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PHYSICOCHEMICAL STUDY OF THE ADSORPTION OF OXPRENOLOL HYDROCHLORIDE BY MONTMORILLONITE

M.J. Sanchez[1], M. Sanchez-Camazano[1], M.T. Vicente[2],
A. Dominguez-Gil[2],

[1]Centro de Edafologia y Biologia Aplicada
Apto. 257. Salamanca

[2]Department of Pharmacy Practice
University of Salamanca
Salamanca. Spain

ABSTRACT

The interaction between oxprenolol hydrochloride and montmorillonite was studied by adsorption isotherms, x-ray diffraction and i.r. spectroscopy.

The adsorption isotherm fits Langmuir's equation and the maximum amount of oxprenolol adsorbed by the clay is 70 mEq/100 g of clay.

The results of x-ray diffraction studies and i.r. spectroscopy reveal that the oxprenolol molecule is adsorbed into the interlayer space of the clay and that the mechanism of adsorption is cation exchange.

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INTRODUCTION

The administration of drugs in a prolonged action formulation is of great interest since their effects may be protracted due to the gradual release of the drug thus permitting a spacing out of the dose.

Among clay minerals, the laminar silicates may be of use as matrices for this kind of formulation, since such silicates, particularly montmorillonite exhibit the property of adsorbing organic compounds into the interlayer space giving rise to the formation of adsorption complexes, (1), (2). The bonding mechanism depends on the chemical structure of the drug in question and on the characteristics of the silicate (3), (4).

Accordingly, research has been begun on the physicochemical aspects of the drug-montmorillonite complex with the idea of possibly using this silicate as a matrix for a prolonged action formulation. Up to the present, the authors have studied the interaction of montmorillonite with chlorpheniramine maleate (5) and propranolol hydrochloride (6). The present work studies the adsorption process and interaction mechanism of montmorillonite and oxprenolol hydrochloride.

MATERIAL AND METHODS

The $< 2 \mu$ fraction of Albagel montmorillonite was used in the study.

Sodium montmorillonite was prepared by successive treatments of the clay with solutions of sodium acetate. The exchange capacity of the clay is 80 mEq/100 g. The oxprenolol hydrochloride used complied to USP standards.

In the studies on adsorption, 100 mg of sodium montmorillonite (equilibrated in an atmosphere of 50% H_2SO_4) in 50 ml volume and a temperature of 40 ºC was used. The suspensions were subjected to continuous shaking in a water bath.

The influence of pH on the adsorption of the drug by the clay was studied by treating the clay with solutions of oxprenolol hydrochloride (0.2 mEq in 50 ml) adjusted to pH values ranging between 3 and 10. The suspension was shaken for 30 min. After this it was centrifuged and the equilibrium concentration in the supernatant fluid was determined by u.v. spectroscopy (absorption maximum at 220 nm).

In order to obtain the adsorption isotherm, the amounts adsorbed as a function of the concentration were determined as described previously, with the following amounts of oxprenolol hydrochloride: 0.02; 0.04; 0.06; 0.08; 0.10; 0.12; 0.15; 0.20 and 0.25 mEq; pH was 7 and contact time was 30 min.

For the study by x-ray diffraction, oriented aggregates of sodium montmorillonite and of montmorillonite-drug complexes, unwashed or previously washed with distilled water were prepared. Diffractograms of the complexes, air-dried and dried under a vacuum of 0.1 mm Hg for 24 h were obtained. In the case of the dehydrated complexes the aggregates were previously wrapped in a film of polyethylene teraphthalate in order to prevent their rehydration.

For i.r. analysis, KBr discs at 1% of the sample of natural montmorillonite, oxprenolol hydrochloride, and of the montmorillonite-oxprenolol complexes were prepared.

RESULTS AND DISCUSSION

The results obtained from the study on the influence of pH (range 3-9) on the adsorption of oxprenolol hydrochloride by sodium montmorillonite show that the amount adsorbed is independent of pH and is 70 mEq/100 g at this is somewhat lower than that necessary to satisfy the cation exchange capacity of the clay (80 mEq/100 g).

The principal reaction which must be taking place in the process is exchange of the sodium ions of the montmorillonite for the organic ions in the solution. At low pH values, not even partial substitution of the sodium ions by the hydrogen ions takes place, since adsorption of the organic cations does not decrease. This has already been described by the authors in the adsorption of propranolol by montmorillonite (6).

At a pH value of 10, the amount of drug adsorbed by montmorillonite (41 mEq/100 g) is less than at lower values. At this pH, greater than the pKa of the compound (pKa = 9.3) most of the molecules must be in the neutral state and only a minimal amount in the form of cations.

