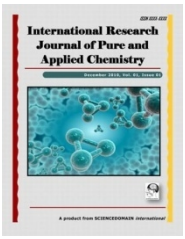

International Research Journal of Pure & Applied Chemistry
4(6): 718-726, 2014

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Investigations of Ferrous Thiamine Complex by Cyclic Voltammetry

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Authors' contributions

This work has been carried out in the department of chemistry, Karachi University. Author SK designed the study, performed experimental work and collected the data. Authors SM and ZM analyze the data and approved the final manuscript. All authors read and approved the final manuscript.

Original Research Article

Received 20th April 2014
Accepted 23rd June 2014
Published 8th July 2014

ABSTRACT

Study of thiamine ferrous complex is carried out by intensive use of cyclic voltammetry. The different mole ratio of ferrous thiamine complexes is assessed. Acidified KCl (1M) solution is used as supporting electrolyte. Mole ratio of complex is established 1:2 (thamine: Ferrous ion) 100 mV/s scan rate is chosen as optimum. By applying the Randles Sevcik equation, their reaction is found reversible and occurred under diffusion control system. Their equilibrium constants values are also determined by using the Ipc values of this complex obtained at different scan rates (100 to 500mV/s). The mechanism of the reaction is tried to discover by these results. Thiamine in AFe_2 complex is oxidized into A^+Fe_2 and then reduces again at a fast scan rate.

Keywords: Thiamine; ferrous ammonium sulphate hexahydrate; Pt electrode; stoichiometry, scan rate.

1. INTRODUCTION

Thiamine hydrochloride plays a very important role in biological compounds and is used as a coenzyme. It belongs to that group of enzymes which was involved in acyl transfer reaction.

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Deficiency of thiamine causes the beriberi disease in human body [1,2,3]. The role of bivalent metals in enzymatic action of thiamine is determined by the bonding mode of the metals to thiamine [4]. Early studies show metal ion binds to thiamine or its derivatives through N1 of pyrimidine ring or pyrophosphate group and form ionic salt such as $[Th]^{2+}[MX_4]^{2-}$, $[Th]^{2+}([MX_3]^-)_2$, or $(Th^+)_2[MX_4]^{2-}$. M could be Zn^{2+}, Co^{2+}, Ni^{2+}, X could be Cl^-, Br^- and Th is for thiamine [2,4]. The presence of positive charge on thiazolium ring and protonation of N1 of pyrimidine ring formed a double charged species. Some partial positive charge migrated toward the sulfur position of the thiazolium ring. This delocalized charge was balanced by bonding of nitrogen, sulfur and oxygen with metals ions. Thiamine and their derivatives can undergo many structural changes at different pH values. In alkaline medium, thiamine HCl may be converted into thiochrome [5]. Therefore, it is stable in acidic media and fully protonated with ionizable proton at the N1 (pKa = 5) and C2 (pKa = 19) of pyrimidine and thiazolium rings respectively Fig. 1 [2,6,7]. Literature shows electrochemical behaviour of thiamine linked with ionization at C2 position of thiazolium ring and it was considered as the key reactivity of thiamine [3,8]. Catalytic behaviour of thiamine was found to be attributed to 4 – amino pyrimidine ring when N1 is protonated [3,9,10]. Polarographic study of thiamine in acidic media is not favourable because mercury electrode can bind with electroactive species of thiamine and participate as catalyst in redox reaction [11]. pH and electrode compositions play very important role in electrochemical determination of thiamine compounds [12]. Platinum compounds have low electrode potential for hydrogen discharging as compared to mercury electrode [13]. In acidic and neutral medium, reduction of thiamine is attributed to multiple adsorption peaks (pre and post adsorption and hydrogen discharge) which are observed at the mercury electrode [2,14]. This behaviour produces more difficulties in determination of the redox properties of thiamine while platinum electrode potential window depends on the composition of solution and pH. In presence of Pt electrode, acidic solution of thiamine (pH 3.5) shows two peaks which are related to two redox processes such as reduction of H^+ and formation of $(Th)^{+2}$ ion. This reduction peak of hydrogen can be removed by using high pH solution [15]. The detail studied of complexation of thiamine is reported with different biological active metals such as Zn^{2+}, Co^{2+},Cd^{2+},Hg^{2+},Pt^{2+} and Pd^{2+} [16,17]. But the interaction of iron with thiamine is not reported however it is more vitally required for human body. Iron plays very important roles in biological system such as oxidation and reduction reaction, bioenergetics and catalytic reactions. In present study, the involvement of thiamine in complexation with ferrous ion in acidic KCl medium is investigated. The mechanism of this type of reaction is also studied.

