compression force was held consistent for all trials at 3,000 lbs.

Drug Dissolution:

Dissolution testing of tablets was performed using a Distek dissolution system. The USP Apparatus 1 paddle with sinkers method was used at an agitation rate of 50 rpm. Dissolution profiles were generated at 37.5°C, with detection at 230 nm. Tablets were introduced into 900 ml of 0.1N HCl.

Results

The average particle sizes of the 3 grades of ethylcellulose were 5 microns (10FP), 40 microns (100FP) and 250 microns (10G). Figure 1 illustrates the effect of particle size of the polymer on release rate in a pure polymer coating system. All of the tablets tested were very hard and maintained their physical integrity throughout the dissolution testing. It was found that as the particle size of the polymer decreased, the release rate slowed (% dissolved/time) and the lag times increased. This suggests that the smaller particle size polymer flows and consolidates more efficiently during the compression process, resulting in a coating with a lower degree of porosity.

Figure 2 shows the effect of the particle size of the polymer when the coating is formulated to contain 50 wt % of a water soluble porosity modifier. Although, as expected, the release rates were increased and the lag times were shortened by the inclusion of the porosity modifier, the significant contribution that the particle size of the polymer makes to permeability of the coating is still quite profound.

As illustrated in Figures 3-5, the final drug release profiles of a compression coating can be modified by changing the concentration of a porosity modifier even when using a micronized version of the insoluble polymer.

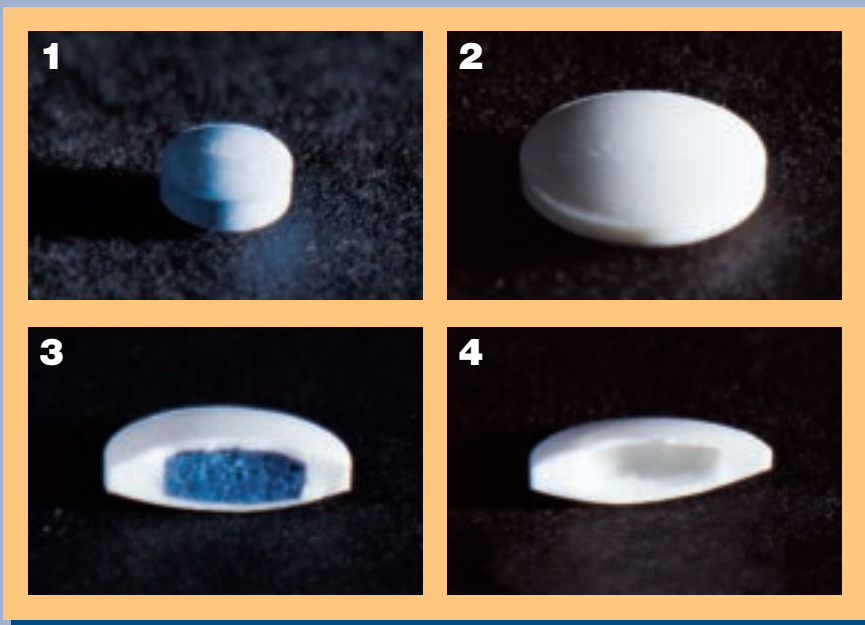
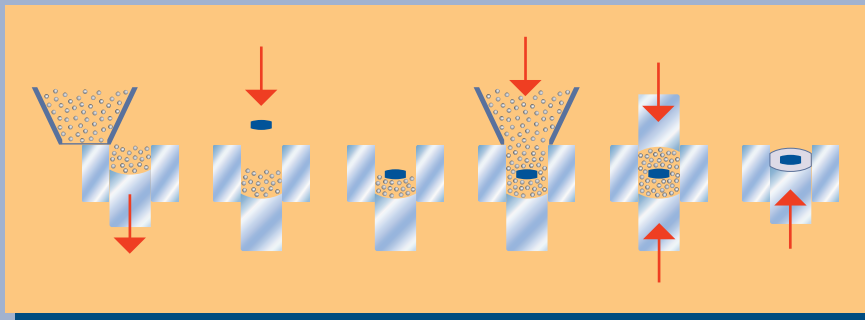
Conclusions

When developing a controlled release dosage form with compression coatings, it has been well demonstrated that the physicochemical properties of added film modifiers can be chosen to yield the desired release profile. The work presented here suggests that another variable that the formulation can manipulate is the particle size of the polymeric film former. The finer the particle size, the less residual porosity will remain in the coating due to efficient consolidation of the polymer powder. This in turn may allow the formulator to use fillers/modifiers not previously available to him to fine tune his release profile.

