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Review Articles

Interaction phenomena in pharmaceutical film coatings and testing methods

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Introduction

Polymers, as a group, are invaluable to man. Their origin can be traced as far back as the beginning of life. For example, the natural polymer, deoxyribonucleic acid (DNA), is an essential component of life itself. Another polymer, cellulose, which is the main structural component of plants, is one of the most plentiful of natural products. The last 100 years have witnessed rapid progress in polymer science and this has made possible the development of numerous commercially important synthetic polymers which have found wide ranging uses in such industries as textiles, paints, plastics and packaging. However, the application of polymeric materials as film coatings to solid dosage forms is still a relatively recent practice. Abbott Laboratories are reported to have pioneered the production of film-coated tablets on a commercial scale in 1954 (Munden et al., 1964). Since then, a number of works on film coating have steadily appeared in the pharmaceutical literature but it appears that until the late 1970's efforts were mainly directed at examining the end-use properties of film coatings such as permeability, mechanical characteristics and drug release profile. Thus film formulation design work was largely based on 'trial-and-error' rather than an adequate understanding of polymer behaviour at the molecular level. Since the late 1970's, however, there has been a greater appreciation of the role played by molecular interactions in determining the product or end-use properties of pharmaceutical film coatings (e.g. Kent and Rowe, 1978; Entwistle and Rowe, 1979; Tufnell et al., 1983; Porter and Ridgway, 1983; Okhamafe and York, 1984a and b) but published works in this area are still relatively few.

A central feature of polymers is the large size of molecular chains which permits the build-up of secondary intermolecular forces. The strength and other properties of polymers are derived from these intermolecular interactions. The magnitude of these interactions, which are mainly hydrogen, van der Waals and dipole–dipole bonds, depends to a large extent on the molecular weight of the polymer, the packing and orientation of the molecular segments, and the flexibility of the

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polymer chains (Harris, 1981). Therefore, a fundamental understanding of the components of film coating formulations and the interplay between them should greatly facilitate the work of formulation and development scientists as well as saving time and reducing costs. It should also make the task of predicting the end-use properties of film coatings easier.

It is intended in this review to highlight a cross-section of works dealing with interaction processes in pharmaceutical film coating. In view of the limited studies on pharmaceutical systems, supplementary materials have been drawn from the polymer science literature. The relationships between interaction phenomena and some end-use properties, and also the evaluation of these phenomena, are emphasised.

(A) End-use properties of pharmaceutical film coatings – role of interaction and formulation factors

In view of the extensive and varied interaction processes that operate in polymeric systems, the film coating scientist has considerable leverage if he decides to modify a film coating system in order to attain certain desirable end-use properties. One approach is to structurally alter the film-former but this process could be potentially expensive, particularly because the new material may have to be subjected to extensive toxicity tests. A more attractive approach, mainly because of its relative simplicity and lower cost, is the application of formulation techniques. This involves the blending of existing film-formers with other materials which may or may not be polymeric. The spectrum of such materials include other film-formers, plasticizers, fillers/pigments and water-soluble additives. This approach has become more important as a result of the current slow rate of discovery of new film-forming materials for pharmaceutical use.

The end-use properties of film coatings that would generally interest the pharmaceutical film formulator may be classified as in Table 1 together with the parameters that are often used to evaluate these properties. Table 2 lists the major formulation factors that influence end-use properties.

Permeation properties

A film coating applied to a solid dosage form, whether for protective, aesthetic, controlled release and/or enteric purposes, is inevitably involved in the transport of one or more molecular species into and/or out of the dosage form. Crank's (1975) relationship (Eqn. 1) essentially summarises the transport of such molecular species.

$$P = D \cdot S \tag{1}$$

where P, D and S are the permeability, diffusion and solubility coefficients, respectively, of the film coating. The transport of the permeant or permeating species, which may be a liquid (e.g. gastric fluid), gas (e.g. oxygen, carbon dioxide and water vapour) or a drug, across the film occurs in two principal stages. The permeant is first dissolved in the polymer matrix (solubility stage) and it is probable that a fraction of the dissolved permeant strongly interacts or binds with some of the functional groups of the polymer and any additives present, and hence will not be available for the

TABLE I

End-use properties of pharmaceutical film coatings and some evaluate parameters

Permeation	Mechanical properties	Adhesion	Appearance
Diffusion coefficient	Tensile strength	Measured adhesion	Opacity
Solubility coefficient	Young's modulus		Gloss
Permeability coefficient	Elongation		Surface roughness
	Hardness		Bridging of intagliation
	Stress crack resistance		
	Incidence of cracking and edge splitting		

TABLE 2

Major formulation factors affecting the end-use properties of pharmaceutical film coatings.

(i) Presence of other film-formers, plasticizers and insoluble additives (pigments/ fillers).
(ii) Solvent system.
(iii) Film coating thickness.
(iv) Operating conditions (type of coating equipment, type of spray pump, spray rate, drying temperature, drying rate, spray droplet size, etc.).

second stage of the permeation process. The second stage involves the free or unbound fraction of the permeant (referred to as the diffusant) being carried along the diffusion channels or pathways, and pores in the polymer matrix.

It is apparent, therefore, that the microstructure of the film coating, as well as the physicochemical characteristics of the film coating components are important considerations in permeation processes. Studies by Burrell (1962) and Michaels (1965) indicate that features such as polarity, crystallinity, chain stiffness and cross-linking have considerable influence on diffusivity. The microstructure of a coating depends, to some extent, on the formulation factors shown in Table 2. The presence of a plasticizer enhances segmental mobility, leading to an increase in the number, size and/or distribution of the diffusion channels (Rogers, 1976; Okhamafe and York, 1983). The effect on diffusivity is illustrated in Fig. 1a. On the other hand, the presence of insoluble additives (including some fillers and pigments), crystallinity and cross-linking in a film hinders polymer chain mobility with a corresponding fall in the size and number of the diffusion pathways, and diffusivity (Michaels and Bixler, 1961; Rogers, 1976; Okhamafe and York, 1983, 1984a). However, pigmentation does not always lower diffusivity (Michaels,

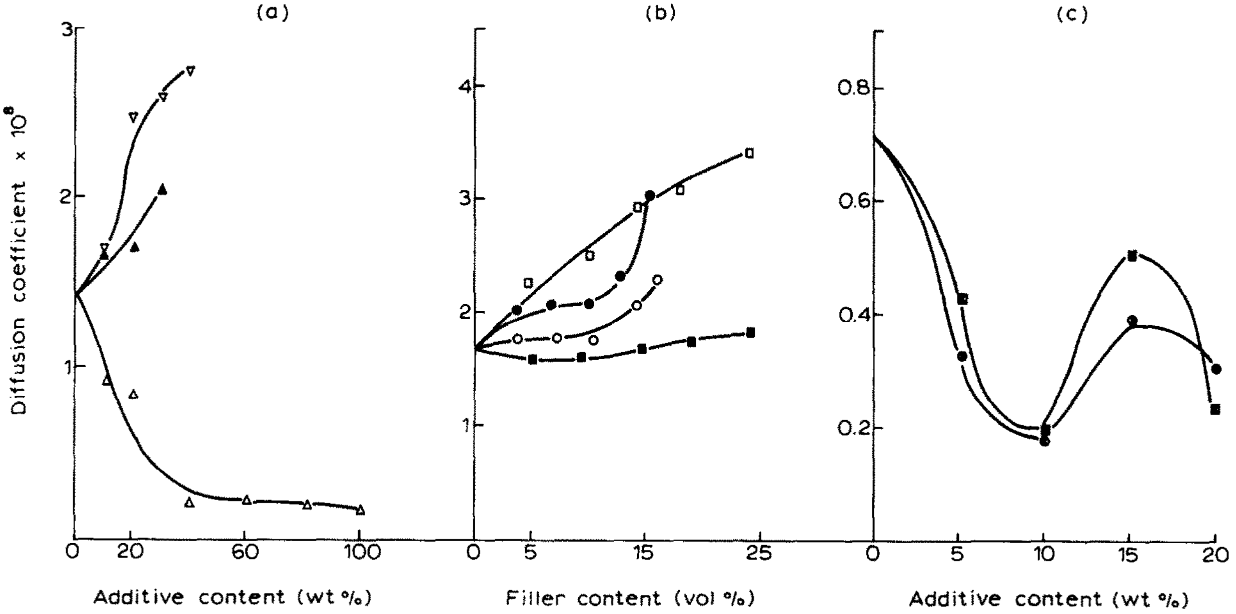

Fig. 1. Moisture diffusion coefficient ($cm^2 \cdot s^{-1}$) of HPMC films containing: (a) PEG 400 (▽), PEG 1000 (▲), PVA (△); (b) fine talc (■), coarse talc (□), anatase TiO_2 (O), surface-treated rutile T_iO_2 (●); (c) citric acid (⊠), urea (⊗) (Okhamafe and York, 1983, 1984a; Okhamafe and Iwebor, 1986).

