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Polymer/polymer interaction in blends of ethyl cellulose with both cellulose derivatives and polyethylene glycol 6000

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Summary

Polymer/polymer interactions in blends of ethyl cellulose with hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose phthalate, cellulose acetate phthalate and polyethylene glycol 6000 have been studied using the torsional braid pendulum. All the film formers were shown to be incompatible with ethyl cellulose exhibiting phase separation throughout the composition range. However, some interaction via the unsubstituted hydroxyl groups did occur, with hydroxypropyl methylcellulose with its increased substitution showing slightly reduced interaction. Both grades of hydroxypropyl methylcellulose phthalate and cellulose acetate phthalate exhibited appreciable interaction and mutual dispersion due to the presence of phthalyl groups. The results are extremely important in understanding the transport mechanisms of such blends when used in pharmaceutical formulations for controlled release.

Introduction

Blends of ethyl cellulose with both water-soluble polymers (hydroxypropyl cellulose, hydroxypropyl methylcellulose and polyethylene glycol 6000) and pH-dependent soluble polymers (hydroxypropyl methylcellulose phthalate, cellulose acetate phthalate) are widely used in the formulation of delayed or sustained release films (Shah and Sheth, 1972; Donbrow and Samuelov, 1980; Rowe, 1985, 1986a). A knowledge of the mutual interaction of these polymers is of prime importance in understanding the morphology or microstructure of the films so formed especially in gaining an insight into their transport mechanisms when applied to granules or tablets. A relatively easy way of studying polymer/polymer interaction in blends is by using dynamic mechanical testing at varying temperatures (Nielsen, 1974) and a version of this technique, the torsional braid pendulum, has been used in this study for blends of ethyl cellulose with both other cellulose derivatives and polyethylene glycol 6000.

Materials and Methods

The polymers studied were ethyl cellulose (EC — Grade N50) and hydroxypropyl cellulose (HPC) (Klucel LF) from Hercules Powder Co., Wilmington, DE, U.S.A.; hydroxpropyl methylcellulose (HPMC) and hydroxypropyl methylcellulose phthalate (HP50 and HP55) — from Shin-Etsu

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Chemical Co., Tokyo, Japan; cellulose acetate phthalate (CAP) from Eastman Chemical Products, Kingsport, TN, U.S.A. and polyethylene glycol (PEG 6000) BDH Chemicals Ltd., Poole, U.K.. All were used as received.

The torsional braid pendulum used in this work has been fully described elsewhere (Rowe et al., 1984; Sakellariou, 1984; Sakellariou et al., 1985). The specimens were prepared by first removing the size from twisted glass yarn braids by heating in an oven at 500°C for 1 h followed by immersion in a 15% solution of the polymer blend dissolved in a solvent mixture consisting of equal parts by volume of dichloromethane and methanol. The methanol content was slightly increased to 60 : 40% v/v for the blend containing high proportions of polyethylene glycol to improve solubility. The braids were dried in an oven at 85°C to constant weight. All the film coatings on the braids were opaque indicating that phase separation had occurred with the formation of dispersed domains of size greater than 10^{-1} μm (Rosen, 1967). The thermomechanical spectra produced were analysed as described previously (Sakellariou et al., 1985). In this study only the logarithmic decrement curves are reported as the relative rigidity curves tended to exhibit poor resolution. The transition width was assessed from the damping/temperature curves as previously described (Sakellariou et al., 1986).

Results and Discussion

The logarithmic decrement/temperature curves for the blends of ethyl cellulose with hydroxypropyl methylcellulose are shown in Fig. 1. At all compositions two transitions were recorded corresponding to the glass transition of the two polymers (131.5°C for ethyl cellulose, 153.5°C for hydroxypropyl methylcellulose—Sakellariou et al., 1985). At blend compositions with ethyl cellulose as the major component a sharp transition was recorded at 132.5–133.5°C while hydroxypropyl methylcellulose yielded a plateau at 153°C. Phase reversal resulted in a broad peak at 153–154°C accompanied by a smaller one at 130–133°C. All blend compositions showed a broadening of the transition due to incomplete separation of the transitions of the components. The damping of the blends at room temperature does not appear to be affected by composition but the peak values do increase with increasing weight fraction of the corresponding component. The results suggest that the mutual solubility of the two polymers is limited although the shift of the transition of the ethyl cellulose from 131.5 to 133°C does suggest that some dispersion does take place which permits the hydroxypropyl methylcellulose to impose restrictions on the mobility of the ethyl cellulose chains within its transition region.