References

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Compression Coating Process



- 1.) Compressed drug core (dyed blue for visualization)
- 2.) Compression coated tablet
- 3.) Cross section of compression coated tablet
- 4.) Cross section of tablet, post-drug dissolution

Figure 1 – Influence of EC Grade

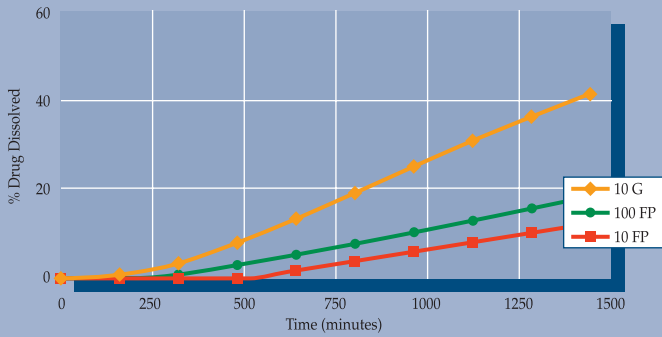


Figure 2 – Ethylcellulose + 50% A-TAB

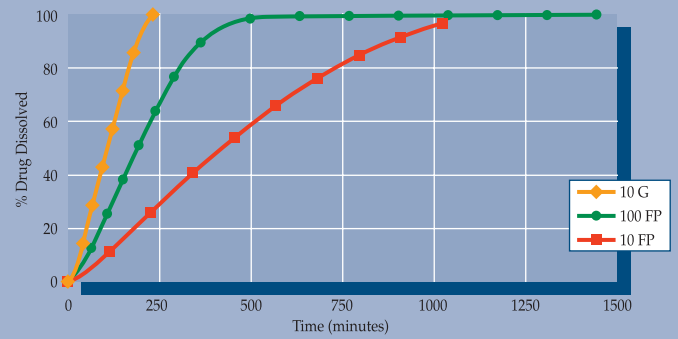


Figure 3 – 10 Granular (250 micron)

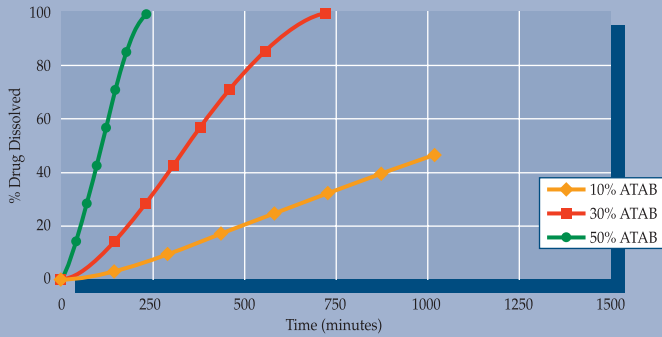


Figure 4 – 100 FP (40 micron)

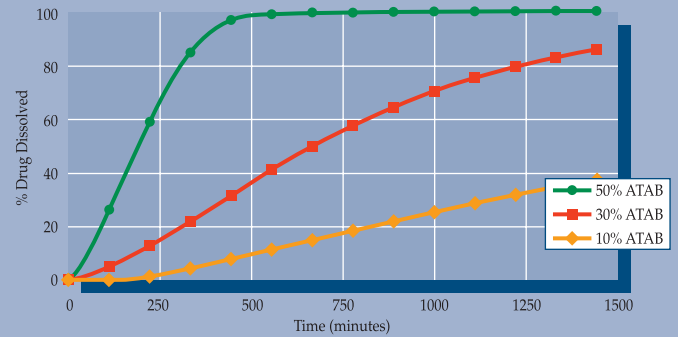
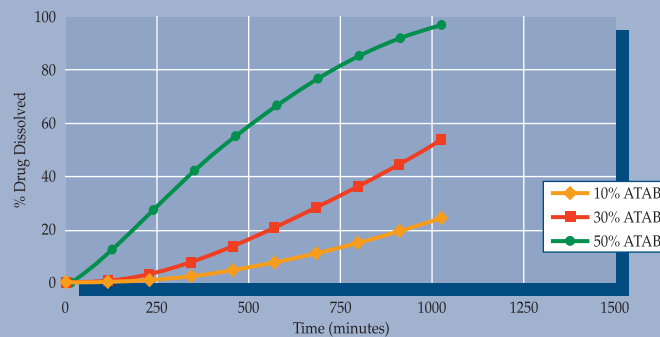


Figure 5 – 10 FP (5 micron)



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