Evaluation of the Effect of Hydro-alcoholic Media on Textural and Rheological Characteristics of Hypromellose Matrices (HPMC)

ABSTRACT SUMMARY

The effect of hydro-alcoholic media on the textural and rheological behavior of hypromellose matrices was investigated. In general, hydro-alcoholic media had little effect on textural properties of the matrices while rheological behavior of hypromellose powder/blends depended on the ethanol content of the media.

INTRODUCTION

Hydrophilic matrices are widely used in the formulation of extended release (ER) systems, with hypromellose being the material of choice as the rate-controlling polymer. Recently, the FDA issued an alert regarding the effect of alcohol on drug release from an ER dosage form (alcohol-Palladone interaction). Rapid hydration of the polymer and formation of a protective gel layer around the matrix when ingested is critical in the performance of hydrophilic matrices. Therefore, the objective of this study was to investigate the effect of hydro-alcoholic solutions on HPMC matrix systems. Textural and rheological properties of the polymer ad matrices were investigated to predict matrix integrity.

EXPERIMENTAL METHODS

HPMC (METHOCEL™, premium cellulose ethers, K100LV Premium CR) was used as a matrix-forming polymer. Felodipine was selected as a model drug, which is practically insoluble in water yet is freely soluble in ethanol.[1&2] Textural and rheological analyses were carried out in hydro-alcoholic media with various ethanol contents, 0, 5, 20, and 40% (v/v). The medium without alcohol was either deionized water for neat METHOCEL™ K100LV or USP phosphate buffer system (PBS, pH 6.5), containing 1% sodium lauryl sulfate (SLS) for felodipine containing ER matrices.[3]

TEXTURAL ANALYSIS

Two batches of matrix tablets were manufactured, Formulation A contained METHOCEL™ only, and Formulation B was a felodipine ER matrix, as shown in Table 1.

Table 1. Composition of Formulations A & B

	mg/tablet	
Ingredients	**Formulation A**	**Formulation B**
Felodipine	-	5.0
Hypromellose (METHOCEL K100LV Premium CR)	297.0	74.0
Lactose (FastFlo)	-	119.0
Fumed Silica (Aerosil 200)	1.5	1.0
Magnesium Stearate	1.5	1.0
Total	300	200

Tablets were allowed to hydrate inside sinkers in 500mL of media, maintained at 37°C in a USP compliant dissolution bath using apparatus II at 100rpm. The tablets were hydrated in the hydro-alcoholic media for the first 2 hours and were then transferred to their respective non-alcoholic media. The tablets were removed at pre-determined time intervals (0-4 hours) and subjected to textural analysis using a texture analyzer (Texture Technologies Inc. US), equipped with a 2-mm round-tipped probe. The force-displacement profiles were used to compare the textural properties of the tablets.

RHEOLOGICAL ANALYSIS

Rheological behavior of METHOCEL™ K100LV and the powder blend of felodipine formulation in hydroalcoholic media was characterized using a TA rheometer (AR-G2, TA Instruments, US), equipped with a rotational concentric cylinder. The samples were prepared by dispersing the respective powder in various media to achieve a 2% (w/v) concentration of the polymer. Prior to analysis, and depending on the viscosity grade, the hydrated METHOCEL™ samples were allowed to deaerate for 2, 24 and 48 hours for K100LV, K4M and K100M, respectively. Viscosity shear stress profiles over a shear rate of 1.5-1500 sec-1 were used for comparing the rheological properties of the samples.

RESULTS AND DISCUSSION

Figure 1 shows an example of typical textural profiles for Formulation A in 5% (v/v) ethanol. Penetration force was calculated for each tablet as the mean force detected by the probe from the point that the probe reaches the tablet up to the first encountered peak on the profile, as shown in Tables 2 and 3.

Figure 1. Typical Textural Profiles of Tablets

(e.g. tablets of formulation (A) in 5% (v/v) ethanol shown below)

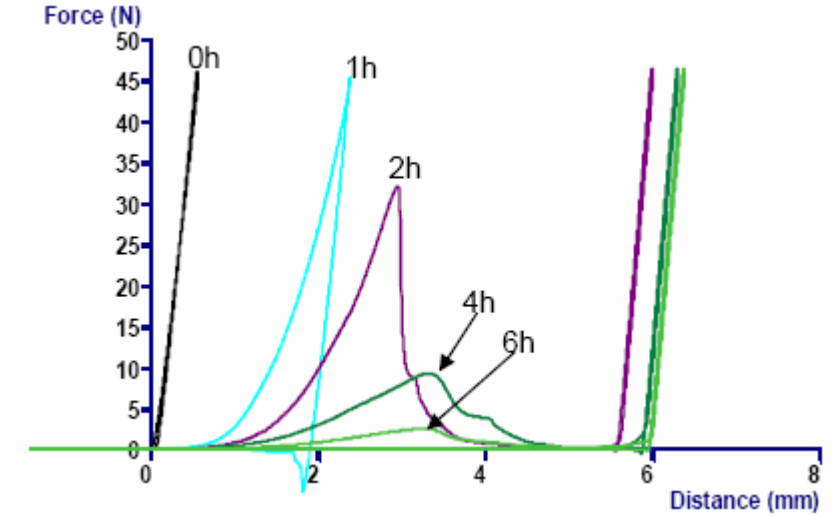


Table 2. Comparison of Penetration Force (N) for Tablets of Formulation (A) in Different Media