Blends of ethyl cellulose with cellulose acetate phthalate (Fig. 2) showed phase separation at all compositions. Although the glass transition temperature of the ethyl cellulose did show a slight decrease by 1.5–4.5°C for all the compositions, that of the cellulose acetate phthalate was reduced by 9–11°C indicating that some form of molecular mixing and interaction between the two components does exist. The heights of the transition peaks were found to be proportional to the weight fraction of the corresponding component while the transition widths narrowed. The damping level at room temperature did not appear to be affected by blend composition. Although the presence of the two transitions indicate a definite phase separation of the two components, the shifts in the transition temperatures do provide evidence of some mutual interaction. The increased shift in the transition of the cellulose acetate phthalate phase suggests a favoured dispersion of the ethyl cellulose in this polymer.

In contrast to the results for blends of ethyl cellulose with cellulose acetate phthalate, blends of ethyl cellulose with the other two pH-dependent polymers HP50 and HP55 showed little resolution of the two transition peaks due to the very small differences between the glass transitions of the components (Figs. 3 and 4). In blends of ethyl cellulose with HP50, with the former as the main component, there was only one major transition occurring at 128°C for the 80 : 20% w/w blend and 131°C for the 60 : 40% w/w blend, the transition of the HP50 phase only appearing as a plateau superimposed on the main transition towards higher temperatures (Fig. 3). When the blend com-

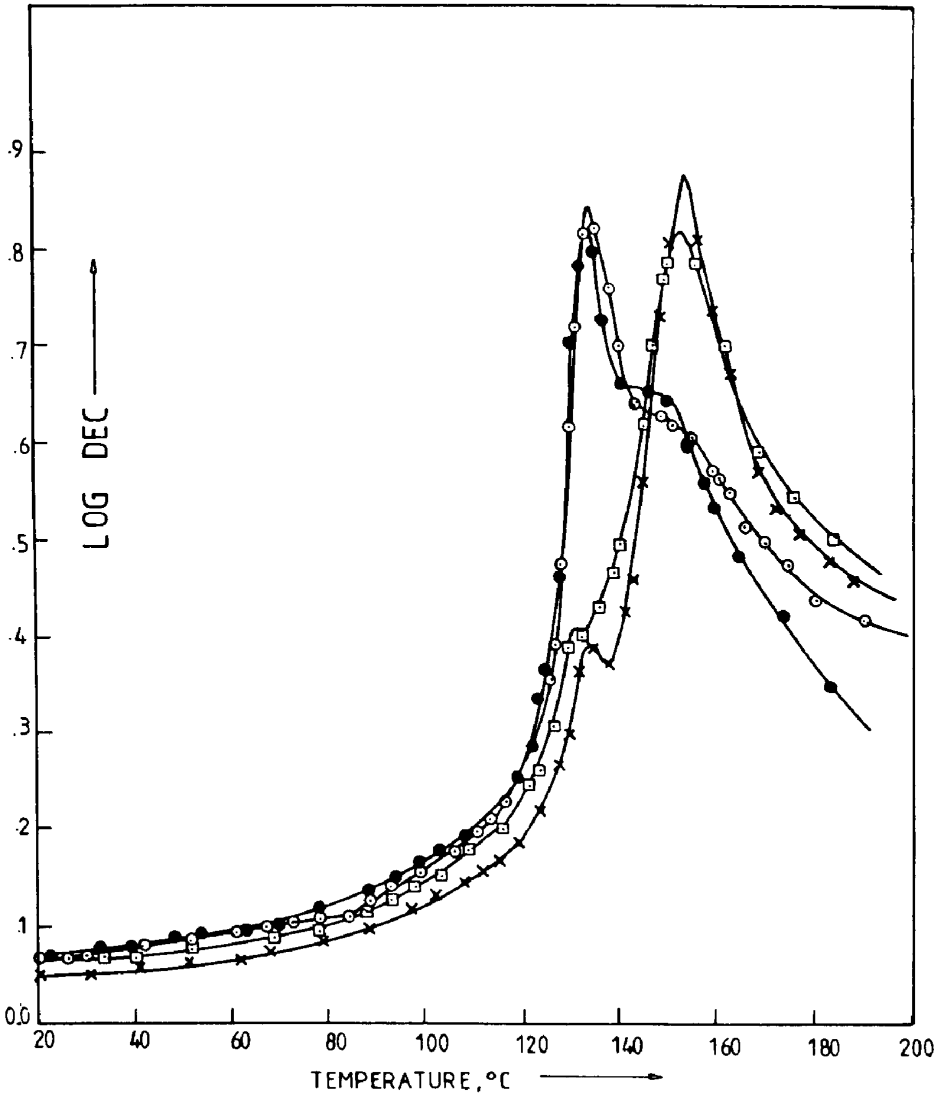

Fig. 1. The thermomechanical spectra (logarithmic decrement curves) for ethyl cellulose/hydroxypropyl methylcellulose blends. ⊙, 80%; ●, 60%; ⊡ 40%; ×, 20% ethyl cellulose by weight.

