Analysis of the permeation and mechanical characteristics of some aqueous-based film coating systems*

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The moisture permeability and mechanical properties of some aqueous-based free films have been evaluated using sorption–desorption and stress–strain techniques, respectively. These properties for blends of two film-formers—hydroxypropyl methylcellulose and polyvinyl alcohol—have been compared with those of hydroxypropyl methylcellulose films plasticized with polyethylene glycols. The polyethylene glycols generally increased the moisture permeability of hydroxypropyl methylcellulose films while polyvinyl alcohol decreased it. Both polyvinyl alcohol and the polyethylene glycols lowered tensile strength at break and Young's modulus but the effects of the polyethylene glycols were more pronounced. These results are discussed in terms of structural interactions between film components. All film systems evaluated, except that containing hydroxypropyl methylcellulose alone, exhibited a degree of anisotropy, a phenomenon with potentially adverse consequences in tablet film coating.

In view of the adverse effects of various environmental factors on product integrity, studies on pharmaceutical film coatings often examine their permeability to water vapour as well as their ability to provide mechanical protection to solid dosage forms. The most widely used technique for measuring moisture permeability is the permeability cup method (Lachman & Drubulis 1964; Banker et al 1966; Porter & Ridgway 1982) based on ASTM method E96–66. This method, though simple, suffers from certain disadvantages (Perera & Selier 1973) in that complete sealing of the cup is difficult and stagnant layers of air in the cup constitute a permeation barrier. In addition, the usual practice of periodic weighing may introduce substantial errors to the results. The sorption–desorption technique (Sacher & Susko 1981), in contrast, does not have these drawbacks and unlike the permeability cup method, the presence of pores in the film has little or no effect on results. The most important feature of this technique, however, is that it provides a deeper insight into permeability mechanisms and thus offers a realistic basis for improving the permeation properties of tablet film coats.

To establish required mechanical properties of films, Marin (1965) reproduced various types of stress-strain curves for polymers. These indicated that for a film to have excellent mechanical characteristics, it must be hard, tough and yet very extensible. Film-coated tablets, unfortunately, are generally unsuitable for assessing the mechanical properties of films because it is extremely difficult to measure tensile strength and elongation. Nonetheless, Rowe (1976) used a microindentation technique to determine the hardness and elastic modulus of films on spray-coated tablets. Tensile measurements on free films, such as those carried out by Allen et al (1972) and Aulton et al (1981), provide stress-strain diagrams, analysis of which can yield tensile strength, Young's modulus, yield point, elongation and energy absorbed under stress.

Although attempts continue to be made to improve the overall properties of pharmaceutical film coatings, few publications consider the use of blends of film-forming materials derived from aqueous systems. With the slow rate of discovery of new film formers, greater attention is likely to be paid in the near future to blending of existing materials with a view to achieving better film characteristics. In this work, we have evaluated the moisture permeability and mechanical properties, using the sorption–desorption and stress–strain techniques, respectively, of free cast hydroxypropyl methyl-cellulose/polyvinyl alcohol film blends and compared them with those of hydroxypropyl methylcellulose plasticized, respectively, with polyethylene glycol 400

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and polyethylene glycol 1000. The possible effect of molecular orientation in tablet film coats is also considered.

MATERIALS AND METHODS

The two film formers employed—hydroxypropyl methylcellulose (Pharmacoat 606) and partially hydrolysed polyvinyl alcohol (Poval PA-5) with a degree of hydrolysis of 88%—were manufactured by Shin-Etsu Chemical Co. Ltd, Japan. Polyethylene glycols 400 and 1000 (British Drug Houses, Poole, U.K.) were used as plasticizers. Coating formulations were prepared from aqueous solutions of the film formers (10% w/v) and of the plasticizers (20% w/v).

