International Journal of Pharmaceutics, 102 (1994) 207–211

IJP 03384

Plasticization and interactions of polyethylene glycol 6000 with hydroxypropyl methylcellulose / polyvinyl alcohol blends

P. Sakellariou [a], H. Hassan [b] and R.C. Rowe [c]

[a] *ICI Paints, Research Department, Wexham Road, Slough (UK),*
[b] *Materials Centre, UMIST, Manchester (UK) and*
[c] *Zeneca Pharmaceuticals, Macclesfield (UK)*

(Received 26 June 1993)
(Accepted 9 August 1993)

Key words: Hydroxypropyl methylcellulose; Poly(vinyl alcohol); Blends; Polyethylene glycol 6000; Interaction; Plasticizer; Tablet coating

Summary

The plasticization of hydroxypropyl methylcellulose/polyvinyl alcohol blends with polyethylene glycol 6000 has been studied by torsional braid analysis. Polyethylene glycol 6000, a poor plasticizer for the two pure homopolymers, had no effect on the behaviour of either hydroxypropyl methylcellulose-rich or polyvinyl alcohol-rich phases of the blends. It segregated into a separate phase due to its thermodynamic incompatibility with both phases of the blend in agreement with theoretical predictions based on the solubility parameters of the individual components and the interaction energy density of the blend.

Introduction

Blends of hydroxypropyl methylcellulose (HPMC) and polyvinyl alcohol (PVA) are used in the formulation of tablet coating films (Okhamafe and York, 1985a). Polyethylene glycols (PEGs) are added to the film formers reducing their modulus and glass transition temperature hence minimising film defects such as film cracking (Okhamafe and York, 1985b). We have reported on the plasticization of HPMC and PVA (Sakellariou et al., 1986, 1993a), individually, showing that the plasticizer efficiency of the PEGs is inversely proportional to their molecular weight, with PEG 6000 virtually a non-plasticizer. We have also shown that HPMC and PVA are thermodynamically incompatible (Sakellariou et al., 1993b) segregating into two, almost pure, phases. This paper reports on the effect of PEG 6000 on a 50:50 w/w blend of HPMC/PVA.

Materials and Methods

The polymers studied were hydroxypropyl methylcellulose (HPMC) from Shin-Etsu Chemical Co., Tokyo, Japan, and polyvinyl alcohol (PVA) POVAL 205 from Kuraray Chemical Co., Tokyo, Japan. Polyethylene glycol with $M_n = 6000$

Correspondence to: R.C. Rowe, Zeneca Pharmaceuticals, Hurdsfield Industrial Estate, Macclesfield, Cheshire SK10 2NA, U.K.

(PEG 6000) was obtained from BDH Chemicals Ltd, Poole, U.K. All materials were used as received.

The torsional braid analyser (TBA) used in this work has been fully described elsewhere (Rowe et al., 1984; Sakellariou et al., 1987a,b). The technique monitors the response of a supported sample to a sinusoidal strain at constant frequency as a function of temperature. Samples were prepared by impregnating heat-cleaned glass braids with 10% aqueous solutions of the polymer blends over several hours. They were dried in an air oven at 50°C to constant weight and stored over dry silica gel until tested. The results are reported in terms of the logarithmic decrement and relative rigidity (p^{-2}, $p =$ period of oscillation) as a function of temperature.

Results and Discussion

Two distinct glass transition temperatures were recorded in the logarithmic decrement (Fig. 1) and relative rigidity (Fig. 2) curves for the 50:50 w/w PVA/HPMC blend plasticized with 5, 10, 20 and 30% w/w PEG 6000. Both transitions remained almost constant (Fig. 3) and occurred at the same temperature as those of the corresponding homopolymers (Sakellariou et al., 1993b) indicating very limited interaction between PEG 6000 and the two phases. A shoulder was also recorded at around 60°C, in agreement with earlier observations with PVA and HPMC homopolymers and is attributed to the melting of PEG 6000-rich phases. This suggests that PEG 6000, being incompatible with both HPMC- and PVA-rich phases, segregates out into small droplets which are dispersed in the film and crystallise during solvent evaporation (Sakellariou et al., 1986).

