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The influence of temperature on the sorption of benzocaine by nylon 6 from aqueous cosolvents

N. E. RICHARDSON AND B. J. MEAKIN*

Pharmaceutics Group, School of Pharmacy and Pharmacology, University of Bath, Bath, U.K.

The influence of temperature on the sorption of benzocaine by nylon 6 powder from aqueous cosolvents has been assessed. At about 30° discontinuities appear in the Van't Hoff plots for sorption from water and aqueous PEG 400, which may be attributed to transitional changes in the polymer structure. No such discontinuities are apparent for sorption from aqueous ethanol over the temperature range 15–60°, which is indicative of plasticization by this cosolvent.

As part of a fundamental study into the parameters which control drug-plastics interactions, we have previously described the effect of such variables as pH, ionic strength, drug and plastics structures, temperature and the presence of cosolvents on the sorption of drugs from aqueous solution, using a model system based on benzoic acid derivatives and pure polyamides (Richardson & Meakin, 1974, 1975). It was observed that the sorption of benzocaine from 0·5M aqueous potassium chloride by nylon 6 powder decreased with increasing temperature according to the Van't Hoff relationship (eqn 1) over the temperature range 30–60°.

$$\log_{10}K = \frac{-\Delta H^{\circ}_{\text{SORPTION}}}{2{\cdot}303\ RT} + \text{constant} \quad .. \quad (1)$$

(K is the sorption constant, R is the gas constant, $\Delta H^{\circ}_{\text{SORPTION}}$ the standard enthalpy of sorption and T is the absolute temperature). Studies by other workers however, have indicated that anomalies can occur at about 30° in the temperature dependency of polyamide interactions. Myers, Meyer & Szware (1961), found that the permeation of water vapour through nylon 6:6 film passed through a minimum at 30° and Iijima (1970) reported a change in slope of the Van't Hoff plot for the diffusion of 4-nitro aniline through nylon 6 film, at about the same temperature. In order to see if similar effects occurred with our sample of nylon 6 powder it was decided to investigate the sorption of benzocaine from aqueous cosolvent mixtures over the temperature range 15–60°.

MATERIALS AND METHODS

Materials. Benzocaine, nylon 6 powder, ethanol and polyethylene glycol 400 (PEG 400) were as described previously (Richardson & Meakin, 1974, 1975). Water was freshly distilled from an all glass still.

Methods. The techniques used for ultraviolet assay, solubility determinations and sorption studies were as before (Richardson 1973; Richardson & Meakin, 1974, 1975).

RESULTS AND DISCUSSION

Sorption isotherms for benzocaine onto nylon 6 powder from water and aqueous cosolvent mixtures containing 10, 20 and 30% w/v of either ethanol or PEG 400 were obtained over the temperature range 15–60°. The sorption data were subjected to linear regression analysis and in all cases correlation coefficients were $>0{\cdot}99$ ($n_{min} = 5$) and intercepts spanned zero within ± 2 standard deviations. All isotherms could therefore be said to be linear and to pass through the origin and could thus be characterized by their slopes or sorption constants (K), which are equivalent to the partition coefficients of the solute between polymer and solvent.

Figs 1 and 2 show the Van't Hoff plots for benzocaine from aqueous ethanol and PEG 400 respectively. In contrast to those from ethanol which are linear over the whole temperature range studied (15–60°), those from both water and PEG 400 show a discontinuity at about 30°, with the K values becoming essentially constant below this temperature except for those from 30% w/v PEG 400 which rise quite sharply. These discontinuities may be associated with a number of factors.

The physical properties of polymers are related to molecular mobility. The temperature range over which polymer segments acquire this mobility is known as the glass transition (Tg). Below the Tg, molecular motion is essentially absent whereas

* Correspondence.

