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Effect of solids–polymer interactions on the properties of some aqueous-based tablet film coating formulations. I. Moisture permeability

Augustine O. Okhamafe and Peter York

Industrial Pharmacy Unit, School of Pharmacy, University of Bradford, Bradford BD7 1DP (U.K.)

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Summary

The effect of interactions between film formers and dispersed solids on the permeation properties of some tablet film coats have been investigated. Two polymer systems were employed: hydroxypropyl methylcellulose (HMPC) and HPMC plasticized with polyethylene glycol (PEG) 400. Two types of titanium dioxide (one of which was surface-treated to increase its hydrophobicity) and two types of talc (differing in particle size) were the solids. The diffusion, solubility and permeability coefficients of the films were obtained from sorption–desorption experiments. Solids–polymer interactions and their effect on the permeation process are interpreted in terms of acid–base interactions and the presence or absence of water at the solid–polymer interface. It is also shown that the values of the critical pigment volume concentration (CPVC) based on permeability and diffusion data are not necessarily identical.

Introduction

Insoluble solids (or fillers or pigments) are incorporated in film coatings, both pharmaceutical and non-pharmaceutical, for a variety of reasons. They serve as opacifiers (e.g. titanium dioxide), colorants (e.g. F.D. and C. pigments), bulking agents and reinforcers (e.g. carbon black in rubber). They may also minimize

Correspondence: P. York, Industrial Pharmacy Unit, School of Pharmacy, University of Bradford, Bradford BD7 1DP, U.K.

tackiness (e.g. talc). Sometimes the desire may be to achieve improved permeability and mechanical properties. No matter what the intended use, the fundamental properties of coatings are likely to be affected to varying degrees when fillers are incorporated.

Generally, the effect of particulate solids on film properties depends on the volume concentration of the filler, its chemical constitution, size, size distribution and shape, degree of dispersion in the film, and the extent of polymer–filler interaction (Elm, 1953; Michaels, 1965). It is difficult to determine precisely the contribution of each of these factors to any particular film property. Funke and his co-workers (1967, 1969) have also shown that the presence of water at the polymer–pigment interface in paint films could accelerate water permeability by disrupting polymer–pigment links. These authors proposed that greater polymer–pigment interaction would minimize interfacial water.

Studies on the moisture permeability of filled pharmaceutical coating systems are few. Parker et al. (1974) reported an initial decrease followed by an increase in the water vapour transmission rate of hydroxypropyl methylcellulose films loaded with increasing concentration of talc and titanium dioxide. Although this observation is in accord with Chatfield's (1962) principle, the authors did not indicate whether the pigments were adequately distributed in the films. Settling of pigments is likely during the drying process because a stationary substrate was used. Porter and Ridgway (1982), using free films cast on vinyl-coated cards fitted in a rotating tablet coating pan observed a similar permeability pattern to that postulated by Chatfield (1962) in cellulose acetate phthalate films containing red iron oxide but not in polyvinyl acetate phthalate films loaded with the same pigment.

However, studies in these areas have generally tended to ignore the effect of interaction between polymers and dispersed solids on the moisture permeability of tablet film coats. It is intended in this paper to consider this factor for plasticized and unplasticized hydroxypropyl methylcellulose films filled with different types of talc and titanium dioxide.

Materials and Methods

Pharmacoat 606 (hydroxypropyl methylcellulose U.S.P.) was manufactured by Shin-Etsu Chem., Japan. Polyethylene glycol (PEG) 400 was supplied by British Drug Houses, Poole, U.K. Two types of talc—Talc 4053NM (talc A) and Talc 4053 (talc B)—which differed only in particle size, were obtained from Richard Baker Harrison, Ilford, U.K. Two types of titanium dioxide were also used. Tioxide AH-R (TiO_2A), a pharmaceutical grade of anatase form, was supplied by B.T.P. (Tioxide, Billingham, U.K.). Bayertitan RC-K-20 (TiO_2B), a rutile form obtained from Bayer U.K., is surface-treated with Al_2O_3 and an undisclosed organic substance which renders it water-repellant. Specific surface area data were obtained from nitrogen adsorption measurements (see Table 1). pH measurements were made with a microprocessor pH/millivolt meter model 811 (Orion Research, Cambridge, MA, U.S.A.).

