

# The Utility of Ultra-High Viscosity Hypromellose in Extended Release Matrix Formulations

Raxit Y. Mehta<sup>1</sup>, Sandip B. Tiwari<sup>1</sup>, Tim Cabelka<sup>2</sup>, Harold Bernthal<sup>2</sup>, Thomas P. Farrell<sup>1</sup>, and Ali Rajabi-Siahboomi<sup>1</sup>

<sup>1</sup>Colorcon, Inc., 275 Ruth Road, Harleysville, PA 19438, <sup>2</sup>The Dow Chemical Company, Midland, MI 48674, [www.colorcon.com/about/contact](http://www.colorcon.com/about/contact)



## Abstract Summary

Hypromellose (HPMC) high viscosity grades K100M and K200M were used to formulate ketoprofen and metformin HCl extended release (ER) tablets. The effects of these two viscosity grades of HPMC on drug release profiles and tablet properties were investigated using 20% to 30% polymer levels. Results indicated that HPMC viscosity did not affect the drug release profiles at either polymer level. The use of HPMC K100M resulted in similar or superior tablet properties compared to HPMC K200M.

## Introduction

HPMC is the most widely used rate controlling polymer in hydrophilic matrices for oral ER drug delivery, providing robust formulations and simplified production. The viscosity grade of HPMC influences drug release profiles by modifying the diffusion and erosion behavior of the matrix system.<sup>1,2</sup> It is generally accepted that drug dissolution from tablets is slower when higher viscosity grades of HPMC polymers are used. However, there have been several instances in the literature that report no difference in release for different viscosity grades. For example, it has been reported that the release rate of theophylline, a slightly soluble drug, was similar from matrices of HPMC K15M and K100M.<sup>3</sup> The relative utility of high viscosity grade of HPMC, for example K100M and K200M, in formulating extended release matrices has not been widely reported. The present study compares the effect of two high viscosity grades of HPMC, K100M and K200M, on drug release of a slightly soluble drug: ketoprofen, and a freely soluble drug: metformin HCl.

## Experimental Methods

Formulations (**Table 1**) were prepared by blending sieved API, filler (microcrystalline cellulose or lactose), HPMC (BENECEL K200M PH-CR or METHOCEL™, premium cellulose ether, K100M CR) and an optional glidant (colloidal silicon dioxide). The powder blends were lubricated with magnesium stearate and compressed using an instrumented rotary tablet press at target

## Experimental Methods (cont'd)

weights of 1000 mg for metformin HCl and 400 mg for ketoprofen. Tablets were produced at compression forces of 10, 15, 20 and 25 kN. Tablet properties were measured using an automated tablet tester (Multicheck, Erweka, Germany). Tablet breaking forces, ejection forces, weight variation, thickness and friability, were determined at each compression force. Tablets produced at 20 ± 2 kN were used for dissolution testing. Drug release for metformin was measured spectrophotometrically using USP Apparatus II, 100 rpm with sinkers and 1000 mL of deionized water. Ketoprofen release was measured spectrophotometrically using Apparatus II with modified hanging basket, 50 rpm and 900 mL of 0.05 M phosphate buffer, pH 5.8.

Table 1. Extended Release Matrix Formulations of Metformin HCl and Ketoprofen

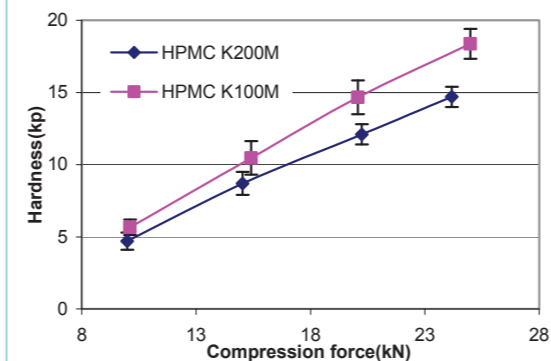
Ingredients	% Composition (w/w)	
Metformin HCl (Wanbury, India)	50	-
Ketoprofen (Spectrum Chemicals, USA)	-	20
BENECEL K200M PH-CR (Hercules Doel BVBA, Belgium) or METHOCEL K100M Premium CR (The Dow Chemical Company, USA)	20 or 30	30
Microcrystalline cellulose (Emcocel 90M, JRS Pharma LP, USA)	29 or 19	-
Lactose monohydrate (Impalpable grade, Sheffield Products, USA)	-	49
Colloidal silicon dioxide (CAB-O-Sil MSP, Cabot Corp., USA)	0.5	-
Magnesium Stearate (Mallinckrodt, USA)	0.5	1
Total	100	100

## Results and Discussion

All the tablet formulations had low weight variation (<1.8% RSD) and breaking forces ranging from 5-22 kP. HPMC K100M and K200M formulations at 20% to 30% polymer levels exhibited similar friability at higher compression forces (>10 kN). However, at lower compression force (10 kN), use of HPMC K200M resulted in higher friability (2.5%-6.5%) compared to HPMC K100M formulations (1.5%-2.0%). At higher compression forces (>15 kN), the use of HPMC K100M resulted in superior mechanical strength of the tablets (Figure 1). The differences in friability and mechanical strength of HPMC K100M and K200M tablets may be attributed to their respective physical differences such as particle size and shape.

