PHARMACY

ADSORPTION OF SOME SALICYLATES ONTO THE SCLEROTIUM OF PLEUROTUS: IMPLICATIONS IN FOOD-DRUG INTERACTIONS

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ABSTRACT

The absorptive properties of powdered sclerotium of Pleurotus tuber-regium were investigated using acetylsalicylic acid and sodium salicylate. Activated charcoal was used as the basis for comparison. The effects of various experimental conditions such as pH, temperature, ionic strength and organic matter (using citrated guinea pig blood) on adsorption were investigated. The results show that the extent of adsorption was dependent on drug type, pH, temperature and ionic strength. The high adsorptive capacity of the powdered sclerotium could have serious implications when co-administered with salicylates.

Keywords: Adsorption, salicylates, sclerotium of Pleurotus, food-drug interactions.

INTRODUCTION

Pleurotus tuber-regium is a basidiomycete found in tropical and sub-tropical regions of the world. The sclerotium of this fungus is commonly used as a food additive among many Nigerian tribes. Oso [1] reported on its use in various disease conditions among Nigerian tribes. The fungal material was reported to be used among traditional medicine practitioners in the treatment of poisoning, headache, fever, cold, asthma, nervous disorder, chest pain, stomach pain and dropsy among others. Recently, Adikwu and Chukwu [2] reported on the use of this fugal material as a disintegrant in aminophylline tablets.

A set of criteria for the evaluation of the adsorptive capacity of any adsorbent would include effect of factors such as pH, particle size, ionic strength, organic matter and thermodynamic considerations. Among these parameters, the rate and extent of solute adsorbed by the adsorbent appear to be the most clinically important in terms of food-drug interactions and use as medicinal adsorbent in diarrhoea diseases and poisoning. It is also essential to evaluate raw materials intended for pharmaceutical formulations to elucidate the possibility of drug-excipient interactions. This study is aimed at evaluating the interactions that may occur between sclerotium of Pleurotus tuber-regium and some salicylates.

MATERIALS AND METHODS

Materials

Activated charcoal (Norit, USA) hydrochloric acid, potassium chloride and sodium citrate (BDH, England) acetylsalicylic acid (Beecham, England), and sodium salicylate (Merck, Germany). All materials were used without further purification. The sclerotium of Pleurotus was purchased locally and processed in our laboratory.

Methods

Preparation of the sclerotium

The outer brownish layer of the sclerotium was peeled off to expose the whitish inner layer. A 100 gm quantity of the material was pulverised in an end-runner mill and screened through a nest of standard sieves. The fraction corresponding to the mean particles size of 150 microns was collected for the adsorptive studies. Earlier work has shown this mean particle size to have the highest adsorptive capacity [3].

Assay of the drugs

Acetylsalicylic acid

Acetylsalicylic acid was made soluble by dissolving 3 parts of the drug in 1 part of strong ammonium acetate solution and then diluted progressively with distilled water to give a final concentration of 10 mg/ml. Various dilutions of this were made in a 100-ml volumetric flask. Five ml of 1N sodium hydroxide solution and 2 ml of five per cent ferric chloride test solution were added and the volume adjusted to the 100-ml mark with distilled water. The absorbances of the various dilutions were determined in a digital colorimeter (model 254, Ciba-Corning) at 540 nm. All other concentrations were determined from the slope of the calibration curve established by this method.

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Sodium salicylate

Various dilutions of sodium salicylate were made in distilled water. Two ml of 5% ferric chloride test solution were added to each of the dilutions and the final volumes made up to 100 ml in a volumetric flask. The absorbances were determined at 540 nm in a digital colorimeter (model 254, Ciba-Corning).

Adsorption isotherms at 30°C

A stock solution of each drug was prepared (as previously described under assay of the drugs) to contain 10 mg ml^{-1}. Different volumes of the stock solutions of the drugs were made up to 20 ml with distilled water. A 0.5 gm quantity of the adsorbent was added to each solution and the mixture agitated for 30 min using a flask shaker (Gallenkamp). The mixture was filtered through a No.1 Whatman filter paper (previously wetted with dilute solutions of the drugs) and assayed at 540 nm after the addition of 2 ml of five per cent ferric chloride test solution. A blank with no adsorbent was treated similarly and assayed.