Films were cast on the inner surface of a lipped Perspex cylinder (length: 18·0 cm and internal diameter: 12·0 cm), rotating at 10 rev min^{-1}, maintained at a temperature of 40–42 °C for 6 h. They were then conditioned, after removal from the cylinder, at 20 °C and 58% rh for one week before test. Preliminary trials showed that film properties became stable within this period. Dried films containing up to 100% w/w polyvinyl alcohol based on the content of hydroxypropyl methylcellulose were obtained but above concentrations of 40% w/w (for polyethylene glycol 400) and 30% w/w (for polyethylene glycol 1000) of hydroxypropyl methylcellulose, films could not be peeled from the casting substrate because they adhered strongly and were too soft.

The moisture permeability measuring apparatus incorporates an automatic recording microbalance (C. I. Electronics, Salisbury, U.K.) to which the rectangular film specimen 4 × 1·5 cm is attached, a vacuum line as well as a controlled humidity line. The whole unit was placed in a controlled temperature room (20 ± 0·5 °C). The system (minus the humidity line) was evacuated overnight at 10^{-4} mbar to remove gases and vapours from the film and eliminate the air barrier around it. (This procedure satisfies one of Crank & Park's (1949) boundary conditions, viz, zero initial moisture concentration in the film.) A stream of moist air at 75% rh was then admitted until the film reached equilibrium sorption weight. We then carried out desorption under vacuum (10^{-4} mbar) until a constant weight was attained. All measurements were in duplicate.

Tensile strength at break, Young's modulus and percent elongation at break were calculated from stress-strain curves obtained using an Instron TT-BM tensile tester (Instron Ltd, High Wycombe, U.K.) at a crosshead speed of 5 mm min^{-1}. The procedure employed was based on ASTM method D638–77a. In order to test for anisotropy, for each test six dumb-bell shaped specimens were cut perpendicular to, and six parallel to, the axis of rotation of the casting cylinder.

Film thickness was determined with a micrometer dial gauge type 130/5 (Thomas Mercer Ltd., St Albans, U.K.) which has a sensitivity of 2 × 10^{-4} cm. Thickness was measured at five different points along the gauge length of samples for both permeability and tensile tests. Mean thickness values were used in evaluating Young's modulus and sorption–desorption data while the minimum thickness values were employed in calculating tensile strength at break. In all cases, thickness at any one point did not vary from the mean value for that specimen by more than 10%.

RESULTS AND DISCUSSION

Films of hydroxypropyl methylcellulose alone and all films prepared from hydroxypropyl methylcellulose/ polyethylene glycol combinations had a satisfactory appearance. Similar observations were made for films containing up to 40% w/w polyvinyl alcohol based on hydroxypropyl methylcellulose content. However above this concentration level irregular spots and patches were observed on the films. We attributed this to excess polyvinyl alcohol being thrown out of the system when the level at which it is compatible with hydroxypropyl methylcellulose was passed. Nonetheless, such films were also evaluated in an attempt to understand the effect of incompatibility on permeation and mechanical properties.

Permeability properties

The sorption–desorption data were analysed using equation (1) which was derived by Long & Thompson (1955). It is based on the Boltzmann solution of Fick's law for the initial stages of Fickian diffusion in films where diffusion is concentration-dependent.

$$\frac{Mt}{Me} = K \sqrt{t/l} \tag{1}$$

where Mt is the weight change (sorption or desorption) at time, t; Me is the weight change (sorption or desorption) at equilibrium; l is the film thickness, and K is a constant. Plots of Mt/Me against $\sqrt{t}/l$ were initially linear and K is the slope of the initial linear portion. The integral (mean) diffusion coefficient, D, was obtained according to equation (2) (Long & Thompson 1955).

$$D = \frac{1}{C_1} \int_{C_0}^{C_1} D' \, dc \equiv \frac{\pi}{32}(K^2_s + K^2_d) \qquad (2)$$

Where D' is the diffusion coefficient at any concentration between C_0 and C_1; C_0 and C_1, respectively, are moisture concentration at $t = 0$ and equilibrium. K_s and K_d represent the initial slopes of the sorption and desorption curves, respectively. According to Henry's law, the solubility coefficient, S, is given by equation (3).

$$S = \frac{C_1}{p} \qquad (3)$$

Where p is the vapour pressure of the moist air. Crank (1975) showed that the solution of Fick's differential equations with proper boundary conditions gives equation (4).

$$P = DS \qquad (4)$$

where P is the permeability coefficient.

