THE INFLUENCE OF CELLULOSE ETHER SUBSTITUTION TYPE ON WATER UP-TAKE AND DISSOLUTION OF PROPRANOLOL HYDROCHLORIDE

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It is generally thought that different grades of cellulose ethers (CE) [hydroxypropylmethylcellulose (HPMC); methylcellulose (MC)] hydrate at different rates. Such differences are reportedly due to variations in the amounts of hydroxypropyl- and methoxy- substituents on the cellulose backbone. However there is little evidence to validate this claim although suggestions have been made that their differing hydrating rates may be used to optimize the formulation of sustained release matrices (Alderman 1984). We have studied the hydration of different grades of CE to ascertain its importance in controlling dissolution. Methocel A4M, E4M, F4M and K4M (Dow Chemicals, USA), equivalent to USP types MC, HPMC 2910, HPMC 2906 and HPMC 2208 respectively were used. For hydration studies, triplicated, accurately weighed ∿10mg samples were compressed into wafers, 6.35mm diameter, and placed in aluminium sample pans into which had been accurately weighed ∿10mg distilled water and held at room temperature for 0.5, 1, 3, 5, 10, 15, 30 or 60 min. Subsequently the pans were cooled to -30°C in a Perkin Elmer DSC7 Differential Scanning Calorimeter. The samples were heated at 10°C min^{-1} to 20°C and the enthalpy of fusion measured to determine the amount remaining of unbound water. 1:1 mixtures of HPMC and water allow complete hydration of HPMC (Mitchell *et al* 1989). Tablets (7.93mm, shallow concave) containing 160mg propranolol hydrochloride [P], 75, 100 or 150 mg CE and 0.75% magnesium stearate were prepared by direct compression. Dissolution was studied using a Copley Series 8000 dissolution tester into 1 litre distilled water at 37°C using the B.P. method 1 monitoring P at 288nm.

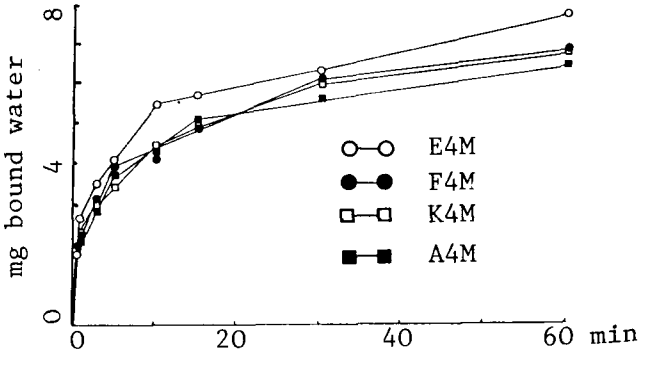
The amounts of water taken up by the Methocel (fig 1) showed little grade dependence with HMPC E4M appearing to hydrate marginally faster than the other grades. ∿20% hydration occurred within 1 min. After 15 min contact (∿50% hydration) the hydration rates decreased substantially. Complete hydration had occurred by 24 h. The dissolution data (table 1) confirmed the lack of difference shown by the grades since no grade consistently gave the highest or lowest dissolution rates at the three P:CE ratios studied.

Table 1. Effect of substitution type of methocel on the dissolution rate ($\%min^{-\frac{1}{2}}$)[a] of P from CE matrices.

	Dissolution Rates		
CE	75mg	100mg	150mg
A4M	5.47	5.24	4.55
E4M	5.61	5.09	3.85
F4M	4.99	4.54	4.02
K4M	5.11	4.43	3.87

[a]mean of 6 tablets.

Fig.1 Water uptake into 10mg of Methocel



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