# The Effect of Film Coating and Storage Conditions on the Performance of Metformin HCl 500 mg Extended Release Hypromellose Matrices

## ABSTRACT SUMMARY

This study investigates the influence of three film coating systems on the performance of metformin HCl (500mg) extended release (ER) hypromellose matrices stored under different conditions up to 12 months.

Keywords: metformin, hypromellose, extended release, film coating, stability

## INTRODUCTION

There is a growing interest for extended release oral drug delivery systems, especially in the design of challenging formulations such as those with high dose, highly water soluble actives.

Metformin HCl is prescribed for the treatment of non-insulin dependent diabetes mellitus.[1] The primary benefit of ER preparations of this active compared to an immediate release (IR) formulation is that a more uniform maintenance of drug blood plasma concentration is achieved, thus potentially avoiding undesirable peaks and troughs associated with multiple IR preparations and the loss of disease control these fluctuations represent. The development of an ER metformin HCl 500 mg formulation using hypromellose (hydroxypropyl methylcellulose, HPMC) was previously investigated.[2] Consistent and robust tablets were produced by direct compression (DC), in which the inclusion of 30% w/w polymer resulted in a drug release profile statistically similar to that of Glucophage XR.

A large proportion of the tablets produced globally are film coated, for a variety of reasons including aesthetics, taste or odour masking, enhanced mechanical strength, improved swallowability; and/or protection from environmental conditions (e.g. moisture, light, air). It is therefore surprising that there are few studies reported in the literature on film coated hypromellose matrices and the enhanced characteristics obtained.[3] However, in this study the influence of three aqueous film coating systems on the performance and stability of metformin HCl ER HPMC tablets, stored under two different ICH conditions for up to 12 months, is investigated.

## EXPERIMENTAL METHOD

Tablet formulation contained 50.0% w/w metformin HCl (Ferico Labs), 19.0% w/w microcrystalline cellulose (MCC), 0.5% w/w fumed silica (Aerosil 200, Degussa) and 0.5% w/w magnesium stearate (Peter Greven). Hypromellose (METHOCEL™, premium cellulose ethers, K100M CR, International Flavors and Fragrances Inc.) was included as a matrix former at 30.0% w/w. MCC and fumed silica were passed through a 500 Ìm sieve prior to use.  All ingredients, with the exception of magnesium stearate, were blended in a Turbula mixer

for 5 minutes. Magnesium stearate was then added and the formulation was mixed for an additional 2 minutes.

Tablets with a target weight of 1000 mg and a target breaking force of 20 kp were manufactured using an instrumented 10 station rotary press (Piccola, Riva), fitted with 7 x 18 mm caplet tooling. Manufactured matrices were coated in a 38 cm side-vented pan (Labcoat II-X, O'Hara) using a Schlick spray gun with three Colorcon IR film coating systems:

- Opadry® II, high performance film coating system, (standard) to 4% weight gain,
- Opadry II (85 series) to 4% weight gain, and
- Opadry® tm, taste mask film coating system, to 5% weight gain

Table 1 shows the coating parameters utilized.

***Table 1. Coating Parameters***

| | **Opadry II (standard)** | **Opadry II (85 series)** | **Opadry tm** |
|---|---|---|---|
| Inlet temperature (ºC) | 55 | 55 | 55 |
| Exhaust Temperature (ºC) | 41 | 42 | 42 |
| Bed Temperature (ºC) | 42 | 42 | 42 |
| Spray Rate (g/min) | 15 | 14 | 14 |
| Atomizing Pressure (bar) | 2.0 | 2.0 | 2.0 |
| Fan Pressure (bar) | 1.5 | 1.5 | 1.5 |
| Pan Speed (rpm) | 18 | 18 | 18 |
| Airflow ($m^3$/h) | 250 | 250 | 250 |

Samples of uncoated and coated tablets were stored in Securitainer polypropylene jars (Jaycare) at 30ºC/65% RH and 40ºC/75% RH for up to 12 months. Tablet weight, mechanical strength and drug release were determined after 1, 3, 6 and 12 months storage.