A plot of diffusion coefficient against concentration (see Fig. 1) shows that while the plasticizers (polyethylene glycols 400 and 1000) increased the diffusion coefficient of hydroxypropyl methylcellulose, the diffusion coefficient fell with increase in polyvinyl alcohol concentration up to 40% w/w of hydroxypropyl methylcellulose. The interaction of the polyethylene glycols with hydroxypropyl methylcellulose results in a decreased molecular order and enhanced chain mobility in the latter. Consequently,
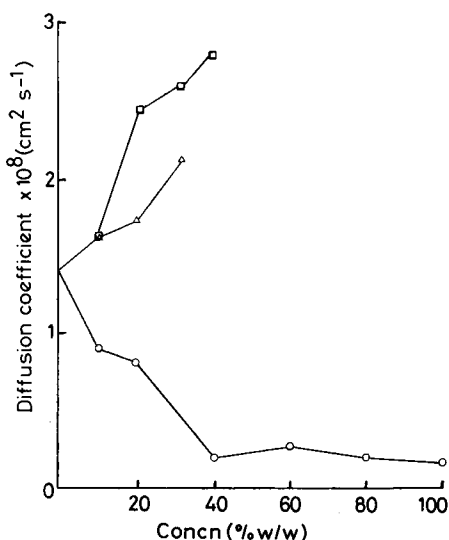

FIG. 1. Effect of concentration of polyethylene glycols 400 (□) and 1000 (△), and polyvinyl alcohol (○) on the diffusion coefficient of hydroxypropyl methylcellulose film at 20 °C, 75% rh.

the diffusion 'holes' or pathways become enlarged and passage of water vapour molecules is facilitated. Polyvinyl alcohol, on the other hand, appears to interact with hydroxypropyl methylcellulose by a mechanism that reduces in size and/or number the diffusion pathways, leading to decreased diffusivity. The largely unchanged diffusion coefficient above the polyvinyl alcohol concentration of 40% w/w is consistent with the observation made earlier, that excess polyvinyl alcohol appeared to be deposited in patches in the film beyond this concentration. This may well be an indication that hydroxypropyl methylcellulose interacts effectively with no more than 40% of its own weight of polyvinyl alcohol.

Fig. 2 indicates that the solubility coefficient of hydroxypropyl methylcellulose decreased as the levels of all three additives were raised in the rank order polyethylene glycol 1000 > polyethylene glycol 400 > polyvinyl alcohol. Solubility coefficient is a useful indication of the affinity of the film for permeating moisture. The polyethylene glycols have twice the number of hydroxyl groups per molecule compared with polyvinyl alcohol. Thus the polyethylene glycols form more hydrogen bonds with hydroxypropyl methylcellulose, leaving it with fewer bonding sites for the permeating water vapour. This explains the comparatively lower solubility coefficient values for hydroxypropyl methylcellulose/polyethylene glycol film combinations. Among the two polyethylene glycols, the lower solubility coefficient achieved by polyethylene glycol 1000 is probably due to its longer ethylene backbone (and hence lower hydrophilicity) which reduces the moisture affinity of the film.

The effect of additive concentration on the permeability coefficient is shown in Fig. 3. The permeability process itself may be divided into two stages, namely, solubility and diffusion. Permeating moisture first dissolves in the film, then travels along the diffusion channels and finally escapes on the other side of the film. It is clear, in view of the similarity of Figs 1 and 3, that in the film systems evaluated, diffusivity plays a far more important role than solubility in determining permeability.

