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# Quantitative assessment of additive–polymer interaction in pigmented hydroxypropyl methylcellulose formulations using immersion calorimetry

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## Summary

The interaction between a series of solid additives (including pigments, opacifiers and talc) and hydroxypropyl methylcellulose has been assessed using immersion calorimetry in both water and an aqueous solution of the polymer. All reactions with the exception of talc in water were exothermic, i.e. they had a negative enthalpy charge. Only titanium dioxide was found to interact significantly with the polymer consistent with glass transmission data generated from differential scanning calorimetry of cast films and inferred from a consideration of literature solubility parameters. The results show that immersion calorimetry can provide a direct, rapid and simple method of assessing additive–polymer interactions.

## Introduction

Additives in the form of pigments (e.g. aluminium lakes of water soluble dyes), opacifiers (e.g. titanium dioxide) and various inorganic materials (e.g. iron oxides and talc) are often included in film-coating formulations (Pickard and Rees, 1974; Porter, 1980; Rowe, 1983). A knowledge of the interaction between these additives and the polymer matrix is important in the optimisation of formulations for specific end use properties (Okhamafe and York, 1987). Interaction generally takes the form of adsorption of the polymer on the additive surface – an exothermic process (Dulog, 1985) capable of being measured using calorimetry. In this preliminary study immersion calorimetry has been used to study the interaction between a variety of solid additives often used in tablet film coating and the polymer hydroxypropyl methylcellulose.

## Materials and Methods

All the additives were obtained from D.F. Anstead Ltd. (Billericay, U.K.) and were used as received. Enthalpies of immersion in distilled water and a 2% w/w aqueous solution of hydroxypropyl methylcellulose (Pharmacoat 606, Shin-Etsu Chemical Company, Tokyo, Japan) were measured using a heat burst calorimeter (Benzinger and Kitzinger, 1963). This instrument operates by

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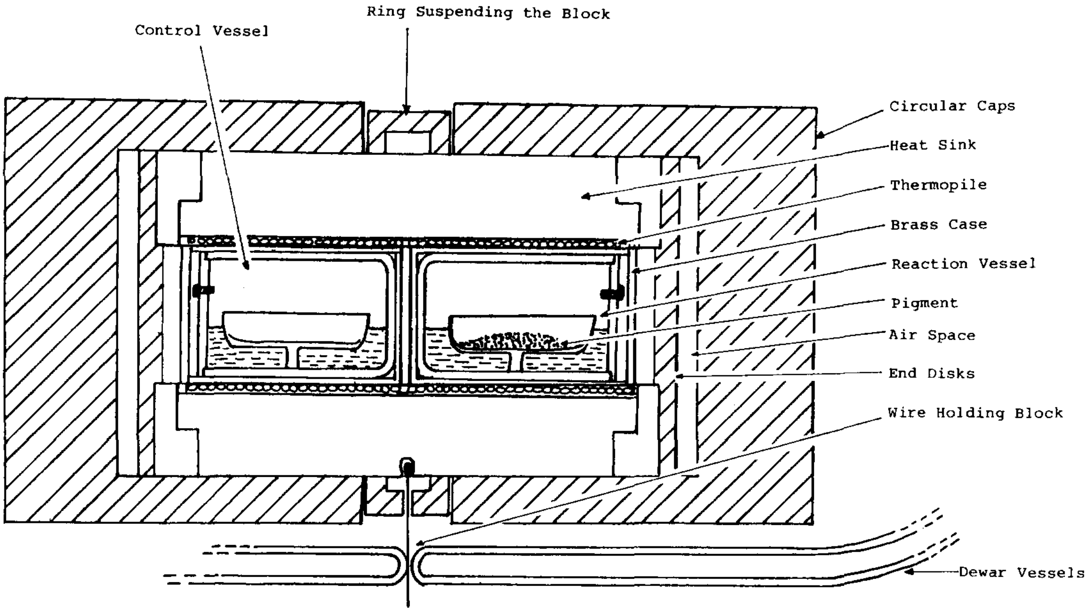

Fig. 1. A diagram of the heat burst calorimeter used (after Benzinger and Kitzinger, 1963).

detecting rapid heat flow from a reaction vessel via a thermoelectric pile into the surrounding heat sink. It consists of two vessels (the reaction and the control) each enclosed in one of two thermopiles connected in series and in opposition, thus cancelling the heat flows originated from the mixing or friction and enabling an accurate measurement of the heat of reaction. Fig. 1 (adapted from Benzinger and Kitzinger, 1963) shows a section through the calorimeter. A weighted sample of the powder is contained in the boat-shaped vessel in the reaction cell, both cells containing the same quantity of water or 2% aqueous hydroxypropyl methylcellulose solution. After assembly the instrument is allowed to attain thermal equilibrium (90 min at 25 °C) before being rotated on its axis to achieve mixing. The heat flow resulting from the reaction is recorded on a chart recorder and the enthalpy change is measured directly from the area under the curve and a knowledge of the instrument calibration.

