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An evaluation of the interaction and plasticizing efficiency of the polyethylene glycols in ethyl cellulose and hydroxypropyl methylcellulose films using the torsional braid pendulum

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Summary

The plasticizing efficiency of the polyethylene glycols when added to both ethyl cellulose and hydroxypropyl methylcellulose films has been evaluated by measuring the glass transition temperatures of formulations using the torsional braid pendulum. Compared to hydroxypropyl methylcellulose, where there was a significant reduction in the glass transition temperature with increasing concentration for all the polyethylene glycols, the effect in the case of ethyl cellulose was relatively small. In both cases the plasticizing efficiency of the polyethylene glycols decreased with increasing molecular weight with the high molecular weight solid members exhibiting phase separation. The experimental data was compared with predicted values using simple models based on the additivity of free volume. Agreement was limited to the systems where the plasticizer and polymer were compatible and no phase separation occurred.

Introduction

Film formers such as the cellulose ethers, ethyl cellulose and hydroxypropyl methylcellulose are now used extensively in the film coating of solid dosage forms. One commonly used method of modifying the properties of these polymers and enhancing their film-forming properties is by the addition of plasticizers. Plasticizers may be defined as low molecular weight substances, ideally of low volatility, which increase the flexibility of the macromolecules hence producing films which are softer, more pliable and often tougher with a subsequent improvement in their resistance to mechanical stress. The most commonly used plasticizers in tablet film coatings include the phthalate esters, polyethylene glycols of molecular weight 200–6000 $g \cdot mole^{-1}$, propylene glycol, glycerol and castor oil in concentrations varying from 5% to 30% by weight of the polymer (Rowe, 1984). Several methods have been suggested for evaluating the efficiency of a plasticizer with respect to the tablet coating requirements including intrinsic viscosity measurements (Entwistle and Rowe, 1979), mechanical strength testing (Entwistle and Rowe, 1979; Porter, 1980; Aulton et al., 1981), incidence of stress-induced defects (Rowe and Forse, 1981) and glass transition measurements (Entwistle and Rowe, 1979; Porter and

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Ridgway, 1983; Rowe et al., 1984; Okamafe and York, 1985; Sakellariou et al., 1985) or softening temperature (Masilungan and Lordi, 1984).

In the present work a dynamic mechanical technique, torsional braid analysis (TBA), recently applied in the determination of the thermomechanical properties and glass transition temperatures of the cellulose derivatives (Sakellariou et al., 1985) has been used to study the plasticization of both ethyl cellulose and hydroxypropyl methylcellulose by a series of polyethylene glycols with molecular weights from 200 to 6000 $g \cdot mole^{-1}$. The application of several free volume models and equations for the prediction of the properties of the plasticized film formers has also been investigated and discussed with respect to the deviations from the free volume theory.

Materials and Methods

The film formers studied were ethyl cellulose (EC — Grade N50, Hercules Powder Co., Wilmington, DE, U.S.A.) and hydroxypropyl methylcellulose (HPMC — Pharmacoat 606, Shin-Etsu Chemical Co., Tokyo, Japan). The plasticizers were a series of polyethylene glycols (PEG, BDH Chemicals, Poole, U.K.) with nominal molecular weights 200, 400, 600, 1000 and 6000 $g \cdot mole^{-1}$. Molecular characterization of the polyethylene glycols using both gel permeation chromatography with tetrahydrofuran as the carrier solvent and vapour pressure osmometry suggested that the materials, as supplied, were effectively monodispersed. All materials were used as received.

The apparatus used to provide the thermomechanical spectra of the systems studied has been fully described elsewhere (Rowe et al., 1984; Sakellariou, 1984; Sakellariou et al., 1985). The glass braids used in this study were prepared by first removing the size by heating in an oven at 500°C for 1 h followed by immersion in a 10 or 15% w/v solution of the formulation dissolved in solvent mixture consisting of equal parts by volume of dichloromethane and methanol. Braids containing the equivalent of 5, 10, 15, 20, 30 and 40% polyethylene glycol (concentration expressed as a weight percentage of the polymer) were dried to constant weight in an oven at 40–70°C. The thermomechanical spectra produced were analyzed as described previously (Sakellariou et al., 1985). The transition width was assessed from the damping/temperature curves where $W_{R\sqrt{2}}$ is the ratio of the area under the logarithmic decrement peak at half power height divided by the peak height.

