Short Communication

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pH-Metric Studies on Some Promethazine Complexes

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The tranquilizer drug, promethazine, has been investigated in the presence of some metal ions using pH-metric technique. The gathered data showed the formation of 1:1 (metal : ligand) complex. The n-half method was used to evaluate the stability constants of the formed complexes. Also ΔG has been calculated.

The present work is aimed to study the interaction of promethazine with some metal ions such as Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Pb^{2+}, Cd^{2+} and Al^{3+}. This compound has been examined analytically using different techniques [1-3]. But it is important to note that little attention has been made to the complexes involving this compound [4,5]. The potentiometric method is by far the most accurate and widely applicable technique currently available for the study of ionic equilibria [6].

Reagents and apparatus. A pH-meter Orion research model 601 digital ion analyzer was used to follow the hydrogen ion concentrations. Oxygen-free nitrogen was bubbled during the titration with constant stirring using magnetic stirrer.

Promethazine (Sigma) and other reagents of A.R. grade were used without further purification. Bidistilled water was used to prepare the solutions. Stock solution of 1.0 M carbonate free sodium hydroxide was prepared and standardized using the usual methods. All the measurements were carried out at 25± 0.1° and constant ionic strength of 0.1M(KCl).

Procedures. The following solutions:

(a) 0.01 mol dm^{-3} HCl.
(b) a + 0.01 mol dm^{-3} promethazine.
(c) b + 2.5 x 10^{-3} mol dm^{-3} metal ion.

are completed to 25 ml and the ionic strength adjusted at 0.1, then titrated separately against 0.1 mol dm^{-3} sodium hydroxide.

Calculations. At the end of titrations, the consumed volumes of sodium hydroxide were drawn against pH values (Fig. 1). From these figures, the values of V_1, V_2 and V_3 were abstracted at different pH values and according to Irving-Rossotti [7], as adopted by Banerjee [8], the protonation and formation constants were evaluated using the following equations:

$$\bar{n}_A = Y + \frac{(V_1-V_2)(E^o+N^o)}{(V_o+V_1)T_L} \quad \text{.............................(1)}$$

where $\bar{n}_A$ is the average number of protons attached per ligand Y is the number of dissociable protons. V_1 and V_2 are the volumes of alkali required for the mineral acid and the ligand titration respectively at a given pH. E^o is the molarity of the free acid. N^o is the molarity of sodium hydroxide. T_L is the total ligand concentration. V_o is the initial volume of the solution.

$$\bar{n} = \frac{(V_3-V_2)(E^o+N^o)}{(V_o+V_2)\bar{n}_A T_M} \quad \text{..................................(2)}$$

$$pL = \log_{10}\left\{\sum_{j=0}^{j=J} \frac{B_J^H[H]^j}{T_L-\bar{n}T_M} \times \frac{V_0+V_3}{V_0}\right\} \quad \text{........................(3)}$$

$\bar{n}$ is the average number of ligand attached per metal ion. pL = -log L,L is the free ligand concentration. V_3 is the volume of alkali required for the metal complex titration at a given pH. T_M is the total metal concentration.

Representative titration curves are shown in Fig. 1. The values of $\bar{n}_A$ were calculated as mentioned above (equation 1) and plotted versus pH (Fig. is not shown). The value of log K^H_1, the proton association constant, is the pH value corresponding