1965; Okhamafe and York, 1984a, 1985c). This is the case when the pigment does not interact adequately with the polymer thus creating voids at the pigment–polymer interface through which the permeant rapidly diffuses. It is possible for a certain degree of cross-linking in a polymer film to reduce the diffusion rate of one permeant while exerting no effect on the diffusion rate of another (Michaels, 1965). This is usually due to differences in the molecular size of the permeants. Thus, while the reduced size of the diffusion pathways (as a result of cross-linking) may substantially hinder the transport of large drug molecules (e.g. theophylline), the diffusion of small molecules such as oxygen and water may hardly be affected.

Michaels and Bixler (1961) have reported that crystallinity levels of 60–80% decreased the diffusivities of some films to between one-tenth and one-thirtieth of values for equivalent amorphous films. A related observation (see Fig. 1a) which has been attributed to crystallinity is the 8-fold reduction in the diffusivity of hydroxypropyl methylcellulose (HPMC) film when polyvinyl alcohol (PVA) was incorporated (Okhamafe and York, 1983). PVA is semi-crystalline (Okhamafe and York, 1985a) and the polymer appears to retain its crystalline feature in the HPMC/PVA blend. An interesting contrast is observed by comparing the effects of two types of water-soluble additives – one type polymeric and the other non-polymeric – on the moisture diffusion of HPMC film (see Fig. 1a and c). Unlike the plasticizers (PEG 400 and 1000) which are polymeric, citric acid and urea generally lowered moisture diffusion. It has been suggested that bonding of a substantial fraction of the diffusing moisture with the non-polymeric additives (which is indicated by increased solubility coefficients) and the obstructive nature of the network of hydrogen bond interactions between the additives (which contain multiple hydrogen bonding groups) and the polymer matrix might have lowered diffusivity. This effect would be dominant over the increase in diffusion due to the enhancement of polymer chain mobility by the additives (Okhamafe and Iwebor, 1986). The influence of pigments/fillers on diffusivity (see Fig. 1b) is generally dependent on the particle size and shape, and the extent of interaction between the polymer and pigment (Michaels, 1965; Okhamafe and York 1984a). As the illustration in Fig. 2 shows, diffusion of moisture through a pigmented film may occur in 3 ways: (i) through the diffusion channels in the polymer matrix; (ii) along pigment surfaces, i.e. 'surface diffusion' (where the pigment substantially adsorbs water); and (iii) free or bulk flow through voids at pigment–polymer interface (due to inadequate pigment–polymer interaction). The overall diffusivity depends on which of these mechanisms predominate. An additional consideration is that plate-like particles, for example, are more effective barriers to diffusants than spherical particles because the former are likely to produce more tortuous diffusion pathways (Chatfield, 1962; Nielsen, 1967; Okhamafe and York, 1984a).

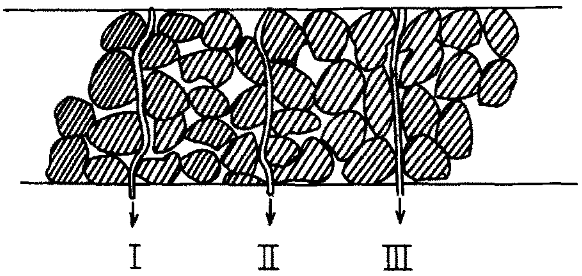

Fig. 2. Paths for moisture transport in filled on pigment films (Michaels, 1965).

An acid–base (electron donor–acceptor) concept which considers polymer–polymer, solvent–polymer and pigment–polymer interactions in terms of acid–base reactions has been proposed by Marmo et al. (1976) and Fowkes (1982). According to this proposition, pigment–polymer interaction, for example, will be promoted if one component is basic in nature (electron donor) and the other acidic (electron acceptor). This hypothesis has been successfully applied to interpret the moisture diffusion properties of some polymer systems loaded with talc and titanium dioxide (Okhamafe and York, 1984a, 1985c).

The solubility coefficient of a film coating is mainly influenced by the physicochemical features of the film components. As can be seen in Fig. 3a, polyethylene glycol (PEG) 400 and 1000, as well as PVA, lowered the solubility coefficient of HPMC probably because by hydrogen bonding with the film-former fewer bonding sites would be available in the polymer matrix for the permeating moisture. Pigmentation also reduced the solubility coefficient of HPMC film (Fig. 3b) but this appears to be primarily due to the considerably lower hydrophilicity of the pigments. In contrast, citric acid and urea, though water-soluble like the PEG's and PVA, increased the solubility coefficient of HPMC (Fig. 3c). This has been attributed to the non-polymeric nature of the additives and their multiple hydrophilic groups which increase the moisture affinity of the films.

Apparently, very little interest has been shown in the effect of operating conditions on the permeation properties of film coatings. While Swarbrick et al. (1972) found no significant difference between the water vapour permeability of poured and sprayed films, Pickard et al. (1972) observed that at 25 wt.% plasticizer level, the moisture permeation of some films based on HPMC/ethyl cellulose (EC) was in the ratio 1.0 : 1.5 : 2.7 for poured, airless- and air-sprayed films, respectively. In a study of the permeation of a 'model' solute, F.D. & C. Red No. 2, through free films of EC/HPMC, Shah and Sheth (1972) reported that although changes in drying conditions caused variations in the physical appearance of the film, solute permeation was essentially unchanged. The authors also noted that the permeation rate increased as film thickness was reduced.

Mechanical properties

The structural and formulation factors which influence permeation often exert predictable effects on the mechanical properties of film coatings. The increase in moisture diffusion arising from enhanced segmental mobility for HPMC film when plasticized with PEG 400 and 1000, has been correlated with the increase in film elongation, and decrease in Young's modulus and tensile strength of similar films (Okhamafe and York, 1983). Enhanced segmental mobility enlarges the diffusion channels which results in a more porous and flexible but less cohesive structure. A correlation can also be established between the permeation and mechanical properties of pigmented films using data from the works of Okhamafe and York (1984a and b). Poor or insufficient pigment–poly-