The two polymer systems employed were hydroxypropyl methylcellulose (HPMC) and HPMC plasticized with 20 wt.% PEG 400 based on the content of the film former. The fillers or pigments were dispersed with a Silverson mixer-emulsifier for 30 min in either 10% w/v aqueous solution of HPMC or 10% w/v aqueous mixture of HPMC/PEG 400. Up to 50 wt.% (14.9–23.5 vol. %), based on total polymer content, of the fillers were examined. Films were cast on the inside of a rotating lipped Perspex cylinder at 40–42°C for 6 h as described in an earlier work (Okhamafe and York, 1983). They were conditioned, after removal from the substrate, at 20°C and 58% R.H. for one week before test. Sorption–desorption data were obtained using an experimental procedure described in a previous study (Okhamafe and York, 1983). Analysis of these data (see Okhamafe and York, 1983) yielded the diffusion, solubility and permeability coefficients, respectively, of the films. Plots of these parameters are shown in Figs. 1–3.

Results and Discussion

Examination of thin sections of each film under the light microscope indicated clearly that the fillers were well distributed in the films.

Diffusion coefficient

This parameter is a measure of the moisture transport rate through the diffusion pathways or channels of a film. A plot of the diffusion coefficient of HPMC film against filler concentration (Fig. 1a) shows that moisture diffusion through the film remained either largely unaffected or increased when filter content was raised. Diffusion was highest in HPMC films loaded with talc A and least in those containing talc B. Films filled with organically surface-treated TiO₂B had higher diffusion coefficients than those loaded with the untreated TiO₂A. It is evident that although films containing TiO₂B (because of its water-repellant properties) would be predicted to exhibit lower diffusion, diffusion nonetheless increased more than with talc B. Films loaded with talc A generally had higher diffusion coefficients than talc B (smaller particle size). The diffusion coefficient data also show that the expected moisture barrier characteristics of the fillers are hardly in evidence. The Chatfield principle (1962) predicts that initially the presence of fillers in a film will increase the tortuosity of the diffusion pathways and therefore reduce the diffusion rate. How-

TABLE 1
SPECIFIC SURFACE AREA AND MAIN FEATURES OF THE FILLERS

Filler	Surface area (m ² ·g ⁻¹)	Particle feature
Talc A	1.34	plate-like, coarse
Talc B	1.81	plate-like, fine
TiO ₂ A	7.89	spherical, anatase, untreated surface
TiO ₂ B	8.42	spherical, rutile, surface treated with alumina and undisclosed organic compound

ever, no such reduction has been observed and in some cases, there was, in fact, an upward trend in diffusion rate.

Fig. 1b is a plot of the diffusion coefficient of HPMC film plasticized with 20 wt.% PEG 400 against filler concentration. It differs in several ways from Fig. 1a. TiO_2B -loaded films now exhibit the highest diffusion coefficients overall although as in Fig. 1a, films filled with talc B had the lowest diffusion. Both TiO_2A and talc A increased diffusion to a lesser extent than in the unplasticized HPMC film while talc B clearly reduced diffusion coefficient.

The effects of the loaded solids on moisture diffusion will be largely influenced by the degree of filler-polymer interaction, the specific surface area of the filler and the particle shape, assuming the degree of dispersion of the solids in the polymer matrix to be the same in all cases. Considering particle shape, talc particles which are plate-like should present a more tortuous barrier to moisture passage than the spherical titanium dioxide particles. However, the difference between the effects of the two types of talc indicates that the specific surface area of a filler is a more important factor than particle shape. Specific surface is directly related to the degree of filler-polymer interaction because the greater the surface area the higher the number of active sites available for interaction. TiO_2A and TiO_2B have specific surfaces 4-6 times those of talcs A and B (see Table 1) and therefore have the potential to interact to a greater extent with the polymer matrix. A comparison of Fig. 1a and b shows that diffusion is inhibited more by the fillers (talc, in particular) in the plasticized system than in the unplasticized film. This clearly indicates a difference in the degree of filler-polymer interaction between the two polymer systems.

