

# EVALUATION OF STABILITY CONSTANTS OF METAL COMPLEXES WITH CHLORAMPHENICOL

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## ABSTRACT

The present paper deals with the study of stability constants of Cr(III), Cu(II), Ni(II), and Zn(II) metal ions with organic ligand chloramphenicol, by paper electrophoresis technique, at 35<sup>o</sup>C and ionic strength I=0.1 mole dm<sup>-3</sup> (HClO<sub>4</sub>), for better understanding of drug metal interaction as the alteration to existing medication. The stabilities of the chelates follow the order Cr(III) > Cu(II) > Ni(II) > Zn(II), which is in accordance with the Irving Williams and Grinberg and Yatsimiki, order for stability constant of the transition metal complexes.

**Keywords:** Binary metal complexes, chloramphenicol, overall mobility, paper electrophoresis, stability constants.

## I.INTRODUCTION

In the quest for novel treatment against safe life form, the alteration of existing medication by mix to a metal complex has picked up consideration as of late. Thus, metal based drug is seen as promising alternatives for possible replacements for some of the current drugs <sup>[1]</sup>. But prior to the synthesis of new metal complexes, it is required to have information about their important chemical properties. One of these properties is the stability constant of the metal ligand complex. Among the most accomplished techniques are complex formation titrations or electrophoretic or chromatographic separations to measure these thermodynamic values <sup>[2] - [7]</sup>. In this study, a scheme was reported for predicting stability constants of metal complex in solution by means of paper electrophoretic technique, because of its simplicity, low cost and availability in most laboratories. The factors affecting the mobility of ions like variation in temperature during the experiment, capillary flow on paper, electro osmosis and adsorption are the usual drawbacks of paper electrophoretic technique. But the technique described here is free from these vitiating factors, and gives result in fair agreement with accepted literature values. The metal ions chosen for complexation Cr(III), Cu(II), Ni(II), and Zn(II) are vital for lives,



hence the formation, stability and reactivity of these complexes have been an active field of research [8]- [9]. Chloramphenicol having the possible three metal-binding sites, an amide and two hydroxyl groups is a well-known antibiotic, but its interaction with Cr(III), Cu(II), Ni(II), and Zn(II) metal ions were not fully established, also the study of stability constants of above metal ligand complexes are still lacking. It was therefore thought of interest to study the chelating properties of chloramphenicol using paper electrophoresis under suitable conditions.

## **II.EXPERIMENTAL**

### **2.1 Instruments**

An electrophoretic apparatus (systronics type 604, India) was used together with the various accessories supplied with the instrument. The apparatus consisted of polyvinyl chloride of the cassette type and chromatogram could be run simultaneously on eight paper strips. The power unit capable of yielding a maximum of 300V. In each case electrophoresis was carried out for 1 hr. at 220V and at 35°C. Whatman no.1 paper strips were used with an applied voltage gradient of 9V Cm<sup>-1</sup>. pH measurements were made with Elico digital pH meter having glass electrode assembly working on 220 volts/ 50 cycles stabilized AC main was used.

### **2.2 Chemicals**

Zn(II), Cu(II), Ni(II) and Cr(III) perchlorates were prepared by precipitating the corresponding carbonates from solutions of nitrate (Anala R grade) with the solution of sodium carbonate, washing the precipitates thoroughly with boiling water and dissolving in a suitable amount of perchloric acid. The resulting solutions were heated to boiling on a water bath and then filtered. The solutions were standardized and diluted with distilled water. As required Anala R/ BDH grade chloramphenicol, NaOH, HClO<sub>4</sub>, and specific color developing reagents were used for different metal ions of binary sets for specific color development. 1-(2-pyridylazo)-2 naphthol(PAN), 0.1% (w/v) in ethanol was used for detecting all the metal ions. A saturated aqueous solution (0.9ml) of silver nitrate was diluted with acetone to 20ml. Glucose was detected by spraying with this solution and then with 2% ethanolic sodium hydroxide, forming a black spot.

