The sorption of benzocaine by nylon 6 (polycaprolactam)

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The sorption of drugs and formulatory adjuvants by plastics can present considerable problems when these materials are used as packaging media. These problems are aggravated by the lack of specific information regarding the individual contributions of the polymer resin and additives such as plasticizers and stabilizers to the product-plastics interaction. Here we report preliminary findings on the interaction of benzocaine in aqueous solution with pure nylon 6 (polycaprolactam) resin.

Powdered nylon 6 (specific surface by krypton adsorption, 7·0 m^2g^{-1}) was prepared from nylon chips by a precipitation process. Infrared spectra were consistent with the α form of nylon 6 containing very little monomer. Sorption was determined by shaking the powder with standard benzocaine solutions for one hour at a constant temperature and assaying the supernatant spectrophotometrically.

Uptake of benzocaine by powdered nylon 6 is rapid reaching equilibrium in less than 30 min and follows a C_1 type partition isotherm (Giles, MacEwan & others, 1960) which is linear over the concentration range studied (0–6 $\times$ 10^{-3}M). No plateau was observed. A similar result was obtained for benzoic acid. This contrasts with the finding of Kapadia, Guess & Autian (1964) who reported that the sorption of benzoic acid by commercial nylon 610 film followed a Langmuir isotherm.

The C_1 isotherms may be described by the expression, $C_n = KC_w$, where C_n is the uptake by nylon (mol kg^{-1}), C_w is the molar concentration in the aqueous phase at equilibrium and K is the equilibrium constant which characterizes the extent of adsorption for the system.

For benzocaine in water at 30°, K = 1·94 $\times$ 10^3 which increases to 2·53 $\times$ 10^3 in the presence of 0·5M potassium chloride. K values also vary with temperature and pH.

K decreases with increase in temperature and a plot of log K against $1/T_{abs}$ is linear, leading to a value of $-12{\cdot}3$ KJ mol^{-1} for the standard enthalpy of adsorption.

K values determined in buffer at ionic strength 0·5M and 30° show that benzocaine is only slightly adsorbed at very acid pH (0·69) but as the pH is increased sorption becomes more extensive, rising to a maximum around pH 5 and thereafter remaining constant. The extrapolated K value of 1·40 $\times$ 10^3 at the pK_a value for benzocaine in 0·5M KCl (2·5) where the drug is 50% ionized is almost exactly midway between the maximum and minimum K values, 2·54 $\times$ 10^3 and 0·2 $\times$ 10^3 respectively.

These results are consistent with the adsorption of a monofunctional solute by a polymeric substrate containing regions of varying crystallinity. It seems likely that principal interaction sites are the amide groups of the polymer which probably form weak hydrogen bonds with the amino group of the free benzocaine base.

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In vitro and *in vivo* studies of the metabolism of phenylbutazone in the alloxan rat and rabbit

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In *in vitro* experiments, liver microsomal preparations of normal and alloxan diabetic rats and rabbits were incubated with phenylbutazone in the presence and absence of appropriate cofactors. These preparations were then assayed for unchanged drug and its metabolites at different intervals. In some of these experiments, preformed NADPH and/or a generating system for it were also incorporated in the incubation milieu. In separate experiments microsomal preparations from diabetic animals pretreated with insulin were similarly used.

In *in vivo* experiments the drug was administered to the normal and diabetic animals. Urine was collected periodically and analysed for unchanged drug and its metabolites. The