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# Adsorption of benzoic acid on sulphadimidine: suppressive effect of some hydrophilic polymers

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The uptake of benzoic acid on sulphadimidine particles has been investigated. Depending on the concentration of sulphadimidine in the system, benzoic acid was adsorbed to the extent of 94%. Data from the adsorption experiments were shown to fit a Langmuir plot for systems containing up to 0·2 g 100 $ml^{-1}$ sulphadimidine. The suppressive effect of three hydrophilic polymers on adsorption was studied; the results followed the sequence: Polyvinylpyrrolidone (PVP) > methylcellulose > sodium carboxymethylcellulose. Dialysis experiments revealed that, within the range of concentrations used, neither PVP nor methylcellulose was significantly bound to benzoic acid.

McCarthy (1969) has pointed to a possible loss in activity of preservatives arising from their adsorption onto solids commonly used as medicaments. Beveridge & Hope (1967) reported that the spoilage of the B.P.C. mixture of sulphadimidine for infants is attributable to possible adsorption of the preservative, benzoic acid, by the suspended sulphadimidine, but no detailed study appears to have been made to support this claim.

We have examined the uptake of benzoic acid by sulphadimidine and the suppressive effect of PVP, methylcellulose and sodium carboxymethylcellulose on adsorption.

## MATERIAL AND METHODS

### *Materials*

*Sulphadimidine* (ICI) (mean volume-surface diameter of 32·6 $\mu$m) and *benzoic acid* (BDH), were B.P. *Polyvinylpyrrolidone* (PVP) was a sample having an average molecular weight of 40 000 (Plasdone K 29–32, GAF Corporation, N.Y.). *Methylcellulose* 20 was used (BDH). Two grades of *sodium carboxymethylcellulose* SCMC 50 and SCMC 100 (BDH) and methyl and propyl hydroxybenzoates (BDH) were of B.P.C. quality.

### *Methods*

*Adsorption isotherm.* Aqueous benzoic acid solution (25 ml) of appropriate concentration was added to each of a duplicated series of weighed quantities of sulphadimidine in 100 ml ground-glass stoppered conical flasks. The flasks were placed in an oscillating water bath at 24° till complete equilibration (30 min). The suspensions were then filtered through a Jena 39 $G_3$ sintered glass funnel and the concentration of benzoic acid in the filtrate was determined spectrophotometrically in an aliquot suitably diluted with 0·05 N HCl.

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*Assay of benzoic acid in the filtrate.* Because of interference by sulphadimidine, the method of Tinker & McBay (1954), for the spectrophotometric determination of a two-component system, was adopted. Measurements were made at 230 and 300 nm and the concentration of benzoic acid (mmol) was calculated using the following equation:

$$C = \frac{aX_1A_2 - aX_2A_1}{aX_1aY_2 - aX_2aY_1} \quad \cdots \quad (1)$$

where $aX_1$ and $aX_2$ are the absorptivity indices for sulphadimidine at 300 and 230 nm respectively, $aY_1$ and $aY_2$ are the corresponding values for benzoic acid. $A_1$ and $A_2$ are the extinctions at 300 and 230 nm respectively.

After substitution, equation (1) becomes:

$$C = \frac{7{\cdot}102A_2 - 12{\cdot}098A_1}{76{\cdot}651} \quad \cdots \quad (2)$$

The validity of equation (2) was tested by assaying known mixtures of benzoic acid and sulphadimidine. The percentage error was $\pm 2{\cdot}3\%$ for benzoic acid.

Methyl and propyl hydroxybenzoates were assayed spectrophotometrically at 295 nm (in 0·01 N NaOH). Sulphadimidine interference (maximum 6·4%) was mainly eliminated by a blank experiment.

*Equilibrium dialysis.* Cellophane bags, prepared from Visking tubing 24/32 inch, were filled with 5 ml of the polymer solution and 5 ml of benzoic acid solution. The bags were immersed in 10 ml of water and shaken at 24° until complete equilibration (8–12 h). The volumes of both the inside and outside solutions were accurately measured and the benzoic acid contents in both solutions were determined spectrophotometrically, after dilution with 0·05 N HCl, at 230 nm. Interference due to either PVP or methylcellulose was negligible.