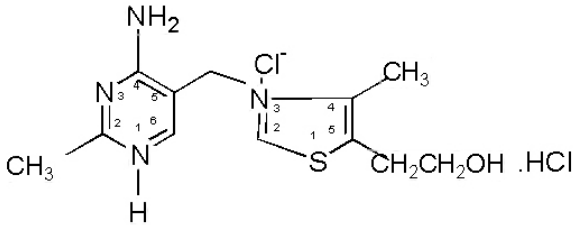

Fig. 1. Structure of thiamine hydrochloride

2. EXPERIMENTALS

Free thiamine of analytical grade is obtained from Sigma™ chemical company. Ferrous ammonium sulfate hexahydrate, sodium hydroxide, oxalic acid, hydrochloric acid, potassium chloride from are obtained from Aldrich™ AG. All solutions are prepared in double distilled

and then deionized water. The pH is recorded at Jenway™ 370 pH meter. Cyclic voltammetry measurements are performed using Computerized Electrochemical workstation, CH-Instruments™ Model CHI – 760D.

Solutions of 4.3 mM ferrous ammonium sulphate and thiamine hydrochloride are prepared separately in acidified 1M KCl of pH 6. Two sets of working standard solutions with different mole ratio 1:1, 1:2, 1:3, 1:4, 1:5 of thiamine to ferrous ion and ferrous ion to thiamine were prepared in acidified KCl solution. The solutions containing complexes are run at 50, 100, 200, 300, 400 and 500mV/s. The base line of 1 M KCl solution is recorded at Pt electrode vs Ag/AgCl reference electrode at temperature 25±1ºC. The horizontally straight line is observed in both sets of solution. The potential range is set as -0.8 V to 0 V in forward scan and then reversed back to 0 V to -0.8 V. The oxidation wave is observed in the potential range of forward scan going from -0.8 V to 0 V. The oxidized species is noticed to be reduced back during the reverse scan from 0 V to initial potential -0.8 V.

3. RESULTS AND DISCUSSION

The working standard solutions of complexes (in which thiamine HCl and Fe^{2+} concentrations are fixed) are scanned at several scan rate. The optimum scan rate is selected to be 100mV/s. Thiamine HCl is showing cathodic and anodic peaks at approximately -505 and -615 mV, respectively (Fig. 3). Plot of Ipc and Ipa versus scan rate is showing linear increase in currents up to 300mv/s scan rate with correlation coefficient of 0.988 regarding Ipc and – 0.999 regarding Ipa (Fig. 2). On further increase in scan rate, namely at values higher than 300mV/s, no proper relationship could be established. The peak potential values for thiamine are same as reported earlier in literature [14].

