

Electrochemical Study of Pb^{+2} -Theophylline Complex

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Abstract: The interaction between Theophylline and Pb^{2+} was investigated using direct current polarography. The polarographic technique was used to determine the stability constants and thermodynamic parameters such as enthalpy change (ΔH), free energy change (ΔG) and entropy change (ΔS) of Pb^{2+} complexes with Theophylline at pH-5 in 0.1M acetate buffer. The study was carried out at two different temperatures 20 °C and 30 °C. Pb^{2+} - Theophylline complexes were formed in 1:1, 1:2 and 1:3 ratios. The electrode processes were reversible and diffusion controlled.

Key words: stability constant, thermodynamic parameters, Pb^{2+} -Theophylline system.

Introduction

A methyl xanthine derivative is diuretic, smooth muscle relaxant, bronchial dilator, cardiac and central nervous system activities stimulant. Theophylline (3,7-dihydro-1,3-dimethyl-1H-purine-2,6-dione) is a methyl xanthine widely used as a bronchodilator for the treatment of bronchial asthma and neonatal apnea.¹ The antibacterial activity of theophylline is well known, especially as this alkaloid is present in tea leaves.² Its primary mode of action is inhibiting phosphodiesterase, thus causing relaxation of the bronchiole walls. Theophylline also exerts excitatory influences on the skeletal muscle, gastric secretion, kidneys and fatty acid metabolism in addition to inhibitory effects on smooth muscle. It is well known that excessive administration of Theophylline occasionally produces serious toxicity, including vomiting, tachycardia, and central nervous system excitation including seizures.^{3,4} Furthermore, Theophylline has biological importance which can be

used in anticancer drugs.⁵⁻⁸ The purines including theophylline, theobromine and caffeine, constitute an important class of anti-inflammatory agents.⁹ Theophylline has biological importance as it is structurally related to nucleic acids components.¹⁰ Thus it can be used as a drug in therapy for respiratory such as COPD or asthma under a variety of brand names and anticancer drugs. A few metal-theophylline complexes have shown significant antitumor activity.¹¹

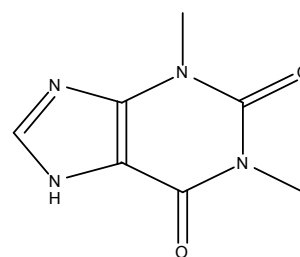


Fig. 1 Theophylline

The anion derived from theophylline has often been used as a model ligand in studying the interaction with metal ions.¹² Theophylline (Fig. 1) has molecular weight 180.1640 g/mol and melting point 272°C.

Lead taken internally in any of its forms is highly toxic; the effects are usually felt after it gets accumulated in the body over a period of time. The symptoms of lead poisoning are anemia, constipation, colic, headache, abdominal pain, memory loss, kidney failure, and weakness, pain, or tingling in the extremities.¹³ Lead based paints and toys made from lead compounds are considered serious hazards for children.¹⁴

The treatment of lead poisoning for people who have significantly high lead levels in blood is given by chelation therapy.¹⁵ A chelating agent is a molecule with at least two negatively charged groups that allow it to form complexes with metal ions with multiple positive charges, such as lead.¹⁶ The chelating agents used for treatment of lead poisoning are edetate disodium calcium, dimercaprol.¹⁷ The interaction of lead with theophylline has been widely studied.¹⁸⁻²⁰

A large number of pharmaceuticals can be reduced or oxidized in the available potential range and their waves can be used in their determination. It seems that often the therapeutic activity is paralleled by electrochemical reactivity. Pharmaceutical companies will use, whenever possible, officially approved methods of analysis. In the past, some polarographic analytical procedures were listed in numerous Pharmacopoeias. It should be a goal of electroanalytical chemists around the world to have them listed again. The lower costs, faster results, and the possibility for quickly detecting mishandlings by technicians, are powerful arguments. To use polarographic methods for analyses of such simple matrices yields results often much faster, with a better accuracy and without using organic solvents.²¹ Numerous examples of such applications have been reported earlier.²²

In this work, we have demonstrated the binding of Theophylline and Pb^{2+} and the thermodynamics of their interaction. Stability constants of complexes in presence of 0.1M Acetate Buffer are determined. Temperature effect on the stability of complexes is also discussed. In order to attain these objectives, we have planned to carry out detailed investigation of Theophylline and Pb^{2+} using Direct current Polarography.