## RESULTS AND DISCUSSION

Preliminary experiments showed that the adsorption of benzoic acid by the sulphadimidine particles was rapid since equilibrium was attained after 10 min. An equilibration time of 30 min was therefore adopted. At 100 mg 100 $ml^{-1}$ initial concentration of benzoic acid, about 94% adsorption occurred at a sulphadimidine concentration of 0·3 g 100 $ml^{-1}$ and remained unchanged up to 10 g 100 $ml^{-1}$ of drug (Fig. 1A). The adsorption pattern at different initial benzoic acid concentrations depended on the concentration of sulphadimidine in the system (Fig. 1B). Below 0·3 g 100 $ml^{-1}$ of drug, saturation regions exist beyond which no more adsorption takes place. For systems containing 0·06, 0·1 and 0·2 g 100 $ml^{-1}$ sulphadimidine, the saturation values are 15·1, 33·8 and 65·6 mg benzoic acid respectively. At higher concentrations of drug no such saturation values were observed and instead, one linear plot was obtained for systems containing from 0·3 to 10 g 100 $ml^{-1}$ sulphadimidine. This would be anticipated if it is considered that about 34 mg of benzoic acid is to be adsorbed by 0·1 g sulphonamide. Higher benzoic acid concentrations could not be used on account of its limited solubility.

Data obtained from the adsorption experiments fitted a Langmuir plot for systems containing up to 0·2 g 100 $ml^{-1}$ sulphadimidine (Fig. 2).

Elution experiments, made by digesting the precipitate in water, showed that the adsorption was irreversible since a constant amount of benzoic acid was eluted which

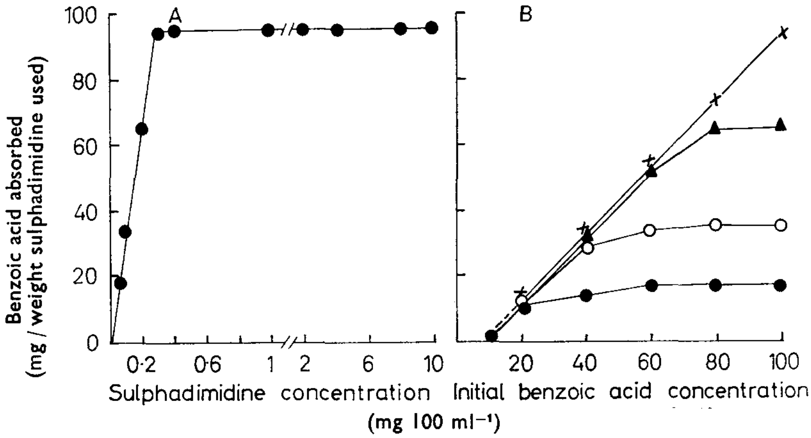


FIG. 1. A. The uptake of 100 mg 100 $ml^{-1}$ benzoic acid by increasing concentrations of sulphadimidine.

B. Effect of benzoic acid concentration on its adsorption by sulphadimidine. Sulphonamide concentrations (g 100 $ml^{-1}$) (●) 0·06; (○) 0·1; (▲) 0·2; (×) 0·3, 0·4, 4 and 10.

amounted only to about 6 mg % (Table 1). This may suggest that adsorption is not of a physical nature.

That the carboxyl group of benzoic acid may be involved in the adsorption process is supported by the finding that sulphadimidine did not adsorb either methyl or propyl hydroxybenzoate.

In an attempt to suppress the adsorption of benzoic acid by sulphadimidine, PVP, methylcellulose and sodium carboxymethylcellulose were compared. The results obtained are shown in Fig. 3 where the percentage suppression was plotted against the polymer concentration. Percentage suppression was calculated from the ratio: mg benzoic acid adsorbed in the absence of the polymer/mg adsorbed in the presence of the polymer/mg adsorbed in the absence of the polymer. The suppressive effect of the three polymers followed the sequence: PVP > methylcellulose > sodium carboxymethylcellulose. PVP, at a concentration of 10 mg % completely suppressed the

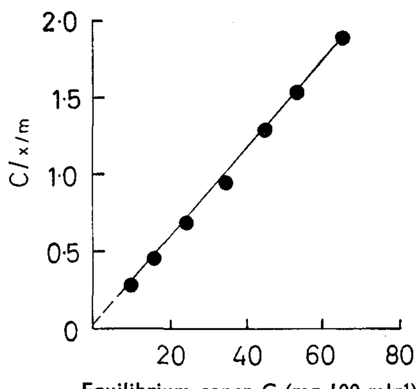


FIG. 2. Langmuir plot for the adsorption of benzoic acid on sulphadimine. Sulphonamide concentration in the system: 0·1 g 100 $ml^{-1}$.

adsorption of benzoic acid in the concentrations used (Tables 2 and 3). Sodium carboxymethylcellulose, on the other hand, had the least effect. The results obtained using the two grades of different viscosities were almost identical (Fig. 3).

