

Ampicillin adsorption by some antacids

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Abstract

In certain situations of peptic ulcers ampicillin has been co-administered with bismuth carbonate with an implication for adsorption of the ampicillin. To quantify this effect the kinetics and extent of adsorption of ampicillin by some commonly used antacids were measured; these are bismuth carbonate, magnesium trisilicate and aluminium hydroxide. The adsorption of ampicillin by bismuth carbonate followed the Langmuir adsorption isotherm, which suggests chemisorptions. It was characterized by a strong adsorption at a low adsorbate (ampicillin) concentration but the % adsorption decreased with increase in adsorbate concentration, which is a feature of a saturated monolayer adsorption. On the other hand, the adsorption by magnesium trisilicate and aluminium hydroxide followed the Freundlich adsorption isotherm characterized by a low adsorption at a low adsorbate concentration but this increased slightly with increase in adsorbate concentration, suggesting a weak physical adsorption. The adsorption capacities (mg/g) of the adsorbate were 1.64 (bismuth carbonate) 0.04 (magnesium carbonate) and 0.03 (aluminium hydroxide). Bismuth carbonate thus gave by far the highest degree of adsorption. The conclusion is that the co-administration of ampicillin and bismuth carbonate in the treatment of certain peptic ulcers is erroneous.

Keywords: Ampicillin, antacid powders, adsorption, adsorption mechanisms, bioavailability. *

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Introduction

Antacids and anti diarrhoeas are potent adsorbents and consequently they impair the bioavailability of concomitantly administered drugs. For instance, the adsorption of promazine by antalgite [1], lincomycin by various anti-diarrhoea preparations [2], and the quinolone – based antibiotic (ofloxacin) due to chelation (i.e. chemisorption) by the metallic antacids (sodium bicarbonate, magnesium trisilicate, and aluminium hydroxide) [3] have been reported by various authors. Now, ampicillin and bismuth carbonate have been used as combination therapy in the management of certain peptic ulcers complicating Helicobacter infection. The objective of this study therefore is to investigate whether the antacid powders appreciably adsorb ampicillin and if so, to investigate the mechanism of adsorption. Besides, reports of ampicillin adsorption by antacids are rare in the literatures; hence this study was undertaken.

Materials and methods

Ampicillin trihydrate (a product of Sigma, U.S.A.) was the test drug. It is sparingly soluble in water dissolving one part in 150 parts of water (i.e. about 7mg/ml) at 20°C. Hence its adsorption, may markedly affect its bioavailability. The test antacid powders were aluminium hydroxide, bismuth carbonate and magnesium trisilicate; all analar grade and received from Halewood chemicals Ltd. Middlesex, London. Their mean particle sizes as determined by photomicroscope were in the range $0.5 - 5 \pm 0.002\mu\text{m}$.

Adsorption studies

Aqueous solutions of ampicillin trihydrate in water (0.5mg/ml – 4.5mg/ml) were prepared. A sample of the antacid powder (1g) was added to 10ml aliquots of the ampicillin solutions and the mixtures shaken $100 \text{ rev. min}^{-1}$ at 37°C for 1 h in a shaker bath. The mixtures were centrifuged at 300 rev. min for 30 min after which the

supernatants were analysed for content of residual ampicillin. The difference between initial amount of ampicillin and the equilibrium content was taken as the ampicillin that was adsorbed; this was expressed as a percentage of the initial amount of ampicillin in solutions. The adsorption capacity was expressed as the milligram of ampicillin adsorbed per gram of the adsorbent.

Analysis of ampicillin

Content of ampicillin in the supernatants was analysed by spectrophotometric methods [4]. A supernatant derived from a suspension of the antacid powder in water (without ampicillin) was used as control in the analysis. In the procedure 0.2 ml supernatant was made up to 10ml with phosphate buffer (pH, 5.5) containing copper ions, 15 μ g/ml. The samples were heated at 75C° for 30 mins to hydrolyse the ampicillin to penicillanic acid, which was the moiety that was determined spectrophotometrically at λ_{max} 320 nm. The determination was carried out in triplicate and mean results calculated.

Results

Adsorptive potentials of the antacids

The extent of adsorption at the various adsorbate concentrations is given in table 1. It can be seen that with bismuth carbonate the adsorption was strong (upto 52% of the initial amount of adsorbate) at the low adsorbate concentration, 0.5mg/ml but this decreased to 13% at the higher adsorbate concentration, 4.5mg/ml. The adsorption reached a plateau at the adsorbate concentration, 2mg/ml. These results suggest a saturation of the adsorptive surface area. With the other two adsorbents (aluminium hydroxide and magnesium trisilicate) the extent of adsorption was weak at the low adsorbate concentration, for instance there was no measurable adsorption at the adsorbate concentration, 0.5mg/ml, but the adsorption increased slightly as the

adsorbate concentration increased and 20% (magnesium up to a maximum of 15% aluminium hydrate). These results suggest that the adsorptive surface area was not readily saturated, as was the case with bismuth carbonate.