Experimental

The general procedure for Direct current Polarography is as follows-

A 10 ml of experimental solution was placed in a polarographic cell and deoxygenated with nitrogen for 13 min. The cell was placed in the thermostat and the capillary was inserted in solution. The current voltage curves were measured manually. Polarographic experiments were carried out with Elico D.C. recording polarograph CL 357. The current voltage measurements were performed with three electrode assembly, a dropping mercury electrode as working electrode, calomel as reference electrode and platinum electrode as counter electrode. A digital pH meter model 111 E was used for measuring the pH of the analytes. The potential was applied to the working electrode with 150 mV/min scan rate and 100 nA/div. sensitivity of current measurement. The dropping mercury electrode had the following characteristics- $m = 2.420$ mg/sec, $t = 3.5$ sec, $h = 60$ cm.

All the solutions were prepared from doubly distilled water and analytical reagent grade chemicals (MERCK).

Theophylline {Sidmak Laboratories (India)} solution was prepared freshly every 5 days.

$Pb(CH_3COO)_2 \cdot 3H_2O$ used was of analytical reagent grade.

0.1 M Acetate buffer (pH-5) has been used as supporting electrolyte.

Triton X-100 (0.001%) was used to suppress polarographic maxima.

Table -1: Polarographic data and $F_j(X)$ values of Pb^{2+} -Theophylline system.

$Pb^{2+} = 1.25$ mM, 0.1 M Acetate buffer (pH-5), $T = 20$ °C

$E_{1/2}(Pb^{2+}) = -0.471$ volts vs. S.C.E

[X] mM	$i_d \times 100$ nA	-Ec V	$-\Delta E_{1/2} = Ec - Em$	FoX	$F_1 X \times 10^2$	$F_2 X \times 10^4$	$F_3 X \times 10^7$
1.25	3.4	0.472	0.0013	1.14	1.15	7.60	5.92
1.56	3.3	0.474	0.0028	1.32	2.05	11.82	7.44
1.88	3.2	0.475	0.0043	1.54	2.87	14.26	7.50
2.18	3.1	0.477	0.0061	1.82	3.77	16.32	7.37
2.50	3	0.479	0.0082	2.24	4.94	18.97	7.51

Where,

i_d = Diffusion current, $\Delta E_{1/2}$ = Difference in $E_{1/2}$ of Pb^{2+} and Pb^{2+} -Theophylline complex.

Em = Half wave potential of Pb^{2+} ion., Ec = Half wave potential of Pb^{2+} -Theophylline complex

Table -2: Polarographic data and $F_j(X)$ values of Pb^{2+} -Theophylline system. $Pb^{2+} = 1.25 \text{ mM}$, 0.1 M Acetate buffer (pH-5), $T = 30^\circ\text{C}$ $E_{1/2}(Pb^{2+}) = 0.468 \text{ volts vs. S.C.E}$

[X] mM	$I_d \times 100 \text{ nA}$	$-E_{1/2c} \text{ V}$	$-\Delta E_{1/2} = E_c - E_m$	F_0X	$F_1X \times 10^2$	$F_2X \times 10^4$	$F_3X \times 10^7$
1.25	3.9	0.469	0.0010	1.11	0.88	05.88	4.55
1.56	3.8	0.470	0.0021	1.24	1.52	08.80	5.54
1.88	3.7	0.471	0.0033	1.39	2.08	10.32	5.43
2.18	3.6	0.472	0.0045	1.57	2.61	11.24	5.07
2.50	3.5	0.474	0.0060	1.81	3.23	12.33	4.88
2.81	3.4	0.476	0.0076	2.11	3.96	13.55	4.77

Table -3: Stability constant of Pb^{2+} -Theophylline system.

System	Ratio	T = 20 °C		T = 30 °C	
		B	log β	β	log β
$Pb(THP)^{+2}$	1:1	$\beta_1 = 20$	1.30	$\beta_1 = 15$	1.18
$Pb(THP)_2^{+2}$	1:2	$\beta_2 = 2000$	3.30	$\beta_2 = 1450$	3.16
$Pb(THP)_3^{+2}$	1:3	$\beta_2 = 7.5 \times 10^7$	7.88	$\beta_2 = 5.0 \times 10^7$	7.70

Result and Discussion

A well-defined two-electron reversible reduction and diffusion controlled wave of Pb^{2+} was observed in 0.1 M Acetate buffer at pH-5. The value of $E_{1/2}$ reversible for Pb^{2+} was -0.469 V vs. Saturated calomel electrode. The nature of the Current-Voltage curve of Pb^{2+} complexes with Theophylline was also reversible and diffusion-controlled.