Results and Discussion

Plasticization of the ethyl cellulose

Incorporation of the polyethylene glycols into ethyl cellulose films brought about considerable changes in the thermomechanical behaviour of the polymer. A typical example of the effect of polyethylene glycol 200 on ethyl cellulose is shown in Fig. 1a and b, while the relevant data of all the systems studied are listed in Table 1. In all cases there is one main transition recorded at a temperature close to the glass transition temperature of the pure polymer. Since this transition moved to slightly lower temperatures with increasing polyethylene glycol concentrations it was assigned to the plasticized polymer. In all the systems studied, with the exception of the unplasticized polymer, there was a broad plateau occurring at temperatures varying between 50 and 80°C. Although the damping level of this plateau increased with increasing polyethylene glycol concentration, no relationship could be established between either the shape or maximum damping and the grade of the polyethylene glycol. Osterwald et al. (1982) reported a similar behaviour for polyethylene glycol 6000 dispersed in hydroxypropyl methylcellulose phthalate interpreting it as an extended melting peak. However, it must be stated, that although the solidification point for the 6000 grade lies within this temperature region, those of the lower molecular weight grades occur at much lower temperatures. Since the plateau is present for all the grades of the polyethylene glycols it can be postulated that this may be due to domains of molten or rubber-like polyethylene glycol dispersed within the polymer matrix. Incorporation of the 6000 grade tended to produce a relatively narrow transition unaffected by concentration whereas the

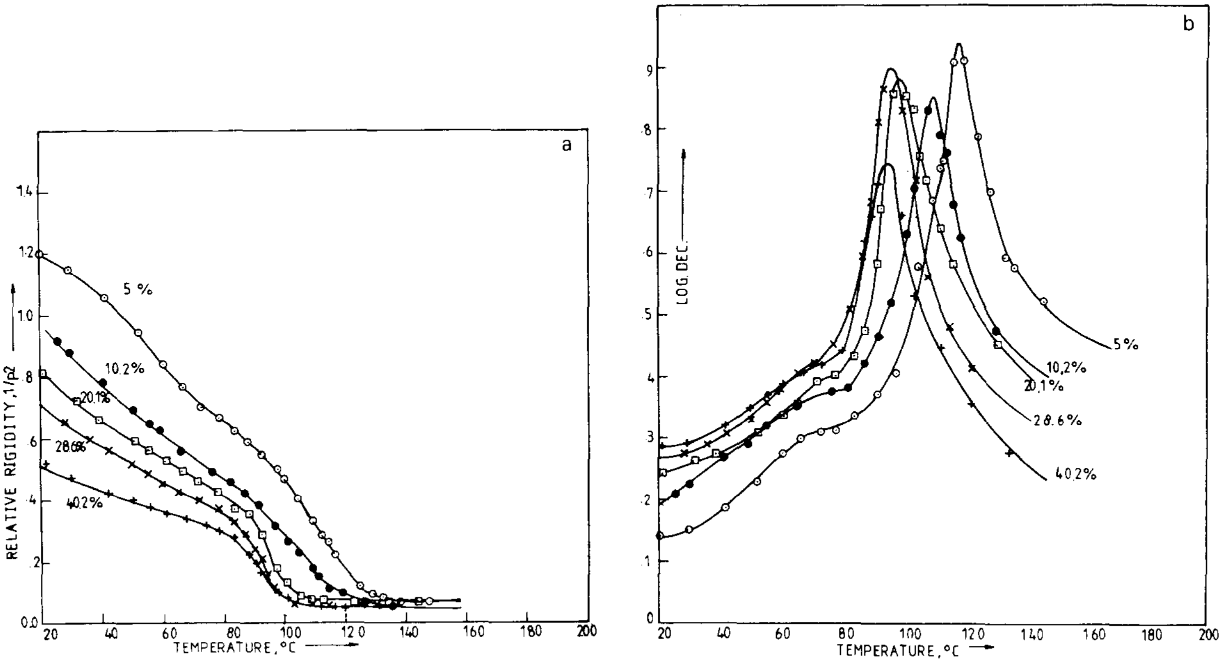

Fig. 1. The thermomechanical spectra of ethyl cellulose plasticized with polyethylene glycol 200. (a) relative regidity; (b) logarithmic decrement.