A concept recently proposed (Marmo et al., 1976; Fowkes, 1982) which views polymer-polymer, solvent-polymer as well as solids-polymer interactions in terms of acid-base reactions can be applied to explain the observed results. According to this concept, solids-polymer interactions will be promoted if one is basic in nature

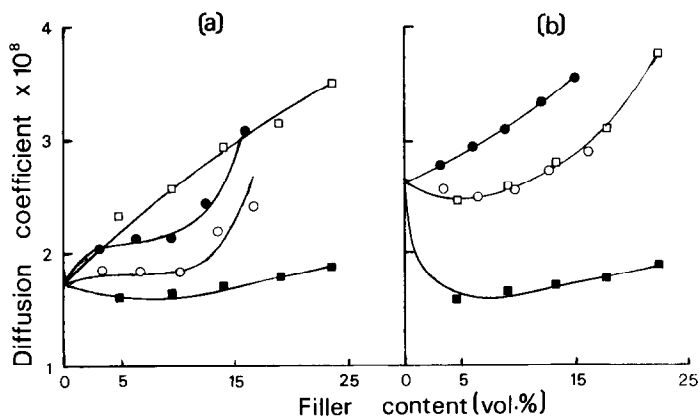


Fig. 1. Plot of diffusion coefficient ($\text{cm}^2 \cdot \text{s}^{-1}$) of (a) HPMC and (b) HPMC/PEG 400 films against filler concentrations at 20°C, 60% R.H. (Note: Talc A = □; Talc B = ■; TiO_2A = ○; TiO_2B = ●).

(electron donor) and the other acidic (electron acceptor). A simple and rapid method of estimating the acidity or basicity of a substance is to measure the pH of its aqueous solution or suspension. Table 2 shows the pH values obtained in this way for the film components used in this study. HPMC is neutral to slightly basic; PEG 400 is acidic; and mixed HPMC/PEG 400 is also acidic. The two talcs are basic while the two TiO_2 appear slightly acidic (TiO_2B) to slightly basic (TiO_2A), although the pH value for TiO_2B may be less valid because of its water-repellant surface. Based on the acid-base concept, greater interaction would occur between talc and HPMC/PEG 400 than talc and HPMC alone. This could partly explain the comparatively greater reduction in diffusion achieved when talc was loaded into the plasticized film. Since the pH of the TiO_2 differed only slightly from those of either HPMC alone or HPMC/PEG 400 blend, interaction would be small and consequently no clear fall in diffusion occurred.

Another factor that may also contribute to higher moisture diffusion in TiO_2 -filled films is the presence of interfacial water. TiO_2 has a strong affinity for water. Ritter (1973) and Day (1973/74) have reported that water may exist in up to three forms on the TiO_2 pigment surface: dissociatively chemisorbed water as surface hydroxyl groups; non-dissociatively chemisorbed water molecules as coordinating ligands to surface cation Lewis acid sites; and physically adsorbed water molecules present in a monolayer or even in a multilayer. The third form of water is of crucial importance because of its masking effect on the active sites of the pigment. This is particularly so because the films used in this study were cast from aqueous systems. (According to Ritter (1973), physically adsorbed water on TiO_2 may be up to two molecules thick at 60-70% R.H.) Thus it is apparent that the physically adsorbed water at the TiO_2 -polymer interface will not only hinder filler-matrix interaction but may, as has been noted by Funke et al. (1969), even facilitate moisture diffusion across the interface. The foregoing applies primarily to TiO_2A and partly to TiO_2B which is surface-treated. Ritter (1973) and Day (1973/74) have indicated that surface treatment frequently leaves a large proportion of the pigment active sites (up to 50%) still uncovered. In view of the water-repellant surface of TiO_2B it is reasonable to assume that the amount of interfacial water would be small when compared with TiO_2A . It would seem, therefore, that the higher diffusion coefficients of TiO_2B -filled films

TABLE 2
pH OF AQUEOUS POLYMER SYSTEMS AND FILLER SUSPENSIONS

System	pH
PEG 400 (10% w/v aqueous solution)	3.05
HPMC (10% w/v aqueous solution)	7.26
HPMC/PEG 400 (10% w/v aqueous solution)	5.71
Talc A/water (10% w/v aqueous suspension)	9.00
Talc B/water (10% w/v aqueous suspension)	9.01
TiO_2A /water (10% w/v aqueous suspension)	7.33
TiO_2B /water (10% w/v aqueous suspension)	6.35

may be due to inadequate filler-polymer interaction as a consequence of surface treatment. Poor filler-polymer interaction of this type would leave voids at the interface through which moisture will diffuse rapidly. Interfacial water if it exists at all in talc-filled films will be minimal in view of the hydrophobic surface of the filler.