Dissolution tests were conducted using an USP compliant bath (Sotax), Apparatus II (paddle method) with sinkers in 1000 mL of purified water (37 ± 1°C) at 100rpm. A dual beam spectrophotometer (Perkin Elmer), fitted with 0.1 mm matched quartz cells, was used for the detection of metformin HCl at a wavelength of 233 nm.

## RESULTS AND DISCUSSIONS

Metformin HCl 500mg ER HPMC matrices displayed low weight variation (less than 1%) and good mechanical strength (19.9 ± 2.2kp). The application of all three film coatings resulted in an increase in tablet breaking force values (Figure 1) and no significant changes to the drug release profile (Figure 2). The rate of metformin HCl dissolution did not change after 1, 3, 6 and 12 months storage at both conditions (Figures 3-6).

***Figure 1. Tablet Breaking Force***

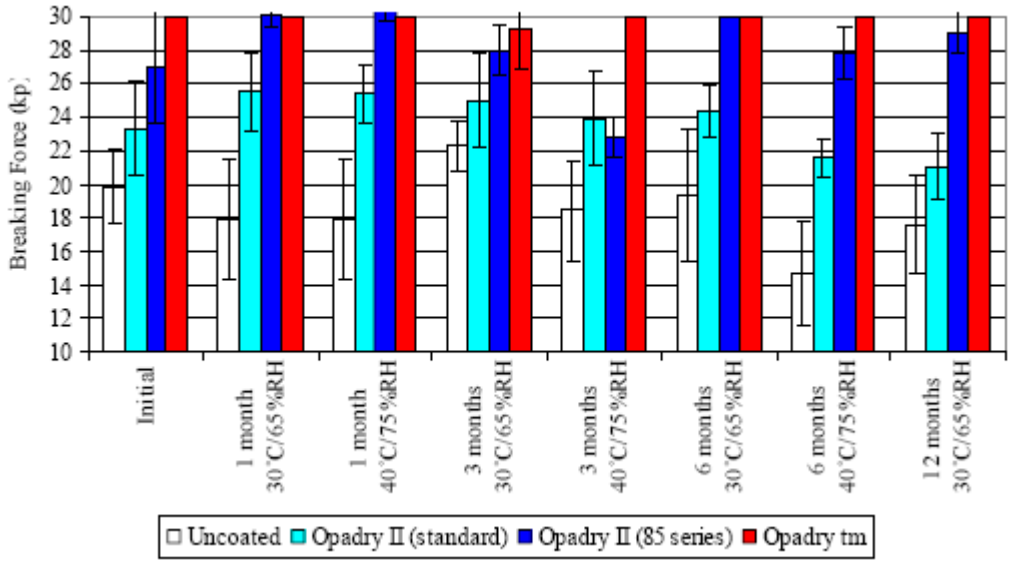



***Figure 2. Drug Dissolution from Uncoated and Coated Tablets – INITIAL***

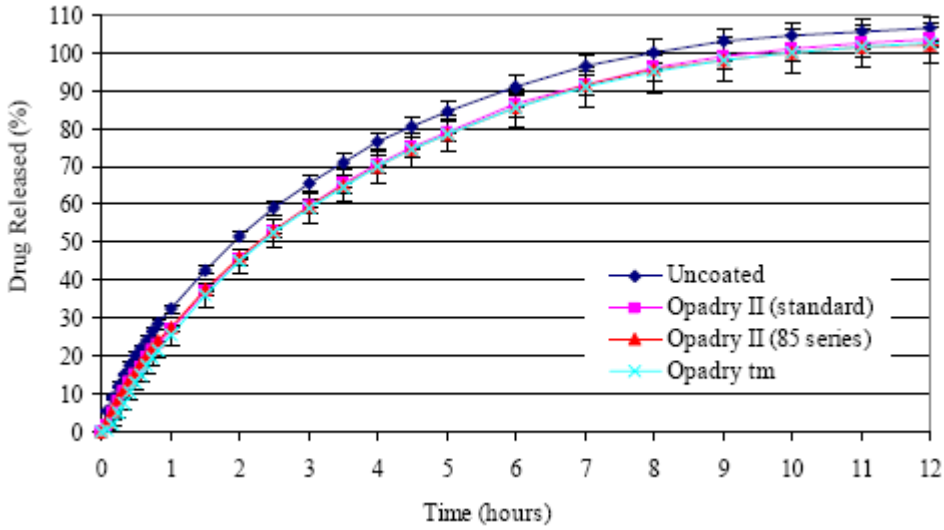



***Figure 3. Drug Dissolution from Uncoated Tablets on Storage***

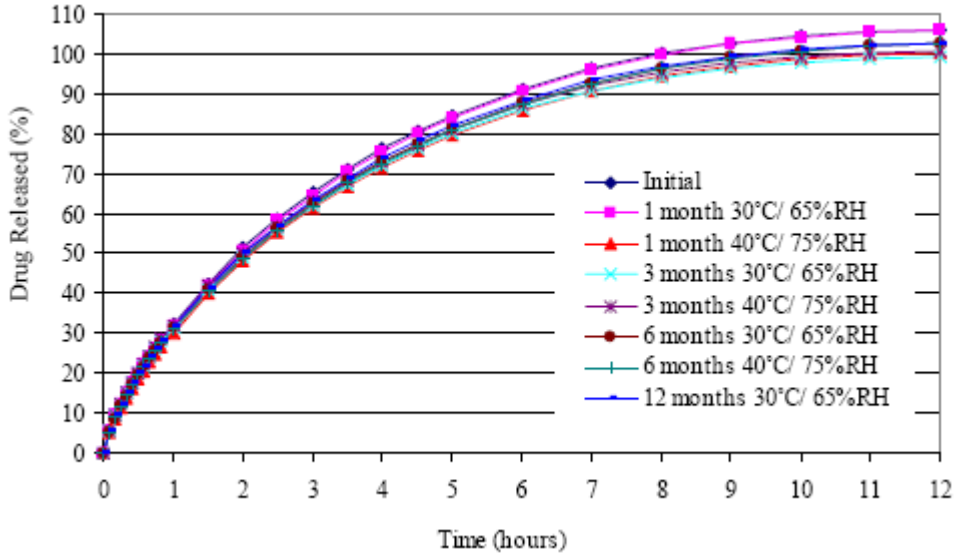


*Figure 4. Drug Dissolution from Coated with Opadry II (Standard) Tablets on Storage*

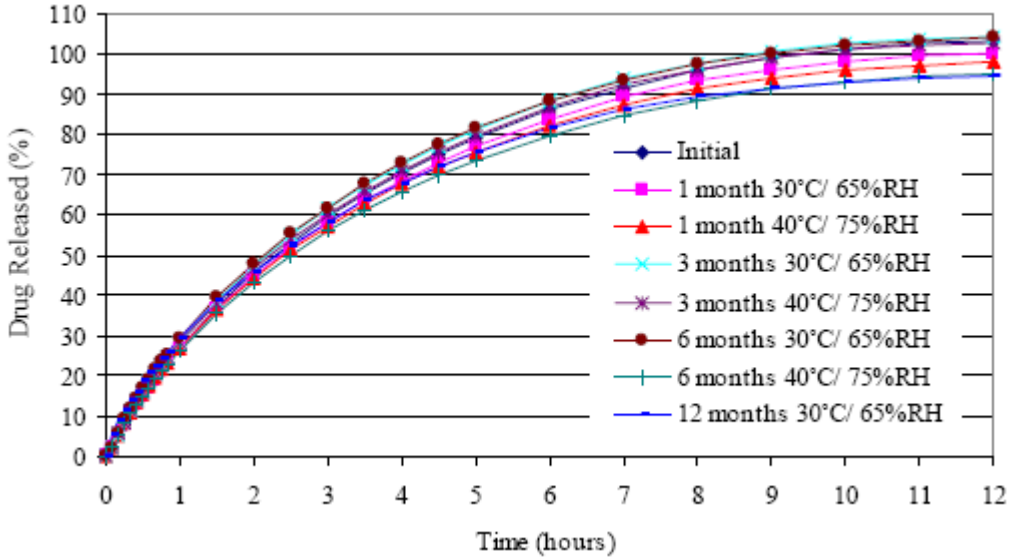



*Figure 5. Drug Dissolution from Coated with Opadry II (85 Series) Tablets on Storage*