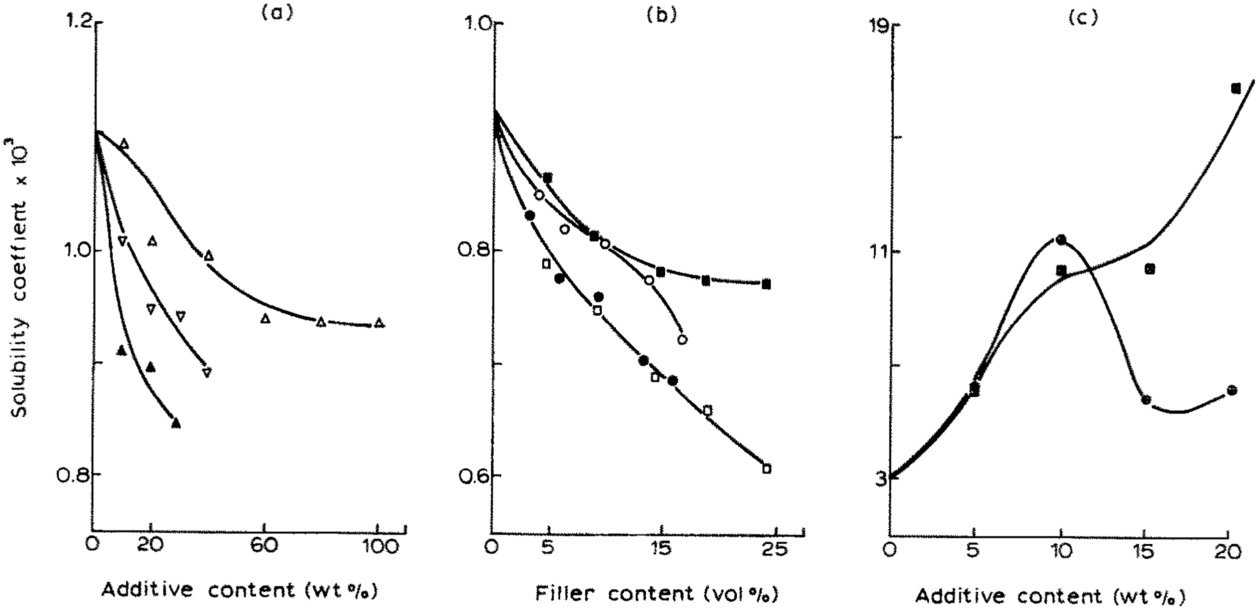

Fig. 3. Moisture solubility coefficient ($cm^3 \cdot cm^{-3} \cdot [cm\ Hg]^{-1}$) of HPMC films containing: (a) PEG 400 (▽), PEG 1000 (▲), PVA (△); (b) fine talc (■), course talc (□), anatase T_iO_2, (○), surface-treated rutile (●); (c) citric acid (⊠), urea (⊗) (Okhamafe and York, 1983, 1984a; Okhamafe and Iwebor, 1986).

mer interaction would leave voids at the pigment–polymer interface which will not only facilitate the diffusion process but also constitute stress locations or concentrations, leading to a fall in tensile strength, elongation and stress crack resistance, and therefore a rise in the incidence of cracking or edge splitting of film-coated tablets (Okhamafe and York, 1985d). On the other hand, good pigment–polymer interaction would minimise interfacial voids and enhance polymer chain stiffness. The consequences would be lower diffusivity, increased modulus and possibly (but not usually) higher tensile strength. The influence of the shape of pigment particles on mechanical properties is generally dependent on the shape factor or aspect ratio. The shape factor of a filler or pigment, as defined by Guth (1945), is the ratio L/d where L is the length of the filler particle and d its diameter. The higher the shape factor the greater the Young's modulus and stress concentrations but the lower the diffusivity (Rowe, 1983a; Okhamafe and York, 1984a and b, 1985d). Qualitative descriptions of the shape of some pigments and fillers used in pharmaceutical film coating are listed in Table 3.

An important parameter for evaluating the mechanical properties of film coatings applied to tablets is the incidence of cracking or edge splitting (Rowe, 1981a, 1982). Generally, the magnitude of internal stress in a film coating has a significant influence on the occurrence of film coating defects. Rowe (1983b) has suggested that the overall internal stress, P, in a film coating applied to a tablet core can be represented as follows:

$$P = \frac{E}{3(1-\nu)} \cdot \left[\frac{\phi_s - \phi_r}{1 - \phi_r} + \Delta\alpha_{\text{cubic}} \cdot \Delta T\right] \qquad (2)$$

where E is the Young's modulus of the film, ν its Poisson's ratio, ϕ_s the volume fraction of the solvent at the solidification point of the coating formulation, ϕ_r the volume fraction of solvent remaining in the dry film at ambient conditions, $\Delta\alpha_{\text{cubic}}$ the difference between the thermal cubical expansion coefficients of the coating and the tablet core and ΔT the difference between the glass transition temperature of the coating and the ambient temperature. Cracking will occur if P is greater than or equal to the tensile strength, σ, of the film (Sato, 1980) i.e.

$$P \geqslant \sigma \qquad (3)$$

Combining and rearranging Eqs. 2 and 3 gives Eqn. 4:

$$\frac{\sigma}{E} \leqslant \frac{1}{3(1-\nu)}\left[\frac{\phi_s - \phi_r}{\phi_r} + \Delta\alpha_{\text{cubic}} \cdot \Delta T\right] \qquad (4)$$

Thus if the right hand side of the equation is assumed to be constant, σ/E may be used to predict the incidence of edge splitting of a film coat (Rowe, 1981a). The larger its value the higher the stress crack resistance of a film. Correlations have been found between the incidence of edge splitting and certain intrinsic and formulation factors. The incidence of edge splitting rises with increase in the molecular weight of HPMC up to a molecular weight of 7.8×10^4 (Rowe and Forse, 1980a). The effect of pigment concentration appears to be dependent on the type of pigments. For example, the incidence of edge splitting of HPMC fell with increase in the content of talc but rose with increasing levels of calcium carbonate (Rowe, 1984a).

TABLE 3

Qualitative descriptions of the shapes of pigments and fillers commonly incorporated in tablet film coatings (Rowe, 1983a).

Pigment/filler	Description of shape
Titanium dioxide	rounded
Black iron oxide	cubic
Red iron oxide	spherical
Yellow iron oxide	acicular
Talc	flaky
Aluminium lakes	irregular

Adhesion

Good adhesion of a film coating to a solid dosage form is an important requirement in film coating practice because complete loss of adhesion will not only adversely affect the appearance of the film-coated dosage form but may also reduce the capacity of the film to protect the dosage form. In addition, moisture could accumulate in substantial quantities at the interfacial voids, a situation that is likely to accelerate the degradation of the moisture-sensitive contents of the dosage form. Adhesion measurements have, in recent years, generated even greater interest as a result of the proposed relationships between adhesion, internal stress of film coatings and film coating defects such as edge splitting, cracking and bridging of intaliations (Sato, 1980; Rowe and Forse, 1981a; Rowe, 1982).

Mittal (1980, 1982) and Rowe (1982) have distinguished between 'practical or measured adhesion' and 'fundamental or intrinsic adhesion' by defining the former as the actual force required to detach a film coating from a unit area of substrate surface, and the latter as the strength of the intermolecular interaction between the film and the tablet. Thus measured adhesion incorporates intrinsic adhesion as well as other non-interfacial factors – the internal stress of the film, type of rupture and the adhesion measurement technique. Internal stress is detrimental to measured adhesion (Sato, 1980), and therefore, if the mode of rupture is adhesive and the measurement technique is constant, the measured adhesion, A_m, may be expressed as follows:

$$A_m = A_i - P \tag{5}$$

where A_i is the intrinsic adhesion and P is the internal stress of the film coating.

A number of factors are known to affect the measured adhesion of a film to tablets. Wood and Harder (1970) found that a rise in the critical surface tension (cohesive energy density) of an aspirin tablet surface improved its adhesion to methyl cellulose (MC) films but a similar effect was not obtained by varying the critical surface tension of the coating solution. Nadkarni et al. (1975) observed that the closer the solubility parameter of a solvent to that of a polymer the stronger the adhesion. The surface tension of the solvent had minimal effect on film adhesion but adhesion was enhanced by an increase in tablet surface roughness. In another study, Fung and Parrott (1980) indicated that the film–tablet adhesion of aqueous-based HPMC was one-half to one-quarter of the values obtained for HPMC cast from some organic solvent systems. Fisher and Rowe (1976) and Rowe (1978), noting that a direct relationship exists between tablet porosity and surface roughness, proposed that film adhesion generally improved as tablet porosity increased. Adhesion initially fell when film thickness was increased to about 35 μm but this was followed by a gradual rise as film thickness was further increased.

The presence of different excipients in tablets has also been reported to influence film adhesion. Microcrystalline cellulose, and stearic acid, which have hydroxyl and carboxylic acid groups, respectively, improved the adhesion of HPMC/ethylcellulose (EC) film to tablets but the presence of calcium and magnesium stearates lowered adhesion (Rowe, 1977). Okhamafe and York (1985e) have investigated the effect of ageing on the adhesion of some film coating formulations to aspirin tablets. The results obtained are summarised in Fig. 4. The general decline in measured adhesion was attributed to greater molecular mobility and re-orientation as the polymer matrix absorbed moisture and heat energy, leading to the creation of new stresses in the film coating and weakening of film–tablet interfacial bonding.