Effect of pH

Twenty ml quantities of the stock solutions of the drugs were adjusted to various pH levels of 2, 4, 6 and 8 with either 1N HCl or 1N NaOH solution as required. A 0.5 gm quantity of the adsorbent was added and agitated for 30 min. The mixture was filtered through a No.1 Whatman filter paper previously wetted with a dilute solution of the drugs. Both drugs were assayed at 540 nm after the addition of 2 ml of 5 per cent ferric chloride test solution.

Effect of ionic strength

Various volumes of 2M potassium chloride solutions were added to 20 ml volumes of the stock solutions of the drugs. Each volume was made up to 50 ml with distilled water and agitated with 0.5 gm of the adsorbent for 30 min At the end of the experiment each mixture was filtered and assayed for the drugs. The ionic strength was calculated from the following relationship:

$$I = {}^{1}/_{2}\, CZ^2 \quad \text{..... Eq.1}$$

where I is the ionic strength; C is the concentration of the ion or electrolyte and Z is the charge on the ionic species.

Effect of temperature

A 20 ml aliquot of the stock solution and 0.5 gm of the adsorbents were mixed and agitated in a thermostated water bath/mechanical shaker at different temperatures for 30 min. The concentration of the drug in each determination was assayed as earlier described.

Effect of organic matter

Citrated blood of guinea pig containing 5×10^5 cells/ml (determined by haemocytometric technique) was employed as the organic matter. Different volumes of the stock solutions of the drugs were each mixed with 0.5 gm of the adsorbent and 5 ml of the citrated blood. The mixture was shaken for 30 minutes and filtered. The filtrate was assayed for the concentration of the unadsorbed drug.

RESULTS AND DISCUSSION

Figs 1a and b show the adsorption isotherms of the drugs on the adsorbents. The adsorption isotherms could be said to follow type I according to the classification of Brunauer et al [4]. The figures show that the smaller the molecular volume of the drug used, the greater is the extent of adsorption.

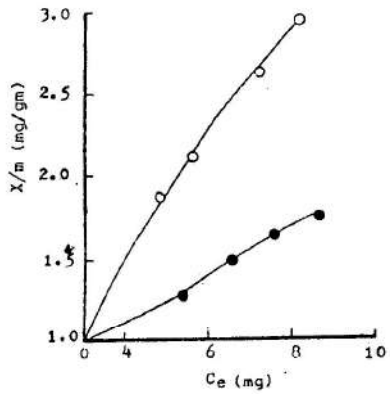

Fig.1a: Adsorption isotherms of acetylsalicylate on the adsorbents at pH 7.2 o activated charcoal, ● pleurotus powder.

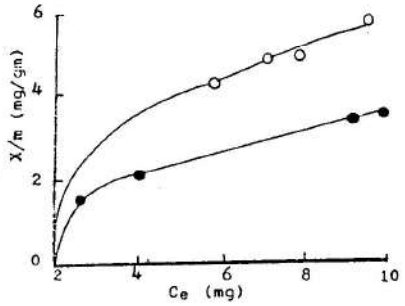

Fig. 1b: Adsorption isotherms of sodium salicylate on the adsorbents at pH 7.2; ▾ activated charcoal; o pleurotus powder.

Type I adsorption isotherms are best described by Freundlich adsorption equation:

$$\frac{X}{m} = aC\bar{e}^{\frac{1}{n}} \quad \text{..... ..... Eq.2}$$

where X/m is the amount of drug adsorbed per unit weight of the adsorbent, Ce is the equilibrium drug concentration, and a and 1/n are constants. The constant, a, depicts the relative adsorbent capacity for a given solid and $\frac{1}{n}$ reflects the affinity of the adsorbent for a particular solute. The equation can be written in the

logarithmic form as shown:

$$\log \frac{X}{m} = \log a + \frac{1}{n} \log Ce \quad \text{..... Eq. 3}$$

Plotted in this linear form, the values of a and 1/n can be determined from the intercept and slope respectively. Linear relations were obtained as shown in Fig 2a and b and the slopes and intercepts were calculated by linear regression analysis. Table 1 shows the values of the Freundlich constants.