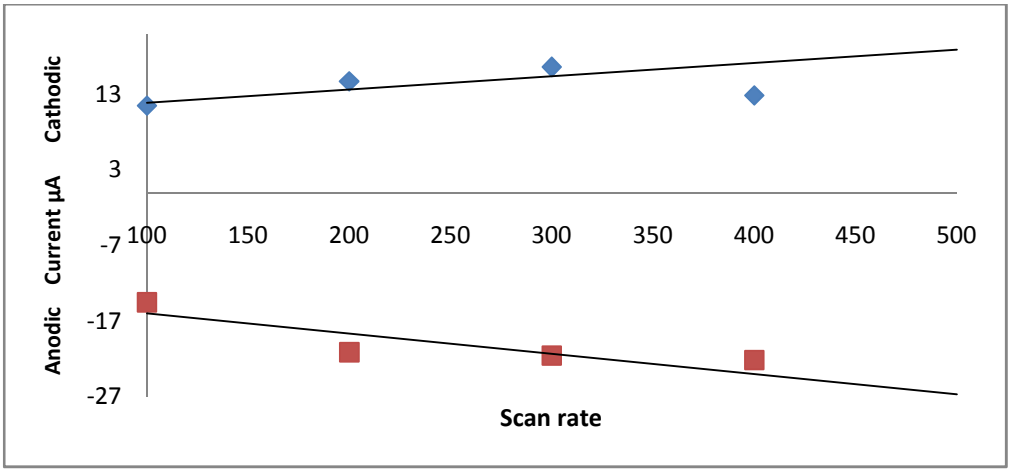

Fig. 2. Plot of Ipa and Ipc values of thiamine HCl at different scan rates

Ferrous ion does not show peaks within this potential window. The overlaid plot of cathodic peaks of complexes formed between thiamine HCl and ferrous ion at 100m V/s, is confirming that the complex formation is optimized at 1:2 thiamine to ferrous ion ratio, which is noticed with decrease in current. This complex peak is not sharp at the upper side and showed the formation of compact type of complex Fig. 3. For other mole ratio compositions, increase in current is due to the presence of free or un-complexed thiamine Fig. 4. Even if complexes

were formed at higher molar ratio, they were extremely unstable, and therefore thiamine is released.

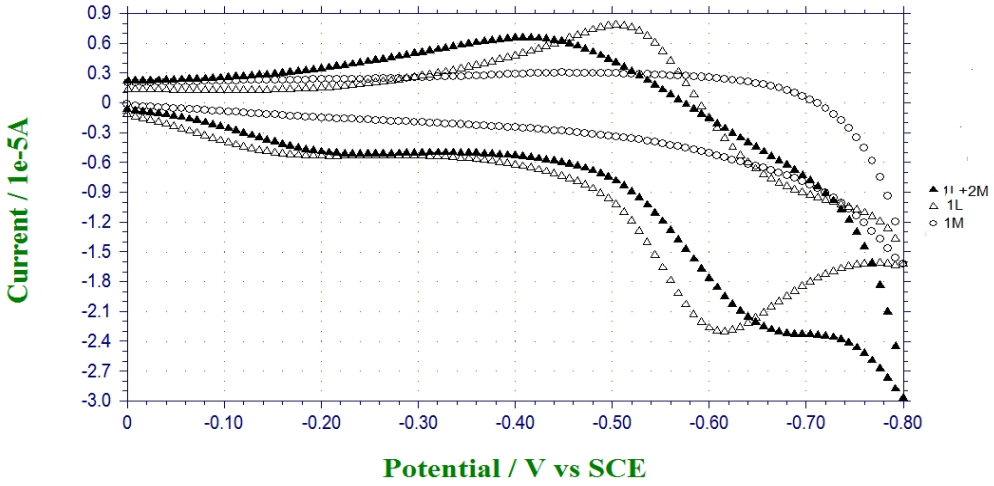

Fig. 3. Voltammogram of ferrous, thiamine and (1L:2M) complex solution at 100 mV/s