TABLE 1

THERMOMECHANICAL DATA FOR THE POLYETHYLENE GLYCOL/ETHYL CELLULOSE SYSTEMS

PEG grade	Concentration (% w/w)	T_g (°C)	$\Delta_{20^\circ C}$	Δ_{max}	$W_{R\sqrt{2}}$ (°C)
200	5.0	118	0.145	0.940	8.4
200	10.2	110	0.200	0.855	7.8
200	20.1	99	0.245	0.880	9.4
200	28.6	96	0.260	0.895	6.8
200	40.2	95.5	0.275	0.745	10.5
400	5.6	124	0.110	0.835	8.8
400	9.5	118	0.135	0.845	7.2
400	15.0	113	0.205	0.725	8.3
400	19.0	111	0.165	0.715	7.7
600	5.0	125	0.105	0.900	4.5
600	10.0	120	0.175	0.805	4.1
600	14.7	117	0.215	0.810	7.1
600	19.7	116	0.215	0.815	8.6
1 000	5.1	127	0.100	0.930	4.9
1 000	10.1	127	0.135	0.900	8.2
1 000	15.3	127	0.135	0.905	10.2
1 000	20.2	127	0.145	0.985	12.3
6 000	4.99	129	0.120	1.045	3.5
6 000	9.98	129	0.120	1.005	3.5
6 000	15.0	129	0.120	0.010	3.7
6 000	19.0	123	0.200	1.005	3.5

lower molecular weight grades exhibited wider transitions which tended to broaden further with increasing concentration. The maximum logarithmic decrement decreased with increasing polyethylene glycol concentration for all grades of the plasticizer although the extent of the depression was considerably less with the higher molecular weight grades.

The variation of the glass transition of the ethyl cellulose with both molecular weight and concentration (Table 1) best describes the plasticizing efficiency of the polyethylene glycols. It can be seen that the efficiency of these materials in lowering the glass transition temperature of the ethyl cellulose decreases with increasing molecular size with the two higher members of the series hardly causing any appreciable change. This effect is probably due not only to molecular size, which would affect the diffusion of the molecules into the ethyl cellulose matrix, but also the effective molar concentration of the hydroxyl groups on the polyethylene glycol molecule since this would certainly decrease dramatically on increasing the molecular weight of the plasticizer.

Plasticization of hydroxypropyl methylcellulose

Typical examples of the thermomechanical behaviour of hydroxypropyl methylcellulose plasticized with polyethylene glycol 200 and 6000 are shown in Figs. 2a, b and 3a, b, while the relevant data for all the systems studied are given in Table 2. A relatively broad transition was recorded in both the logarithmic decrement and relative rigidity curves. Since the position of the maximum logarithmic decrement was shifted to lower temperatures with increasing polyethylene glycol concentration this was assigned to the plasticized polymer. A number of samples exhibited a shoulder before the glass transition temperature at approximately 40°C and extending to approximately 80°C analogous to the plateau region seen on the ethyl cellulose systems. Although the level of the maximum damping of this shoulder was proportional to the polyethylene glycol concentra-