### **2.3 Background Electrolyte**

Stock solution of 5.0 M perchloric acid was prepared by its 70% solution (Anala R grade) 2.0m sodium hydroxide (Anala R grade), 0.5M chloramphenicol were prepared. Each solution was standardized as usual. The background electrolytes used in the study of binary complexes were 0.1M perchloric acid and 0.01M chloramphenicol.

### **2.4 Procedure**

The midpoint of each paper was marked and moistened with the background electrolyte. Excess electrolyte was allowed to drain off and papers were mounted on the plate of electrophoretic chamber. A spot of the metal solution was then applied at the marked point with the help of a fine glass capillary. For recording observations

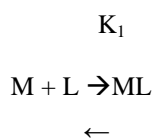


of particular metal ion two strips were spotted with the metal ion solution along with additional two spotted with glucose. The electrode compartment was filled with the equal volumes of the desired background electrolyte solutions. The lid of the chamber was then placed; it was left for 10 minutes to ensure wetting of strips. Subsequently a direct 220-volt potential was applied between the electrodes. Electrophoresis was carried out for 60 minutes after which these strips were removed from the tanks with a glass rod and dried. The metal ion and glucose spots were detected by specific reagents. The leading and tailing edge were measured from the marked Centre point and the mean were taken. The distance moved by glucose was subtracted (in case the migration towards anode) to obtain correct path length. Migration towards anode and cathode were designated by negative and positive signs respectively. The actual distance of the sample spot was measured after taking into account the distance travelled by the reference glucose spot. The distance recorded in the duplicated differed within  $\pm 5\%$  and the average of two distances was noted. The mobilities were then calculated and expressed in  $10^3 \text{cm}^2 \text{v}^{-1} \text{min}^{-1}$ . The mode of dissociation of pure chloramphenicol is shown in Figure 2.

### III.RESULTS AND DISCUSSION

Several workers<sup>[10]-[11]</sup> have been employed graphical methods for determination of stability constants of metal complexes using ionic mobilities data. A plot of electrophoretic mobility against pH gives a curve with a number of plateaus (Fig1). Two plateaus with all the four metal ions are observed. The first plateau in each case corresponds to a region of pH where metal ion is uncomplexed. In this low pH protonated form of chloramphenicol is maximum. Further increase in pH from this region onwards which naturally leads to increase in ligating chloramphenicol anion concentration and brings about a progressive decrease in overall ionic mobility of the metal ion species. This decrease indicates formation of complex of the metal ion with the ligand. A point is reached beyond which mobility of the metal ion species remain constant regardless of the increase of pH of reaction mixture. This is the second plateau which corresponds to a pH region in which 1:1 binary complex of cationic nature is formed. A further increase of pH has no effect on the mobility of metal ions, which indicates no further interaction between the metal ions and ligands. It is significant that these studies give clear evidence of the complexation of the anionic species of chloramphenicol with metal ions forming binary complexes of 1:1 in composition

In view of the above observation the complexation of metal ions with these ligands may be represented as



The metal ion moving under the influence of electrical field, the overall mobility is given by the equation.

$$u = \sum u_n f_n$$

Where,  $u_n$  and  $f_n$  are mobility and mole fraction of a particular complex species. This equation is transformed into the following form. On taking into consideration of different equilibria.

$$u = \frac{u_0 + u_1 K_1 [L] + u_2 K_1 K_2 [L]^2 + \dots}{1 + K_1 [L] + K_1 K_2 [L]^2 + \dots}$$

Where  $K$ 's ( $K_1 K_2$ ) are the stability constants of complexes and  $[L]$  is concentration of chloramphenicol.  $u$ 's ( $u_0, u_1, u_2$ ) are the ionic mobilities of different species of the metal ions, which can be accessed from the plateaus of the Fig1. In the region between first and second plateau, the system consists, mixture of free metal ion and 1:1 complex. The existence of 1:2 complex can be excluded and hence the third term in the numerator and the denominator of the above equation can be neglected.  $u$  would be equal to  $(u_0 + u_{1/2})$  provided  $K_1 [L] = 1$ .