Moisture diffusion through the films examined in this study can thus be summarized as follows. Filler particles are expected to reduce diffusion by making the diffusion channels more tortuous. Water at the filler-polymer interface will hinder interaction and speed up moisture diffusion. Filler-polymer interaction will be improved if one phase is basic (electron donor) and the other acidic (electron acceptor). Inadequate filler-polymer interaction may create voids around particles through which diffusion will be promoted. The size and/or number of voids will vary inversely with the degree of filler-polymer interaction. Where facilitated diffusion through the interfacial water layer and/or voids more than compensates for the fall in diffusion arising from the more tortuous pathways, there is an overall rise in moisture diffusion. This appears to be the case in the filled films except those containing talc B. Although the surfaces of talcs A and B are chemically similar, the latter interacted quantitatively more (as a result of its greater specific surface area) with the polymer matrix and therefore reduced moisture diffusion because interfacial voids were smaller and fewer.

Solubility coefficient

Solubility coefficient is a measure of the affinity of the film for the permeant. The solubility coefficient of all the filled films decreased with increase in the content of the solid additives (Fig. 2a and b). This effect would normally be expected since they are more hydrophobic than the polymeric matrix, and therefore increase in filler concentration reduces correspondingly the hydrophilic fraction of the films. In both plasticized and uplasticized HPMC films, those loaded with the more hydrophobic

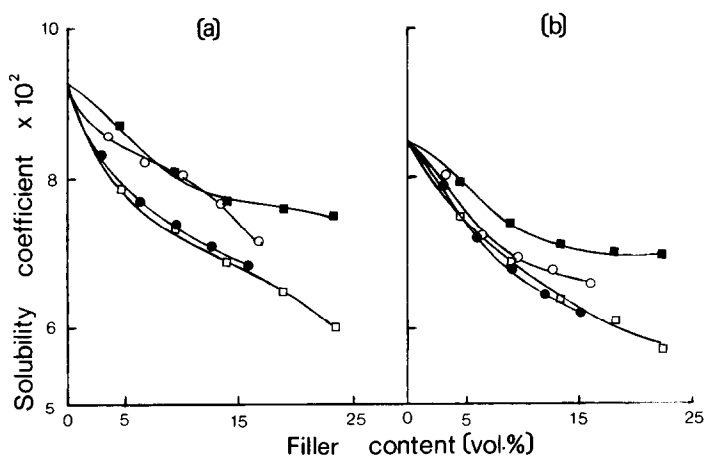


Fig. 2. Solubility coefficient ($\text{cm}^3 \cdot \text{cm}^{-3} \cdot [\text{cm Hg}]^{-1}$) of (a) HPMC and (b) HPMC/PEG 400 films versus filler concentration at 20°C, 60% R.H. (Note: Talc A = □; Talc B = ■; TiO₂ A = ○; TiO₂ B = ●).

TiO₂B had lower moisture solubility than those containing TiO₂A. Solubility coefficients were lower in films containing talc A than in those loaded with the smaller particle size talc B. This may be due to the larger surface area of talc B which adsorbs more polymer onto its surface than talc A. Consequently, a larger polymer surface overall was exposed to the permeating moisture.

Permeability coefficient

This parameter is the product of the diffusion and solubility coefficients and is a measure of the rate of moisture transport from one surface of a film, through it, to the other surface. It is plotted against filler content in Fig. 3a and b. The magnitude of the moisture permeability is in the rank order; talc A > TiO₂B > TiO₂A > talc B for HPMC films and is identical with that found for diffusion coefficient. Except for the unplasticized films loaded with talc A where permeability increased with solid concentration, all the films showed permeability minima that were generally lower than those of appropriate unfilled films. The solids-loaded HPMC/PEG 400 films were all generally less moisture-permeable than the unfilled film. On the whole, the permeability data show that neither diffusion nor solubility had a clearly dominant influence on the moisture permeability of the filled films. This contrasts with findings in a previous study (Okhamafe and York, 1983) where polymeric additives (including plasticizers), rather than pigments, were blended with HPMC. In that work, diffusion played the dominant role in moisture permeability. Reductions of up to 20–30% in solubility coefficient achieved in the present study had a considerable effect on moisture permeability.

