Influence of soluble and insoluble excipients on drug release from hydroxypropyl methylcellulose tablets

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Objective

The objective of this study is to investigate the influence of soluble and insoluble excipients on drug release from hydroxypropyl methylcellulose (HPMC) tablets.

Methodology

Benecel K4M PH CR (HPMC) was used as the matrix former. Lactose (X1) and ethyl cellulose (X2) were selected as soluble and insoluble excipients. Naproxen and theophylline were used as the model drugs. Tablets were made from the dry blend of the drug and polymer according to the composition in Table 1. Dissolution tests were carried out in USP Apparatus II using phosphate buffer at pH 6.8. Mean dissolution times for 50% drug release (MDT-50) were calculated from the dissolution data and the dissolution profiles were compared using the similarity factor (f2). SEM photomicrographs of the tablets containing highest levels of soluble and insoluble excipients were taken after 12 hours of dissolution.

Results & Discussions

Figures 1 and 2 show the dissolution profiles of various formulations containing theophylline and naproxen respectively. In presence of highest level of ethyl cellulose in HPMC matrices, the f2 values for theophylline and naproxen release are 53.2 and 51.6 signifying a low degree of similarity in their release profiles to that ones without ethyl cellulose (batch F1 Vs F3). Presence of lactose at its highest level in the matrix, however, exhibits f2 values of 69.4 and 49.6 for theophylline and naproxen release profiles, respectively (batch F1 Vs F7). This dissimilarity in release of poorly soluble drug is attributed to the channeling and hydrophilization effects of the soluble excipients.

The MDT-50s are 3.12, 4.08, and 2.91 hours for theophylline tablets containing HPMC alone, HPMC and an insoluble, and HPMC and a soluble excipient, respectively; while those values for naproxen containing tablets are 9.2, 12.1, and 6.3 hours (Table 1). Readily soluble drugs rapidly escape from the periphery of the matrix leaving channels for the rest, resulting in an overall faster release. Presence of soluble excipients does not appreciably change the release behavior of the soluble drugs. In case of poorly soluble drugs like naproxen, besides creating channels, the soluble excipients hydrophilize and enhance wetting of the drug resulting in significant improvement in dissolution.

There are no apparent differences in the photographic images before dissolution of the tablets containing different excipients (Figures 3 and 5). After 12 hours of dissolution, however, the photographs exhibit significant difference between the tablets containing soluble and insoluble excipients (Figures 4 & 6). Insoluble excipient in the matrix moves along with the moving boundary and remains in the gel impeding drug release. On the contrary, the soluble excipient readily goes into solution leaving channels for the drug to escape from the matrix. SEM photomicrographs of tablets containing soluble excipient revealed pores with increase in diameter, while tablets with insoluble excipient did not make distinguishable pores for the drug to escape from the matrix (figures 7, 8, & 9). The difference in drug release among the tablets containing excipients such as lactose and ethyl cellulose can be attributed to the excipients solubility.

Conclusions

The presence of soluble excipient results in a higher rate and a greater extent of drug release than the insoluble excipient from the HPMC matrix. The soluble excipient is believed to behave as a channeling as well as a wetting agent for the drug particle facilitating its dissolution, while the insoluble excipient remain in the matrix or move along with the moving gel boundary without contributing to the drug release process.

Batch Code	Variable levels in coded form*		Theophylline			Naproxen		
	X1	X2	% released	MDT-50	*f2*	% released	MDT-50	*f2*
F1	-1	-1	89.6	3.12	-	52.1	9.2	-
F2	-1	0	84.7	3.44	71.3	49.9	9.3	91.2
F3	-1	1	81.5	4.08	53.2	44.6	12.1	51.6
F4	0	-1	91	3.05	73.8	58.1	7.6	65.4
F5	0	0	88.7	3.31	91.7	55	8.8	79.9
F6	0	1	88.4	3.68	95.6	50.7	9.6	90.9
F7	1	-1	94.1	2.91	69.4	63.9	6.3	49.6
F8	1	0	90.9	3.35	84.1	61.1	7.3	58.2
F9	1	1	86.3	3.92	74.6	56.7	8.7	74.3

Coded Values*	Actual Values (mg)	
	X1	X2
-1	0	0
0	25	25
1	50	50

Table 1. Experimental design layout and dissolution outputs for theophylline and naproxen formulations.