The observed behaviour is consistent with theoretical predictions based on Hansen solubility parameters (Barton 1983; van Krevelen 1972) Table 1. The dispersive component, δ_d, was similar for all three materials, as expected, whereas the polar and hydrogen bonding components were significantly different. The data of Table 1 suggest that phase separation between HPMC, PVA and PEG 6000 would be expected due to the inability of these molecules to participate in hydrogen bonding and dipole-dipole/induced dipole interactions with each other. In earlier publications (Sakellariou et al., 1993a,b), we showed that in the case of PVA and HPMC, the two polymers are both mainly Lewis bases with weak acid characteristics, and hence are unable to set up acid-base interactions to induce compatibility.

The PVA used in this study was essentially a random copolymer of poly(vinyl alcohol-co-vinyl acetate) with 88% vinyl alcohol content. Literature data (Paul and Barlow, 1984) have shown that compatibility can be introduced into systems containing mutually incompatible copolymers by virtue of significant differences in the extent of incompatibility between blend components. A typical example is that of styrene/acrylonitrile copolymers which are miscible with polymethyl methacrylate over a certain acrylonitrile range while neither polystyrene nor polyacrylonitrile is miscible with polymethyl methacrylate.

A necessary condition for miscibility is that the free energy of mixing

$$\Delta G_m = \Delta H_m - T\Delta S_m \tag{1}$$

is negative. Since the combinatorial entropy of mixing for polymer blends is negligible, the compatibility between the two components will be largely dependent on the heat of mixing. The latter can be expressed in a van Laar type expression:

$$\Delta H_m = (V_A + V_B) B \Phi_A \Phi_B \tag{2}$$

where B is a binary interaction energy density, V_A and V_B denote the actual volumes of these components in the blend and Φ_A and Φ_B are the corresponding volume fractions. Eqn 2 for any homopolymer blend can be rewritten as:

$$\Delta H_m = V \sum_{i>j} B_{ij} \Phi_i \Phi_j \tag{3}$$

where V is the total system volume.

In the presence of a copolymer Eqn 2 must be corrected for the 'heat of mixing' of the copolymer. It is this contribution which accounts for the presence of miscibility windows in copolymer-homopolymer blends. If the incompatibility between copolymer segments exceeds that between copolymer and homopolymer, the system can exhibit compatibility over a certain composition range. In the case of PVA/HPMC blends with PEG 6000 the heat of mixing for the blend can be expressed in terms of the blend interaction energy density, B:

$$B = \Phi'_1(B_{13} + B_{14}) + \Phi'_2(B_{14} + B_{24}) - \Phi'_1\Phi'_2 B_{12} \quad (4)$$

where B_{ij} is the interaction energy density between segments i and j, and Φ'_1 and Φ'_2 represent the volume fractions of vinyl alcohol (VAl) and vinyl acetate (VAc) units in PVA, respectively, with $\Phi'_1 + \Phi'_2 = 1$. Subscripts 1, 2, 3 and 4 correspond to vinyl alcohol, vinyl acetate, HPMC and PEG 6000 components, respectively. Compatibility requires that $B < 0$ and that, according to Eqn 4, can be achieved only when the final term is greater than the contribution from the first two. This corresponds to the case when the

TABLE 1

Calculated Hansen and Van Krevelen solubility parameters for PVA (as used here), pure polyvinyl alcohol (PVAl), polyvinyl acetate (PVAc), HPMC and PEG 6000

Polymer	δ_d	δ_p	δ_h	δ	δ [a]
PVA	16.4	14.7	24.2	32.7	–
HPMC	14.4	5.8	16.7	22.8	24.4
PEG 6000	17.5	1.0	9.4	19.9	22.4
PVAl	–	–	–	–	33.7
PVAc	–	–	–	–	18.9

Values expressed as $\text{MPa}^{1/2}$.

[a] Values of Van Krevelen (1972).