The adsorption reaction is rapid and no additional adsorption of the compound takes place after 15 min, according to the study of the influence of contact time.

Figure 1-a shows the adsorption isotherm of oxprenolol hydrochloride by montmorillonite. In it, the equilibrium concentration is represented as a function of the amount adsorbed and it may be seen that the maximum amount adsorbed is 70 mEq/100 g of clay and that this does not increase with concentration. When the adsorption data are plotted according to the Langmuir equation, a straight line is obtained (figure 1-b).

To confirm the adsorption of oxprenolol into the interlayer space of the silicate, x-ray diffractograms of sodium montmorillonite and of the same montmorillonite treated with solutions of oxprenolol hydrochloride at different pH values and with solutions at different concentrations were made (figure 2).

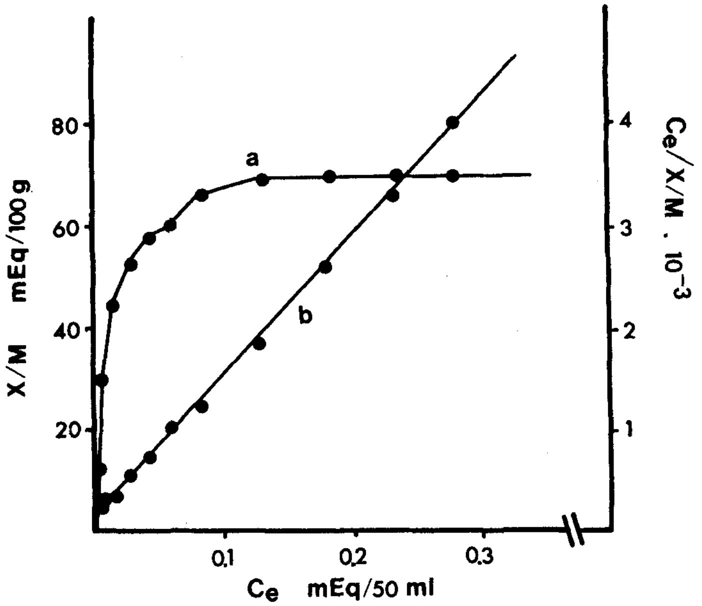

Fig. 1: Adsorption isotherm of oxprenolol hydrochloride by sodium montmorillonite, a: amount adsorbed/100 g of the clay (x/m), against the equilibrium concentration (Ce). b: Langmuir plot.

The results obtained agree with the adsorption data and show that the organic cations penetrate into the interlayer space of the montmorillonite, giving rise to an increase in its d_{001} basal spacing which is independent of the pH of the solution within the range studied but which does depend on the concentration of the solution - (Table 1). Therefore, with the solutions at different pH values, the d_{001} spacing obtained is consistently 17.66 Å, representing an increase of 8,06 Å with respect to the value of 9.6 Å of the dehydrated montmorillonite.

When the clay is treated with solutions of oxprenolol hydrochloride at different concentrations, the d_{001} basal spacing increases with the increase in the concentration of the solution until it reaches a value of - 17.66 Å. The low values of the spacing would correspond