Differential scanning calorimetry was performed on cast films using a Perkin Elmer DSC 2 instrument over the temperature range 30 °C–200 °C with a heating rate of 20 °C/min.

## Results and Discussion

All reactions with the exception of talc in water were exothermic, i.e. they had a negative enthalpy change. The coefficient of variation of the results for the immersion in water (5–14% for the coloured pigments and titanium dioxide, 17% for the talc) was always higher than that for the immersion in the polymer solution ($< 4\%$ for the coloured pigments and titanium dioxide, 10% for the talc). However, the measurement technique is more precise than such a variation indicates, almost all the experimental scatter being caused by the intrinsic variability of the samples. The heats of immersion in water of the titanium dioxide and red iron oxide (Table 1) are much lower than literature values for comparable pigments ($+592$ mJ/m$^2$ for anatase titanium dioxide, Wade and Hackerman, 1961; $+350$ mJ/m$^2$ for red iron oxide, Zettlemoyer and McCafferty, 1969).

However, whereas in these previous studies the pigments had been pretreated by outgassing at high temperatures (a process which has a large effect on the measured heat of immersion due to the removal of water from and, sometimes, a

TABLE 1

*Heat of immersion data for additives studied*

| Additive | Surface area $m^2/g$ | Heat of immersion | | | |
|---|---|---|---|---|---|
| | | in water | | in aqueous HPMC | |
| | | mJ/g | $mJ/m^2$ | mJ/g | $mJ/m^2$ |
| Titanium dioxide | 7.60 | +751.2 | +98.8 | +861.1 | +113.3 |
| Red iron oxide | 7.56 | +997.4 | +131.9 | +972.4 | +128.6 |
| Black iron oxide | 3.84 | +688.4 | +179.3 | +669.4 | +174.3 |
| Yellow iron oxide | 13.07 | +1 224.5 | +93.7 | +1 226.9 | +93.9 |
| FD&C yellow 6 lake | 93.10 | +6 648.1 | +71.4 | +6 214.2 | +66.7 |
| Talc A | 2.99 | −28.3 | −9.5 | +160.0 | +53.5 |
| Talc B | 14.33 | −127.4 | −8.9 | +622.5 | +43.4 |

Surface areas are measured using nitrogen (BET). A positive heat of immersion is indicative of an exothermic reaction, i.e. a negative enthalpy and vice versa.

chemical change of the surface, Wade and Hackerman, 1961) in this study the pigments were used as received. In fact, immersion calorimetry has been used to study the physical adsorption of water vapour onto red iron oxide showing that in this case, the measured heat of immersion can fall as low as +118 $mJ/m^2$ (Healey et al., 1956). The effect of adsorbed water on the surface of titanium dioxide can be demonstrated by comparing the enthalpy change in Table 1 with that for another sample equilibrated overnight over water for which a heat of immersion of +54.7 $mJ/m^2$ was recorded.

The presence of adsorbed water is probably the reason for the low enthalpy change in water recorded for the aluminium lakes since these pigments have very high moisture contents (15–25% w/w). A similar argument can be applied to the data for the iron oxides since in this series the yellow form has the highest water of hydration (15% w/w). The negative heats of immersion for the talcs imply little or no wetting by the water — an expected result since it is well known that talc is a hydrophobic material.

If the results for the enthalpy changes in water and in aqueous polymer solution are compared, then the most notable differences occur with the talcs and the titanium dioxide. With the talcs the change in the reaction from an endothermic to an exothermic one is a result of the promotion of wetting by the polymer solution due to reduced surface tension. However, the 14.7% increase in enthalpy occurring with the titanium dioxide implies a positive interaction for this system.