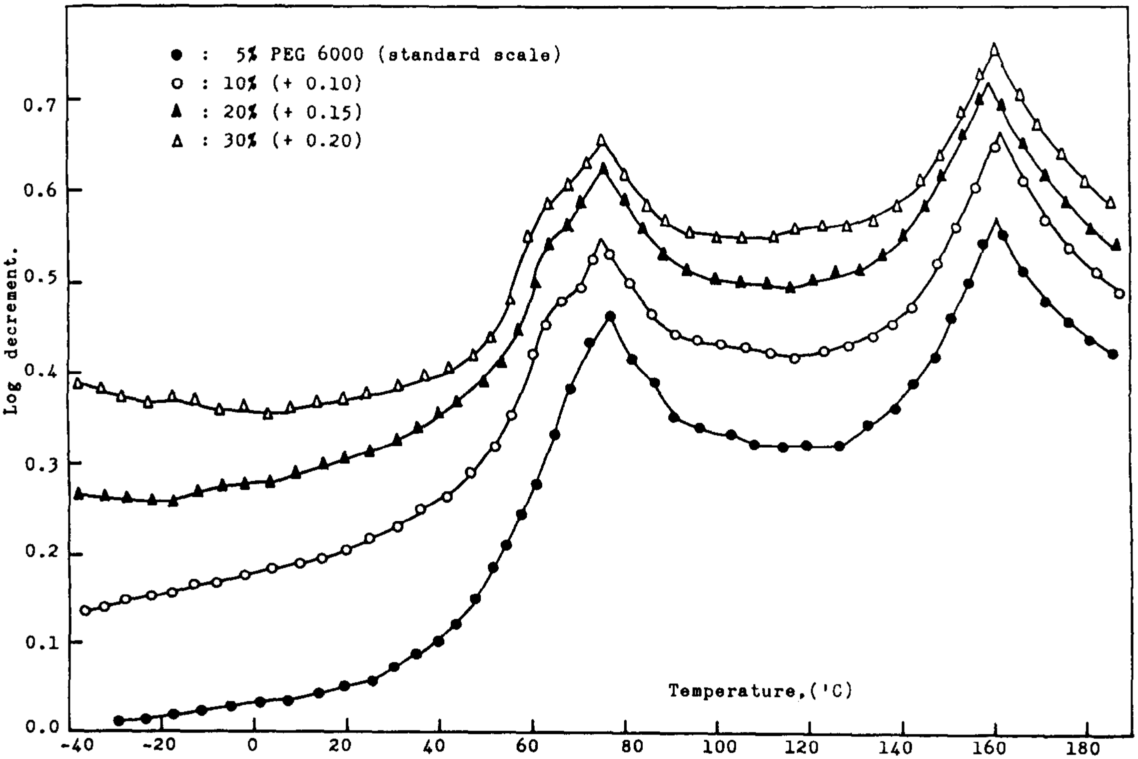

Fig. 1. Logarithmic decrement curves for 50:50 w/w PVA/HPMC blend containing 5, 10, 20 and 30% w/w PEG 6000. Curves have been offset vertically for clarity.