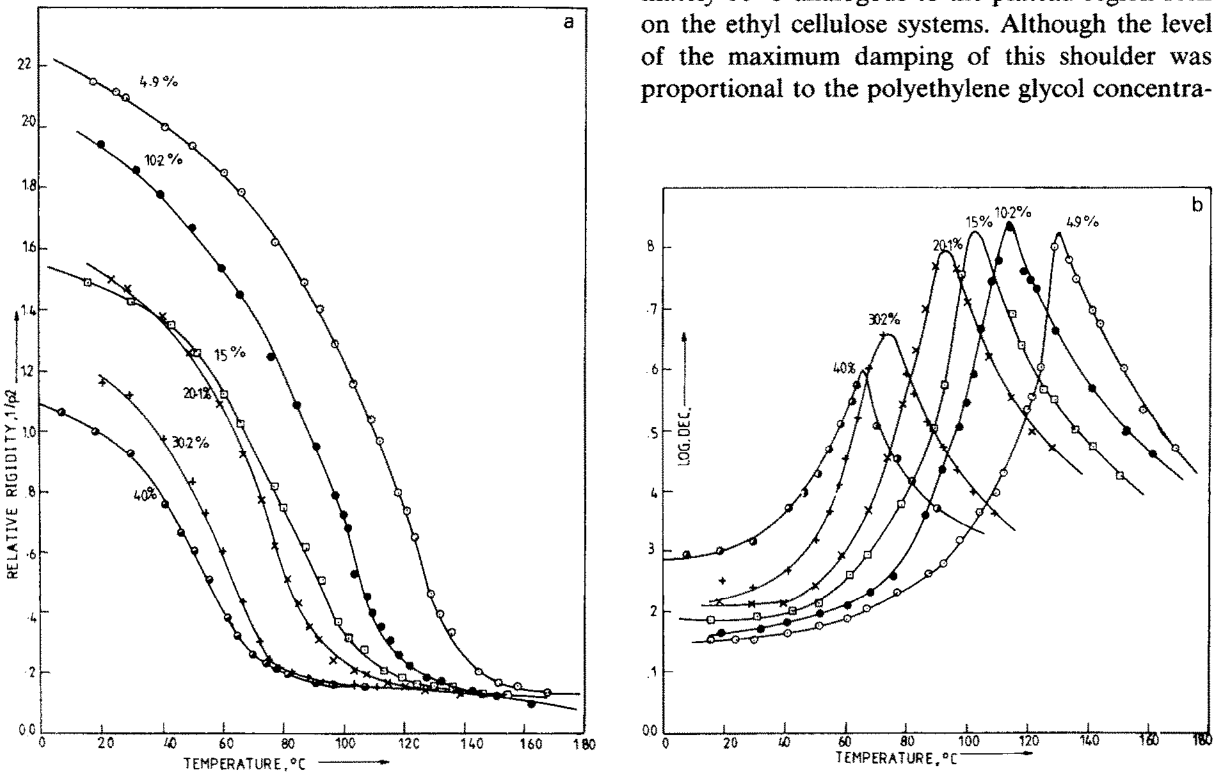

Fig. 2. The thermomechanical spectra of hydroxypropyl methylcellulose plasticized with polyethylene glycol 200. (a) relative rigidity; (b) logarithmic decrement.

TABLE 2

THERMOMECHANICAL DATA FOR THE POLYETHYLENE GLYCOL/HYDROXYPROPYL METHYLCELLULOSE SYSTEMS

PEG grade	Concentration (% w/w)	T_g (°C)	$\Delta_{20°C}$	Δ_{max}	$W_{R\sqrt{2}}$ (°C)
200	3.7	136.5	0.115	0.760	6.5
200	4.9	130.5	0.150	0.830	8.3
200	7.5	121	0.135	0.740	6.2
200	10.2	114	0.160	0.645	7.7
200	12.6	108.5	0.160	0.690	7.6
200	15.0	103	0.190	0.830	11.8
200	20.1	93	0.215	0.795	14.6
200	30.2	74.5	0.230	0.660	15.1
200	40.0	66	0.290	0.600	16.1
400	4.8	136.5	0.115	0.825	9.4
400	10.0	119	0.120	0.665	14.0
400	13.0	111	0.140	0.645	9.5
400	20.0	99	0.170	0.590	13.8
400	28.0	90.5	0.190	0.616	16.3
400	39.0	83	0.240	0.560	21.7
600	4.9	138	0.100	0.695	12.1
600	11.7	119	0.135	0.617	10.4
600	15.0	115	0.175	0.670	19.1
600	19.8	104.5	0.175	0.537	20.0
600	29.3	96	0.150	0.575	14.5
600	39.6	86	0.180	0.590	26.4
1000	5.0	139	0.09	0.710	13.9
1000	8.8	131	0.125	0.660	14.0
1000	14.6	122	0.145	0.630	16.8
1000	19.0	115	0.150	0.685	21.6
1000	36.2	105.5	0.215	0.460	25.1
6000	5.0	155	0.100	0.830	10.1
6000	10.3	154	0.160	0.766	10.1
6000	14.5	153	0.120	0.805	9.8
6000	20.3	152	0.130	0.740	15.8