Mechanism of adsorption

In order to investigate the adsorption mechanism (i.e. the adsorption isotherm) the data in table 1 were analysed according to the Freundlich and the Langmuir isotherms, which describe adsorption from dilute solutions [5]. The Freundlich isotherm is given by

$$\frac{x}{m} = KC^{1/n} \quad (1)$$

where x is the amount of adsorbate adsorbed by an adsorbent of mass, m , C is the equilibrium concentration of the adsorbate. K and n are constants, which for a given adsorbate are measures of the adsorptive capacity of the adsorbent, and the adsorbate – adsorbent affinity respectively. In systems obeying the Freundlich isotherm a plot of $\log \frac{x}{m}$ vs $\log C$ is linear with a slope = $\frac{1}{n}$ and a Y – intercept = $\log K$. In the analysis the correlation coefficients for linear regression were calculated. A coefficient close to unity (i.e. ≥ 0.90) indicates conformity with the isotherm. The values of the correlation coefficients for the various adsorbents were as follows: 0.980 (aluminium hydroxide), 0.946 (magnesium trisilicate), and 0.749 (bismuth carbonate). These results show that aluminium hydroxide and magnesium trisilicate conformed with Freundlich adsorption while bismuth carbonate deviated. However when the data for bismuth carbonate were analysed for low adsorbate concentrations only (0.5mg/ml – 2mg/ml) bismuth carbonate now conformed with Freundlich adsorption with a correlation coefficient, 0.966. The values of K and n were thus obtained at this low adsorbate concentration only.

The Langmuir adsorption isotherm is given by [5]:

$$C \cdot \frac{m}{x} = 1/b C + 1/ab \quad (2)$$

where a and b are constants for a given adsorbent – adsorbate system. In systems obeying the Langmuir isotherm a plot of $C \cdot \frac{m}{x}$ vs C is linear with a slope = $1/b$ and a Y – intercept = $1/ab$. The linear correlation coefficients by this Langmuir analysis for the three adsorbents were 0.9705 (bismuth carbonate), 0.8152 (aluminium hydroxide) and 0.6273 (magnesium trisilicate), thus indicating that only bismuth carbonate conformed to the Langmuir adsorption isotherm.

Adsorption capacity of the adsorbents and their affinity for the adsorbate

The adsorption capacity (K) of the adsorbents and their affinity (n) for the adsorbate were obtained from the Freundlich isotherm (equation 1). The K values (mg/g) were as follows: 1.64 (bismuth carbonate) 0.04 (magnesium trisilicate), and 0.03 (aluminium hydroxide). The K value is a measure of the extent of adsorption as adsorbate concentration tends to zero bismuth carbonate displayed a stronger adsorptive capacity compared with the other two adsorbents. The affinity index values were 2.5 (bismuth carbonate), 0.66 (aluminium hydroxide), and 0.62 (magnesium trisilicate); which also means that bismuth carbonate displayed the strongest affinity for the adsorbate.

Table 1: Amount of ampicillin adsorbed by the various antacid powders

Initial ampicillin concentration (mg/ml)	Amount of ampicillin adsorbed by the various antacid powders					
	Aluminium hydroxide		Bismith carbonate (mg/g)		Magnesium trisilicate	
	(mg/g)	%	%		(mg/g)	%
0.5	–	–	2.6	52	–	–
0.75	–	–	2.7	36	0.6	8
1.0	0.9	9	3.3	33	1.6	16
1.5	1.2	8	4.2	28	2.1	14
2.0	1.8	9	5.7	29	3.9	20
3.0	4.5	15	5.7	19	5.4	18
4.0	5.8	15	5.8	15	6.0	15
4.5	6.0	13	6.0	13	6.8	15

Note: – no measurable adsorption, the percentages represent the proportion of the initial amount of ampicillin (in the test solution) which was adsorbed.

Discussion

The Freundlich adsorption isotherm is associated with weak physical adsorption involving van Der Waal's forces and this may involve a multilayer adsorption. On the other hand the Langmuir isotherm is associated with strong chemisorption leading to saturation of the bonding forces, hence a saturated monolayer adsorption may occur when the functional groups involved in the chemical bonding are saturated⁵. The results thus suggest that the strong adsorption of ampicillin by bismuth carbonate even at the low ampicillin concentration (see table 1) was by a chemisorption mechanism possibly involving hydrogen bonding between the -COOH group of ampicillin and the -CO₃ functional group of bismuth carbonate. The decrease in percentage adsorption with increase in initial concentration of ampicillin is an evidence for monolayer saturation. On the other hand the weak adsorption of ampicillin by the other two adsorbents is attributable to a physical adsorption mechanism possibly involving multilayer adsorption, which explains the increase in the percentage adsorption with increase in initial concentration of adsorbate (table 1).

Differences in the specific surface area of a powder may influence the extent of adsorption. However, as noted above the particle size distribution in the adsorbent powders were not markedly different. Hence the difference in adsorptive capacity relates more to the difference in the adsorption mechanisms rather than particle size differences.

Conclusion

The study has shown that bismuth carbonate adsorbs ampicillin strongly. This finding has important implication in the co-administration of these two drugs in the treatment of certain peptic ulcers. The bioavailability of the ampicillin would be impaired; hence, the practice is erroneous.

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