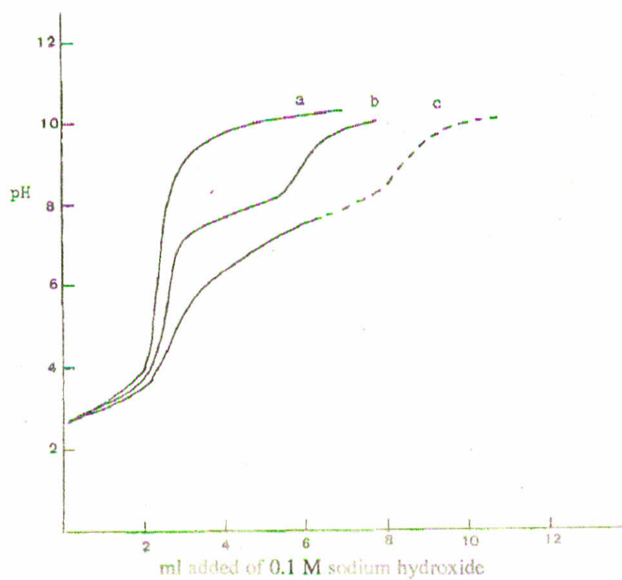

Fig. 1. pH-Metric titrations curves of (a) 0.01 mol dm^{-3} HCl, (b) a + 0.01 mol dm^{-3} promethazine, (c) b + 2.5 x 10^{-3} mol dm^{-3} Pb (II).

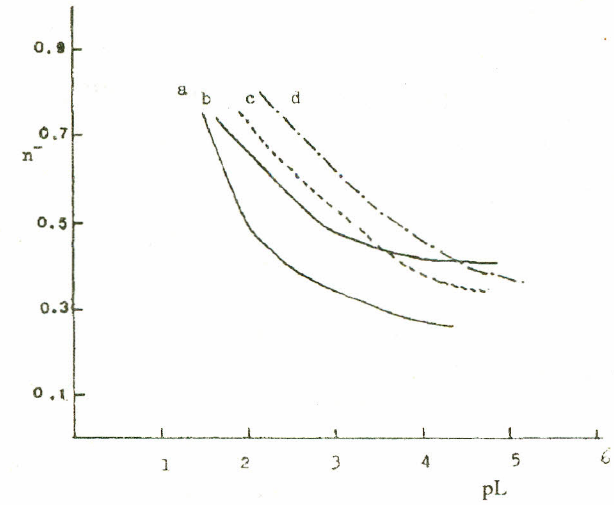

Fig. 2. $\bar{n}$ -pL relation for: (a) Mg(II)-Promethazine complex. (b) Ca(II)-Promethazine complex. (c) Sr(II)-Promethazine complex. (d) Ba(II)-Promethazine complex.

to $\bar{n}_A = 0.5$. The resulted value ($\log K^H_1 = 9.0$) is agree very well with the reported values.

The titration curves of the metal ligand solutions (c) are well separated from the ligand solution (b) indicating the complex formation. To evaluate the formation constants, both of n and pL values are needed. The $\bar{n}$ values were plotted against the corresponding pL to get the formation curves of the metal complexation equilibria. The obtained formation curves are shown in Fig. 2. The values of stability constants were determined using the half integral method and are listed in Table 1. The gathered data indicate the formation of only one complex by the ratio 1:1 (metal:ligand). The metal ion may coordinates the nitrogen atom of tertiary amine.

For alkaline earth metal ions studied, the stability constants of the 1:1 complexes formed with promethazine decrease in the order agree with their ionic potential, i.e. the stability constants decrease in the sequence, $Mg^{2+} > Ca^{2+} > Sr^{2+} > Ba^{2+}$ [9].

For Cd^{2+} and Pb^{2+}, the values of $\bar{n}$ and pL were calculated upto pH = 7, in which at pH > 7, a precipitate has been appeared. Cd^{2+} and Pb^{2+} form a complex with log K = 5.04 and 4.29 respectively.

TABLE 1. STABILITY CONSTANTS OF M-PROMETHAZINE COMPLEXES IN AQUEOUS SOLUTION, T=25 ± 0.1°, μ = 0.1

ion	log K	– Δ G* (K cal/mol)
Mg^{2+}	3.55 ± 0.07	4.823
Ca^{2+}	3.15 ± 0.07	4.280
Sr^{2+}	2.85 ± 0.07	3.872
Ba^{2+}	1.98 ± 0.07	2.690
Pb^{2+}	4.29 ± 0.07	5.824
Cd^{2+}	5.04 ± 0.07	6.848
Al^{3+}	7.90 ± 0.07	10.735

* Δ G = -2.303 RT log K

Al^{3+} forms a stronger complex in comparison with the other metal ions. However, a precipitate was been observed at pH > 5.5, so the calculations are stopped [8] at this pH value.

Key words: pH metry, Promethazine, Formation constant.

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