Similar values of a (adsorptive capacity) were obtained for the adsorption of acetylsalicylic acid onto the adsorbents. The different values of 1/n obtained may suggest the existence of different mechanisms of adsorption of the drug onto the adsorbents. A higher value of adsorptive capacity was obtained with the adsorption of sodium salicylate onto Pleurotus powder than that for the drug onto activated charcoal. Generally, higher values of adsorptive capacity were obtained with sodium salicylate onto the two adsorbents than those obtained with adsorption of acetylsalicylic acid. This may be related to the molecular nature of the drugs. The acetylsalicylic acid with a bulkier structure than sodium salicylate, is less readily adsorbed - a type of physical steric hinderance. The similar values of 1/n obtained for sodium salicylate onto the two adsorbents may suggest a similar mechanism of adsorption of the drug onto the adsorbents.

Figs. 3a and b show the influence of pH on the quantity of the drug adsorbed. The adsorption of both drugs on the two adsorbents decreased with increase in pH. pH influences adsorption by changing the solubility and extent of ionization of drug molecules. pH also alters the charge distribution on the surface of adsorbents [5]. The decrease in adsorption noticed for the two drugs as the pH increased could be related to increased solubility. The equation relating solubility, pKa and pH is given by [6]:

$$S_T = K_S \left(1 + \frac{K_a}{[H^+]}\right) \quad \text{..... Eq.4}$$

and was modified to give:

$$[H^+] = \frac{K_a K_s}{S_T - K_S} \quad \text{..... Eq.5}$$

where S_T is the solubility of the drug, K_a is the dissociation constant of the drug, K_S is solubility constant and $[H^+]$ is the hydrogen ion concentration.

As $[H^+]$ increases, pH decreases and the solubility of drug adsorbed is known to decrease with increase in solubility [7]. At low pH (pH 2) more of the salicylate is converted to the acid. The acid is less soluble in the aqueous phase, hence adsorption is increased.

Figs. 4a and b show the effect of ionic strength on the adsorption of the drugs by the adsorbents. The quantity of acetylsalicylic acid adsorbed by activated charcoal was independent of changes in the ionic strength of the solution. The initial increase in the extent of adsorption of acetylsalicylic acid onto Pleurotus powder to a maximum at an ionic strength of 0.75 followed by a decrease

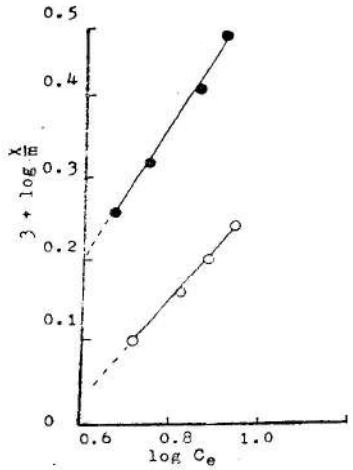

Fig.2a: Logarithmic plot of the adsorption isotherms of acetylsalicylic acid on the adsorbents • activated charcoal o pleurotus powder.

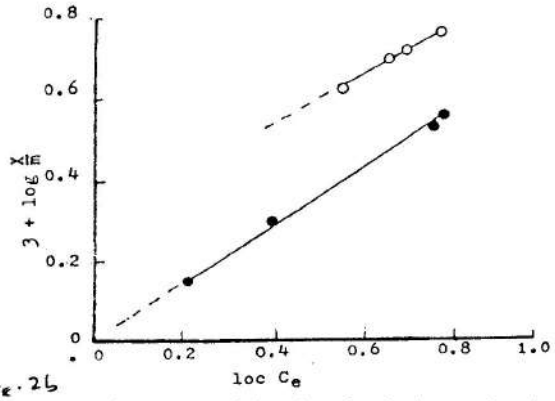

Fig.2b Logarithmic plots of the adsorption isotherms of sodium salicylate on the adsorbents • activated charcoal, o pleurotus powder.

Table 1: Freundlich constants for the adsorption of the drugs onto the adsorbents

		Activated charcoal	Pleurotus powder
Acetylsalicylic acid,	a	-3.80	-3.90
	1/n	0.92	0.63
Sodium salicylate,	a	-0.14	0.18
	1/n	0.75	0.67

may be due to the effect of ions on the nature of charges at the active sites of the adsorbent. Both electrostatic and non-electrostatic binding are involved during adsorption [8]. Ionic strength alters the surface charges and dielectric constants of adsorbents in aqueous suspensions [9].