tion, there was no relationship with molecular size. The level of the maximum logarithmic decrement decreased with increasing polyethylene glycol concentration indicating an appreciable interaction between the polymer and the plasticizer. Polyethylene glycol 6000 showed a depressed tendency for such an effect indicating a poorer interaction. Although there was scatter in the determination of the peak width, it did tend to increase with plasticizer concentration for all but the polyethylene glycol 6000. From both the logarithmic decrement and relative rigidity curves, it was possible to investigate the compatibility limits for phase separation of the plasticizer in the film (Table 3). This suggests that there is a definite relationship between the molecular weight of the polyethylene glycol and its interaction with the polymer. The limits are similar to those reported by Okamafe and York (1985) and were confirmed by producing films and observing them for any signs of blushing indicating migration of the plasticizer.

The variation of glass transition temperature with increasing plasticizer concentration (Table 2) shows that the plasticizing efficiency of polyethylene glycol decreases with increasing molecular weight with polyethylene glycol 6000 being virtu-

TABLE 3

COMPATIBILITY LIMITS FOR THE POLYETHYLENE GLYCOL/HYDROXYPROPYL METHYLCELLULOSE SYSTEM

PEG grade	Compatibility limit (% w/v)
200	40
400	28
600	28
1000	15
6000	10

ally a non-plasticizer for the polymer. These observations are in good agreement with both intrinsic viscosity data which showed a maximum viscosity for hydroxypropyl methylcellulose dissolved in polyethylene glycol 200 (Entwistle and Rowe, 1979) and with data on the mechanical properties of hydroxypropyl methylcellulose films plasticized with polyethylene glycols of varying molecular weight (Aulton et al., 1981).

Theoretical considerations

It is interesting to compare the experimental data with those predicted using equations relying on the additivity of the free volume of both the polymer and the diluent/plasticizer. The first equation chosen was that of Garfield and Petrie (1964) which relates the plasticizing efficiency parameter, β, of a plasticizer at a reference temperature, T, to the glass transition temperatures and thermal expansion coefficients of the polymer and plasticizer, i.e. T_{gp}, T_{gd}, α_p, α_d, respectively:

$$\text{i.e. } \beta(T) = \alpha_p(T - T_{gp}) - \alpha_d(T - T_{gd}) \quad (1)$$