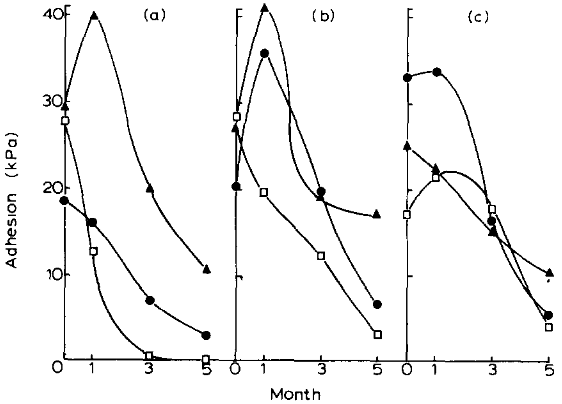

Fig. 4. Effect of ageing at 37% and 75% R.H. on the adhesion of HPMC (●). HPMC/PVA (▲) and HPMC/PEG 400 (□) film coatings to aspirin tablets. Note: (a) = unpigmented films; (b) = talc-filled films; (c) = T_iO_2-filled films (Okhamafe and York, 1985e).

Appearance

The film coating applied to a solid dosage form, in addition to its permeation and mechanical roles, also serves an aesthetic function as well as facilitates product identification. A rough surface reduces glossiness, and in general surface roughness rises with increase in the solution concentration of HPMC but decreases with increase in the molecular weight of the polymer (Rowe, 1976, 1979). The effect of the mean particle size of filler or pigment on the surface roughness of pigmented coatings varies from one pigment to another. While the mean particle size of dolomite influenced film surface roughness (Rowe 1981b), this parameter was independent of particle size for films pigmented with various grades of iron oxide (Rowe, 1985).

When the engraving, also referred to as intagliation or monogram on a tablet, is bridged across by a film coating thus obscuring product identification this phenomenon or defect is known as bridging of intagliation or monogram (Rowe and Forse, 1980b). Bridging occurs when residual stresses due to film shrinkage (during drying) exceed the adhesive forces holding the film to the tablet at the intagliation. A direct correlation exists between film thickness, residual stresses and the incidence of bridging of intagliation (Rowe and Forse, 1980b). Plasticization reduces residual stresses and consequently, the incidence of bridging. For some plasticizers incorporated in HPMC, the rank order of plasticizer, measured by the degree of lowering of the incidence of bridging, was shown to be: PEG 200 > propylene glycol > glycerol (Rowe and Forse, 1981b).

There has always been a need to protect photolabile medicinal substances from light. Film coatings loaded with opacifying substances, usually coloured pigments, conveniently provide such protection. Glossy and coloured film coatings also promote elegance and facilitate product identification. However, the degrees of opacity, colour and gloss are often a function of the pigment type, particle size and concentration, as well as the polymer system and the coating method used. The degree of opacity of HPMC/EC film coatings pigmented with coloured lake pigments has been reported to be in the rank order: blue > red > orange > yellow, but for various iron oxide pigments which showed very high degrees of opacity, the pigment colour had no effect on opacity (Rowe, 1984b). Rowe (1984b) also noted that unlike TiO_2, calcium carbonate, calcium sulphate and talc exhibited low opacifying properties; in addition, increasing the level of TiO_2 and F.D.&C. Yellow 5 enhanced opacity but increase in the particle size of white dolomite resulted in a fall in opacity.

A phenomenon that has an important implication in the evaluation of the appearance of film coatings is optical anisotropy. The capacity of a material to reflect light, and hence its opacity, is greatly influenced by its refractive index. Pigments that are optically anisotropic possess refractive indices which vary depending on their alignment or orientation. Rowe (1983c) has observed that as a consequence of the optical anisotropy exhibited by talc and calcium carbonate, HPMC coatings (loaded with either of these pigments) applied to tablets were essentially transparent except at the intagliations where the film appeared opaque (white).

(B) Evaluation of interaction phenomena in film coating and other polymer systems

Although intrinsic phenomena in non-pharmaceutical polymer systems have been researched for at least half a century, complete characterisation of interactions in any polymer remains a difficult task. This is due to the complexity of polymers and their interactions and also because most polymers do not exhibit a definitive molecular weight; usually, they are made up of fractions of varying molecular weights. This perhaps explains the proliferation over the decades of instruments and techniques designed to help unravel the complex nature of polymers and their interactions. Many of the well known techniques are listed in Table 4 along with the intrinsic/interaction phenomena that are generally examined. The techniques used are now critically evaluated.

Viscometry

This is perhaps one of the simplest and oldest methods of examining interactions in polymer sys-

TABLE 4

Some methods of evaluation of intrinsic/interaction phenomena in polymeric systems

Method	Intrinsic phenomenon/parameter
Viscometry	compatibility, solvent–polymer and polymer–polymer interactions
Solubility studies	compatibility, solvent–polymer and polymer–polymer interactions
Differential scanning calorimetry (DSC)	glass transition temperature (T_g), compatibility, crystallinity, moisture interactions, polymer–polymer, plasticizer–polymer and pigment–polymer interactions
Thermogravrimetric analysis (TGA)	moisture interactions, thermal stability
Thermomechanical analysis (TMA)	T_g, softening point (T_s), melting point (T_m), plasticizer–polymer and pigment–polymer interactions
Electrophoresis	pigment–solvent and pigment–polymer interactions, zeta potential.
Microcalorimetry	solvent–polymer, solvent–polymer and pigment–polymer interactions, differential enthalpies
Nuclear magnetic resonance spectroscopy (NMR)	moisture interactions
Radiotracer	solvent retention, moisture interactions
Infrared spectroscopy (IR)	hydrogen bond interactions, moisture interactions, acid–base interactions, structural features.
X-ray diffraction	crystallinity

tems. The intrinsic viscosity of a polymer in a dilute solution generally provides a measure of the polymer – solvent interaction. This concept has been extended to ternary systems, i.e. systems consisting of two polymers and a common solvent, by Krigbaum and Wall (1950) who attempted to quantify polymer–polymer and polymer–solvent interactions. However, Cragg and Bigelow (1955) considered viscosity interaction parameters directly based on intrinsic viscosity data for binary or ternary systems as unsatisfactory since the intrinsic viscosity of a polymer varies considerably with its molecular weight, and intrinsic viscosity is dependent on the type of solvent employed. As a result, viscosity interaction parameters obtained would not be sufficiently accurate measures of interactions. The authors proposed the Huggins viscosity slope constant, k, as a more acceptable parameter which is obtained from the following equation:

$$\eta_{sp/c} = [\eta] + k[\eta]^2 \qquad (6)$$

where $\eta_{sp/c}$ is reduced viscosity, $[\eta] = \lim_{c \to 0} (\eta_{sp/c})$ and c is the concentration of the solution. Unlike intrinsic viscosity, k is independent of polymer molecular weight and varies less with the type of solvent used.

Investigations of interactions in pharmaceutical film coating systems by viscometry are still few. Kent and Rowe (1978) measured the intrinsic viscosity of ethylcellulose (EC) in a number of solvents ranging from poorly hydrogen bonding types to those with strong hydrogen bonding qualities. The highest intrinsic viscosities were shown by the polymer solutions prepared with poorly

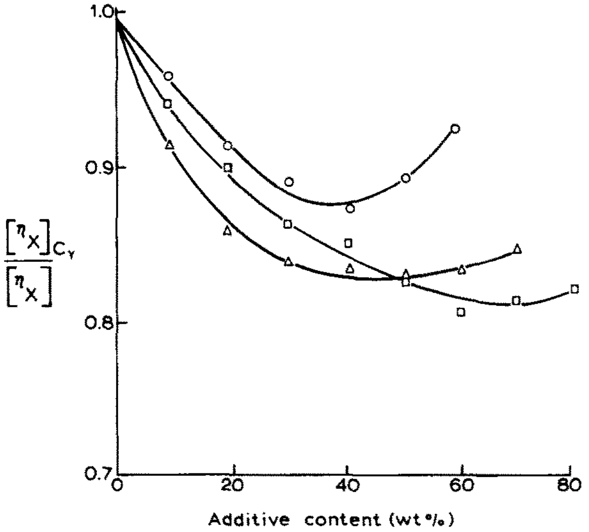

Fig. 5. Plot of the HPMC/polymer additive: HPMC intrinsic viscosity ratio against polymer additive content. Note: ○ = PVA; □ = PEG 400; △ = PEG 1000 (Okhamafe and York, 1985a).

hydrogen bonding solvents, suggesting that solvents in this class are best for ethylcellulose. Intrinsic viscosity measurements have also been employed to determine the most efficient plasticizers in two homologous series, viz. dialkyl phthlates and ethylene glycol derivatives, for EC and HPMC, respectively (Entwistle and Rowe, 1979). The higher the intrinsic viscosity the greater the degree of polymer–plasticizer interaction and hence the higher the plasticizer efficiency. Based on a qualitative assessment of polymer–solvent interaction in a dilute aqueous solution of HPMC containing increasing concentrations of either PVA, PEG 400 or PEG 1000 (see Fig. 5), Okhamafe and York (1985a) proposed that the greater the depression of the intrinsic viscosity of HPMC by the polymer additives, and also the higher the polymer additive concentration at which intrinsic viscosity minimum was observed, the greater the degree of solvent–polymer additive interaction. Thus the rank order of interaction of the polymer additives (with the solvent) is: PEG 400 > PEG 1000 > PVA.