There was a decrease in the adsorption of sodium salicylate onto the two adsorbents before a final rise. This may be associated with the two pKa of the drug

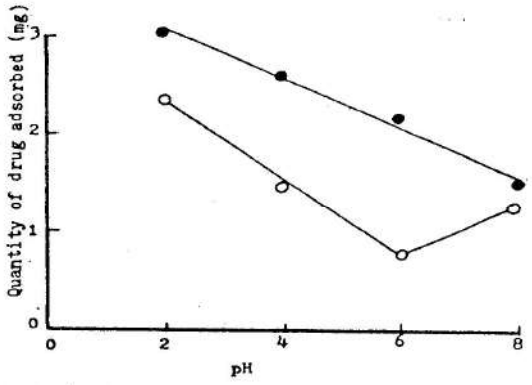

Fig.3a: Effect of pH on the adsorption of acetylsalicylic acid onto 0.5 gm of adsorbent at 23oC. ● activated charcoal, o pleurotus powder.

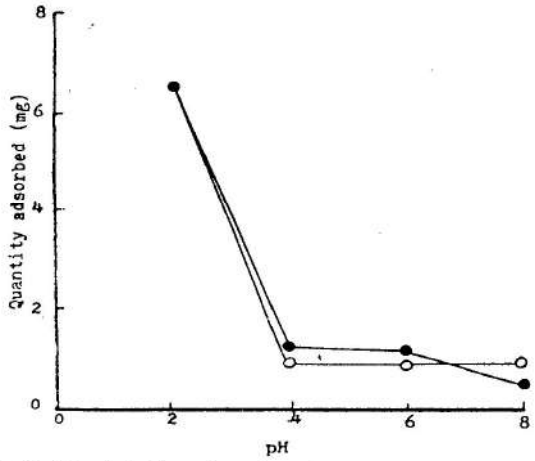

Fig.3b: Effect of pH on the adsorption of sodium salicylate onto 0.5 gm of the adsorbents at 28oC, ● activated charcoal, o pleurotus powder

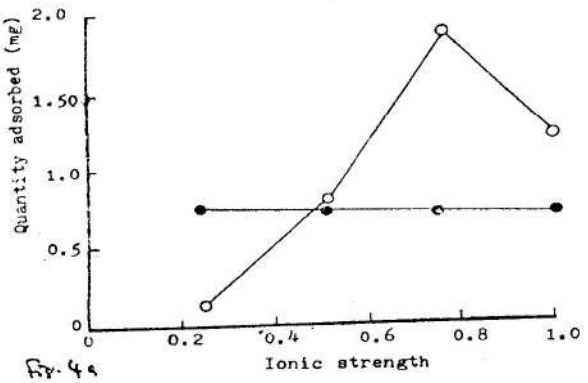

Fig.4a: Effect of ionic strength on the adsorption of acetylsalicylic acid onto 0.5 gm of adsorbent at pH 7.2, ● activated charcoal, o pleurotus powder.

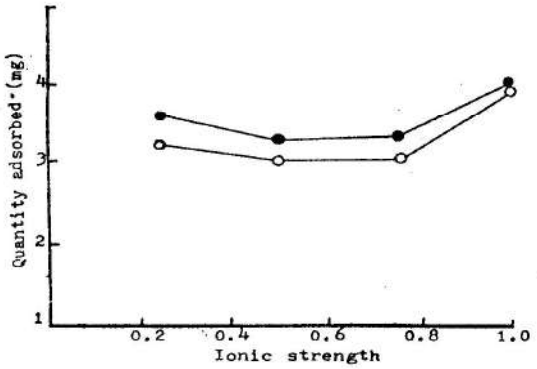

Fig. 4b: Effect of ionic strength on the adsorption of salicylate onto 0.5 gm of the adsorbent at pH 7.2, ● activated charcoal, o pleurotus powder.

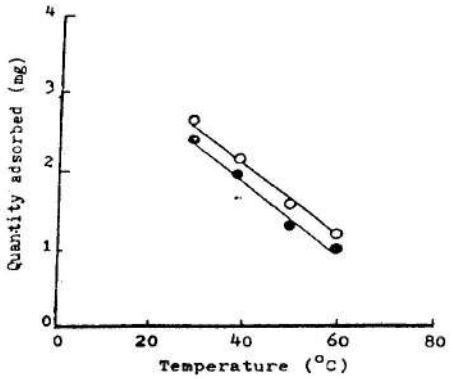

Fig 5a: Effect of temperature on the adsorption of acetylsalicylic acid onto 0.5 gm of the adsorbents at pH 7.2, ● activated charcoal, o pleurotus powder