position was reversed (i.e. ethyl cellulose was the minor component), one relatively narrow peak was obtained at slightly elevated temperatures indicating that the transition of the ethyl cellulose phase had been shifted towards the transition of the HP50. The incorporation of HP50 into the ethyl cellulose caused a lowering in the peak values of the damping which together with the slight lowering of the glass transition temperature of the ethyl cellulose suggests a plasticization of the ethyl cellulose. The transition peaks for the ethyl cellulose HP55 blends were all relatively sharp occurring at between 128 and 129°C (Fig. 4), i.e. at lower temperatures than the glass transition temperatures of both polymers. This suggests that HP55 does, in fact, act as a more efficient plasticizer for ethyl cellulose than the HP50. This effect is thought to be due to its increased phthalyl

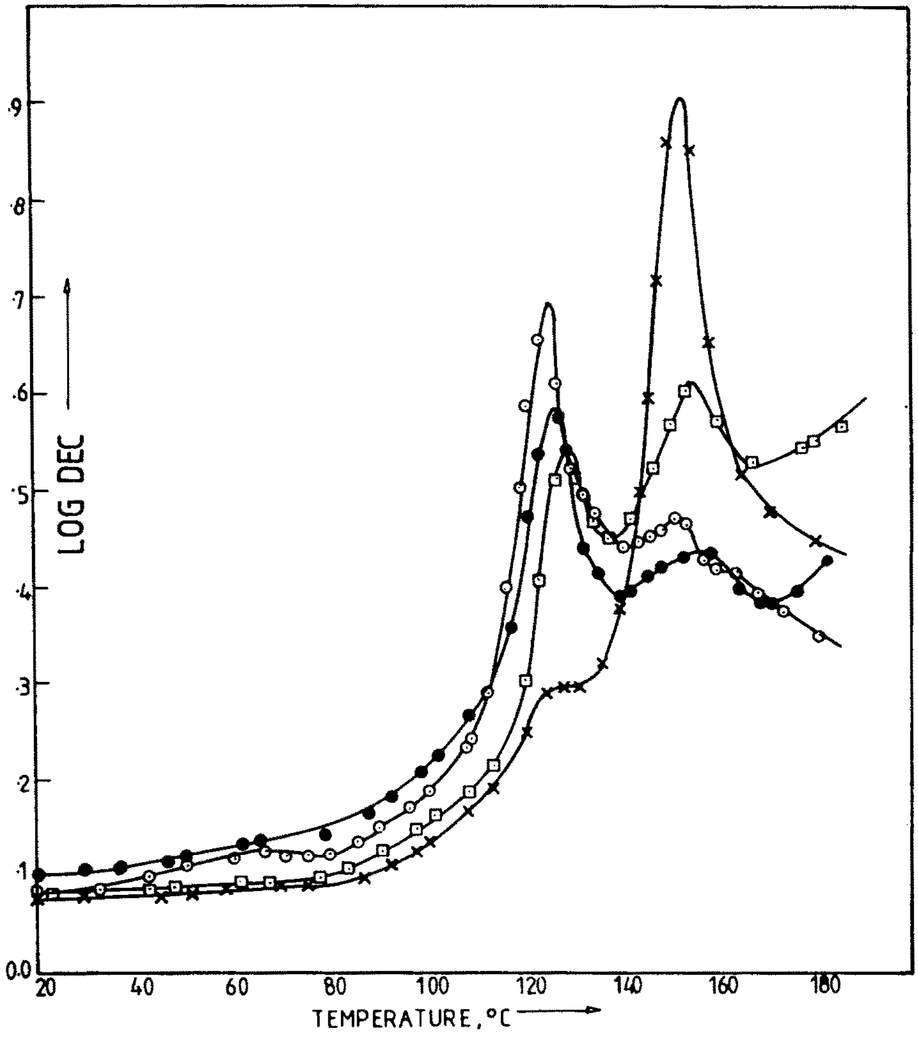

Fig. 2. The thermomechanical spectra (logarithmic decrement curves) for ethyl cellulose/cellulose acetate phthalate blends. ⊙, 80%; ●, 60%; ⊡, 40%; ×, 20% ethyl cellulose by weight.

content (25–35% w/w for HP55; 20–24% w/w for HP50) since it is known that these groups do facilitate chain flexing in the ethyl cellulose (Rowe et al., 1984).

