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# STABILITY CONSTANTS OF ALKALINE EARTH METAL COMPLEXES WITH MEDICINAL DRUGS

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## ABSTRACT

The stability constants of binary complexes of alkaline earth metal ions with tazobactum ($L_1$) and chloropheniramine maleate ($L_2$) medicinal drugs have been determined at 27°C temperature and 0.1 M ionic strength ($NaClO_4$) in aqueous solution pH metrically. The proton and metal ligand stability constants of complexes were determined by using Calvin Bjerrum method as modified by Irving and Rossotti titration technique and discussed in terms of order of stability and basicity of ligands.

**Key words**: Stability constants, Complexes, Tazobactum, Chloropheniramine maleate, Basicity.

## INTRODUCTION

The alkaline earth metal ions like Mg (II) and Ca (II) plays an essential role in biological process in the form of coordination compounds[1]. The most of the drugs acts as ligands to form complexes with metal ions during their mode of action and metabolism[2]. The metal complexes also act as drugs and involved in detoxification, storage and transportation process[3]. Literature survey reveals that a very few researchers have done such type of work[4-6]. In view of above consideration, the present investigation deals with the systematic study of stability constant of binary complexes of alkaline earth metal ions with tazobactum ($L_1$) and chloropheniramine maleate ($L_2$) medicinal drugs.

## EXPERIMENTAL

The chemicals were used for present work were of A. R. grade. All the solutions were prepared in double distilled $Co_2$ free water having pH 6.70-6.90. The concentration of solutions were determined by standard procedures[7].

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The pH measurements were done by Elico pH meter (Model L1-120 Elico Pvt. Ltd. Hyderabad) with combined electrode by using Calvin Bjerrum method as modified by Irving Rossotti titration technique. The titration procedure for determination of stability constants of binary complexes were involved three steps.

(1) Free acid + $NaClO_4$ (A)

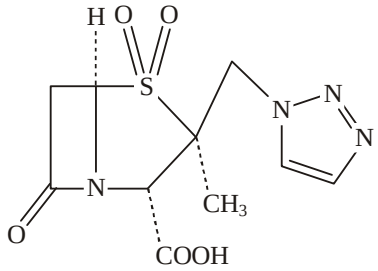
(2) Free acid + $NaClO_4$ + Ligand (A + L)

(3) Free acid + $NaClO_4$ + Ligand + Metal (A + L + M)

These three sets were titrated separately with standard NaOH solution at 27°C temperature in aqueous solutions pH metrically by using Irving Rossotti titration technique[8]. The ionic strength of each solution was maintained constant at 0.1 M by addition of $NaClO_4$.

## RESULTS AND DISCUSSION

The medicinal drugs used in the present study were antibiotic third generation tazobactum ($L_1$), drugs which inhibit the action of beta – lactamase[9] and chloropheniramine maleate ($L_2$), is a anti allergic drug[9], acts as anti histamine relieves symptom of allergy. The structures of drugs are shown in Fig. 1 and 2.



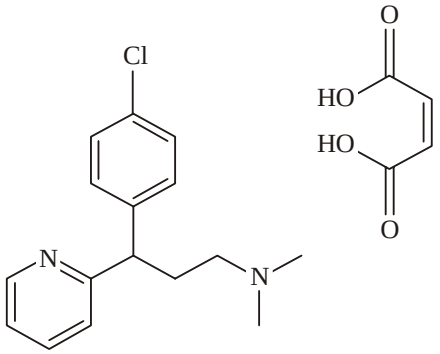




**Fig. 1: Tazobactum drug ($L_1$)** **Fig. 2: Chloropheniramine maleate drug ($L_2$)**

### Proton ligand stability constants (pK)

The proton ligand stability constants (pK) of drugs determined by point wise calculation method as well as half integral methods. In $L_1$ drug, highest value of n~A is around one, indicates only one pKa (2.17) value which may be attributed to the dissociation of (-COOH) group of beta lactum thiozolidine ring. The pK value of tazobactum is found to be less than thiazolidine carboxylic acid (6, 19) which may be attributed to the electron with drawing inductive effect of sulphone and carbonyl groups.

The acid ligand curve of chloropheniramine maleate shows higher pH than acid curve along volume axis which indicates the deprotonation of tertiary amino groups. The highest values of n~A in between 0.2 to 2.0 which indicate the presence of two pK (pK1 = 7.63 and pK2 = 10.97) values. The average pK value (9.30) of drug L2 is near to the pK value of histamine (pK = 10.00) which may inhibit the stimulated secretion of gastric acid[10]. The pK values indicate that durg $L_1$ has low basicity than drug $L_2$.

## Metal ligand stability constants

The considerable deviation of metal titration curves with respect to ligand titration curve along volume axis indicates the formation of complex species and lies at pH region where hydrolysis is not possible. The metal ligand stability constants (log K) of Mg (II) and Ca (II) metal ions with $L_1$ and $L_2$ drugs were determined by point wise calculation method as well as hald integral method. The pK, log K and log β values were enlisted in Table 1.

**Table 1: pK, log K and log β values of alkaline earth metal ions with drugs**

| Metal | Stability constants | L1 | L2 |
|---|---|---|---|
| - | $pK_1$ | - | 7.63 |
| - | $pK_2$ | 2.17 | 10.97 |
| Mg (II) | log $K_1$ | 2.92 | 9.39 |
| | log $K_2$ | 2.76 | 6.75 |
| | log β | 5.68 | 16.14 |
| Ca (II) | log $K_1$ | 2.69 | 8.34 |
| | log $K_2$ | 2.43 | 5.31 |
| | log β | 5.12 | 13.65 |

The highest value of n - obtained was about 2.0 which clearly indicate the formation of 1 : 1 and 1 : 2 binary complexes. The Mg (II) and Ca (II) metal complexes of $L_2$ drugs shows high stability than $L_1$ drug which may be attributed to the strength of basicity.

The stability order of Mg (II) and Ca (II) alkaline earth metal complexes with drugs in the present study are as follows –

$L_1$ : Mg (II) > Ca (II)

$K_2$ : Mg (II) > Ca (II)

Which has been reported by Chakrawarti et al.[11] The plot of log K versus atomic number, atomic radii were plotted and observed that the order of stability of Mg (II) and Ca (II) complexes follows the usual order as low ionic radius more stable will be the complexes[12]. The low values of log K in $L_1$ drug indicates ionic interactions whereas high log K values of $L_2$ drug may be attributed to covalent interactions. The 1 : 1 complexes are found more stable than 1 : 2 complexes due to the statistical effect[13].

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