A major weakness of the viscometric method is the lack of a universally applicable viscosity parameter for quantifying interactions in polymer systems. Parameters such as the Huggins viscosity slope constant are inadequate because it is usually assumed that interactions between the components of a polymer system are solely hydrodynamic but in reality thermodynamic forces are also involved (Bohmer et al., 1970). Determined efforts to overcome this difficulty (e.g., Staszewska et al., 1980) have not been particularly successful. Another drawback of viscometry is that the magnitude of polymer–polymer interaction in a ternary systems in inevitably influenced by the presence of a solvent and, therefore, cannot accurately reflect the level of polymer-polymer interaction in the solid state, e.g. in a tablet film coating. Nonetheless, this method remains a useful tool for the qualitative examination of compatibility and other interaction phenomena in polymer systems.

Solubility techniques

These usually involve solubility studies and the use of the solubility parameter concept. In order for two polymers to be mutually compatible, or for a polymer to dissolve in a solvent, the Gibb's free energy of mixing (or dissolution), ΔG, must be negative (see Eqn. 7).

$$\Delta G = \Delta H - T \cdot \Delta S \tag{7}$$

where ΔH is the heat of mixing, T the absolute temperature and ΔS the entropy of mixing. In most cases, mixing or dissolution involves a gain in entropy, and therefore the value of ΔH could be crucial if complete compatibility or dissolution is to be assisted. ΔH may be obtained from the following relationship (Hildebrand and Scott, 1950):

$$\Delta H = V_m \left[\left(\frac{\Delta E_1}{V_1} \right)^{1/2} - \left(\frac{\Delta E_2}{V_2} \right)^{1/2} \right]^2 \phi_1 \cdot \phi_2 \tag{8}$$

where V_m is the total volume of the mixture, ΔE the energy of vaporisation of components 1 or 2, V the molar volume of component 1 or 2 and ϕ the volume fraction of component 1 or 2. The term $\Delta E/V$ is generally referred to as the cohesive energy density (CED) and its square-root as the solubility parameter, δ. Eqn. 8 can then take the following form:

$$\Delta H = V_m (\delta_1 - \delta_2)^2 \phi_1 \cdot \phi_2 \tag{9}$$

If δ_1, and δ_2 are the same, the heat of mixing is zero, and consequently maximum interaction as well as solubility and compatibility in all proportions should be expected.

The solubility parameter approach has been adopted by Kent and Rowe (1978) and Entwistle and Rowe (1979) for the evaluation of the solubility of ethylcellulose in a range of solvents and the comparative assessment of polymer–plasicizer interaction, respectively. Aulton et al. (1985) combining the solubility parameter concept and the Flory-Huggins interaction parameter (Flory, 1953), predicted that polyvinyl pyrrolidone (PVP) should be mutually compatible with the PEG's (up to a molecular weight of 6000) and propylene glycol.

Although the solubility parameter is helpful in the qualitative investigation of polymeric interactions, it is, however, not a totally dependable tool for the quantitative prediction of intrinsic phenomena. For example, Aulton et al. (1985) reported that the observed limited compatibility of the solid PEG's/PVP systems was at variance with the prediction of complete miscibility. This discrepancy was attributed to the crystallinity of the solid PEG's and the generally low entropy of mixing for polymers. Tager (1984) has also noted that polyarylates based on aromatic bisphenols and aromatic acids with solubility parameters in the range $21.5–21.9 \times 10^{-3}$ $(\mathrm{J \cdot m^{-3}})^{0.5}$ dissolve well in nitrobenzene but not in acetone, although both solvents have a common solubility parameter value of 20.5×10^{-3} $(\mathrm{J \cdot m^{-3}})^{0.5}$. However, working with cellulose polymers and several plasticizers, Rowe (1986) has plotted two-dimensional solubility parameter maps and has shown the value of such graphs as a guide in predicting compatibility between film components, and illustrated the potential of this approach.

Thermal methods

Methods involving thermal analysis are particularly appropriate for the study of interaction processes in pharmaceutical film coating formulations. Unlike viscosity and solubility studies, thermal investigations are generally performed on the cast or applied coatings rather than on the film solution. The 3 principal thermal methods frequently used to examine intrinsic phenomena in pharmaceutical coating systems are differential scanning calorimetry, thermogravimetric analysis and thermomechanical analysis.

Differential scanning calorimetry (DSC)

Polymer features such as moisture interactions, glass transition temperature (T_g), compatibility and crystallinity may be determined using this technique. Fig. 6 is an illustration of the DSC thermogram of a hypothetical polymer that exhibits 3 thermal transitions, viz, melting of frozen water in the polymer at about 0 °C, transition from a glassy to a rubbery state (glass transition) and fusion of the polymer. The area of the first endotherm yields the heat of fusion of free (freezable or unbound) moisture and can be used to determine the free water content (Davies and Webb, 1969; Nelson, 1977; Bair, 1981). DSC studies may also provide an insight into the bound moisture content of polymers (Roland, 1981; Hatakeyema and Yamauchi, 1984).

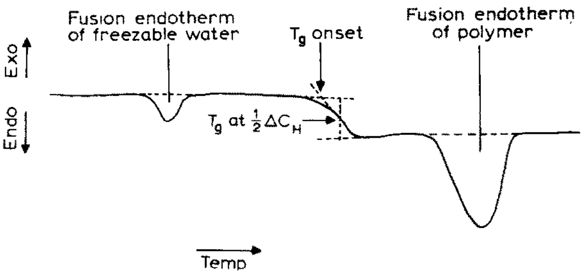

Fig. 6. A hypothetical DSC thermogram of a polymer system showing three thermal transitions.

Glass transition is usually manifested as an endothermal shift in the baseline of a thermogram. T_g is generally taken as either the onset of glass transition or the mid-point of the heat capacity change (ΔC_H) at glass transition. The significance of T_g lies in its relationship with the other properties of polymers. At T_g, a polymer undergoes a change from a state of relatively low segmental mobility to one of considerable chain mobility. Although the T_g's of many polymers used in pharmaceutical film coating lie well above room temperature, changes in the T_g of a polymer usually affect various film properties. As shown in Fig. 7, plasticization generally lowers T_g (Okhamafe and York, 1985a) while pigmentation often enhances T_g (Okhamafe and York, 1984/85). Comparison of Fig. 7a and Fig. 1b indicates that a correlation can be established between the fall in the T_g of HPMC film in the presence of a plasticizer (PEG 400) and the rise in the moisture diffusivity of the film since it is well known that plasticization enhances segmental mobility. Another correlation exists between the increased Young's modulus of HPMC in the presence of pigments (see Okhamafe and York, 1984b) and the rise in the T_g of the polymer (Fig. 7b) because pigmentation generally lowers polymer chain mobility which manifests as an increase in film stiffness or rigidity.