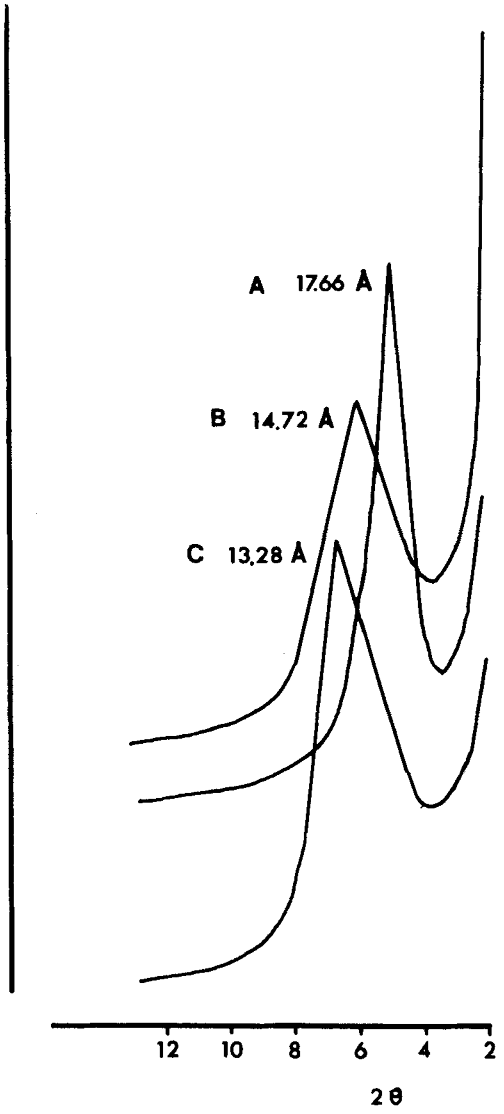

Fig. 2: X-ray diffractograms of A) montmorillonite-oxprenolol at pH 7 (70 mEq/100 g); B) montmorillonite-oxprenolol at pH 7 (30 mEq/100 g); C) montmorillonite-oxprenolol at pH 10 (41 mEq/100 g).

Table 1: Spacing d_{001} of sodium montmorillonite treated with solutions of oxprenolol hydrochloride at different concentration.

AMOUNT OF ORGANIC COMPOUND		UNWASHES SAMPLES		WASHED SAMPLES	
Added mEq/50 ml	Adsorbed mEq/100 g	Vacuum d_{001} Å	Dried ΔÅ	Vacuum d_{001} Å	Dried ΔÅ
0,020	12	12,70	3.40	12,98	3,38
0,040	30	13,28	3,68	13,28	3,68
0,060	45	17,31	7,71	17,31	7,71
0,080	53	17,66	8,06	17,66	8,06
0,100	57	17,66	8,06	17,66	8,06
0,120	60	17,66	8,06	17,66	8,06
0,150	66	17,66	8,06	17,66	8,06
0,200	70	17,66	8,06	17,66	8,06
0,250	70	17,66	8,06	17,66	8,06

to the interstratified phases due to partial replacement of inorganic ions for organic ones.

The d_{001} spacings of the comlexes are not modified by washing with distilled water nor by subjecting them to 0.1 mm Hg vacuum, suggesting that the molecules must be tightly retained in the interlayer space and that there is no physical adsorption and that there are no molecules retained by Van der Waals forces.

The diagram of the montmorillonite treated with solutions of oxprenolol at pH 10 gives a lower basal spacing (14.72 Å) in agreement with the adsorption data. This - spacing changes to 13.08 Å when the complex is washed - with distilled water. This seems to indicate that in the treatment with solutions at high pH values, the existing neutral molecules are adsorbed by the montmorillonite by a weaker bonding mechanism than the electrostatic bonding of cation exchange.

Figure 3 shows the i.r spectra of sodium montmorillonite, oxprenolol hydrochloride and montmorillonite treated with solutions of oxprenolol hydrochloride at different concentrations and at different pH.

The study of these spectra of the complexes suggests that oxprenolol is present in the interlayer space of the silicate since adsorption bands of oxprenolol may be seen in the spectrum of the complex after several washes with water. The variation in the intensity of the bands shows that the amount of organic cation present in the interlayer space of the montmorillonite increases with the concentration of the solution. Similarly, it may be seen that there is a decrease in the intensity of the bands at 3420 and 1630 cm^{-1} (corresponding to the stretching and bending bands of the water associated to the clay); this is due to the fact that the drug progressively displaces the water in the interlayer space of the clay.

The deformation band of the NH_2^+ in the oxprenolol spectrum appears at 1500 cm^{-1} and in the complex shifts towards lower frequencies; this could be due to the interaction between the NH_2^+ groups and the negative surface of the O_2 atoms of the silicate.

In the spectrum of montmorillonite treated with drug at pH 10, the intensity of the band corresponding to the bending bands of the water increases, in agreement with the adsorption and x-ray results. When this complex is washed several times with distilled water, the bands corresponding to the organic compound remain in the spectrum, though to a lesser extent though with less intensity, showing that displacement of the organic compound by the water is not complete and that in the original complex there are molecules that in fact are adsorbed in neutral and in cation form.