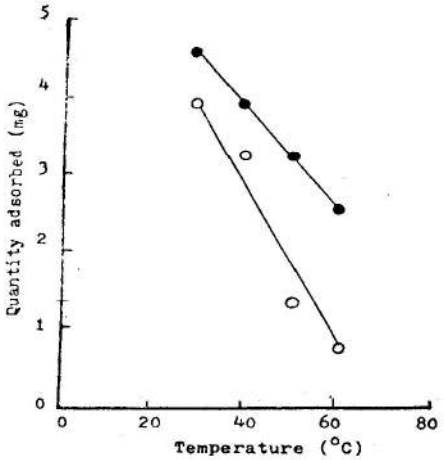

Fig. 5b Effect of temperature on the adsorption of sodium salicylate onto 0.5 gm of the adsorbents at pH 7.2, ● activated charcoal, o pleurotus powder

(pKa 3.0 and 13.4 at 25°C) and /or changes in the porosity of the adsorbent. Probcan et al [10] have stated that changes in the porosity of an adsorbent could lead to increased adsorption.

Figs. 5a and b show the effect of temperature on the extent of adsorption. Increase in temperature decreased the quantity of the drugs adsorbed. The decrease shows that the adsorption is a physical phenomenon. Physical adsorption is an exothermic process [8]. Adoption is governed by the thermodynamic equation [11]:

$$\Delta G = \Delta H \quad T \quad S \ldots\ldots\ldots \quad \text{Eq.6}$$

where ΔG is changed in free energy, ΔH is change in enthalpy of adsorption, T is temperature expressed in Kelvin and ΔS is enthropy change.

Increase in temperature causes an increase in ΔG while adsorption causes a decrease in ΔG. If ΔS is negative, the freedom of the adsorbed molecule is restricted and the entropy change is decreased. Therefore, less adsorption takes place at elevated temperature except for some form of chemisorption [12].

Figs. 6a and b show the effect of organic matter on the extent of adsorption onto the adsorbents. The quantity of the drugs adsorbed decreased with increased organic matter (citrated guinea pig blood). This may be associated with some blood cells and other serum components competing for binding sites (on the adsorbents) with drug molecules.

CONCLUSIONS

It has been shown in this study that salicylates are adsorbed by powdered scleotium of Pleurotus. The sclerotium is commonly employed as food in many Nigerian societies. In vivo animal studies have shown that activated charcoal reduces gastro-intestinal adsorption of acetylsalicylic acid and salicylamide [13]. A similar effect may exist with the Pleurotus powder. However, it may be necessary to carry out in vivo studies with the Pleurotus in order to correctly related in vitro and in vivo observations.

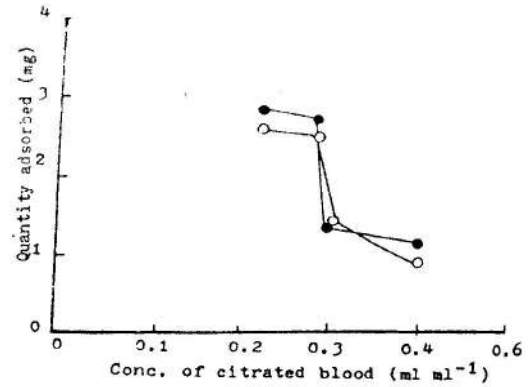

Fig. 5a: Effect of organic matter on the adsorption of acetylsalicylic acid onto 0.5 gm of the adsorbents at pH 7.2, ● activated charcoal, o pleurotus powder

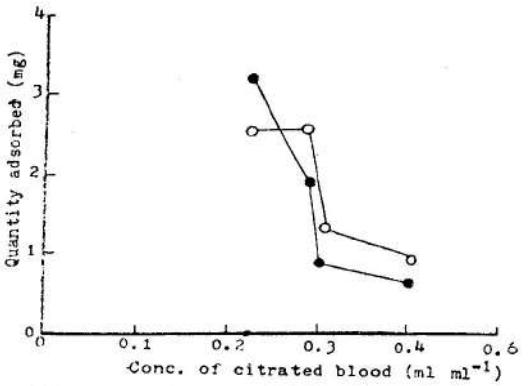

Fig.6b: Effect of organic matter on the adsorption of sodium salicylate onto 0.5 gm of the adsorbent at pH 7.2, ● activated charcoal, o pleurotus powder.

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