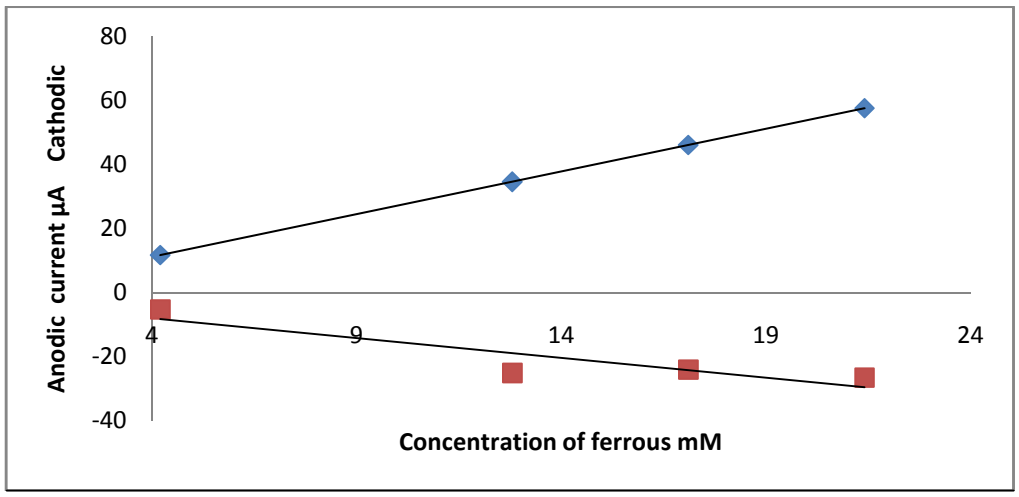

Fig. 4. Plot of Ipa and Ipc versus different concentration of ferrous complexes at 100 mV/s scan rate except 1:2 mole ratio complex

Randles Sevcik equation is applied on that complex formation reaction for determination the diffusion coefficient and reversibility of the reaction.

$$Ip = -2.69 \times 10^5 n^{3/2} C D^{1/2} v^{1/2} \quad (1)$$

The graph is plotted between Ipa or Ipc and $v^{1/2}$, and the linear dependence was obtained with 0.992 coefficient of regression (Fig. 5). It shows that the reaction is reversible and is occurring under diffusion control system. The average diffusion coefficient values were found between 400 to 500 for both Ipa and Ipc current by using Randles Sevick equation (Eq-1).

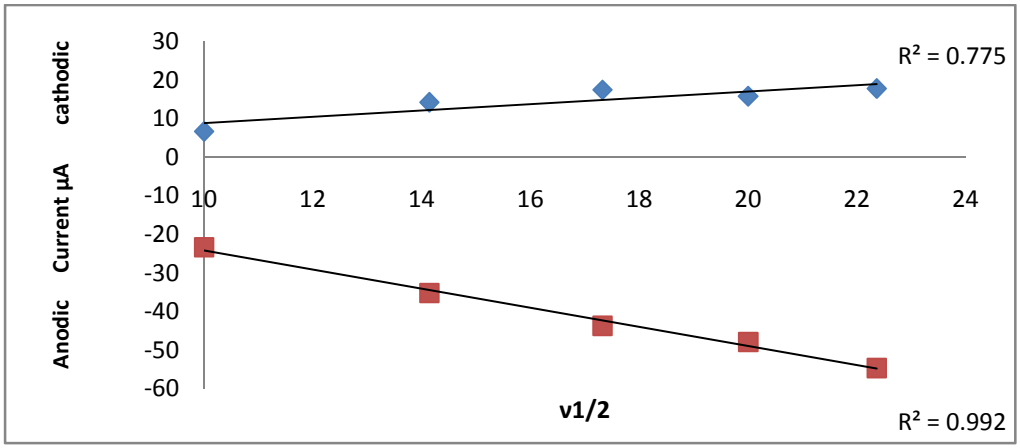

Fig. 5. Plot of v ½ and Ipa or Ipc of 1:2 mole ratio complex

The graph is plotted with Ipa versus variable mole ratio of ferrous ion at different scan rates showed that the Ipa values sharply increasing till two to three mole ratios of ferrous ion and then remain constant Fig. 6. This sharp increase is also confirming that two or three ferrous ions may be involved in complex formation.