It is common (e.g. Parker et al., 1974; Porter and Ridgway, 1982) to refer to the permeability minima of solids-loaded films as the critical pigment volume concentration (CPVC). CPVC is the filler concentration at which diffusion is minimum; beyond this concentration, voids are created as a result of the inability of the polymer matrix to bind all filler particles. This usually then leads to increase in the

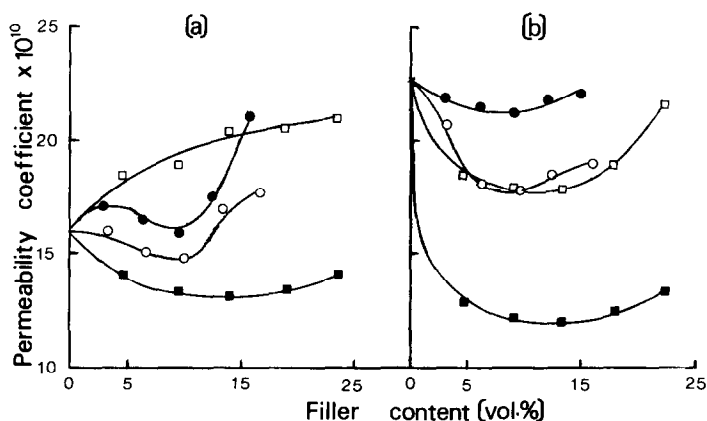


Fig. 3. Permeability coefficient ($\text{cm}^2 \cdot \text{s}^{-1} \cdot [\text{cm Hg}]^{-1}$) of (a) HPMC and (b) HPMC/PEG 400 films versus filler concentration at 20°C, 60% R.H. (Note: Talc A = \square ; Talc B = \blacksquare ; TiO₂A = \circ ; TiO₂B = \bullet).

diffusion rate. It follows, therefore, that CPVC is better assessed from diffusion rather than permeability data. As Figs. 1a, 1b, 3a and 3b show, CPVCs based on diffusion and permeability results would not necessarily be identical, due no doubt to the influence of solubility on permeability. Where CPVC was observed it tended to be higher when estimated from permeability results.

References

- Chatfield, H.W., *Science on Surface Coating*, Van Nostrand, New York, 1962, p. 452.
- Day, R.E., The characterisation of the surface of titanium dioxide pigments. *Progr. Org. Coatings*, 2 (1973/74) 269–288.
- Elm, A.C., Some mechanical properties of paint films. *Official Digest, Fed. Soc. Paint Technol* 25 (1953) 750–774.
- Fowkes, F.M. Acid–base interactions in polymer adhesion. In Georges, J.M. (Ed.), *Microscopic Aspects of Adhesion and Lubrication*, Elsevier, Amsterdam, 1982, pp. 119–137.
- Funke, W., On the relation between the pigment–vehicle interaction and liquid water absorption of paint films. *J. Oil Col. Chem. Ass.*, 50 (1967) 942–975.
- Funke, W., Zorll, U. and Murthy, B.G.K., Interfacial effects in solid paint films related to some film properties. *J. Paint Technol.*, 41 (1969) 210–221.
- Marmo, M.J., Mostafa, M.A., Jinnai, H., Fowkes, F.M. and Manson, J.A., Acid–base interaction in filler–matrix systems. *Ind. Eng. Chem., Prod. Res. Develop.*, 15 (1976) 206–211.
- Michaels, A.S., Water and the barrier film. *Official Digest, Fed. Soc. Paint Technol.*, 37 (1965), 638–653.
- Okhamafe, A.O. and York, P., Analysis of the permeation and mechanical characteristics of some aqueous-based film coating system. *J. Pharm. Pharmacol.*, 35 (1983) 409–415.
- Parker, J.W., Peck, G.E. and Banker, G.S., Effects of solids-loading on moisture permeability coefficients of free films. *J. Pharm. Sci.*, 63 (1974) 119–125.
- Porter, S.C. and Ridgway, K., The permeability of enteric coatings and the dissolution rates of coated tablets. *J. Pharm. Pharmacol.*, 34 (1982) 5–8.
- Ritter, H.S., Surface properties of titanium dioxide pigments. In Patton, T.C. (Ed.), *Pigment Handbook*, Vol. III: Characterisation and Physical Relationship, John Wiley and Sons, New York, 1973, pp. 169–184.