Accordingly, the pH corresponding to the average value of  $u_0$  and  $u_1$  is found from the fig.1 and with the knowledge of the dissociation constant of chloramphenicol ( $pK_a$  6.94), the concentration of chloramphenicol ion at this pH is calculated. Its reciprocal gives the stability constant  $K_1$  of the 1:1 complex

The concentration of chelating chloramphenicol anion  $[L]$  is determined as

$$[L] = \frac{[L]_{tot}}{1 + [H]/K_1 + [H]^2 K_1 K_2}$$

Where  $[L]_{tot}$  is the total concentration of the ligand chloramphenicol (0.01M) and  $K_1$  and  $K_2$  are first and second dissociation constants of the chloramphenicol respectively.

#### IV.FIGURES AND TABLES

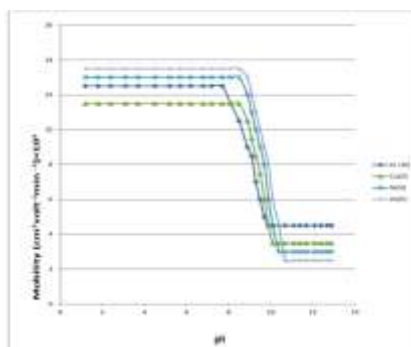


Fig. 1 Mobility curves for metal(II)/metal(III)- chloramphenicol systems -----. = Cr(III) – chloramphenicol-- --- Cu(II)-chloramphenicol - - - - - + - - - - = Ni(II) –chloramphenicol; - - - - - =Zn(II)- chloramphenicol. The paper strips were spotted with 0.1 µl of sample solution and glucose (for making osmotic correction)

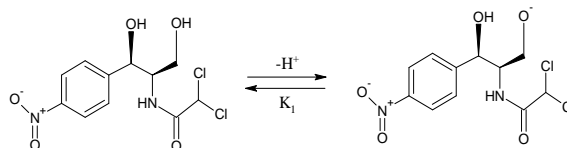


Fig. 2 Figure 2. Mode of dissociation of pure chloramphenicol. Ionic strength: 0.01 M. Temperature: 35 °C.

TABLE -1 Stability Constant Of

M- Chloramphenicol Complexes

Temp. 25<sup>0</sup> Ionic Strength – 0.1M

S.No.	Metal ions	Calculated Values log K <sub>1</sub>	Literature values log K <sub>1</sub>
1	Cr(III)	3.9346	-
2	Cu(II)	3.5427	-
3	Ni(II)	3.3300	-
4	Zn(II)	3.1612	-

From table 1 it can surely be deduced that for a given, the chelation potential of Cr(III) was highest whereas that of Zn(II) was lowest. The metal ion drug ratio was found to be 1:1, for all four metal cations. This is in accordance with the Irving Williams <sup>[12]</sup> and Grinberg and Yatsimiki <sup>[13]</sup> order for stability constant of the transition metal complexes.

V.CONCLUSION

The use of the term stability is without any qualification mean that complex is existent under suitable condition and it is possible to store complex for appreciable time. Thus the term stability is very important to determine whether the complex is suitably stable or not.



The research results open up the prospects to design promising antimicrobial transition metal complexes of chloramphenicol with Zn(II), Cu(II), Ni(II) and Cr(III) metal ions, which would be a help to the working scientists or researchers in the biological and medicinal field and is expected to hopefully produce analogues with better biological profiles and with the minimal requirement to maintain the activity. The stability constants of metal complexes can be very easily calculated by this technique. The present paper technique is limited to charged species, and the precision of the method is not as accurate as other physicochemical methods. However, uncertainty in the results is ( $\pm 5\%$ ). It is not felt that it can replace the other methods, yet it is an alternate approach used.

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