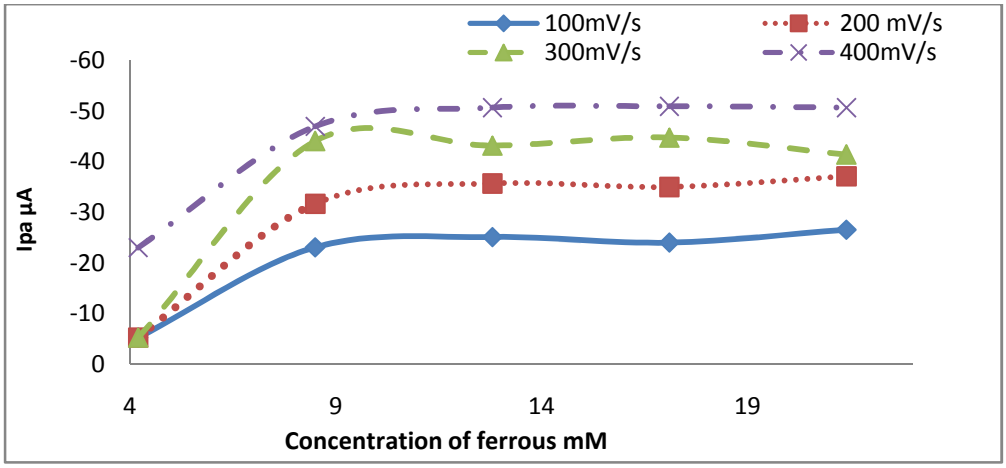

Fig. 6. Plot between Ipa versus variable concentration of ferrous ion than thiamine HCl complexes solution in acidify pH at 100mV/s scan rate

The constant concentration thiamine is varied keeping Fe^{2+} at fixed concentration. Then complex solutions are scanned at 100 mV/s. All complexes showed approximately same cathodic and anodic potential as thiamine HCl but difference is noticed in their current values. The Ipa or Ipc values of thiamine HCl were lower than Ipa or Ipc values of ferrous thiamine complexes. The Ipa and Ipc values of complexes were found to increases with the increasing concentration of thiamine HCl but it was not linear. The graph plotted between Ipc values of complexes versus the concentrations of thiamine HCl. The plot is not showing a linear dependence, due to involvement of the thiamine in equilibrium with HCl, this is also showing that the thiamine is unavailable for complexation at very low concentration. Fig. 7.

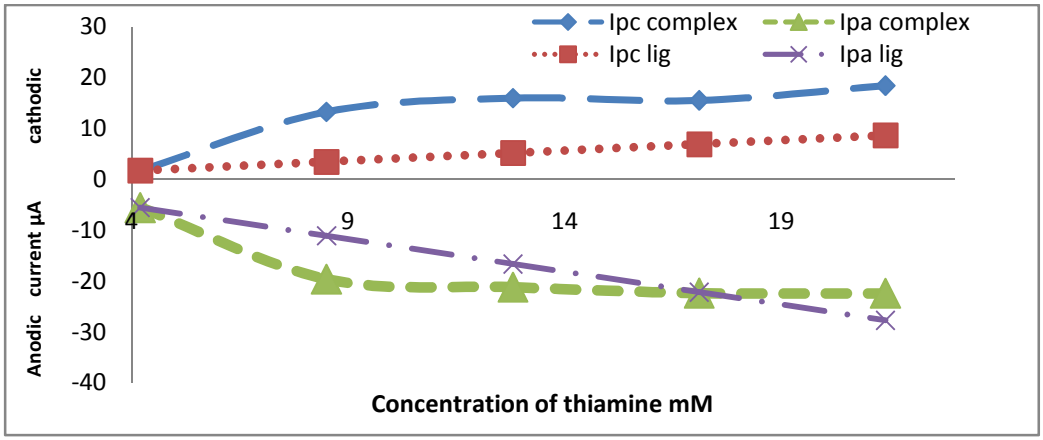

Fig. 7. Plot between Ipc verses variable concentration of thiamine HCl than ferrous ion complexes solution in acidify pH at 100mV/s scan rate

The equilibrium constant values of all complexes are calculated through the plot of Ipc (Fig 6-7) values versus variable concentrations of thiamine and ferrous ion at different scan rates. These values of equilibrium constants are increasing with variable concentration of metal ion upto 300 mV/s given in Table 1. The equilibrium constant values are calculated by using the following formulas

$$2M + A \leftrightarrow M_2A$$
$$K_{eq} = [M_2A]/[M]^2 [A]$$

$$i_d = a[M_2A]$$

$$[M] = [M]_{eq} - 2\,[M_2A]_{eq}$$

$$[A] = [A]_{eq} - [M_2A]_{eq}$$

where '*i*' is diffusion current, $[M_2A]$ is concentration of complex form between metal M and ligand L, '*a*' is voltammetric constant (containing upon various factors such as diffusion coefficient, area of electrode, number of electron involved in reaction, nature, distance between electrodes etc).

