Comparative Study of High Viscosity Grade of Hydroxypropyl Cellulose (HPC-H) for Hydrophilic Matrix, Sustained Release Formulation

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SUMMARY

Hydrophilic matrix is widely used for oral sustained release drug delivery formulation. As a controlling material for this application, higher viscosity grade of Hypromellose (HPMC) is commonly used and use of hydroxypropyl cellulose (HPC) is not so common. In this study, we carried out the comparison of tablet properties and drug release for high viscosity grade of HPC and HPMC in formulations prepared by direct compression and wet granulation methods using theophylline as model drug. As a result of the comparison, HPC-H was found to have equivalent tablet properties and control release performance to HPMC while its viscosity was much lower.

INTRODUCTION

Hydroxypropyl Cellulose (HPC) is considered as an effective controlled release (CR) material since it is a hydrophilic polymer which swells and becomes a state of hydro-gel in water, and releases drug slowly with dissolution and diffusion. In this study, we evaluated tablet properties and drug release for high viscosity grade of HPC compared to Hypromellose (HPMC), which is similarly a hydrophilic polymer and widely used as CR material for hydrophilic matrix. Formulations were prepared by both direct compression (DC) and wet granulation (WG) methods using theophylline as model drug.

EXPERIMENTAL METHODS

CR Materials

CR Materials	Viscosity* (mPa*s)	D_{50} (μm)
HPC-H (Nippon Soda Co., Ltd.)	3040	150
HPC-H-FP (Nippon Soda Co., Ltd.)	3090	56
HPMC 4000 (Metolose 90SH-4000SR, Shin-Etsu Chemical Co., Ltd.)	4040	46
HPMC 100000 (Metolose 90SH-100000SR, Shin-Etsu Chemical Co., Ltd.)	90200	48

* 2% aqueous solution at 20℃

Tablet Formulation

Ingredients	Composition (%)
Theophylline (Shiratori Pharmaceutical Co., Ltd.)	50
Microcrystalline Cellulose PH-101 (AVICEL PH-101, FMC Corporation)	19
CR Materials(HPC or HPMC)	30
Silica (Sylysia350, Fuji Silysia Chemical, Ltd.)	0.5
Magnesium Stearate (Wako Pure Chemical Industries, Ltd.)	0.5

Preparation of Direct Compression (DC) Tablet

Powder for tablet was prepared by dry-mixing of materials except Magnesium Stearate in PE bag for 3 minutes. This was followed by addition of Magnesium Stearate and further dry-mixing for 30 seconds.

Laboratory scale rotary tablet press machine (VELA5 0312SS2MZ, KIKUSUI SEISAKUSHO Ltd. was used to compress tablet at 10kN of compression force. Tablet weight was 200mg and its diameter was 8mm.

Preparation of Wet Granulation (WG) Tablet

Wet granulation process was carried out in high shear mixer granulator (Type FS-GS-5, Fukae Pawtec Co., 500g Scale). All powder except Silica and Magnesium Stearate were added to the granulator and dry blended for 1 minute. Granulation was operated for 4 minutes with pouring 30g of D.I. water. The impeller and chopper were operated at constant speeds of 400 rpm and 1500 rpm respectively. The granules were pre-dried and milled using 3mm grated screen, followed by drying at 52℃ with fluidized bed system (FL-LABO, FREUND Co., Ltd.) and milling using 1 mm grated screen. Powder for tablet was prepared by dry-mixing granules of 30 mesh pass and silica in PE bag for 3 minutes. This was followed by addition of Magnesium Stearate and further dry-mixing for 30 seconds.

Tablet was prepared at 15kN of compression by the same tablet machine as DC method. Tablet weight was 200mg and its diameter was 8mm.

Measurement of Tablet Properties and Dissolution

Tablet hardness of 10 tablets per lot was measured by ERWEKA model TBH28 tablet tester. Friability was measured according to JP method. Release of theophylline was also measured according to JP method and concentration of theophylline at each time point was determined by measurement of absorbance at 271nm with UV spectrophotometer.