Polymer–polymer compatibility or miscibility may also be evaluated from T_g data (Fried et al., 1978; Min and Pearce, 1981; Okhamafe and York, 1985a). If the two polymers in a binary film system are compatible, one T_g (that of the compat-

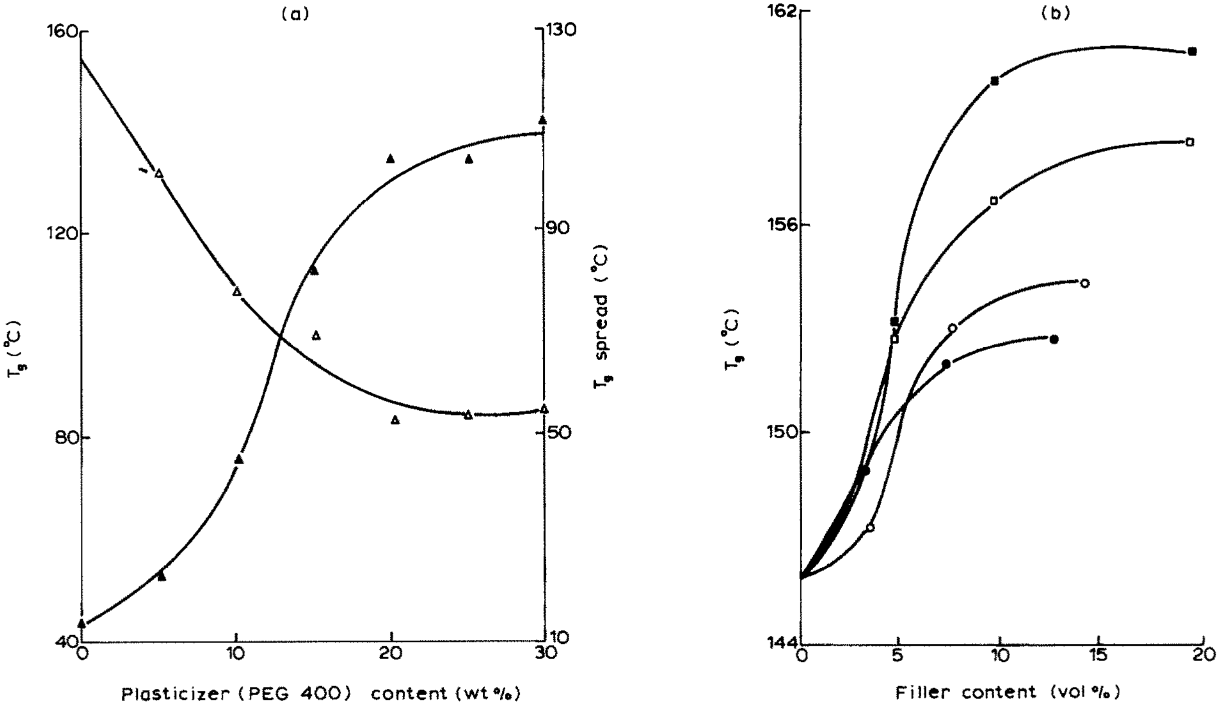

Fig. 7. Glass transition plots for (a) plasticized and (b) pigmented, HPMC films. △ = T_g of plasticized system; ▲ = glass transition spread, T_g spread, of plasticized system: ■ = fine talc; □ = coarse talc; ○ = anatase T_iO_2; ● = surface-treated rutile T_iO_2 (Okhamafe and York, 1984/85, 1985a).

ible phase), lying between the T_g's of the individual polymers in the blend, is observed. For partially compatible polymers, two T_g's are detectable if the compatibility limit is exceeded: one for the blend and the other for the polymer which is in excess. Moreover, the glass transition spread or width (i.e. the temperature range over which glass transition occurs) for partially compatible polymer blends increases as the content of the second polymer is raised until just before incompatibility sets in (see Fig. 7a).

As a result of the lengthy nature of polymer chains, polymers cannot be completely crystalline (Van Krevelen, 1976) although completely amorphous polymers exist. This has given rise to the term 'crystallinity' which is used to define crystalline phenomena in polymers. There is lack of agreement on the form crystallinity takes in polymers, but two models have been reported (Van Krevelen, 1976). The older one, known as the 'fringed micelle model', views crystallinity in polymers as areas of perfectly ordered polymer chains (referred to as crystallites) coexisting with disordered polymer chains constituting the amorphous phase (see Fig. 8). The crystalline and amorphous regions of the polymer are well defined and as a result, interpretation of crystallinity is simple with this model. The second model is much more complex in that the X-ray diffraction patterns of a polymer are interpreted in terms of statistical disorder in which the amorphous phase constitute small 'defect' sites within a polymer matrix consisting largely of perfectly ordered lamellae (folded chains) and paracrystalline features. Certain polymer properties such as creep and fracture are claimed to be better explained using this model (Van Krevelen, 1976).

Since it is only the crystalline phase of a polymer that undergoes fusion (Beaman, 1952), the heat of fusion of a polymer (calculated from the melting endotherm shown in Fig. 6) relative to the heat of fusion of the polymer standard (which is assumed to be 100% crystalline) provides an estimate of the degree of crystallinity (Gray, 1970;

Fig. 8. Diagrammatic representation of the fringed micelle model of polymer crystallinity (Van Krevelen, 1976).

Peppas and Merrill, 1976; Runt and Rim, 1982). Comparative crystallinity data for HPMC/PVA film blends obtained by this technique are listed in Table 5 (Okhamafe and York, 1985a).

Thermogravimetric analysis (TGA)

TGA may be used for measuring changes in film sample weight with respect to temperature. TGA thermograms often provide useful information on the moisture interactions, residual solvents and thermal stability of polymers. A typical thermogram is shown in Fig. 9. It shows a transition at 40–140 ° C due to moisture loss, and a sharper transition beginning at about 260 ° C as a result of thermal degradation. It has been proposed (Okhamafe and York, 1985b) that for PVA and HPMC film formulations, the smaller transition corresponds to the loss of moderately bound water from the film systems, the magnitude of which may be employed to estimate polymer–polymer compatibility. Table 6 provides a comparison of the compatibility limits of some polymer additives in HPMC films based on both T_g and moderately bound water content data.

TABLE 5

Comparative crystallinity data for HPMC/PVA film systems (Okhamafe and York, 1985a)

Polymer additive	wt. %	Heat of fusion ($J \cdot g^{-1}$) ± S.D. [a]	Comparative crystallinity index (%)
PVA	10	5.86 ± 0.54	17.58
	20	6.31 ± 0.70	18.8
	30	5.99 ± 0.53	17.8
	40	7.26 ± 0.65	21.6
	50	9.45 ± 0.65	28.1
	60	13.12 ± 1.16	39.0
PVA alone (standard)		33.60 ± 0.60	100.0

[a] Standard deviation.

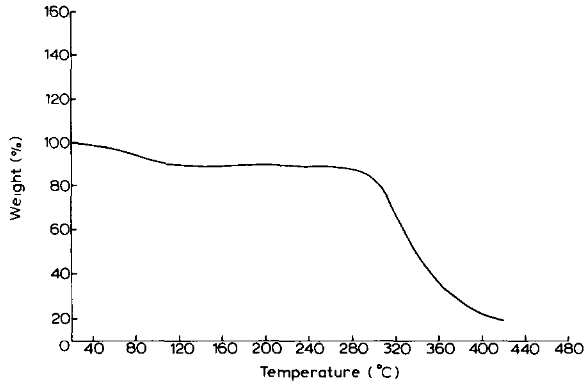

Fig. 9. TGA thermogram for PVA film (Okhamafe and York, 1985b).

Thermomechanical analysis (TMA)

This technique permits the monitoring of very small changes in sample dimensions as a function of temperature, applied load or time. A typical analysis can be used in a variety of modes including penetration, expansion, extension and flexure.

TABLE 6

Compatibility limits of some polymer additives in HPMC based on T_g (Method 1) and bound moisture content data (method 2) (Okhamafe and York 1985a and b).