The logarithmic decrement/temperature curves for blends of ethyl cellulose with hydroxypropyl cellulose are shown in Fig. 5. A single main transition peak was recorded at 130.5–131.5°C all through the composition range with its height decreasing and its width increasing with increasing concentration of hydroxypropyl cellulose. This was attributed to the ethyl cellulose phase being superimposed on the complex damping curve of hydroxypropyl cellulose described previously (Sakellariou et al., 1985). The damping at room temperature also increased with increasing concentration of hydroxypropyl cellulose. The relaxation seen previously at 105°C with the hydroxypropyl cellulose was only seen at the blend containing the highest concentration of this polymer. This suggests that the ethyl cellulose does interact with the hydroxypropyl cellulose via the available

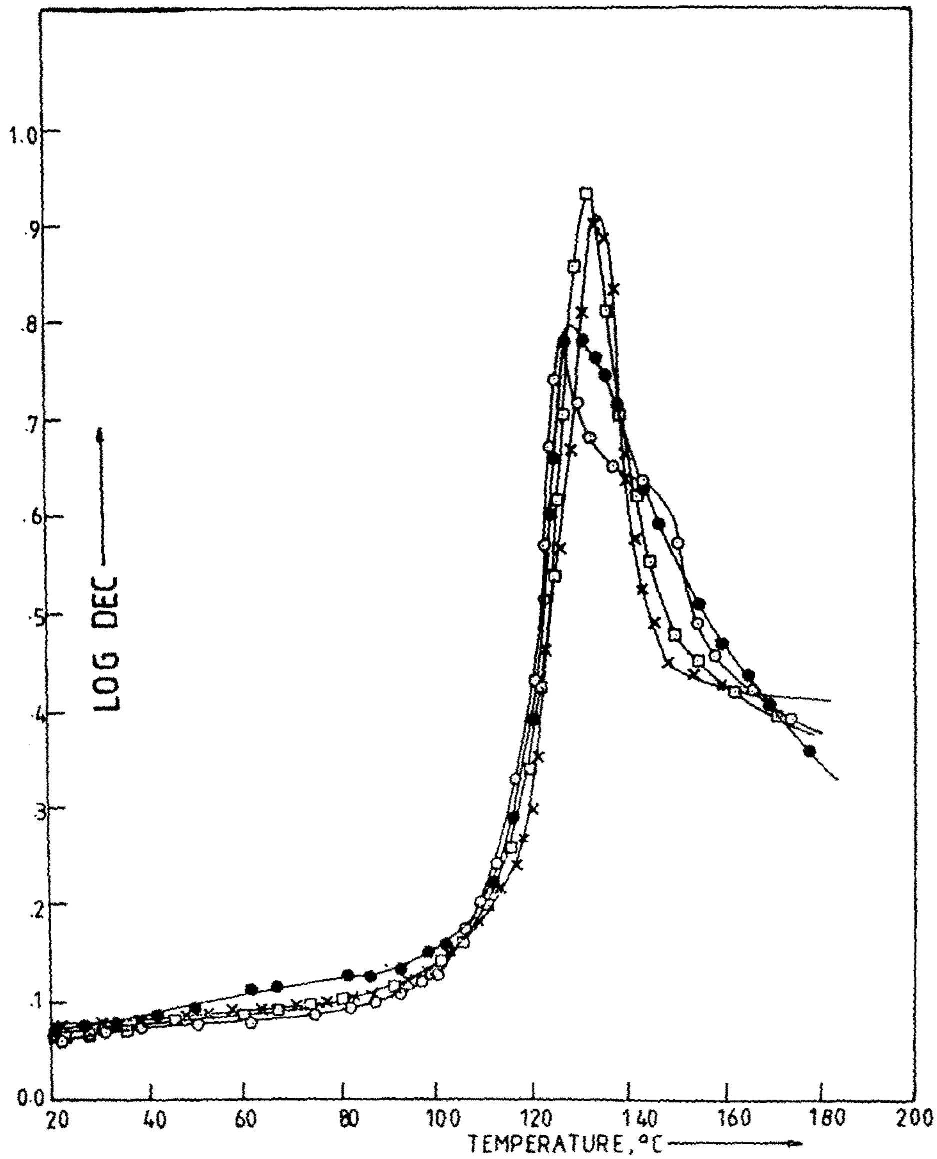

Fig. 3. The thermomechanical spectra (logarithmic decrement curves) for ethyl cellulose/hydroxypropyl methylcellulose phthalate (HP50) blends. ⊙, 80%; ●, 60%; ⊡, 40%; ×, 20% ethyl cellulose by weight.

hydroxyl groups thus hindering the interaction of the hydroxypropyl cellulose with water — the cause of this relaxation peak (Sakellariou et al., 1985). The glass transition of the hydroxypropyl cellulose at 124°C could not be resolved because it was hidden within the ethyl cellulose relaxation but the plateaus at 145–150°C and 63–67°C seen with this polymer alone were both present in the blends. However, the peak at 178°C seen previously and thought to be associated with the softening and commencement of viscous flow of the hydroxypropyl cellulose and/or some localised disorientation of the hydroxypropyl cellulose chains (Sakellariou et al., 1985) could not be seen in any of the blends. The thermomechanical spectra suggest that while ethyl cellulose imparts rigid-