When aqueous solution of Theophylline(THP) was added, half wave potential was shifted towards more negative direction i.e. towards more cathodic value, the difference being related to the free energy of dissociation of complex²³ and The diffusion currents were found to decrease with increase of ligand concentration, which suggests complex formation. The complex ion formed is of much larger size as compared to the aqua metal ion hence there is the low value of diffusion currents with the increase of ligand concentration.²⁴ (Fig. 2, Fig. 3 and Fig.4).

The slope values of the plots of $\log(i/i_a - i)$ vs. E (mV) are found in the range $28 \pm 2 \text{ mV}$ suggesting the reversible nature of electrode reaction.

The plot of $\Delta E_{1/2}$ against $\log [X]$ consists of a smooth curve which is convex with respect to the abscissa axis, with increase of the activity of the ligand, complexes with a larger coordination number are

formed and the slope of the plot increases.²⁵(Fig.5 and Fig.6).

The Deford and Hume method²⁶ confirmed the formation of 1:1, 1:2 and 1:3 complexes of Pb^{2+} with Theophylline. Complexation has been carried out at two (20°C and 30°C) temperatures. At 20°C more shifts in half wave potential was observed. The temperature coefficient of the half wave potential is between -0.30 to -0.52 mV/degree so the system is reversible.²⁷ The plots of $F_j(X)$ vs. X (where X is the concentration of Theophylline in mole/liter) are given in Fig. 7 & 8 and results are summarized in Tables 1 & 2 at 20°C & 30°C respectively.

Fig. 7 & 8 illustrates plots of the functions $F_j(X)$ for the Pb^{2+} -Theophylline system. Evidently three complexes are formed in this system: $Pb(THP)^{+2}$, $Pb(THP)_2^{+2}$ and $Pb(THP)_3^{+2}$. From the plots of $F_j(X)$ vs. X values of β_1 , β_2 and β_3 have been evaluated.

Value of intercept gives the value of β , whereas value of $\log\beta$ represents the stability constant. More will be the value of stability constant more will be stability.

As shown in Table 3 stability constant values increases with increases in coordination number suggesting more stability of Pb^{2+} -Theophylline complexes in 1:3 ratio. The stability constant values suggest that 1:3 complex is more stable at 20°C than at 30°C .