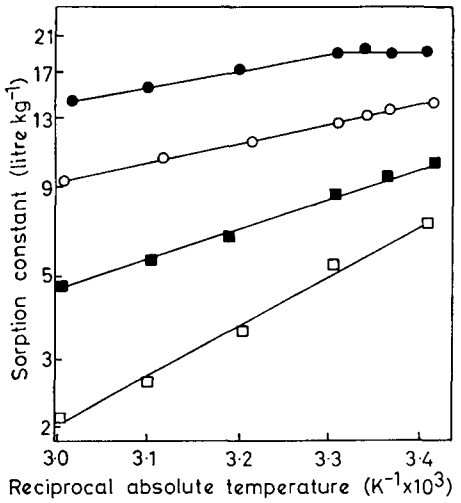


FIG. 1. Van't Hoff plots for the sorption of benzocaine from water and aqueouse thanol (● water, ○ 10%, ■ 20%, □ 30% ethanol).

above Tg segmental motion increases with temperature until molecular motion is possible; these effects occur predominantly in the non-crystalline regions of the polymer. The diffusion of a penetrant molecule into a polymer will therefore depend on the extent of both segmental and molecular motion. The Tg value for nylon 6 has been reported to lie within the range 15–80° according to the physical characteristics of the polymer and the conditions under which the measurements were made (Marx, Smith & others 1955; Ke & Sisko, 1961; Brandrup & Immergut, 1967; Brennan, 1973). In the dry state a value of about 50° seems to be most commonly quoted and this would be lowered in the presence of water. One conclusion that would therefore seem likely, is that in the sorption of benzocaine from water, 10 and 20% PEG 400, regions of the polymer are becoming impermeable to the drug at temperatures below 30°. This reduction in the number of available interaction sites would then compensate for the increased extent of sorption predicted from simple partition theory as a result of the drug solubility in the aqueous phase decreasing with fall in temperature (Richardson & Meakin, 1974, 1975), thus accounting for K becoming invariant with temperature.

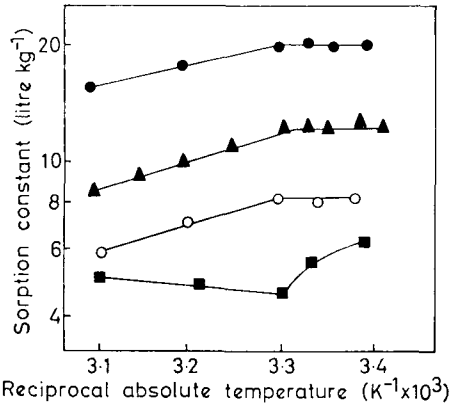
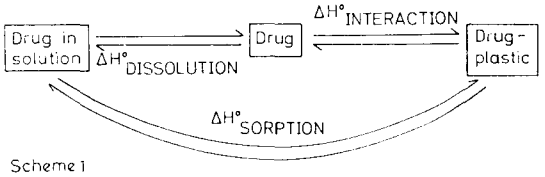


FIG. 2. Van't Hoff plots for the sorption of benzocaine from water and aqueous PEG 400 (● water, ▲ 10%, ○ 20%, ■ 30% PEG 400).

An alternative explanation arises from the conclusions of Lord (1973), based on differential thermal analysis, that the parallel polymer chains in nylon 6 can undergo a thermal twist at about 30–40° and that these twisted regions are prevented from crystallizing to any degree of perfection by the constraints of the neighbouring antiparallel regions. Any such decrease in crystallinity would have a similar influence to increase in segmental and molecular motion on the sorption process.

Solvent penetration of a polymer results in plasticization and lowers Tg values. Comparison of the solubility parameters of the pure solvents (water 23·4, ethanol 12·7, PEG 400 8·6) with that for nylon 6 (13·5) suggests that ethanol might be a better plasticizer than the others, which could explain the absence of breaks in the Van't Hoff plots for systems containing ethanol (Figs 1 and 2).

The overall interaction between a drug in solution and a polymer will involve the removal of drug molecules from their solvent environment, followed by interaction with the plastic (Scheme 1).