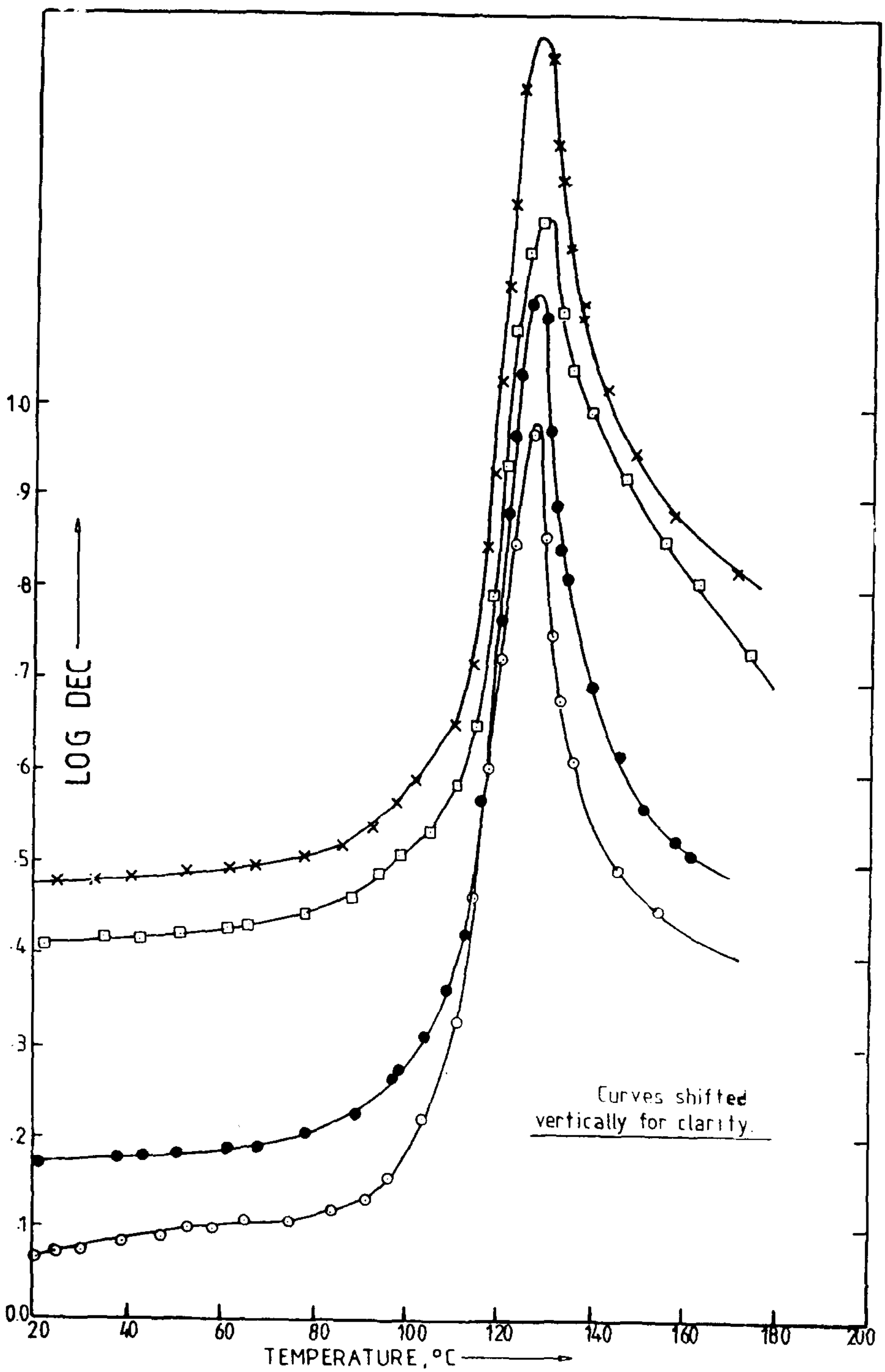

Fig. 4. The thermomechanical spectra (logarithmic decrement curves) for ethyl cellulose/hydroxypropyl methylcellulose phthalate (HP55) blends. ⊙, 80%; ●, 60%; ⊡, 40%; ×, 20% ethyl cellulose by weight.