The significantly lower moisture permeability of hydroxypropyl methylcellulose/polyvinyl alcohol film blend is interesting. Although films of polyvinyl alcohol alone were observed in preliminary trials to be slightly less permeable to water vapour than films of hydroxypropyl methylcellulose alone, the permeability coefficient of a blend of the two film formers (polyvinyl alcohol 40% w/w of hydroxypropyl methylcellulose) exhibits an approximately
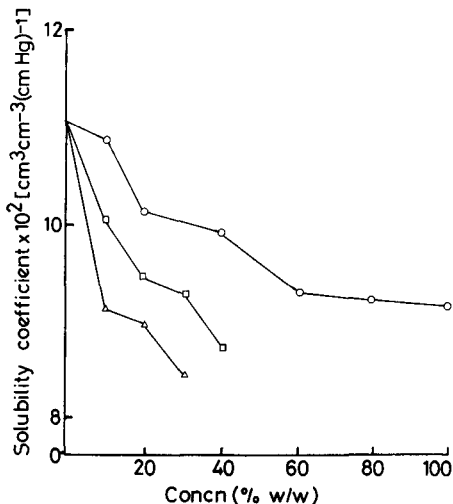
FIG. 2. Effect of concentration of polyethylene glycols 400 (□) and 1000 (△) and polyvinyl alcohol (○) on the solubility coefficient of hydroxypropyl methylcellulose film at 20 °C, 75% rh.

polycarbonate cast from mixed solvents which Jackson & Caldwell (1967) attributed to crystallinity. Polyvinyl alcohol exhibits crystallinity (Banker 1966). Hydroxypropyl methylcellulose with a melting point of 260 °C* is also semi-crystalline since wholly amorphous polymers do not have a melting point (Beaman 1952). The crystalline phase of a film is virtually impermeable to water molecules (Michaels 1965) because diffusion 'holes' are either not present or are too small to allow passage of moisture. Thus water vapour bypasses the crystalline areas and is exclusively transported across the amorphous areas of the film. Michaels & Bixler (1961) found that crystallinity levels of 60–80% decreased diffusivities in some films to between one-tenth and one-thirtieth of values for equivalent amorphous films. The diffusion coefficient of hydroxypropyl methylcellulose/polyvinyl alcohol film was approximately one-eighth of that of hydroxypropyl methylcellulose film alone.
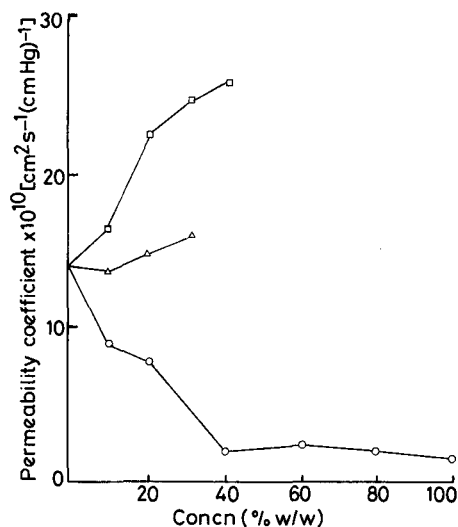
eightfold reduction in permeability coefficient compared with that of a film of hydroxypropyl methylcellulose alone. The large fall in diffusion rate in this instance is not attributed to the formation of hydrogen bonds between polyvinyl alcohol and diffusing water molecules, as Porter (1980) suggested may occur when certain additives are employed. This is because the polyethylene glycols with more hydroxyl groups per molecule, and which are therefore capable of forming more hydrogen bonds with penetrating water molecules, actually increased diffusion rate. A crosslinking mechanism is also not considered to be responsible since cross-linking, which involves primary valence bonding between adjacent polymer segments, would almost certainly have rendered the film insoluble. In addition, Michaels (1965) postulated that because of the small size of a water molecule the degree of cross-linkage required to reduce its diffusivity significantly will have to be high. Such magnitude of cross-linking will greatly enhance chain stiffness and inevitably lead to increased tensile strength and Young's modulus, but as is shown later, these mechanical properties were decreased in hydroxypropyl methylcellulose/polyvinyl alcohol films.