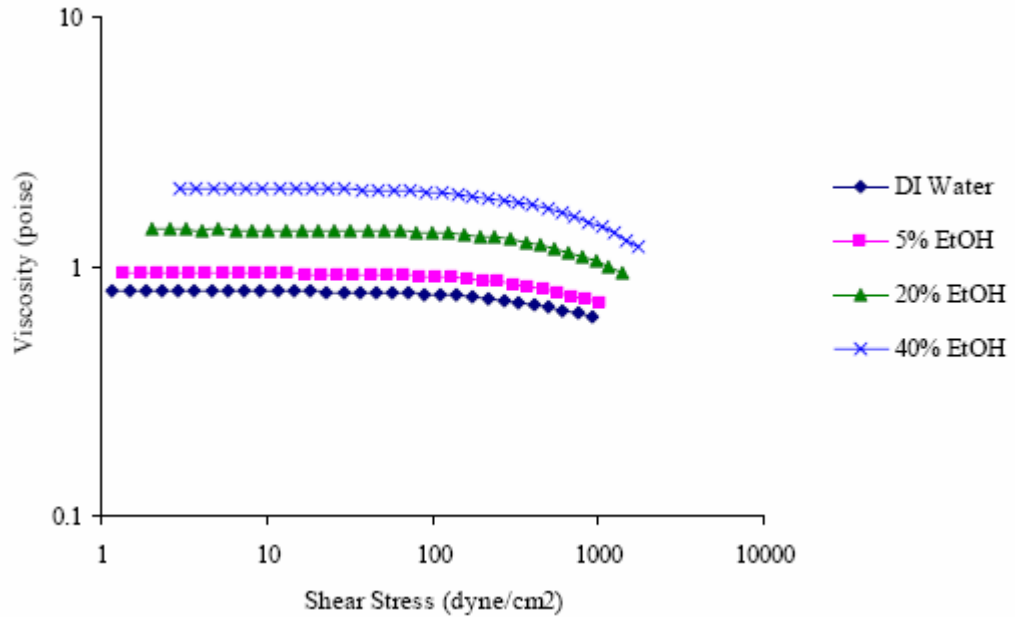
Time (h)	DI water	5% Ethanol	20% Ethanol	40% Ethanol
0	20.8 ± 0.2	20.8 ± 0.2	20.8 ± 0.2	20.8 ± 0.2
1	11.0 ± 0.4	11.0 ± 0.5	12.5 ± 0.4	12.7 ± 0.3
2	7.8 ± 1.0	8.1 ± 0.3	8.7 ± 1.1	6.9 ± 0.6
4	2.7 ± 0.6	3.0 ± 0.2	4.0 ± 0.1	3.4 ± 0.2

Table 3. Comparison of Penetration Force (N) for Tablets of Formulation (B) in Different Media

Time (h)	PBS (pH6.5)/SLS	5% Ethanol	20% Ethanol	40% Ethanol
0	22.5 0.1	22.5 0.1	22.5 0.1	22.5 0.1
1	8.5 0.8	9.0 0.7	9.9 0.4	11.8 0.2
2	3.6 1.2	5.7 1.5	6.8 0.4	6.4 0.3
4	0.4 0.0	0.2 0.0	0.7 0.1	0.7 0.2

These values are an indication of tablet resistance to the probe penetration. In general, as the hydration time increases, the gel strength decreases; hence, the force needed for the probe to penetrate the tablet is reduced. Tablets from Formulation A in water exhibited gradual selling over time, whereas tablets from Formulation B in phosohate buffer and SLS appeared to undergo faster erosion, (indicated by smaller penetration forces in Table 3 with time). This could be due to the smaller tablet size of Formulation B, lower polymer content and the presence of other ingredients in these tablets which contribute to faster gel erosion. However, an increase in the ethanol content of the media appeared to cause higher axial swelling (data not shown) and an increased resistance for tablets of Formulation B, where the penetration force values seemed to be more comparable for tablets of Formulation A. Meanwhile, the rheological data showed that the higher ethanol contents of the media led to an increase in the viscosity of all samples (Figure 2), which might be due to the reduced volume of water in the hydro-alcoholic mixture or dielectric constant of the hydro-alcoholic media, leading to the formulation of new bonds/structures.[4]

Figure 2. Rheological Behavior of METHOCEL™ K100LV in Various Media*



**same trend was seen for felodipine blends*

CONCLUSIONS

The presence of ethanol in the media did not affect the textural properties of tablets containing only METHOCEL™ K100LV CR. Felodipine ER tablets eroded faster than METHOCEL™ K100LV CR tablets which may be due to their composition and smaller size. The rheological data showed that an increase in the ethanol content of the media led to higher viscosity for all samples. Overall, it may be concluded that when a hypromellose matrix is exposed to the hydroalcoholic media, gel formation and thus integrity of the matrix is not significantly affected by the level of ethanol up to 40% (v/v).

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REFERENCES

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2. Physician's Reference Desk, 2006
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