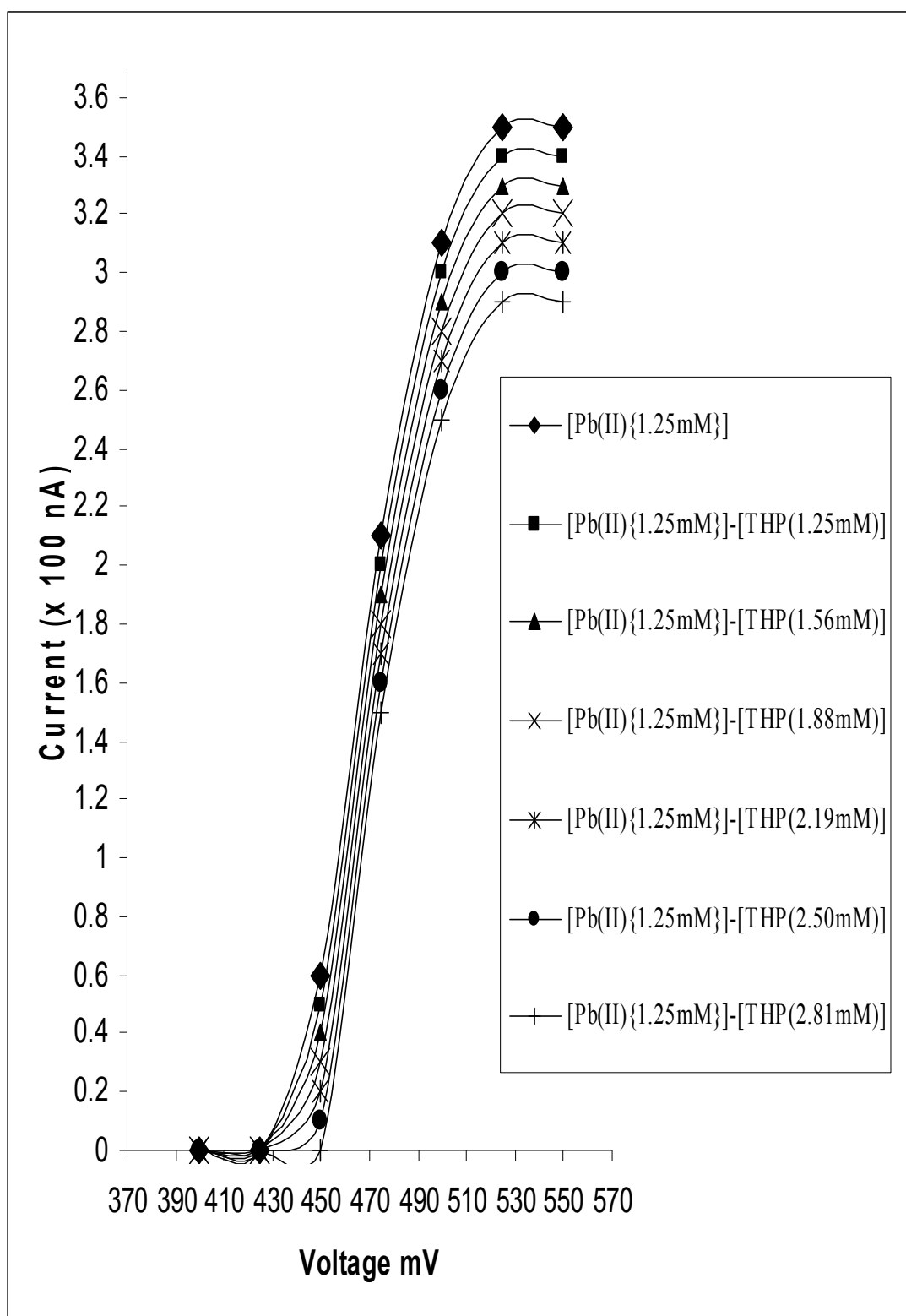


Fig. 2.A. Polarograms of Pb^{2+} - Theophylline system at 20 °C.