The variable concentrations of ferrous complex solutions are also prepared in different buffer solution, such as sodium acetate (pH 4), potassium hydrogen phthalate (pH 5 & 7) and sodium tetraborate (pH 8) and scanned at 100mV/s, but they are giving meaningless results except for potassium chloride at pH 6.

The mechanism of complexation reaction could be suggested by the assumption that one electron transfer reaction may occur in one step at fast scan rate and in two steps at slow scan rate. Literature also shows that the one electron transfer reduction process of thiamine occurs in aqueous solution [18]. In 1:1 mole ratio complex, AFe (where A is ligand) is oxidized at Pt electrode and converts into A^+Fe, which reduces with fast scan rate and it may be converted into A^+ and Fe at slow scan rate, then A^+ was reduced into A and reacted with Fe atom and converted into AFe complex. The charge balance of complexes is not considered here, they could be balanced by some counter ions.

$$[AFe] \overset{k_o \text{ fast}}{\leftrightarrow} A^+Fe + e^-$$

$$A^+Fe + e^- \overset{k_{-1} \text{ slow}}{\rightarrow} A^+ + Fe$$

$$A^+ + \bar{e} \rightarrow A$$

$$A + Fe \overset{k_1}{\rightarrow} [AFe]$$

Table 1. Equilibrium constant values determined from Ipc of different mole ratio complexes at each scan rate

Scan rate mV/s	Equilibrium constants	
	At constant concentration of ferrous (4.3mM)	**At constant concentration of thiamine (4.3mM)**
100	0.02	0.166
200	0.015	0.269
300	0.026	0.33
400	0.0108	0.141
500	0.013	0.181

In case of AFe_2 complex, thiamine may oxidize and converts into $A^+ Fe_2$ which further reduces at fast scan rate. At slow scan rate $A^+ Fe_2$ may converted into A^+Fe and that reduces in the presence of Fe atom and converts into AFe_2 complex or may be converted into A^+ and Fe atom. A^+ reduces into A and reacted with two moles of Fe atoms and formed AFe_2 complex.

$$AFe_2 \overset{k_o \text{ fast}}{\leftrightarrow} A^+ Fe_2 + e^-$$

$$AFe_2 \overset{k_o \text{ fast}}{\leftrightarrow} A^+ Fe_2 + e^- \overset{k_{-1} \text{ slow}}{\rightarrow} A^+Fe + Fe + e^- \rightarrow AFe_2$$

$$A^+Fe \overset{k_{-2}}{\rightarrow} A^+ + Fe$$

$$A^+ + e^- \rightarrow A$$

$$A + 2Fe \overset{k_1}{\rightarrow} [AFe_2]$$

4. CONCLUSION

Electrochemical study for ferrous and thiamine complex are carried out by cyclic voltammetry using Pt electrode vs Ag/AgCl reference electrode. The acidified 1M KCl (pH 6) is found to be a suitable electrolyte for the complex formation as compared to different buffer solutions such as sodium acetate (pH 4), potassium hydrogen phthalate (pH 5 & 7) and sodium tetraborate (pH 8). Mole ratio of 1:2 is established between thiamine to ferrous ion in acidified 1 M KCl (pH 6) solution. Scan rate of 100mV/s is selected. The complexation reaction is found reversible and average diffusion coefficient value is observed between 400

- 500 for both Ipa and Ipc current. The equilibrium constant values are also calculated through Ipc values of 1:2 mole ratio complex and these values are increasing up to 300mV/s and confirmed that 1:2 mole ratio exist between the thiamine and ferrous ion in the complex. At the fast scan rate thiamine in AFe_2 complex oxidized into A^+Fe_2. This is further converts into A^+Fe at slow scan rate. A^+Fe may react with another Fe ion and reduce to complex or may convert into A^+ and Fe atom. A^+ may reduce and reacted with two moles of Fe atoms to form complex.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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