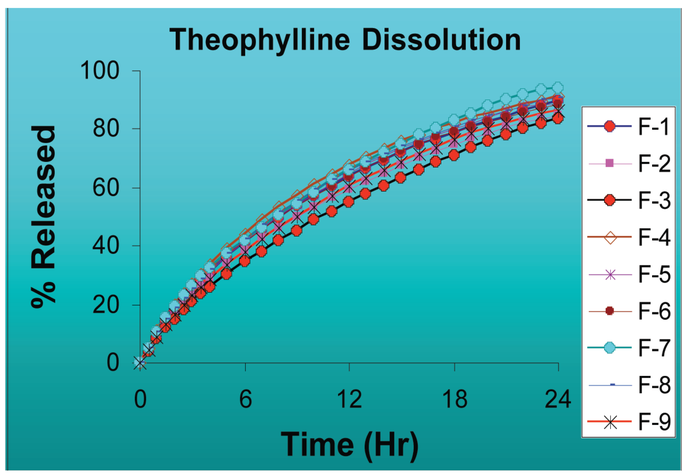

Figure 1. Dissolution profiles of theophylline formulations

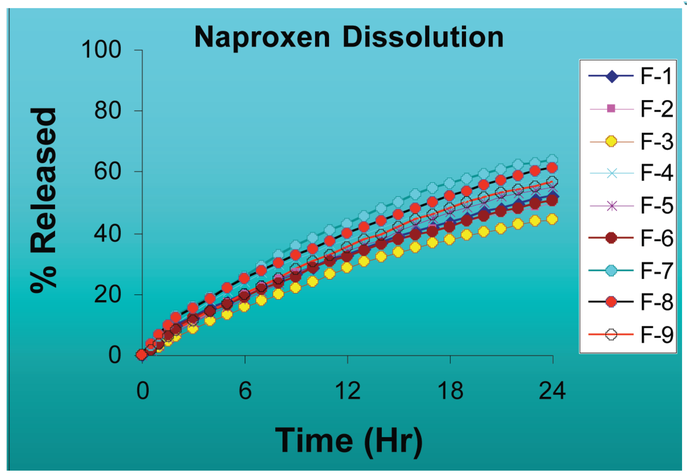

Figure 2. Dissolution profiles of naproxen

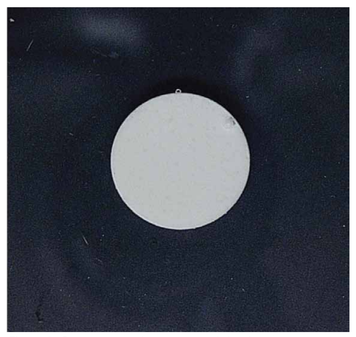

Figure 3. Photograph of tablet containing insoluble excipient before dissolution

Figure 4. Photograph of tablet containing insoluble excipient after 12 hours of dissolution

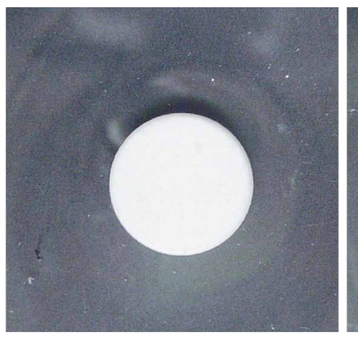

Figure 5. Photograph of tablet containing soluble excipient before dissolution

Figure 6. Photograph of tablet containing insoluble excipient after 12 hours of dissolution

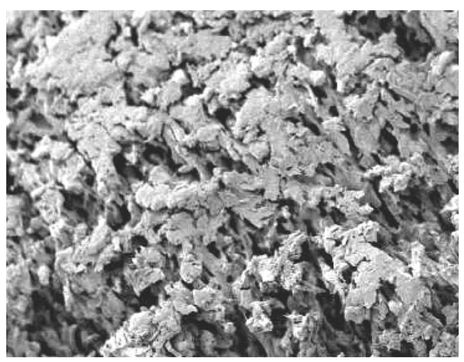

Figure 7. SEM Photo of HPMC tablet after 12 hours of dissolution

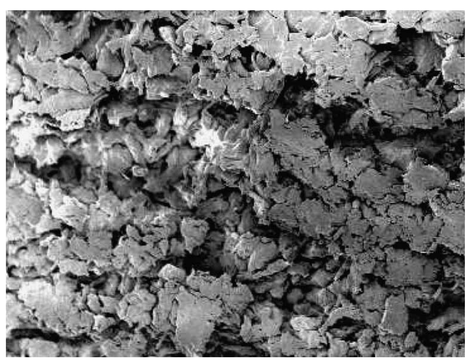

Figure 8. SEM Photo of HPMC tablet containing insoluble excipient after 12 hours of dissolution

Figure 9. SEM Photo of HPMC tablet containing soluble excipient after 12 hours of dissolution