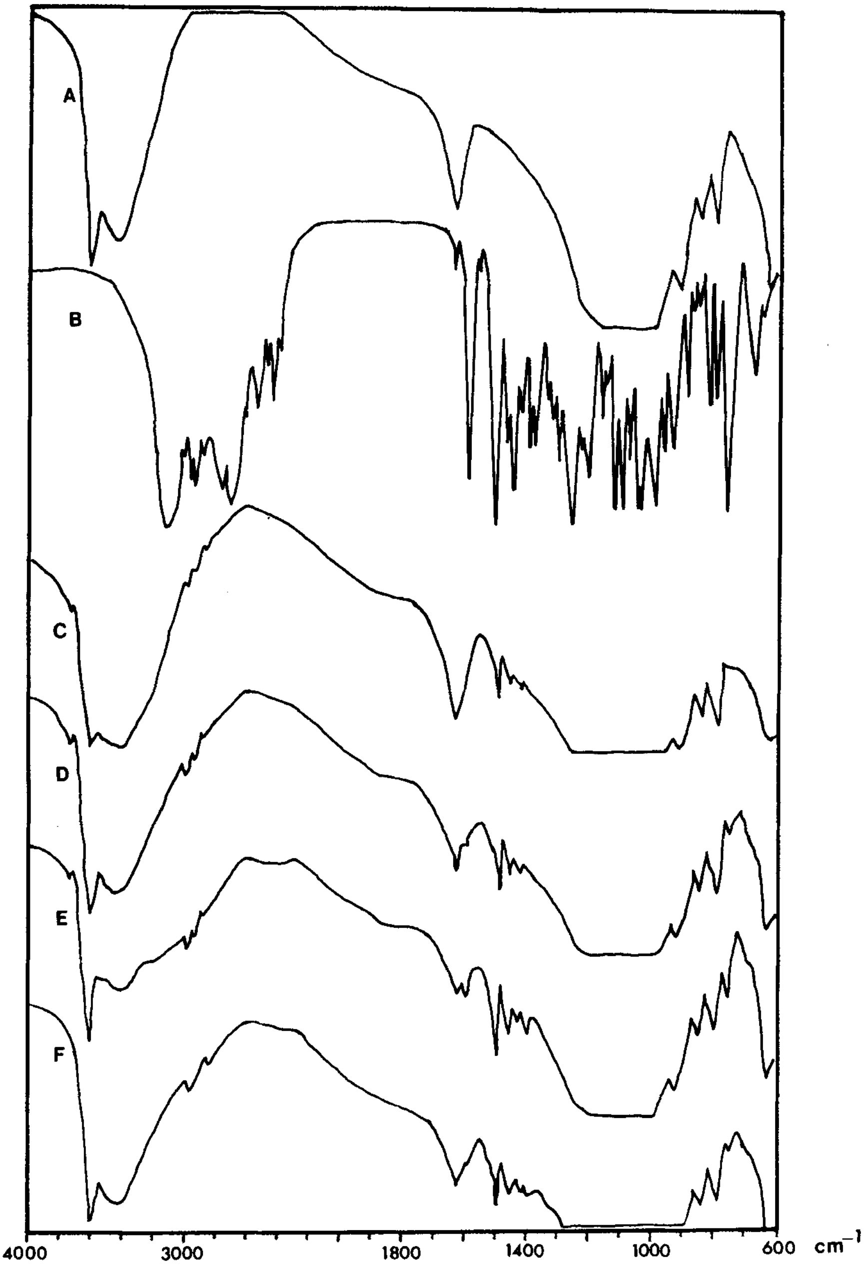

Fig. 3: I.R. spectroscopy of A) sodium montmorillonite; B) oxprenolol hydrochloride; C), D), E) montmorillonite-oxprenolol at pH 7,0 (0,02 mEq; 0,04 mEq and 0,25 mEq) and F) montmorillonite-oxprenolol at pH 10,0.

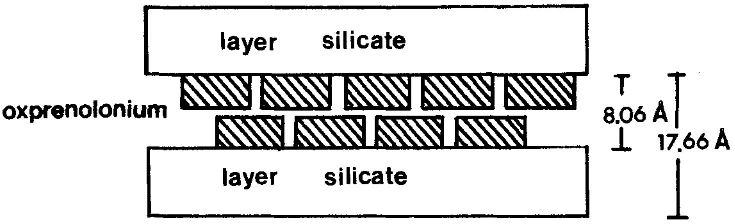

Fig. 4: The possible disposition of the organic cations in the interlayer space of the silicate.

In order to confirm the possible disposition of the organic cations in the interlayer space of the montmorillonite, a comparison was made between the molecular size of oxprenolol and the 8.06 Å increase in spacing undergone by the clay in the expansion, bearing in mind the orientation which the NH_2^+ group should adopt and with the use of molecular models.

The flat surface of the molecule (119 $Å^2$) is greater than the surface available in the montmorillonite per monovalent exchange cation (80 Å). Thus, taking adsorption into account, close to the exchange capacity of the clay, the flat disposition requires the formation of a bilayer complex (figure 4). The thickness of each layer with a flat disposition is approximately 4.0 Å and the thickness of the two superimposed layers governs the spacing.

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