## Results and Discussion (cont'd)

Figure 1. Breaking Force vs. Compression Force Profile for Metformin HCl 500 mg ER Tablets (30% Polymer) (Mean ± SD, n=10)



Ketoprofen and metformin HCl formulations with HPMC K100M and K200M showed similar drug release profiles at polymer levels of 20% or 30%. The similarity factor ( $f_2$ ) for ketoprofen and metformin HCl formulations was 81 and 97, respectively, at 30% polymer level (Figure 2 & 3). Even at 20% polymer level, metformin formulations with HPMC K100M and K200M showed similar drug release profiles ( $f_2 = 72$ , Figure 4). This suggests that these two polymers have similar diffusion and erosion properties in the formulations studied here. There is no apparent benefit of using ultra-high viscosity HPMC (K200M) versus K100M for designing ER formulations for high dose, high solubility APIs like metformin HCl, or for slightly soluble APIs like ketoprofen. These data confirm those reported in the literature, where it has been postulated that a threshold effect may be attained at a specific viscosity grade of HPMC for a drug. In both cases here, the threshold has been reached at K100M.

Figure 2. Dissolution Profile of Ketoprofen 80 mg ER Tablets (30% Polymer) (Mean ± SD, n = 6)

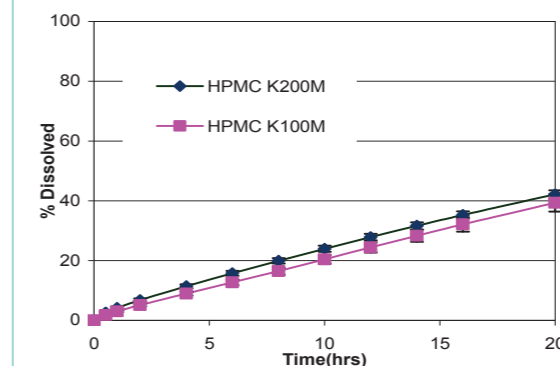


Figure 3. Dissolution Profile of Metformin HCl 500 mg ER Tablets (30% Polymer) (Mean ± SD, n = 6)

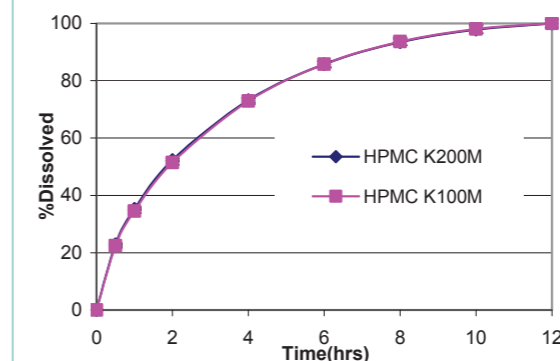
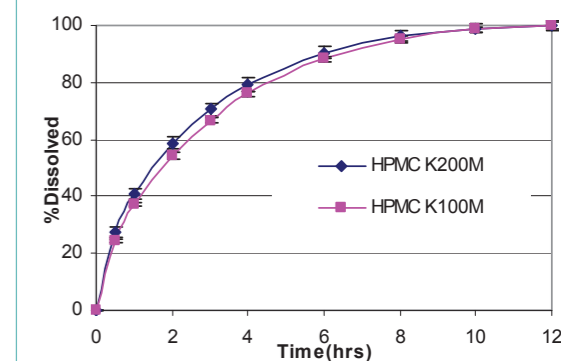


Figure 4. Dissolution Profile of Metformin HCl 500 mg ER Tablets (20% Polymer) (Mean ± SD, n = 6)



## Conclusions

The use of ultra-high viscosity HPMC K200M in an extended release matrix system of a slightly soluble drug or a freely soluble drug did not show any advantage in drug release retardation over the more widely used viscosity grade (ie, METHOCEL K100M). Indeed, the use of METHOCEL K100M resulted in similar or superior tablet properties and release profiles compared to HPMC K200M.

## References

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