RESULTS AND DISCUSSION

Table 1: Comparison of Tablet Properties

	Hardness (kgf)		Friability (%)	
Method	DC	WG	DC	WG
HPC-H	-	14.8	-	0.19
HPC-H-FP	16.6	15.8	0.15	0.18
HPMC 4000	11.9	15.6	0.10	0.12
HPMC 100000	14.3	16.5	0.14	0.11

Comparison of tablet property is as shown in Table 1. In the case of DC method, tablet prepared by HPC-H-FP showed better properties than HPMC. On the other hand, hardness of tablet prepared by HPC-H was slightly lower than the others in the case of WG method. In the comparison of preparation method or CR material, much difference of friability was not seen.

RESULTS AND DISCUSSION (Continued)

Fig. 1: Comparison of Drug Release from HPC tablet (DC vs WG)

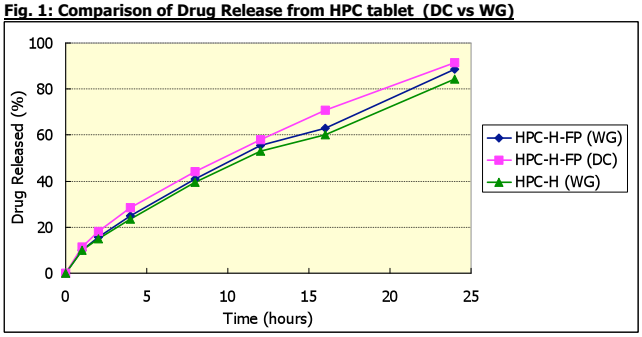


Fig. 2: Comparison of Drug Release from DC Tablet

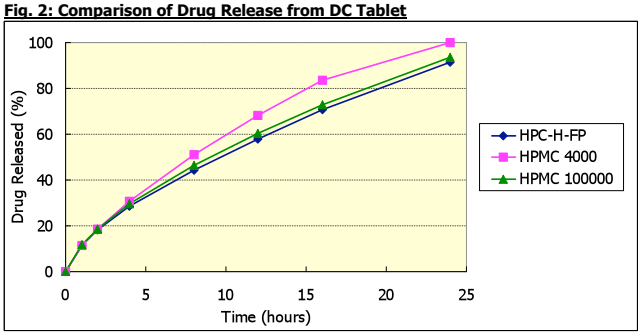
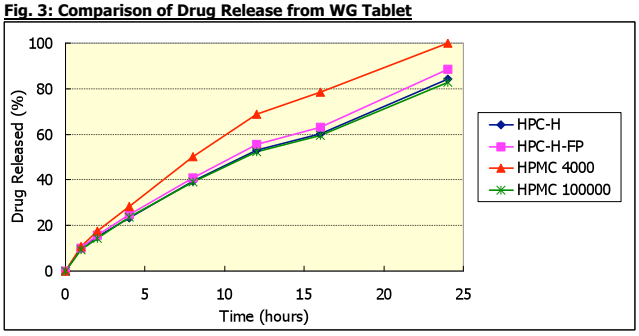


Fig. 3: Comparison of Drug Release from WG Tablet



Comparison of drug release is as shown in Fig. 1-3. In comparison of preparation method, the result showed drug release from WG was sustained a little more than DC. The reason seems formation of hydrophilic matrix of granule level is more effective to sustain drug release than the one of tablet level. (Fig.1)

In the case of DC method, HPC-H-FP sustained drug release more than HPMC 4000, and showed equivalent release control performance to HPMC 100000 while its viscosity was much lower. (Fig. 2)

In the case of WG method, much difference was not seen in comparison of drug release from tablet prepared by HPC-H and HPC-H-FP. Also, both HPC-H and HPC-H-FP showed equivalent control release performance to HPMC 100000. Drug release from tablet prepared by HPMC 4000 was much faster than the others. (Fig.3)

CONCLUSIONS

(1) HPC-H-FP was found to provide better tablet hardness than HPMC in the case of DC method.
(2) It was suggested that hydrophilic matrix of granule level was more effective to sustain drug release than tablet level.
(3) HPC was found to sustain drug release more effectively than HPMC in the case of the equivalent viscosity.
(4) In both DC and WG method, HPC-H was found to have equivalent control release performance to HPMC 100000 while its viscosity is much lower.

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