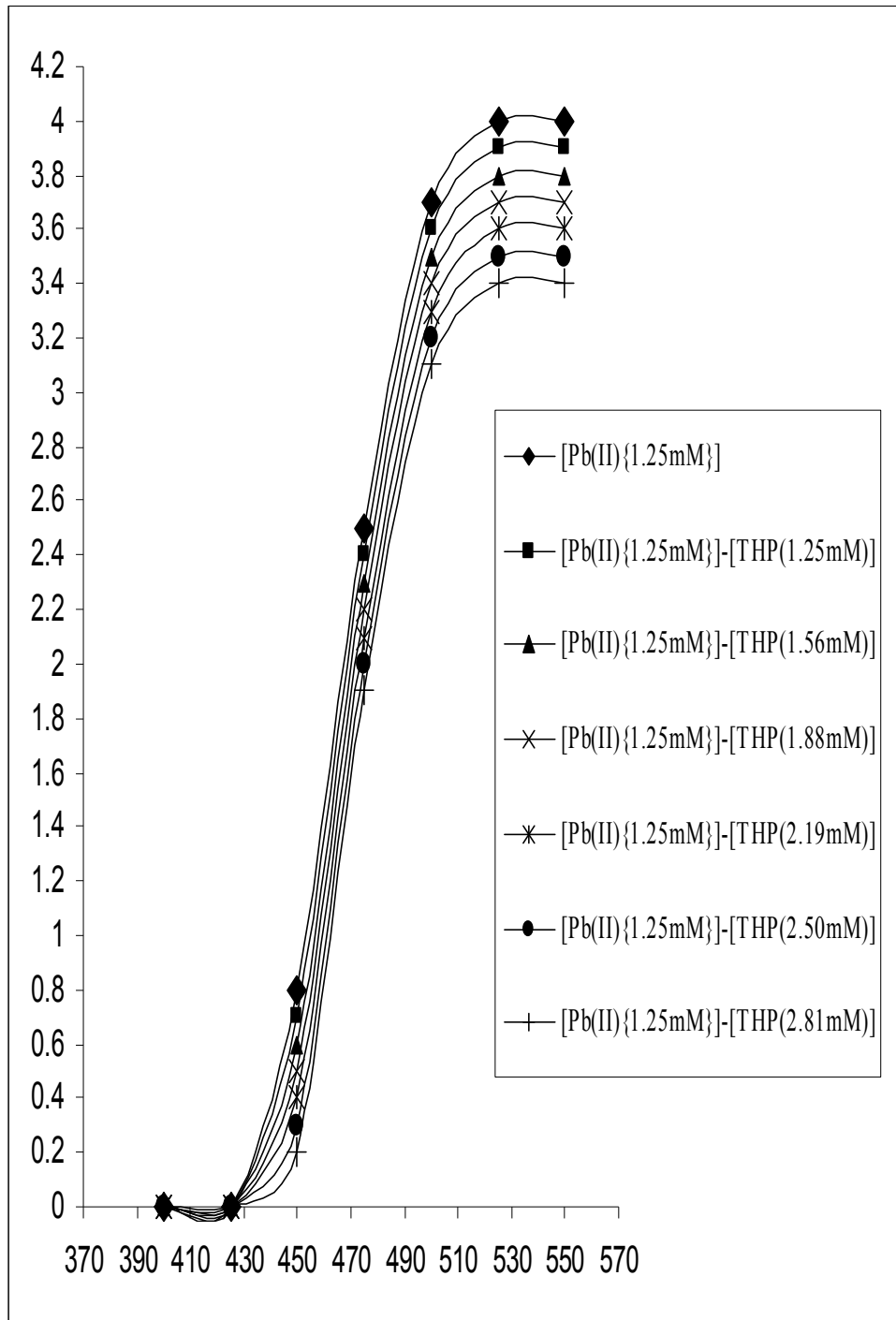


Fig. 2.B. Polarograms of Pb²⁺ - Theophylline system at 30 °C.

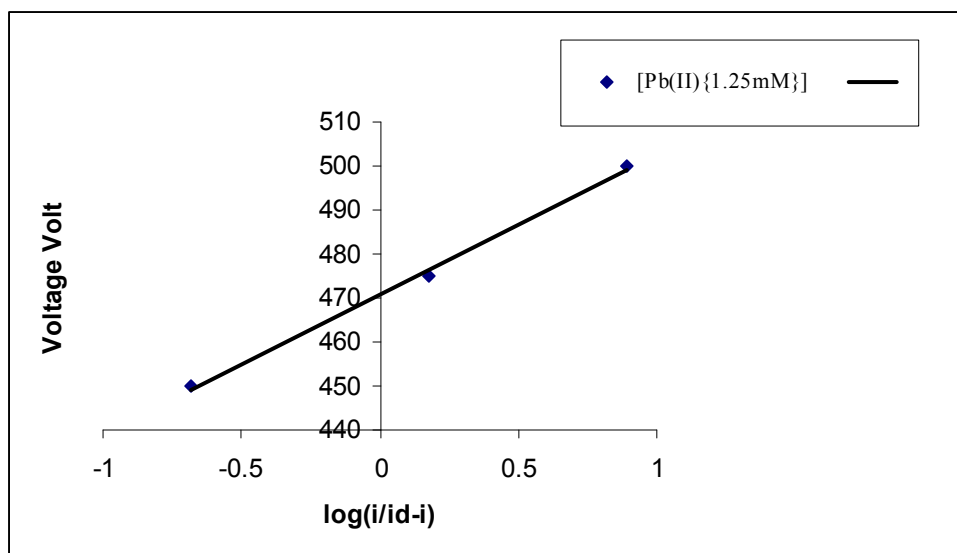


Fig. 3.A.