The second equation chosen was that of Kelley

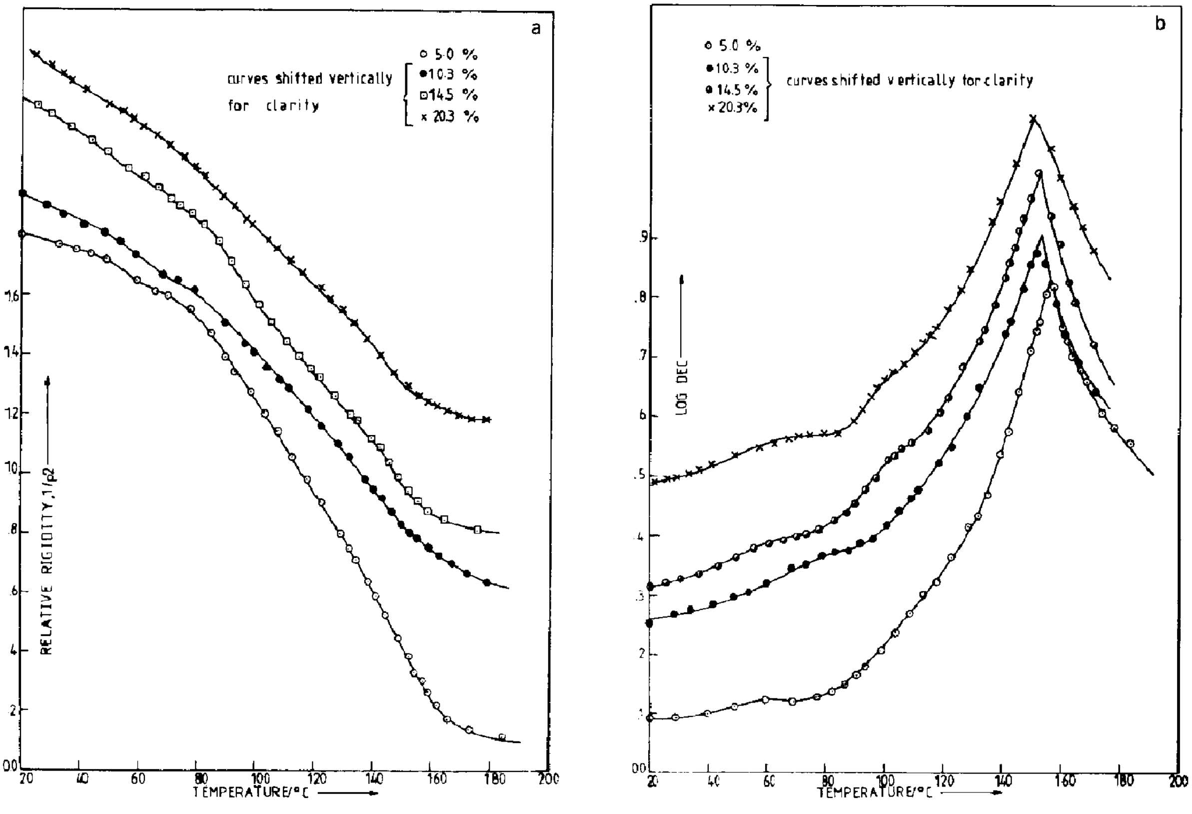

Fig. 3. The thermomechanical spectra of hydroxypropyl methylcellulose plasticized with polyethylene glycol 6000. (a) relative rigity; (b) logarithmic decrement.

and Bueche (1961) which relates the predicted glass transition temperature of the plasticized polymer, T_g, with the volume fractions of the polymer and plasticizer, V_p, and V_d respectively:

$$T_g = \frac{\alpha_p \cdot V_p \cdot T_{gp} + \alpha_d \cdot V_d \cdot T_{gd}}{\alpha_p \cdot V_p + \alpha_d \cdot V_d} \tag{2}$$

Table 5 shows values for β (using constants for the equation as given in Table 4) at two reference temperatures, firstly at the glass transition temperature of the polymer and secondly at 40°C to facilitate comparison with data produced by Fujita and Kishimoto (1958). It can be seen that the β parameters for the ethyl cellulose system are generally lower than those for the hydroxypropyl methylcellulose, decreasing with increasing polyethylene glycol molecular weight for both systems. It is interesting to note that the maximum β parameter for the ethyl cellulose system is similar to that for the hydroxypropyl methylcellulose system containing polyethylene glycol 6000 (cf. the experimental data which shows phase separation and poor interaction in these systems). Although the calculated values for the β parameter are of the expected order (0.05–0.30; Fujita and Kishimoto, 1958) they do not provide any information on the validity of the assumptions made in the derivation of the equation.

Application of the Kelley and Bueche (1961) equation does provide information of the validity of the approach by comparing predicted glass transition temperatures with experimental data. It can be seen (Fig. 4) that for hydroxypropyl methylcellulose the predicted values compare favourably with the experimental data for all plasticizer concentrations up to 15% for all the grades of polyethylene glycol studied with the exception of PEC 1000 where the concentration was reduced to 10% and of PEG 6000 where there was poor agreement at all concentrations. For ethylcellulose (Fig. 5), with the exception of the PEG 200 at concentrations below 10%, there was poor agreement in all cases. It is interesting to note that in every case where there is poor agreement the experimental curves always deviate toward higher temperatures. These observations added to the fact that poor agreement was invariably seen in systems where there were signs of phase separation would suggest the assumptions in the equation are invalid.