Polymer additive	Compatibility limit (wt%)	
	Method 1	Method 2
PEG 400	20	15
PEG 1000	15	10
PVA	40	40

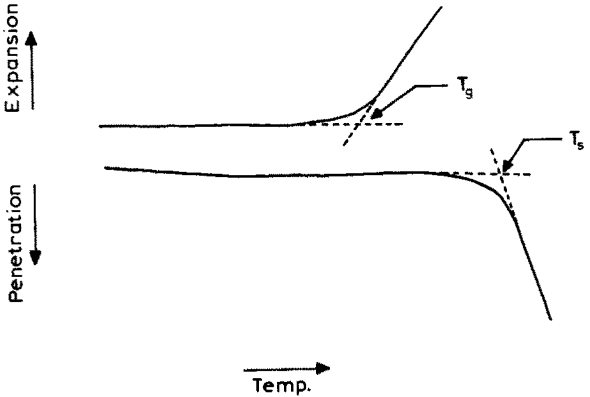

Fig. 10. An illustration of the TMA thermograms of a polymer film obtained using the expansion and penetration modes, respectively.

In the first two modes, the test sample is under a compressive force while in the latter two, the sample experiences a pull and is therefore in a state of tension. Typical thermograms from two of the commonly used modes are illustrated in Fig. 10. Melting points (T_m), softening points (T_s) and glass transition temperature (T_g) are just a few of the parameters that can be obtained from TMA studies but T_s and T_g are particularly useful in the evaluation of interaction phenomena in polymers. T_s indicates the point at which the polymer softens prior to melting and usually lies between T_g and T_m. It is readily detected when the TMA is used in the penetration mode as the temperature at which the probe rapidly penetrates the film coating. At T_s, polymer chain mobility is so high that some intersegmental bonds are ruptured and as a result, the polymer matrix is more porous and resistance to penetration becomes low. T_g measurement, usually in the expansion mode, is based on the principle that at T_g the rigid polymer chains become more mobile, thus increasing the free volume. This is manifested as a thermal expansion of the film coating which vertically displaces the expansion probe.

TMA has proved very useful, rapid and convenient in the investigation of paints, plastics and fibres (Holsworth et al., 1974; Cassel, 1977; Brennan, 1977) but it has not been widely applied to the study of pharmaceutical film coatings. Porter and Ridgway (1983), using a pneumatic microindentation apparatus, obtained and plotted Brinell hardness values for some plasticized and unplasticized cellulose acetate phthalate (CAP) and polyvinyl acetate phthalate films against temperature. The temperature at which hardness inflected was taken as the T_g by the authors. Since the technique employed involved penetration of the film coatings by an indenter, it is probable that the actual parameter measured was T_s rather than T_g. Masilungan and Lordi (1984) used a Du Pont thermomechanical analyser to examine the effect of some plasticizers on the T_s of EC, HPMC and hydroxypropyl methylcellulose phthalate (HPMCP) films. The authors applied the relationship of Moelter and Schweizer (1949) to calculate the softening point depression coefficients (k) of the film systems thus:

$$T_p = T_o \, e^{-kn} \tag{10}$$

where T_p is the T_s of the plasticized film, T_o the T_s of the unplasticized film and n is the mole fraction of the plasticizer. The slope of the linear plots of ln T_p against n yields k, and is considered a measure of plasticizer efficiency. Typical k values obtained by Masilungan and Lordi (1984) are listed in Table 7.

TABLE 7

Softening point depression coefficient (k) of some plasticizers for EC, HPMC and HPMCP films (Masilungan and Lordi, 1984)

Film-former	Plasticizer	*k*
EC	DEP	2.34
	TA	2.04
	PEG 400	1.00
	PG	0.07
	CO	1.77
HPMC	DEP	2.30
	TA	2.40
	PEG 4000	8.86
	PG	0.35
HPMCP	DeP	1.59
	TA	1.63
	PEG 400	2.96

EC = ethyl cellulose; HPMC = hydroxypropyl methylcellulose, HPMCP = HPMC phthalate; DEP = diethyl phthalate; TA = triacetin; PG = propylene glycol; PEG = polyethylene glycol; CO = castor oil.

Another technique used in TMA in the dynamic mode is the torsional braid pendulum, a method originally used for following rigidity changes during the curing of polymers. Recent work has examined several pharmaceutical polymer systems (Osterwald et al., 1982; Rowe et al., 1984; Sakellariou et al., 1985). Analysis of graphs of relative film rigidity and the logarithmic decrement, a function of the energy loss of the system under test, versus temperature enabled glass transition temperatures to be measured with a high degree of precision.

Electrophoresis

The properties exhibited by pigments in film coatings such as dispersibility and opacity are partly dependent on the level of pigment–polymer interaction (Day, 1973/74). Therefore, the nature and magnitude of the charge on the pigment surface, which can be determined by electrophoresis, is important. It has in fact been suggested that the most important feature of titanium dioxide is its surface charge, either as an induced electrostatic charge or an electrophoretic charge resulting from adsorption of ions from polymer solution (Day, 1973/74). The magnitude of the electrophoretic charge is directly related to the electrophoretic or zeta potential, ξ, which is evaluated by measuring the rate of migration, v, of the pigment particles in the liquid medium when a potential difference is applied, and is calculated from Helmholtz's (or Smoluchowski's) equation thus (van der Minne and Hermaine, 1952):

$$\xi = \frac{v 4 \pi \eta}{E e} \tag{11}$$

where η and e are the viscosity and dielectric constant, respectively, of the liquid medium, and E the voltage gradient. Since η and e in the immediate vicinity of the pigment particles are difficult to measure accurately, the rate of particle migration, v, is often taken as a measure of the zeta potential (Ritter, 1973). A direct relationship exists between the electrophoretic charge and zeta potential. Low zeta potential implies low pigment–polymer interaction (Fowkes, 1982). When, for example, the forces of attraction (due to van der Waals and London forces) of the pigment particles exceed their repulsion forces as a result of a low electrophoretic charge, flocculation occurs producing a poor dispersion. On the other hand, adequate pigment–polymer interaction ensures that polymer is adsorbed onto the pigment surface as the film dries and this enables the pigment particles to retain some degree of mobility, prevent agglomeration and facilitate even distribution in the dry film.

A number of factors affect the zeta potential of pigments in liquid media. Fowkes (1982) proposed that the high zeta potential observed in a system consisting of calcium carbonate (which is basic) and post-chlorinated polyvinyl chloride (acidic) in dioxane was due to the donation of electrons by the filler to the polymer. The presence of trace amounts of water in organic solvents has been found to exert considerable influence on zeta potential especially when the pigments are metal oxides such as silicon dioxide, iron oxide and titanium dioxide (Micale et al., 1966; Kitahara, 1973/74). This is of significance in pharmacy because organic solvent systems are still widely used in the formulation of film coatings. The effect of trace water has been explained in terms of a proton-exchange phenomenon with the acidic active sites of the metal oxides (negatively charged) attracting H^+ from water and therefore acquiring a more positive electrophoretic charge. Thus the pigments become more basic and the positive values of the zeta potential increases. Trace metal ions (e.g. Na^+) and other ions also exert a similar effect (Kitahara, 1973/74).

Microcalorimetry

This method provides a direct means of determining the enthalpies of immersion, adsorption, mixing and wetting. At least two variations of this technique are available – batch cell and flow cell. Heats of immersion and mixing are obtained if the batch cell approach is adopted. It involves the mixing of a liquid with another liquid or particulate material and monitoring the enthalpy changes. In the flow cell technique, a gas or vapour (usually water vapour or nitrogen) is allowed to pass through a bed of the evacuated powdered material and the heat of adsorption or wetting is measured. Differential enthalpies, derived from enthalpy data are useful in evaluating solvent–polymer, pigment–polymer, pigment–polymer and moisture interactions (Boesen, 1970; Day, 1973/74; Dulog, 1985). It has also been indicated (Ritter, 1973; Day, 1973/74) that the polarity or electrostatic field strength of pigment surfaces (a measure of the degree of interaction between pigment surfaces and molecules through their permanent or induced dipoles) can be characterised from the slopes of the plots of heat of immersion in various liquid media as a function of the dipole moments of the liquids.