One possible explanation of the reduced diffusivity of the film blend is that its degree of crystallinity is higher than that of hydroxypropyl methylcellulose film. The slight haziness of the film blend (which was, nevertheless, transparent) can be compared with the haziness of transparent films of bisphenol A

FIG. 3. Effect of concentration of polyethylene glycols 400 (□) and 1000 (△), and polyvinyl alcohol (○) on the permeability coefficient of hydroxypropyl methylcellulose film at 20 °C, 75% rh.

One of the main attractions of the sorption-desorption technique is that by utilizing the information it provides on permeability mechanisms, the film formulator is in a better position to modify permeability by employing suitable additives to inhibit diffusion and solubility without rendering the film insoluble. A weakness of this method, however, lies in the fact that the permeability data produced

* Dow Chemical Corp. handbook on Methocel products.

does not take account of moisture transport across pores and microscopic cracks, a process that may occur in film coats applied to tablets.

Mechanical properties

An ideal tablet film coat should be hard, tough and extendible. This implies that a film with these features will have a high tensile strength, Young's modulus and yield point as well as a satisfactory elongation. Plasticization generally leads to a reduction in tensile strength at break and Young's modulus and an increase in elongation of hydroxypropyl methylcellulose films (Aulton et al 1981). The results in Figs 4 and 5 as well as Table 1 support this observation. Increasing the concentration of polyethylene glycols 400 and 1000 progressively lowers tensile strength at break and Young's modulus. Although the same picture emerges with the hydroxypropyl methylcellulose/polyvinyl alcohol blend, the decrease in these properties is much less up to the polyvinyl alcohol concentration of 40% w/w of hydroxypropyl methylcellulose, the level at which the components of the blend are compatible. Table 1 shows that while increase in the concentration of the polyethylene glycols generally improved the elongation of the films, polyvinyl alcohol lowered elongation, implying that unlike the plasticizers the latter inhibited polymer chain mobility. Polyethylene glycol 400, with a lower molecular weight than polyethylene glycol 1000, has greater effects than the latter on tensile strength and Young's modulus, indicating that it is a more effective plasticizer of hydroxypropyl methylcellulose. This is in agreement with the findings of Entwistle & Rowe (1979) and

Aulton et al (1981) who noted that the higher the molecular weight of the polyethylene glycols the less the reduction in ultimate tensile strength and modulus of elasticity of hydroxypropyl methylcellulose films.
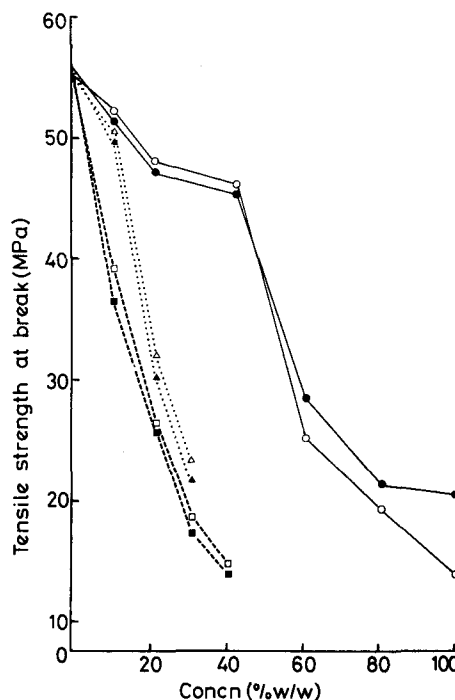

FIG. 4. Effect of concentration of polyethylene glycols 400 (□, ■) and 1000 (△, ▲), and polyvinyl alchol (○, ●) on the tensile strength at break of hydroxypropyl methylcellulose film at 20 °C, 60% rh [Open symbols = 'parallel' samples, closed symbols = 'perpendicular' samples.]