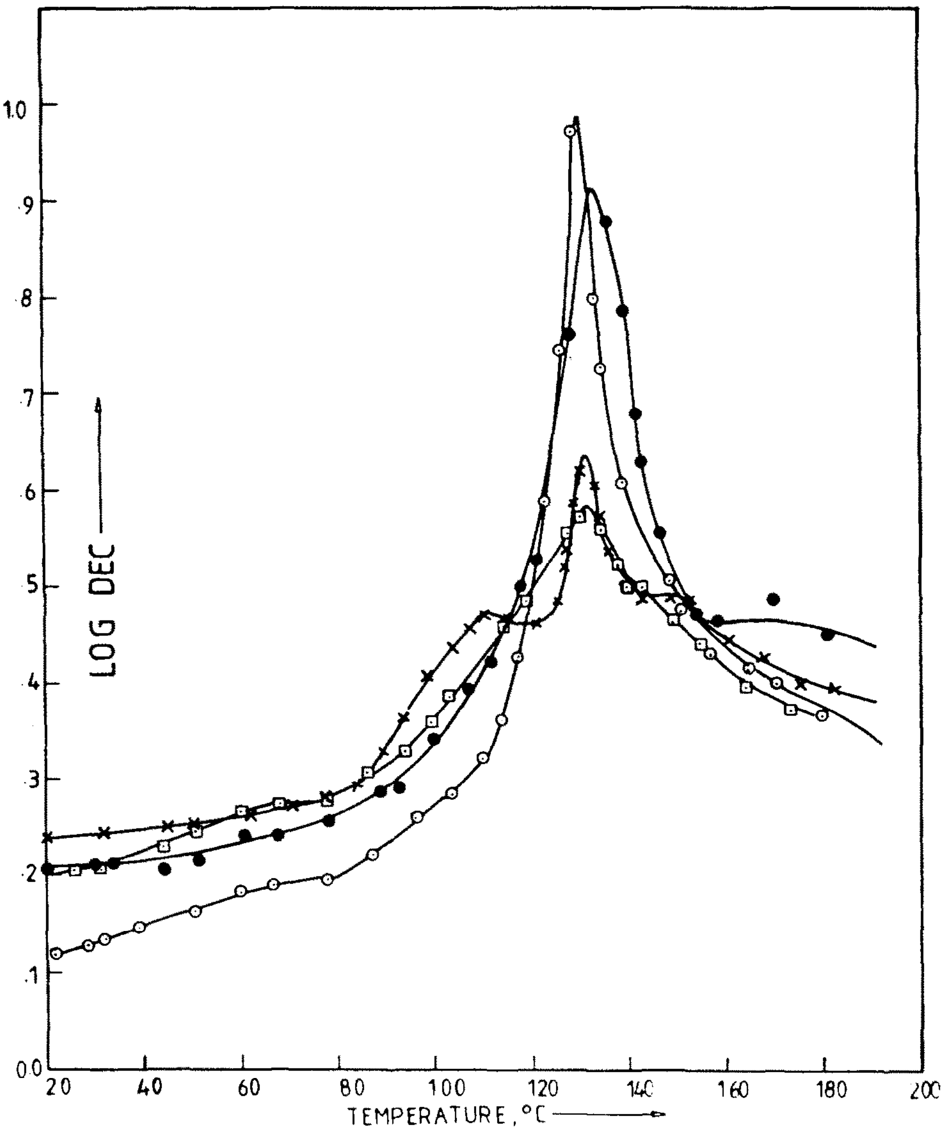

Fig. 5. The thermomechanical spectra (logarithmic decrement curves) for ethyl cellulose/hydroxypropyl cellulose blends. ⊙, 80%; ●, 60%; ⊡, 40%; ×, 20% ethyl cellulose by weight.

ity to the hydroxypropyl cellulose, the latter imparts increased toughness and film formability to the blend. The mechanical properties of the blend are dominated by that of the hydroxypropyl cellulose even at hydroxypropyl cellulose concentrations as low as 40% w/w.

The logarithmic decrement/temperature curves for the blends of ethyl cellulose with polyethylene glycol 6000 (Fig. 6) are different from the others reported since this system consists of a mixture of an amorphous polymer (ethyl cellulose) with a crystalline polymer (polyethylene glycol 6000). Three relatively sharp transitions were recorded, one at − 40° to − 47°C, one at 60°C and one at 118–126°C. The variation of these transitions with blend composition is shown in Fig. 7. The first