Moriguchi & Kaneniwa (1969) showed that the effect of PVP in suppressing the adsorption was dependent on the drug: PVP ratio. This is borne out in Tables 2 and 3 where the suppressive effect of PVP is seen to be dependent on the sulphadimidine content in the system. At a constant sulphonamide concentration, the suppressive effect of PVP was also dependent on the initial benzoic acid concentration (Table 3). This may suggest that for suppression of the adsorption, the sulphadimidine particles had to be 'protected' by the polymer since PVP is known as a good protective colloid.

The data of equilibrium dialysis show that no significant interaction occurred between benzoic acid and either PVP or methylcellulose, within the concentration range used. This is in agreement with the findings of Higuchi & Kuramoto (1954)

Table 1. *Elution rate of benzoic acid adsorbed on sulphadimidine after digestion in water at 24°.** (Initial benzoic acid concentration 100 mg 100 $ml^{-1}$.)

| Time (h) | Benzoic acid eluted (mg %) from concentrations of sulphadimidine of 0·2 | 1 | 4 | 10 g 100 $ml^{-1}$ |
|---|---|---|---|---|
| 0·25 | 5·81 | 5·64 | 5·75 | 5·78 |
| 0·50 | 5·95 | 5·77 | 5·88 | 5·89 |
| 1·0 | 6·01 | 6·13 | 6·11 | 6·15 |
| 3·0 | 6·15 | 6·18 | 6·13 | 6·20 |
| 6·0 | 6·13 | 6·17 | 6·19 | 6·22 |

* The precipitate, after the adsorption experiment, was digested in 50 ml water and agitated at a speed of 18 ± 2 strokes $min^{-1}$ at 24°.

Table 2. *Effect of PVP on the uptake of benzoic acid by sulphadimidine.* (Initial benzoic acid concentration: 100 mg 100 $ml^{-1}$.)

| Sulphadimidine (g 100 $ml^{-1}$) | Benzoic acid adsorbed (mg/weight sulphadimidine used) at concentrations of PVP of 0 | 2 | 5 | 10 mg % |
|---|---|---|---|---|
| 2 | 94·3 | 75·0 | 0·0 | 0·0 |
| 4 | 94·0 | 92·2 | 50·1 | 0·0 |
| 8 | 93·8 | 93·1 | 73·0 | 0·2 |
| 10 | 94·6 | 94·2 | 82·3 | 0·4 |

Table 3. *Effect of PVP on the uptake of benzoic acid by sulphadimidine at various initial benzoic acid concentrations.* (Sulphadimidine concentration: 4 g 100 $ml^{-1}$.)

| Initial benzoic acid concentration (mg 100 $ml^{-1}$) | Benzoic acid adsorbed (mg/4g sulphadimidine) at concentration of PVP of 0 | 2 | 5 | 10 mg % |
|---|---|---|---|---|
| 40 | 35·1 | 0·0 | 0·0 | 0·0 |
| 60 | 55·0 | 28·6 | 0·0 | 0·0 |
| 80 | 74·9 | 52·4 | 0·0 | 0·0 |
| 100 | 94·2 | 92·2 | 50·1 | 0·3 |

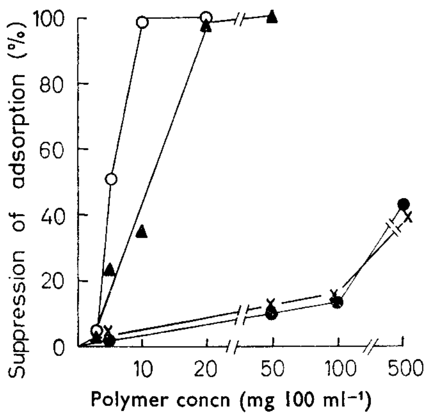


FIG. 3. Effect of some hydrophilic polymers on the suppression of benzoic acid adsorption by sulphadimidine. Polymer: (○) PVP; (▲) methylcellulose; (×) sodium carboxymethylcellulose 50; (●) sodium carboxymethylcellulose 100. Sulphadimidine concentration: 4 g 100 $ml^{-1}$; initial benzoic acid concentration: 100 mg 100 $ml^{-1}$.

who found that below 0·1 % PVP no binding occurred with benzoic acid. It follows, therefore, that the suppressive effect of either PVP or methylcellulose on benzoic acid adsorption by sulphadimidine cannot be attributed to benzoic acid/polymer interaction. It seems probable that the suppressive role of PVP and methylcellulose is due to the adsorption of either polymer onto the sulphadimidine particles. Supporting evidence for this can be found in the work of Simonelli, Mehta & Higuchi (1970) and Moriguchi & Kaneniwa (1969).

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