TABLE 4

CONSTANTS USED IN THE PREDICTIVE EQUATIONS

	T_{gp} [a] (°C)	α_p [b] (°C^{-1})	T_{gd} (°C)	α_d [c] (°C^{-1})
Ethyl cellulose	131.5	4.8×10^{-4}		
Hydroxypropyl methylcellulose	153.5	4.8×10^{-4}		
PEG 200			−77	7.3×10^{-4}
PEG 400			−70	7.3×10^{-4}
PEG 600			−67	7.3×10^{-4}
PEG 1000			−65	7.3×10^{-4}
PEG 6000			−56	7.3×10^{-4}

[a] Sakellariou et al. (1985).

[b] Williams et al. (1955).

[c] Trade Literature, Hoechst Polyglycol Manual (1977).

TABLE 5

PLASTICIZING EFFICIENCY (β) PARAMETERS AT A — THE GLASS TRANSITION TEMPERATURE OF THE POLYMER AND AT B — 40°C

PEG grade	A		B	
	PEG/ HPMC	PEG/ EC	PEG/ HPMC	PEG/ EC
200	0.168	0.152	0.240	0.168
400	0.163	0.147	0.173	0.163
600	0.160	0.144	0.169	0.159
1000	0.156	0.139	0.166	0.155
6000	0.153	0.137	0.163	0.152

Further information on this point can be obtained by involving the theory of Braun and Kovacs (1965) who proposed that the introduction of an interaction constant, k, to account for the non-additivity of the free volumes of the components. From their theory it is possible to derive a modified Kelley and Bueche equation.
i.e.

$$T_g = \left[\frac{\alpha_p \cdot V_p \cdot T_{gd} + \alpha_d \cdot V_d \cdot T_{gd}}{\alpha_p \cdot V_p + \alpha_d \cdot V_d} \right]$$

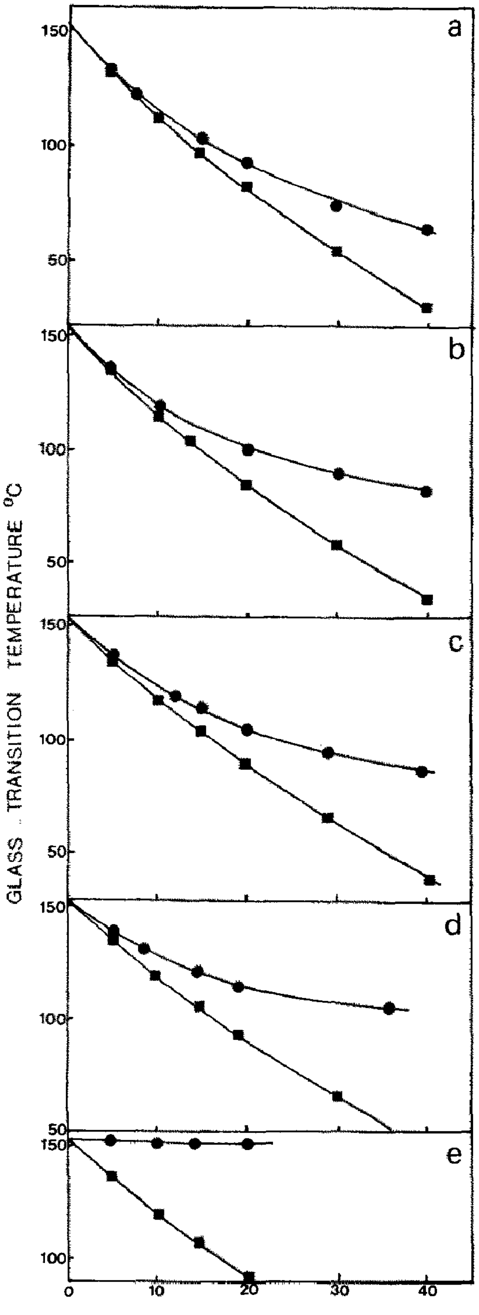

Fig. 4. The effect of concentration and grade of polyethylene glycol on the glass transition temperature of hydroxypropyl methylcellulose. (a) PEG 200; (b) PEG 400; (c) PEG 600; (d) PEG 1000; (e) PEG 6000. ●, experimental values; ■, calculated values.