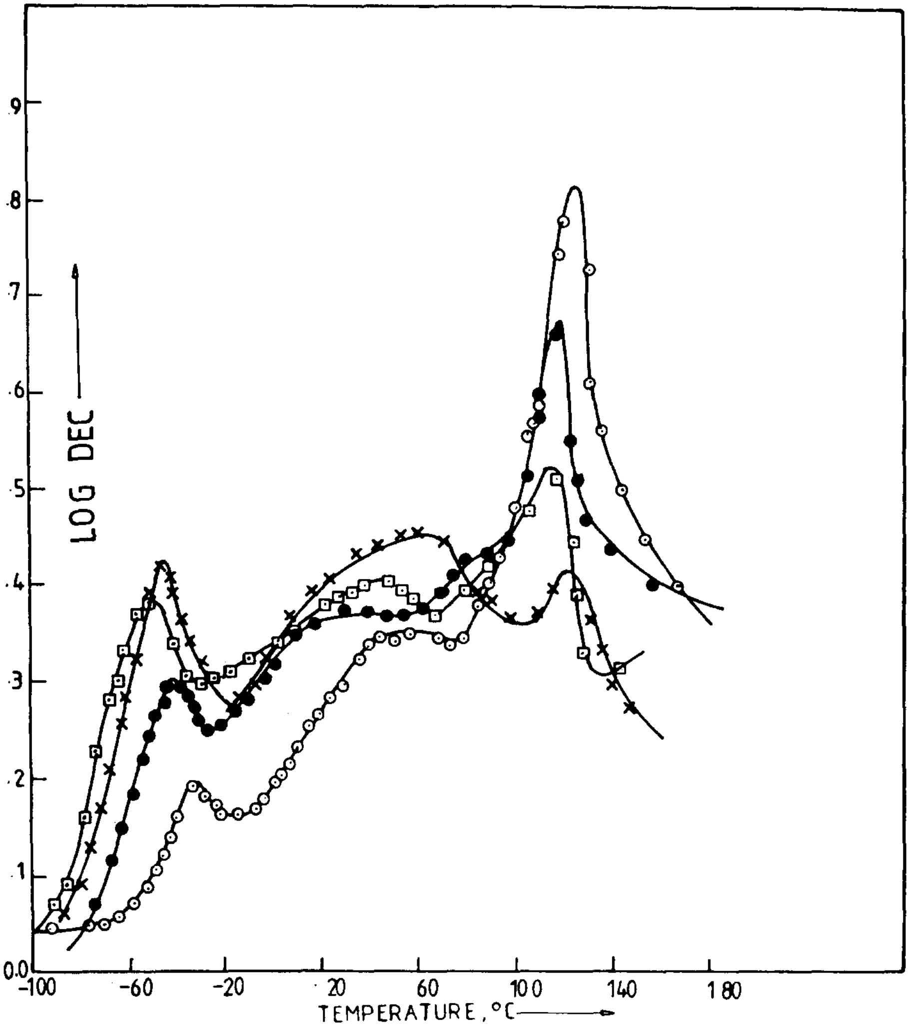

Fig. 6. The thermomechanical spectra (logarithmic decrement curves) for ethyl cellulose/polyethylene glycol 6000 blends. ⊙, 80%; ●, 60%; ⊡, 40%; ×, 20% ethyl cellulose by weight.

transition is thought to be due to the amorphous part of the polyethylene glycol that gives rise to a glass transition. In this case the transition height increased with increasing polyethylene glycol content but its breadth decreased. It is thought that increasing the concentration of the amorphous polymer ethyl cellulose results in an increased restriction in movement of the polyethylene glycol chains. Furthermore this behaviour is associated with the depression of the degree of crystallinity of the polyethylene glycol. The second transition of 60 °C is associated with the melting of the polyethylene glycol crystallites and the subsequent increase in mobility of this polymer within a rigid matrix of ethyl cellulose. The decrease in the temperature at which this transition was seen at high ethyl cellulose concentrations (Fig. 7) confirms that there is a decrease in the degree of crystallinity and reduced crystallite size in the polyethylene glycol phase with increasing presence of amorphous material (Paul and Altamirano, 1974). The third transition occurring within the temperature range 118–126 °C can be attributed to the ethyl cellulose phase since its height in-

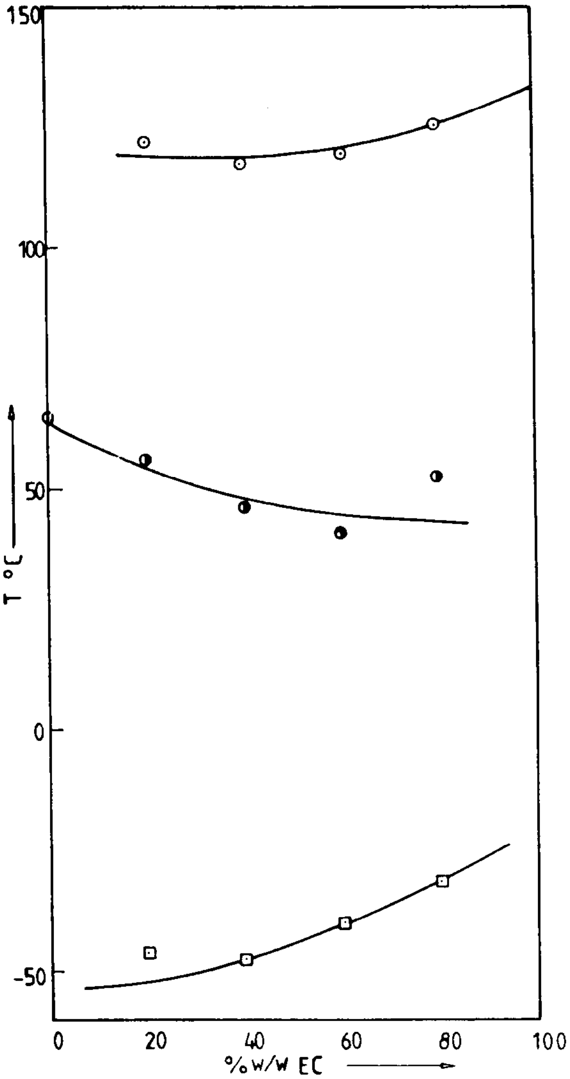

Fig. 7. The variation in the transition temperatures with blend composition for ethyl cellulose/polyethylene glycol 6000 blends: ○, glass transition temperature of ethyl cellulose; ◑, melting temperature of the polyethylene glycol 6000 crystallites; ⊡, glass transition temperature of the polyethylene glycol 6000.

creases and breadth decreases with increasing ethyl cellulose concentration. The variation in the glass transition temperatures with blend composition is in agreement with that seen in a previous study on the plasticization of ethyl cellulose with polyethylene glycols (Sakellariou et al., 1986).