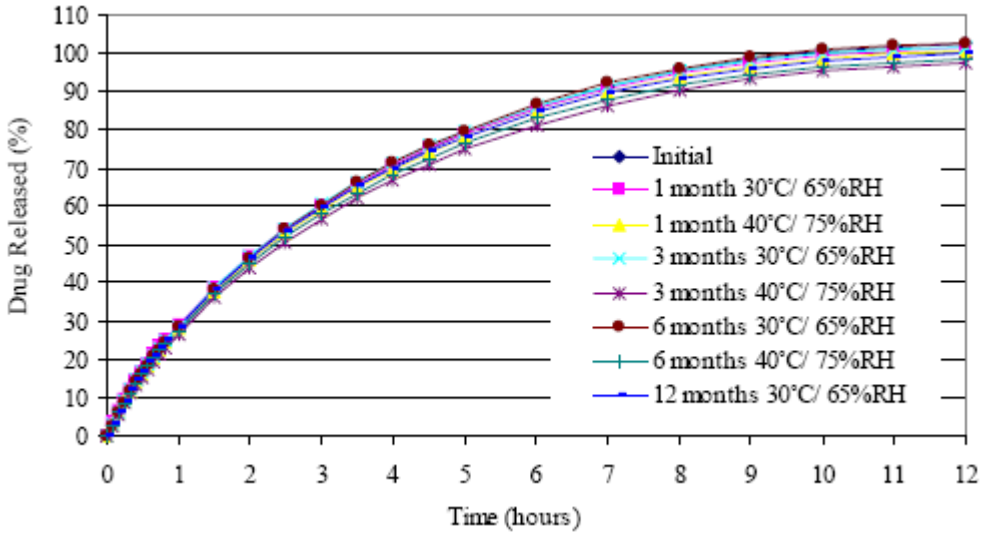
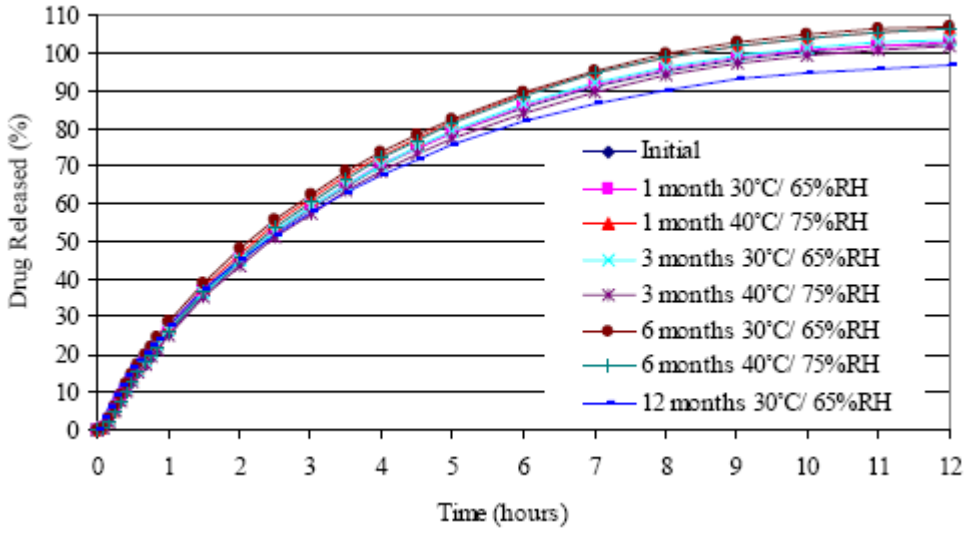



*Figure 6. Drug Dissolution from Coated with Opadry tm Tablets on Storage*



## CONCLUSION

Application of all three Colorcon immediate release film coating systems resulted in a significant increase in mechanical strength of metformin HCl 500 mg hypromellose ER tablets and no change to the drug dissolution. Uncoated and coated matrices exhibited consistent release rates at all storage conditions after 1, 3, 6 and 12 months.

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3. Levina M., Influence of fillers, compression force, film coatings and storage conditions on performance of hypromellose matrices, Drug Del. Tech. 4(1) (2004) 34-42.



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