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HYDROXYPROPYLMETHYLCELLULOSE SUSTAINED RELEASE TECHNOLOGY

J.E. Hogan

Colorgon Limited, Murray Road,

St. Pauls Cray, Orpington, Kent BR5 3QY

ABSTRACT

The use of polymers in controlling the release of drugs has become important in the formulation of pharmaceuticals. Watersoluble polymers such as polyethylene glycol and polyvinylpyrrolidone may be used to increase the dissolution rates of poorly soluble drugs (Ford)[1] and slowly soluble, biodegradable polymers such as polylactic acid may be used for controlled release implants (Rak et al.[2]). Hydrogels provide the basis for implantation, transdermal and oral-controlled release systems. Hydroxypropylmethylcellulose (HPMC) are cellulose ethers which may be used as the basic for hydrophilic matrices for controlled release oral delivery.

In tablet matrix systems the tablet is in the form of compressed compact containing an active ingredient,

lubricant, excipient, filler or binder. The matrix may be tabletted from wet-massed granules or by direct compression.

This review article examines a previously published series of work and concentrates on the following aspects of the subject; the relationship between release rate and quantity of polymers, such consideration allow a certain predicability in release rates to be made. Also the effect of drug particle size, tablet shape and the presence of additional diluents in the formula are examined.

INTRODUCTION

The use of polymers in controlling the release of drugs has become important in the formulation of pharmaceuticals. Water-soluble polymers such as polyethylene glycol and polyvinylprrolidone may be used to increase the dissolution rates of poorly soluble drugs (Ford[1]) and slowly soluble, biodegradable polymers such as polylactic acid may be used for controlled release implants (Rak et al.[2]). Hydrogels provide the basis for implantation, transdermal and oral-controlled release systems. Hydroxypropylmethylcellulose (HPMC) are cellulose ethers which may be used as the basis for hydrophilic matrices for controlled release oral delivery.

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The operative principle controlling drug release in matrix tablets is that on exposure to aqueous fluids the tablet surface becomes wet and the polymer starts to partially hydrate to form a gel layer. An initial burst of soluble drug from the external layer may be relased. There follows an expansion of the gel layer when water permeates into the tablet increasing the thickness of the gel layer and soluble drug diffuses through the gel barrier. Concomitantly the outer layers become fully hydrated and dissolve, a process generally referred to as erosion. Water continues to penetrate towards the tablet core until it has dissolved.

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MATERIALS AND METHODS

All drugs were B.P. grade. Hydroxypropylmethylcellulose, Methocel (Dow Chemical, U.S.A.) was used without further preparation. Magnesium

stearate (B.D.H., U.K.) was used as lubricant. Calcium phosphate (B.D.H.) or spray-dried lactose were used as required as diluents. Compaction was accomplished using direct compression of the blends that had been thoroughly mixed for 15 min using a tumbler mixer. The following variables were examined.

Influence of Drug:HPMC Ratios

Blends were compressed to the following formulae.

(i) Promethazine hydrochloride (250-500 μm): 25mg, HPMC K15M: 20, 25, 40, 50, 80, 120 or 160mg, magnesium stearate: 0.75%. Compaction pressure was 1395 $MN.m^{-2}$ (as Ford[3]).

(ii) Aminophylline (125-180 μm): 225mg, HPMC K15M: 45, 60, 90, 180 or 270mg, magnesium stearate: 0.85%. Compaction pressure was 455 $MN.m^{-2}$ (as Ford et al.[4]).

(iii) Propranolol hydrochloride (125-180 μm): 160 mg, HPMC K15M: 57, 71, 95, 140 or 285mg, magnesium stearate: 0.75%. Compaction pressure was 348.5 $MN.m^{-2}$ (as Ford et al.[4]).

(iv) Indomethacin (90-125 μm): 25mg, HPMC K15M: 25.8, 36, 61.5 or 200mg, magnesium stearate: 0.75%. Compaction pressure was 1395 $MN.m^{-2}$ (as Ford et al.[5]).

(v) Tetracycline hydrochloride (125-180 μm): 250mg, HPMC K15M: 45, 60, 90, 180 or 270mg,

magnesium stearate: 0.75%. Compaction pressure was 455 $MN.m^{-2}$.

(vi) Theophylline hydrochloride (125-180 μm): 225mg, HPMC K15M: 60, 90, 180 or 270mg, magnesium stearate: 0.75%. Compaction pressure was 455 $MN.m^{-2}$.

(vii) Diazepam (125-180 um): 10mg, HPMC K15M: 50, 61.5, 80, 114.3 or 200mg, magnesium stearate: 0.75%. Compaction pressure was 1395 $MN.m^{-2}$.

Compaction was accomplished using flat-faced punches on a Manesty F3 single-punch tableting machine. Propranolol tablets were 0.5 inch diameter, promethazine, indomethacin and diazepam tablets were 0.25 inch diameter, the remainder were 0.4375 inch diameter.

Dissolution Studies

The dissolution rates of the tablets were monitored using a Copley-Series 8000 dissolution tester (Copley Instruments, Nottingham, U.K.). 1000ml of distilled water was used as dissolution media and maintained at 37°C. The USP 1 dissolution method was used at a rotation speed of 100 rpm. Dissolution was continuously recorded using a spectrophotometer (Kontrol, model Uvikon 810) at 250 nm connected to a Commodore Model 8032 microprocessor. Dissolution studies were performed in triplicate for each batch of tablets.

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