Since the effects of the additives on hydroxypropyl methylcellulose film are a consequence of structural interaction, it may be possible to correlate the moisture permeability of the examined films with their mechanical properties. The mode of plasticizer interaction with film formers generally involves severance of bonds (mainly hydrogen bonds in the case of hydroxypropyl methylcellulose) between adjacent segments of the film former in which the plasticizer then becomes sandwiched. The result is a loose structure in which reduced links between the segments of the film former not only lead to enhanced segmental mobility (and hence increased diffusion) but also lower resistance to stress (as indicated by diminished tensile strength at break) and deformation (as shown by decreased Young's modulus).

Table 1. Percent elongation at break (± standard deviation) of hydroxypropyl methylcellulose films containing polyethylene glycols 400 and 1000 (PEG 400 and PEG 1000), and polyvinyl alcohol (PVA), respectively, at 20 °C, 60% rh.

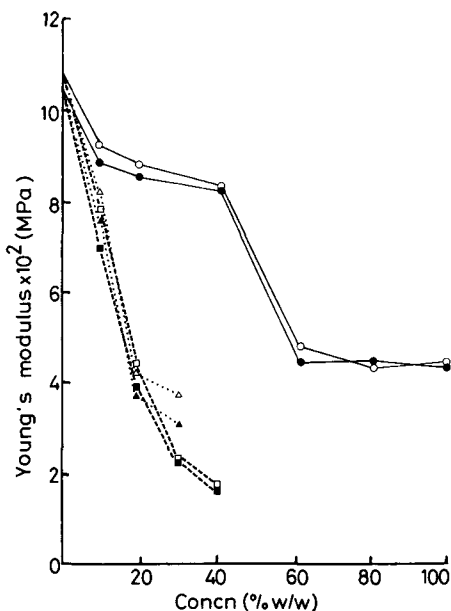|		% elongation	
Additive (% w/w)		'Parallel' specimens	'Perpendicular' specimens
HPMC alone		14·4 ± 1·3	14·9 ± 1·0
PVA	10%	13·0 ± 1·9	20·9 ± 1·4
	20%	11·9 ± 1·7	19·0 ± 2·4
	40%	9·4 ± 1·3	16·7 ± 2·5
	60%	9·2 ± 0·9	16·3 ± 2·9
	80%	5·8 ± 0·5	12·0 ± 2·6
	100%	3·3 ± 0·9	4·7 ± 1·1
PEG 400	10%	11·2 ± 1·1	17·0 ± 2·1
	20%	27·3 ± 2·9	35·5 ± 2·8
	30%	23·7 ± 3·1	36·2 ± 3·0
	40%	18·6 ± 2·9	33·5 ± 2·7
PEG 1000	10%	11·0 ± 1·0	14·5 ± 1·2
	20%	18·4 ± 2·1	24·7 ± 2·2
	30%	10·9 ± 3·0	19·4 ± 3·6

FIG. 5. Effect of concentration of polyethylene glycols 400 (□, ■) and 1000 (△, ▲), and polyvinyl alcohol (○, ●) on the Young's modulus of hydroxypropyl methylcellulose film at 20 °C, 60% rh [Open symbols = 'parallel' samples, closed symbols = 'perpendicular' samples.]

Although the mechanism of interaction between hydroxypropyl methylcellulose and polyvinyl alcohol has not yet been established, it was previously suggested that increased film crystallinity might account for the decreased diffusion coefficient of the film blend. In view of the virtual non-existence of diffusion 'holes' in the crystalline regions of a film, the higher the degree of crystallinity, the more compact the film. Crystallinity indicates a state of high molecular order with little or no polymer chain mobility which will therefore have the effect of increasing the mechanical properties of films. Thus the proposed increase in crystallinity in hydroxypropyl methylcellulose/polyvinyl alcohol films while reducing permeability substantially prevented a large drop in tensile strength at break and Young's modulus compared to hydroxypropyl methylcellulose films plasticized with the polyethylene glycols.