Scheme 1

$\Delta H^\circ_{SORPTION}$ calculated from the Van't Hoff plots using equation 1 thus gives the standard enthalpy associated with both steps of the process. It is therefore possible to calculate the interaction enthalpy if the standard enthalpy of dissolution is known, using equation 2.

$$\Delta H^\circ_{SORPTION} = -\Delta H^\circ_{DISSOLUTION} + \Delta H^\circ_{INTERACTION} \quad (2)$$

Table 1. *Thermodynamic parameters for the dissolution in and sorption of benzocaine by nylon 6 powder from aqueous cosolvents.*

Solvent	$\Delta H^\circ_{SORPTION}$ (KJ mol^{-1})	$\Delta S^\circ_{SORPTION}$ at 30° (J mol^{-1} K^{-1})	$\Delta H^\circ_{DISSOLUTION}$ (KJ mol^{-1})	$\Delta H^\circ_{INTERACTION}$ (KJ mol^{-1})
Water	−8·8 (0·7)[a]	−4·6 (2·6)	+32·7 (1·5)[c]	+23·9 (1·7)
10% Ethanol	−9·9 (0·7)[b]	−11·6 (2·6)	+37·9 (2·3)[c]	+28·0 (2·4)
20% Ethanol	−17·1 (1·0)[b]	−38·9 (6·3)	+46·6 (2·5)[c]	+29·5 (3·1)
30% Ethanol	−28·4 (0·6)[b]	−79·5 (2·6)	+53·0 (1·5)[c]	+24·6 (1·6)
10% PEG 400	−13·7 (0·9)[a]	−24·8 (3·3)	+32·8 (1·6)[c]	+19·1 (1·8)
20% PEG 400	−12·5 (3·2)[a]	−23·8 (10·9)	+31·9 (2·2)[c]	+19·4 (3·9)
30% PEG 400	+5·3 (1·6)[a]	+30·0 (6·0)	+27·2 (1·5)[c]	+32·5 (2·2)

Temperature ranges a = 30–60°; b = 15–60°; c = 20–45°. Figures in brackets are standard deviations.

$\Delta H^\circ_{SORPTION}$ values were obtained by linear regression analysis of the data shown in Figs 1 and 2 and are given in Table 1; the values for water and aqueous PEG 400 systems were obtained from K values determined at 30° and higher. $\Delta H^\circ_{DISSOLUTION}$ values were calculated similarly from solubility measurements between 15–45° (Richardson, 1973).

Table 1 shows that $\Delta H^\circ_{INTERACTION}$ values for benzocaine from both aqueous ethanol and water are not significantly different with a mean value of +26·5 KJ mol^{-1} ($\chi^2_{calc} = 4{\cdot}01$, $\chi^2_{tab} = 7{\cdot}81$, $P = 0{\cdot}05$) which is indicative that at temperatures above 30° the addition of ethanol does not change the mechanism of the drug-plastic interaction.

A similar situation has been reported by Suda, Susuki & Nakajima (1971) for the sorption of dyes by cellulose acetate from a series of n-alcohols. The data for PEG 400 do not quite fit this pattern however. The values for $\Delta H^\circ_{INTERACTION}$ for 10 and 20% PEG 400 are slightly lower than for aqueous ethanol and water their being about 19 KJ mol^{-1} which would suggest that the polymeric cosolvent modifies the drug-nylon 6 interaction. The anomalous behaviour from 30% PEG 400 (Fig. 2) is further evidenced by the positive sorption enthalpy of +5·3 KJ mol^{-1} and this is also the only solvent system which showed a positive entropy for sorption (+30 J mol^{-1} K^{-1}) even allowing for the errors associated with value of this parameter. At present there is no satisfactory explanation for this behaviour.

Pharmaceutical implications. These results show that transitional changes which can occur with all plastics materials can influence the temperature dependence of drug-plastics interactions and also suggest the temperatures at which these transitions occur can be considerably modified by the type of cosolvent present in a formulation. Such effects are relevant to accelerated storage testing of formulations in their final containers. Extrapolations from data determined above the Tg to sub-Tg temperatures would seem likely to underestimate shelf life whilst the presence of cosolvents which can plasticize the polymer and so lower the Tg may tend to promote drug loss by sorption processes.

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