At this point it is pertinent to discuss these results in the context of data generated by other techniques for assessing/predicting additive–polymer interaction viz differential scanning calorimetry of cast films and solubility parameter methods. Adsorption of a polymer by an additive generally results in an increase in the glass transition of the polymer film and this was exactly the effect seen with cast films of hydroxypropyl melthylcellulose pigmented with titanium dioxide where, over the

TABLE 2

*Solubility parameter data used in this study*

| Material | Hansen parameters ($MPa^{1/2}$) | | | Radius of interaction ($MP_{\alpha}^{1/2}$) | Ref. |
|---|---|---|---|---|---|
| | $\delta_d$ | $\delta_p$ | $\delta_h$ | | |
| Titanium dioxide | 24.1 | 14.9 | 19.4 | 17.2 | Hansen (1967b) |
| Red iron oxide | 20.7 | 12.3 | 14.3 | 11.5 | Hansen (1967b) |
| Hydroxypropyl methylcellulose | 14.4 | 5.8 | 16.7 | – | Rowe (1988) |

pigment concentration range studied (0–25%), an increase in glass transition temperature of 8–12 ° C was recorded. However, in the case of the iron oxides only a marginal increase of between 1–5 ° C was recorded implying an increased interaction between titanium dioxide and the polymer.

Pigment–polymer interactions can also be predicted using a 3-dimensional solubility parameter approach where the solubility parameter, $\delta$, is divided into components representing dispersion interactions, $\delta_d$, dipole–dipole and polar interactions, $\delta_p$, and hydrogen bonding, $\delta_n$ (Hansen 1967a). Such an approach predicts that when plotted on a 3-dimensional projection every solvent will be represented by a point in space and every polymer or pigment will be characterised by a volume formed by all the solvents which either dissolve it (in the case of a polymer) or suspend it (in the case of a pigment) (Hansen, 1967b). For polymers it has also been shown that the degree of overlap between the projections will provide information on their mutual compatibility (Hansen, 1967c).

Applying this concept to the pigments titanium dioxide and red iron oxide and the polymer hydroxypropyl methylcellulose results in Figs. 2 and 3. Unfortunately the only data for the polymer (Table 2) are those determined from calculations based on the structure of a repeating unit using literature values for the group molar attraction constants and hydrogen bonding energies (Rowe, 1988) represented by the point P in the figures. However, even from this limited information it can be seen that while in the case of titanium dioxide, the polymer falls well within the sphere of interaction of the pigment, in the case of the red iron oxide it is very much towards the periphery. This implies a greater interaction in the case of the titanium dioxide consistent with the data generated by both immersion calorimetry and differential scanning calorimetry.

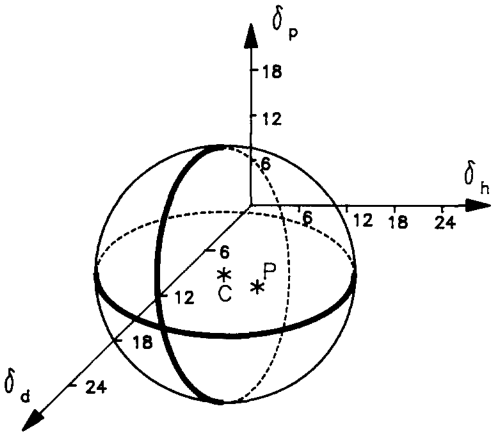

Fig. 2. A 3-dimensional solubility parameter projection for titanium dioxide (after Hansen, 1967b). C, the centre for the titanium dioxide; P, the calculated value for hydroxypropyl methylcellulose.

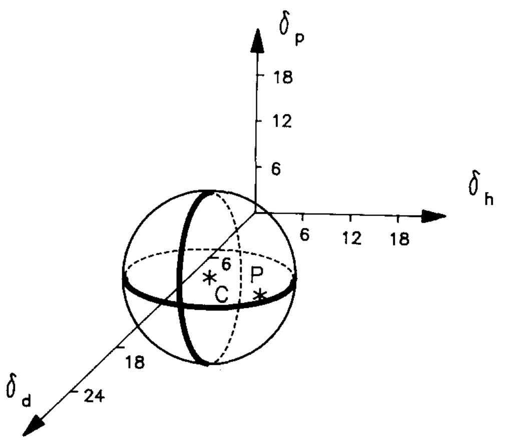

Fig. 3. A 3-dimensional solubility parameter projection for red iron oxide (after Hansen, 1967b). C, the centre for the red iron oxide; P, the calculated value for hydroxypropyl methylcellulose.

In conclusion, the results show that immersion calorimetry can provide a direct, rapid, simple method of assessing additive polymer interaction. The results are comparable with those generated by other methods and consistent with the known theories of polymer adsorption on pigment surfaces.

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