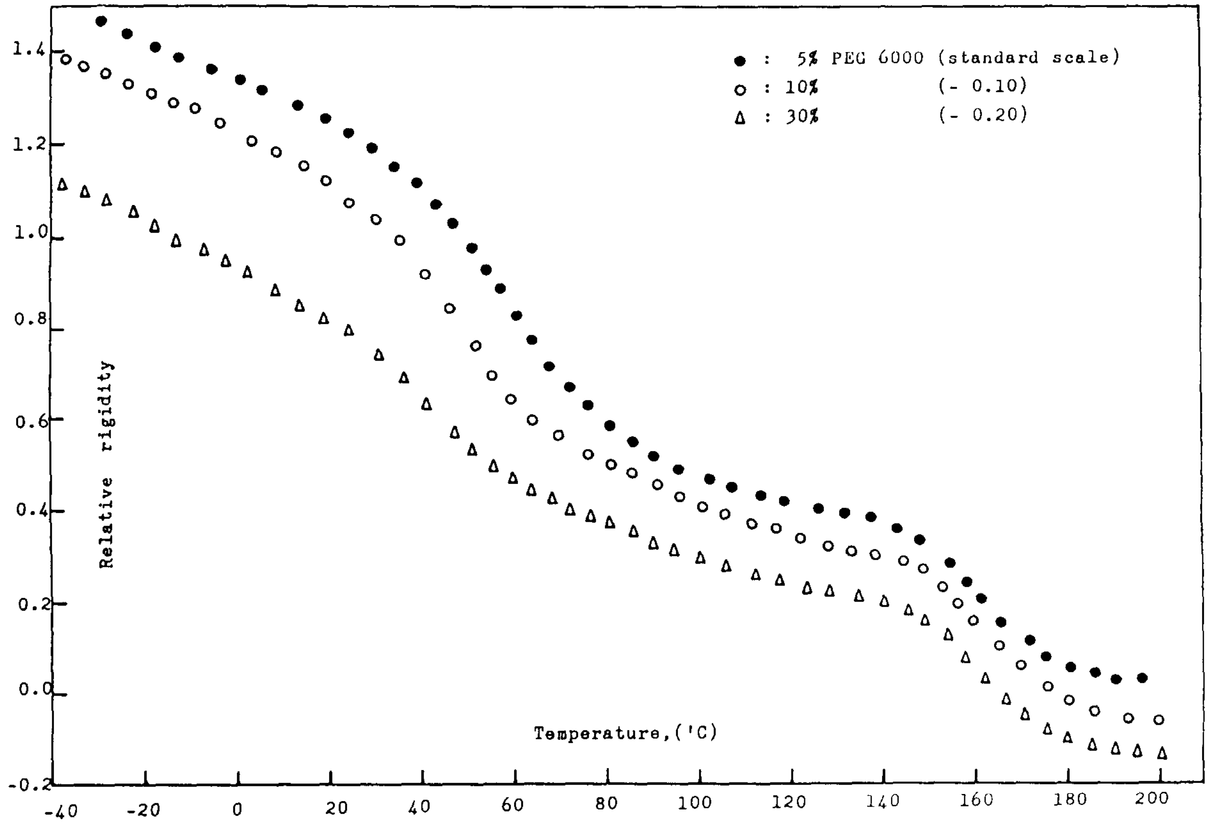

Fig. 2. Relative rigidity curves for 50:50 w/w PVA/HPMC blend containing 5, 10, 20 and 30% w/w PEG 6000. Curves have been offset vertically for clarity.

incompatibility between the two components in the copolymer outweighs that between the two homopolymers.

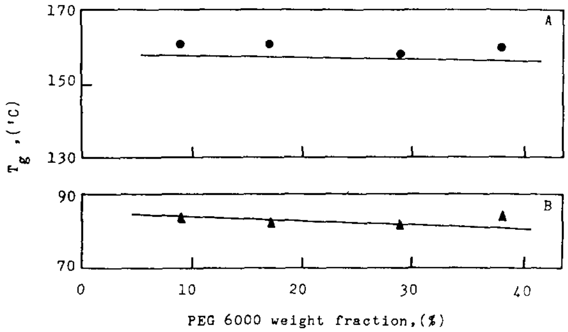

Fig. 3. Variation of the glass transition temperature of HPMC-rich (A) and PVA-rich (B) phases in 50:50 w/w PVA/HPMC blends with PEG 6000 concentration. Continuous lines are those obtained from the homopolymers with PEG 6000 taken from Sakellariou et al. (1986, 1993a).

Expressing B_{ij} in terms of the solubility parameters we obtain:

$$B = \Phi_1'\left[(\delta_1 - \delta_3)^2 + (\delta_1 - \delta_4)^2\right] + \Phi_2'\left[(\delta_1 - \delta_4)^2 + (\delta_2 - \delta_4)^2\right] - \Phi_1'\Phi_2'(\delta_1 - \delta_2)^2 \tag{5}$$

The total solubility parameters (Table 1), calculated from the molar attraction and molar volume constants of Van Krevelen (1972), were used to compute the blend interaction energy density for our blend for PVA with different vinyl alcohol contents (Fig. 4). In all cases B was positive, characteristic of a phase separated system. It is interesting to note that the degree of incompatibility was reduced for blends with PVA grades