All the film formers studied in this work have been shown to be incompatible with ethyl cellulose throughout the composition range. This is in agreement with literature predictions (Petersen et al., 1969; Krause, 1978). Despite the phase separation recorded, one would expect that some form of interaction would occur due to the similarities in their chemical structure (Rowe, 1986b). Indeed the data generated here do imply that there is interaction via the unsubstituted hydroxyl groups, with hydroxypropyl methylcellulose with its increased substitution showing slightly reduced interaction. The appreciable interaction between ethyl cellulose and the pH-dependent soluble polymers has already been discussed above.

Equations relating the glass transition of a polyblend (T_g) with the composition of the blend can be used to determine the phase composition especially in blends exhibiting two sharp glass transitions. The equations used in this work were those derived by Fox (1956).

$$\frac{1}{T_g} = \frac{W_1}{T_{g1}} + \frac{W_2}{T_{g2}} \tag{1}$$

and Stoetling et al. (1970)

$$T_g = W_1 \cdot T_{g1} + W_2 \cdot T_{g2} \tag{2}$$

where W_1 and W_2 are the weight fractions of the components and T_{g1} and T_{g2} are their glass transition temperatures. Data for the ethyl cellulose/cellulose acetate phthalate and ethyl cellulose/polyethylene glycol 6000 blends are shown in Tables 1 and 2.

TABLE 1

COMPOSITIONS OF THE TWO PHASES OF ETHYL CELLULOSE (EC)/CELLULOSE ACETATE PHTHALATE (CAP) BLENDS AS CALCULATED FROM EQNS. 1 AND 2

Blend composition EC:CAP	Eqn. 1		Eqn. 2	
	Wt.% EC/[CAP]	Wt.% CAP/[EC]	Wt.% EC/[CAP]	Wt.% CAP/[EC]
80:20	31	14	32	14
60:40	23	11	25	11
40:60	26	5	28	5
20:80	32	5	32	5

TABLE 2

COMPOSITION OF THE TWO PHASES OF ETHYL CELLULOSE (EC)/POLYETHYLENE GLYCOL 6000 (PEG) BLENDS AS CALCULATED FROM EQNS. 1 AND 2

Blend composition EC:PEG	Eqn. 1		Eqn. 2	
	Wt.% EC/[PEG]	Wt.% PEG/[EC]	Wt.% EC/[PEG]	Wt.% PEG/[EC]
80:20	21	2	12.3	3
60:40	15	4	8.5	7
40:60	8	4	4.3	7
20:80	9.5	3	5.3	6

The results indicate that an appreciable amount of the ethyl cellulose had dispersed into the cellulose acetate phthalate-rich phase whereas the ethyl cellulose-rich phase contained distinctly less cellulose acetate phthalate, the amount of which decreases with decreasing ethyl cellulose content. This suggests that increased interaction takes place between the ethyl cellulose and the cellulose acetate phthalate in polyblends with ethyl cellulose as the major component. The corresponding data for the ethyl cellulose/polyethylene glycol 6000 indicates a lower compatibility, with the dispersion of the ethyl cellulose into the polyethylene glycol phase appearing to be favoured over the reverse one. Unfortunately the remaining polyblends could not be analysed using the equations because of the merging of the transitions of the individual components.

The area beneath the logarithmic decrement peak is associated with energy dissipation and can thus be used as an indication of the overall toughness of the specimen tested. Introduction of a second component into an ethyl cellulose film caused either a broadening of the peak or the introduction of a second peak or shoulder indicating a general toughening effect. Such an effect would invariably be beneficial in films applied to tablets or granules. Furthermore, the variation of the damping peak heights with the concentration of the corresponding component recorded for all the blends except those containing hydroxypropyl cellulose and hydroxypropyl methyl cellulose phthalate provides evidence for a domain morphology consisting of the minor component dispersed in the matrix of the major component as opposed to a laminate morphology.

In conclusion it can be seen that all the polyblends studied exhibited phase separation although with some mutual interaction at specific blend compositions. Such a finding is extremely important in understanding their transport mechanisms when used in pharmaceutical formulations especially when immersed in an aqueous environment, e.g. the gastrointestinal tract, since in such cases it would be expected that the soluble component would be leached out leaving aqueous-filled pores.

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