The rotating cylinder technique used in film casting in the present study may cause one or both components of the film to align preferentially in a particular direction. Such a directional orientation of molecular chains is usually referred to as anisotropy (Nielsen 1962). Films possessing this property are anisotropic while those that do not are termed isotropic. The tensile properties of anisotropic films are dependent on whether measurements are made perpendicular or parallel to the direction of alignment. Although the mean values of tensile strength at break and Young's modulus of 'parallel' specimens were slightly greater than those of the corresponding 'perpendicular' specimens (see Figs 4 and 5) for all three film systems, the t-test at the 95% confidence level showed, however, that the difference between the sets of values in each case was not significant. We, nevertheless, found significant differences between the percent elongation results of 'parallel' samples and those of 'perpendicular' samples, with the exception of the film containing hydroxypropyl methylcellulose alone (Table 1). There is therefore some evidence that the two-component films are anisotropic and this property is directly linked to the inclusion of additives.

Although anisotropy is indicated by the elongation results, it is not yet clear why the tensile strength and Young's modulus data do not further reflect this observation. It may be that during film formation the nature, strength and even number of bonds linking the molecular segments of hydroxypropyl methylcellulose (which itself is not oriented) are not affected by the orientation of the additives. Therefore, the same resistance to the severance (tensile strength) and deformation (Young's modulus) of the bonds will occur whether stress is applied in a direction parallel or perpendicular to the alignment of the additive molecules. On the other hand, elongation is not primarily influenced by the strength or deformability of intersegmental bonds. As a result of the molecular linearity of the polyethylene glycols and polyvinyl alcohol, greater elongation values would be expected when stress is applied in the direction of molecular alignment than when the same stress is applied perpendicular to the direction of orientation.

Theoretically, the consequences of anisotropy are potentially unfavourable. Rowe (1981a,b) and Rowe & Forse (1981) have shown that the internal stresses inherent in tablet film coats may lead to film defects such as edge splitting, cracking, peeling, bridging of intagliations and even microscopic cracks. Anisotropy could result in significant variation in stress distribution not only between tablet coats but also within the film coat of any one tablet.

The implication in tablet film coating using the various equipment currently available is debatable. It is thought unlikely that fluidized bed coaters and coating procedures which employ a rotating chamber similar to the film casting cylinder used in the present study, would produce film coats that exhibit this phenomenon because the sprayed coating solution

dries rapidly. It is not known at present whether the anisotropy in the examined film systems was inherent, or might have been created by the rotatory motion of the casting substrate.

CONCLUSIONS

The moisture permeability and mechanical properties of a film blend of two film-formers —hydroxypropyl methylcellulose and polyvinyl alcohol—have been evaluated and compared with those of hydroxypropyl methylcellulose film plasticized with polyethylene glycols 400 and 1000.

Permeation properties were determined using the sorption–desorption technique while mechanical properties were obtained from stress-strain measurements. The sorption–desorption technique, apart from affording distinct practical advantages, offers a deeper insight into permeability mechanisms than the permeability cup method.

Plasticization of hydroxypropyl methylcellulose with the polyethylene glycols increased moisture permeability as a result of enhanced segmental mobility. The film blend of hydroxypropyl methylcellulose and polyvinyl alcohol, however, substantially lowered moisture permeability which was attributed to an increase in film crystallinity.

Tensile strength at break and Young's modulus of hydroxypropyl methylcellulose films were decreased by the inclusion of either polyvinyl alcohol or the polyethylene glycols but the effect of the former on these properties was comparatively small. Elongation was enhanced by the polyethylene glycols but lowered by polyvinyl alcohol.

Some evidence of anisotropy in the film systems studied was found. This phenomenon has potentially unfavourable consequences in tablet film coating.

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