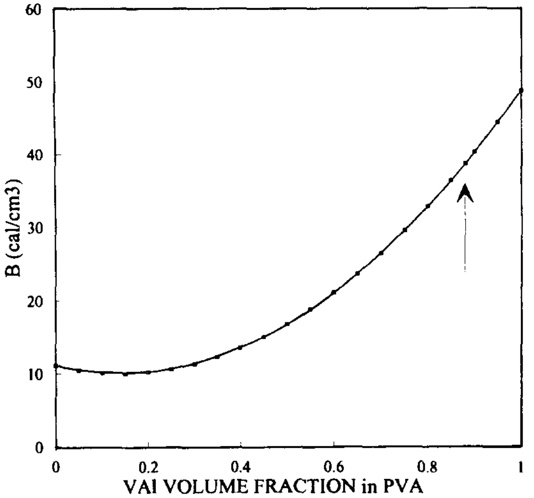

Fig. 4. Variation of the blend interaction parameter energy density, B, with volume fraction of vinyl alcohol segments in PVA, Φ_1' (arrow indicates the data for PVA as used in this study, i.e., 88% hydrolysed).

with lower degrees of hydrolysis but was significantly higher for grades with high degrees of hydrolysis equivalent to those generally used in tablet film coating.

Conclusion

It is now well recognised that the structural complexity and end use properties of tablet film coatings are derived from the inter- and intramolecular interactions in the polymeric film formers complicated by the presence of plasticizers and/or other additives (Okhamafe and York, 1987). As illustrated in this work, these interactions can be examined and predicted employing techniques commonly used in polymer science. Not only does this approach allow a detailed scientific study of the system under examination but also extrapolations can be made enabling formulators to optimise their formulations for compatibility or incompatibility depending on the end use property required.

References

Barton, A.F.M., *Handbook of Solubility Parameters and Other Cohesion Parameters*, CRC Press, FL, 1983.

Okhamafe, A.O. and York, P., Interaction phenomena in some aqueous-based tablet coating film coating polymer systems *Pharm. Res.*, 1 (1985a) 19–23.

Okhamafe, A.O. and York, P., Stress crack resistance of some pigmented and unpigmented tablet coating film coating systems *J. Pharm. Pharmacol.*, 37 (1985b) 449–454.

Okhamafe, A.O. and York, P., Interaction phenomena in pharmaceutical film coatings and testing methods *Int. J. Pharm.*, 39 (1987) 1–21.

Paul, D.R. and Barlow, J.W., A binary interaction model for miscibility of copolymers in blends *Polymer*, 25 (1984) 487–494.

Rowe, R.C., Kotaras, A.D. and White, E.F.T., An evaluation of the plasticizing efficiency of the dialkyl phthalates in ethylcellulose films using the torsional braid pendulum *Int. J. Pharm.*, 22 (1984) 57–62.

Sakellariou, P., Hassan, A. and Rowe, R.C., Phase separation and polymer interactions in aqueous poly(vinyl alcohol)/ hydroxypropyl methylcellulose blends *Polymer*, 34 (1993b) 1240–1248.

Sakellariou, P., Hassan, A. and Rowe, R.C., Plasticization of aqueous poly(vinyl alcohol) and hydroxypropyl methylcellulose with polyethylene glycols and glycerol *Eur. Polym. J.*, 29 (1993a) 937–943.

Sakellariou, P., Rowe, R.C. and White, E.F.T., An evaluation of the interaction and plasticizing efficiency of the polyethylene glycols in ethyl cellulose and hydroxypropyl methylcellulose films using the torsional braid pendulum *J. Pharm. Pharmacol.*, 29 (1986) 55–64.

Sakellariou, P., Rowe, R.C. and White, E.F.T., The interactions and partitioning of low molecular weight polyethylene glycols and diethyl phthalate in ethylcellulose/ hydroxypropyl methylcellulose blends *J. Appl. Polym. Sci.*, 34 (1987b) 2507–2716.

Sakellariou, P., White, E.F.T. and Rowe, R.C., The development of a torsional braid analyser interfaced to microprocessor and some factors affecting the optimization of the technique *Br. Polym. J*, 19 (1987a) 73.

Van Krevelen, D.W., *Properties of Polymers, Correlations with Chemical Structure*, Elsevier, Amsterdam, 1972.