An interesting application of enthalpy data in the elucidation of polymeric interactions has been reported by Fowkes (1982). According to Fowke's (1982) acid–base (electron donor–acceptor) concept, interaction between the components of a polymer system will be promoted if one component is basic (electron donor) and the other acidic (electron acceptor). The enthalpy of acid–base interaction, H_{ab} may be evaluated from the equation of Drago et al. (1971, 1977) (see Eqn. 12) for small molecules:

$$-\Delta H_{ab} = C_A C_B + E_A E_B \tag{12}$$

where C_A and E_A (in $J \cdot mol^{-1}$) are measures of the degree of acidity of the electron accepting sites and C_B and E_B are measures of the degree of basicity of the electron-donating sites. Details of the determination of the constants C and E and ΔH_{ab} by calorimetry, infrared and NMR are provided in the works of Drago et al. (1971, 1977) and Fowkes (1982).

Nuclear magnetic resonance spectroscopy (NMR)

This method was initially employed in the study of moisture interactions in cellulosic materials (Ogiwara et al., 1969; 1970; Child, 1972; Carles and Scallan, 1973; Froix and Nelson, 1975) but is now being used in the examination of other polymers such as PVA (Hatakeyema and Yamauchi, 1984). One NMR approach, referred to as the 'wide-line technique', provides a rapid and non-destructive analysis of water in solid polymeric materials. Typical spectra (Fig. 11) exhibit broad peaks which are due to protons in the test material; the degree of broadening of the peaks, termed 'line width' are related to the mobilities of the protons. The peak due to water has a smaller line width than that of cellulose because the protons in the latter are less mobile. However, the peak due to water present in cellulose is usually wider than that of free (or unbound) water because interaction between cellulose and water hinders the mobility of the water protons. Ogiwara et al. (1969, 1970) have classified moisture in cellulose into 'free' and 'bound' based on the plots of line width at half value versus the water contents of some moistened modified wood pulps.

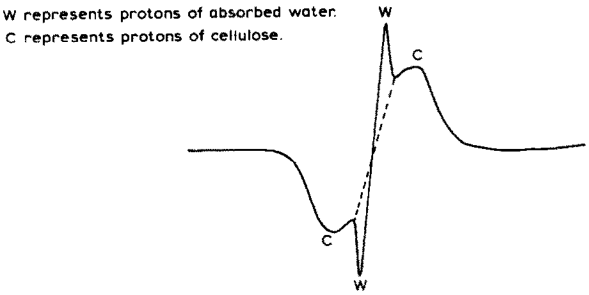

Fig. 11. Typical NMR spectrum of moist cellulose (Mitchell, 1976).

Another approach, known as pulsed NMR, makes use of the spin-lattice and spion–spin relaxation times. Details of this technique are provided in the works of Child (1972), Carles and Scallan (1973), Froix and Nelson (1975) and Hatakeyema and Yamauchi (1984).

Radiotracer method

Moisture interactions (Okhamafe and York, 1985b) as well as residual solvents (Murdock and Wirkus, 1963; Hays, 1964) in film coatings have been investigated by this method. Usually, a β-emitting radioisotope tracer – ^3H and ^{14}C for moisture and organic solvent determinations, respectively – is incorporated in the film coating formulation prior to the casting. Measurements are normally carried out in a liquid scintillation counter. This technique has been used to obtained the levels of tightly bound moisture (i.e. water bound within the crystalline phase) and total moisture of some aqueous – based HPMC film coating systems (Okhamafe and York, 1985b). One principal benefit that may be derived from these data is that tightly bound moisture contents can provide an indication of the degrees of crystallinity and plasticization of film coatings (Okhamafe and York, 1985b).

Infrared spectroscopy (IR)

The primary application of this method in film coating is the microstructural analysis of polymer films and film additives. The IR spectrum, for example, of nylon shows a strong band at about 1100 cm^{-1} which indicates the presence of aliphatic ether linkages and hydroxyl groups (Haas et al., 1955). Maddams and Woolmington (1985) have used IR to study the type of alkyl branches of 5 linear low density polyethylenes (LLDPE) containing methyl, ethyl, butyl, isobutyl and hexyl branches. The magnitude, breadth and frequency of the bands in the 800–1200 cm^{-1} were utilized by the authors to distinguish between the alkyl groups, and also between the methyl branches in the crystalline and amorphous regions of the polymer.

IR has also been found useful in the study of the surface features of pigments, particularly those of silica and alumina (Little, 1966; Hair, 1967). Day (1973/74) has classified the water adsorbed on titanium dioxide pigments, using data from IR investigations, into three types: dissociatively chemisorbed water, present as surface hydroxyl groups; non-dissociatively chemisorbed water molecules as a co-ordinating ligand to surface cation Lewis acid sites; and physically adsorbed water molecules existing as a monolayer or multilayers.

TABLE 8

Water contents of some polymers obtained by infra-red spectroscopy (Mitchell, 1976)

Polymer	Frequency (cm^{-1})	Water content (%)
Acrylic resins	5260 (approx. 1.9 μm)	0.1–1.2
Cellophane	5260	Several
Cellulose	3500 (approx 2.8 μm)	0.1– >1
Polyamides	5260	0.0–0.3
Polyethylene terephthalate	3400–3700 (2.94–2.70 μm)	Tenths
Polyols	5260	0.1–0.3
Polypeptides	3500	Tenths

Another area where IR has proved a useful tool is the characterisation of moisture interactions in polymers. Malcolm (1970) has applied this technique in the evaluation of the water adsorbed on α-helical synthetic polypeptides. A broad account of the IR method is given in a review by Mitchell (1976), and Table 8 is a summary of reported levels of water in some polymers. Perhaps it is pertinent to mention also that enthalpies of acid–base interactions can be derived from IR data as indicated earlier in the section on 'microcalorimetry'.

X-Ray diffraction

This technique is mainly used to study the crystallinity of polymers and pigments/fillers. It can be employed to differentiate between oriented crystalline and unoriented crystalline polymers (Van Krevelen, 1976). The X-ray diffraction patterns of the latter, like those of low molecular weight powder crystals, are characterised by diffraction rings rather than by spots. When an isotropic polymer undergoes orientation (i.e. molecular and crystallite realignment or rearrangement) as a result of a directed external stress, the diffraction rings contract into arcs and spots (Van Kevelen, 1976). The significance of orientation lies in the fact that oriented polymers are anisotropic, i.e. they exhibit physical properties which vary in different directions. Differences in the crystal structure of apparently identical pigments can also be detected by X-ray diffraction. The higher refractive index (and hence opacity) of rutile titanium dioxide when compared with the anatase form, has been ascribed to the longer Ti–O (atomic) distance of rutile by Ritter (1973) who quoted atomic distances of 1.946 ± 0.003 and 1.984 ± 0.004 Å for rutile, and 1.937 ± 0.003 and 1.964 ± 0.009 Å for anatase, based on X-ray diffraction work.

X-ray diffraction studies on pharmaceutical film formulations are apparently few. Porter and Ridgway (1983) were unable to obtain evidence of crystallinity in cellulose acetate phthalate (CAP) and polyvinyl acetate phthalate (PVAP) films from X-ray diffraction. Attempts to use this technique to detect crystallinity in PVA and HPMC, either in the powder form or as films have also not been successful (Okhamafe and York, unpublished data) although it has been shown from DSC investigations that these polymers exhibit crystallinity (Okhamafe and York, 1985a).

Final remarks

The increasing application of film coatings to solid dosage forms and the insufficient knowledge of their intrinsic characteristics have highlighted the need to adopt a fundamental approach in finding solutions to the problems encountered in film coating practice. Considerable improvements in the properties of existing film coating systems would be more readily achieved if adequate information on interaction phenomena is available. This approach may be less time-consuming and more cost-effective than synthesizing entirely new polymers. The structural complexity of film coatings is mainly derived from the extensive inter/intramolecular interactions found in polymeric materials, and is often further complicated by the presence of residual solvents and additives such as pigments and plasticizers. In this review, the various roles played by polymers, solvents, additives and moisture in the complex interrelationships that exist in film coatings have been addressed, and where appropriate, a correlation has been drawn between certain interaction phenomena and end-use properties. The discussions of the techniques used in the evaluation of interaction phenomena have been necessarily brief. Several recent methods such as small angle light scattering (SALS), low energy electron diffraction (LEED), Auger spectroscopy and electron spectroscopy for chemical analysis (ESCA) otherwise known as X-ray photoemission spectroscopy (XPS) have not been described. This is not due to a lack of merit but as a result of a desire to focus attention on the well established and better known methods.

Acknowledgements

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