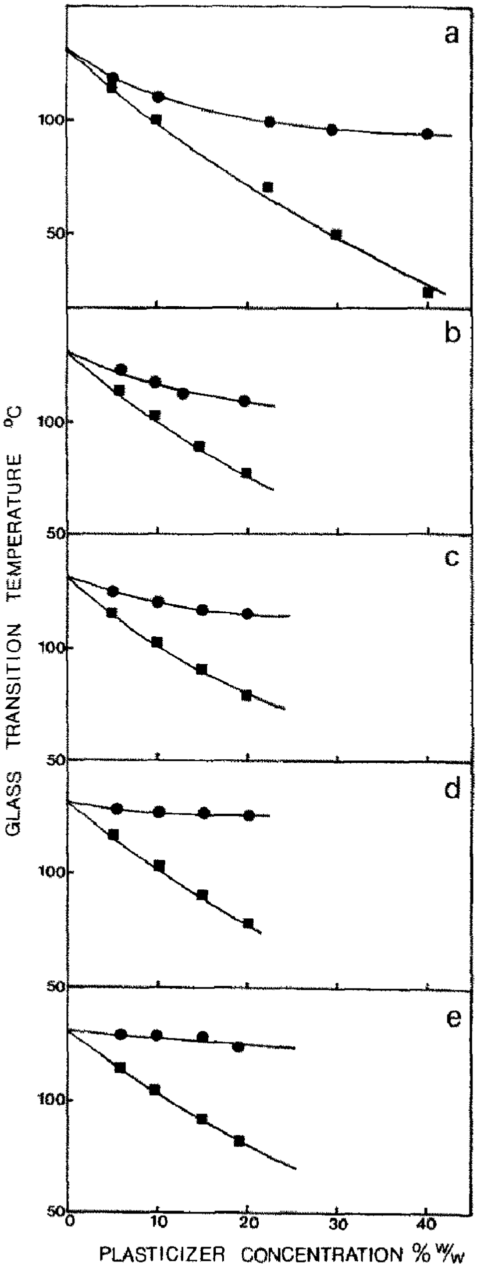

Fig. 5. The effect of concentration and grade of polyethylene glycol on the glass transition temperature of ethyl cellulose. (a) PEG 200; (b) PEG 400; (c) PEG 600; (d) PEG 1000; (e) PEG 6000. ●, experimental values; ■, calculated values.

TABLE 6

INTERACTION CONSTANTS (k) AND CORRELATION COEFFICIENTS CALCULATED FOR EQN. 3

PEG grade	PEG/HPMC		PEG/EC	
	k	Correlation coefficient	k	Correlation coefficient
200	0.1980	0.9413	0.1165	0.9036
400	0.1417	0.9517	0.1448	0.8927
600	0.1453	0.9899	0.1260	0.8725
1000	0.2070	0.9916	0.1699	0.9401
6000	0.1535	0.9924	0.1953	0.9970

$$+k\left[\frac{V_p \cdot V_d}{\alpha_p \cdot V_p + \alpha_d \cdot V_d}\right] \qquad (3)$$

According to the model proposed by Braun and Kovacs (1965), the deviation of the theoretical from the experimental data will vary linearly with the quantity $V_p \cdot V_d/\alpha_p \cdot V_p + \alpha_d \cdot V_d$ and the slope of the graph will be of the order of 10^{-2}. Table 6 summarizes the so calculated k values for both the polymers studied and it can be seen than k exceeds the expected value by a factor of 10. This implies that the non-additivity of the free volumes in the mixture is only partially responsible for the deviations in the predicted and experimental data, and that other factors are involved. Okamafe and York (1985) have suggested that the broad molecular weight distribution of the cellulose ethers might be responsible but, although such a factor would affect the recorded value of the T_g, it is unlikely that it depresses the plasticizing efficiency of the polyethylene glycols with increasing concentration. The depressed plasticizing efficiency of the polyethylene glycols above their compatibility limits must be due to their phase separation and their aggregation into small domains dispersed in the polymer matrix. Consequently the actual amount of the plasticizer dispersed at a molecular level is less than the nominal. These phase separated domains will have a specific effect on the mechanical behaviour of the films so prepared but will have little effect on their glass transition temperature.

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