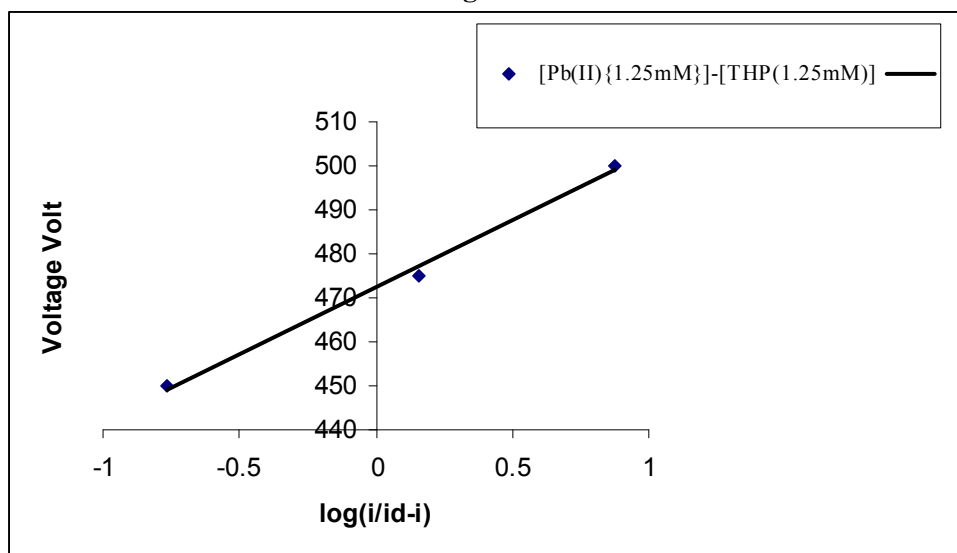


Fig. 3.B

Fig. 3.(A & B) plot E vs. $\log(i/i_d-i)$ at 30 °C

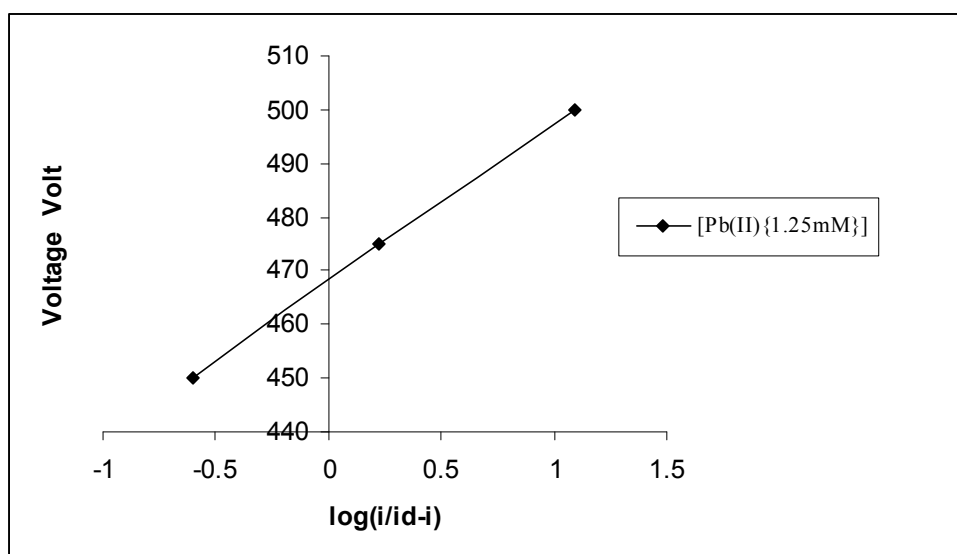


Fig. 4.A.

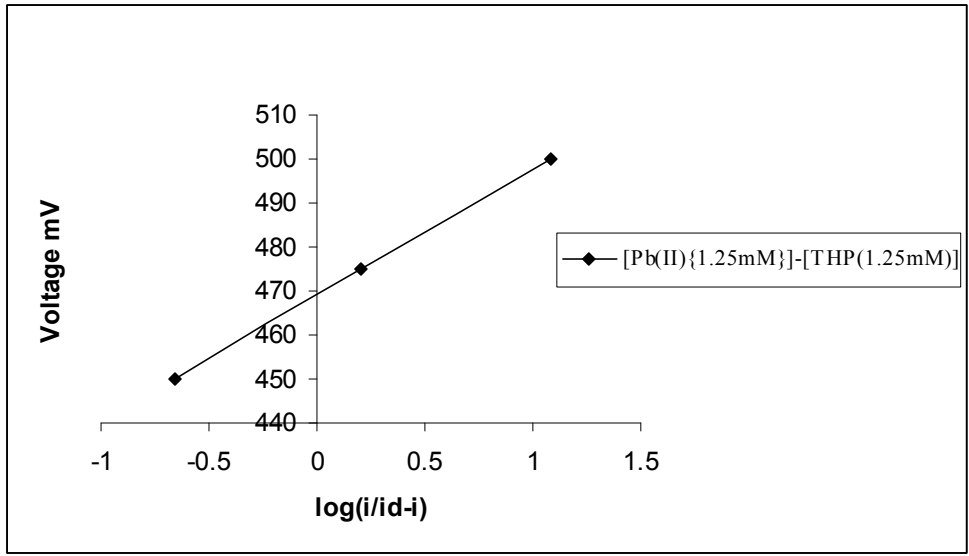


Fig. 4.B.
Fig. 4.(A & B) plot E vs. $\log(i/i_d-i)$ at 30 °C

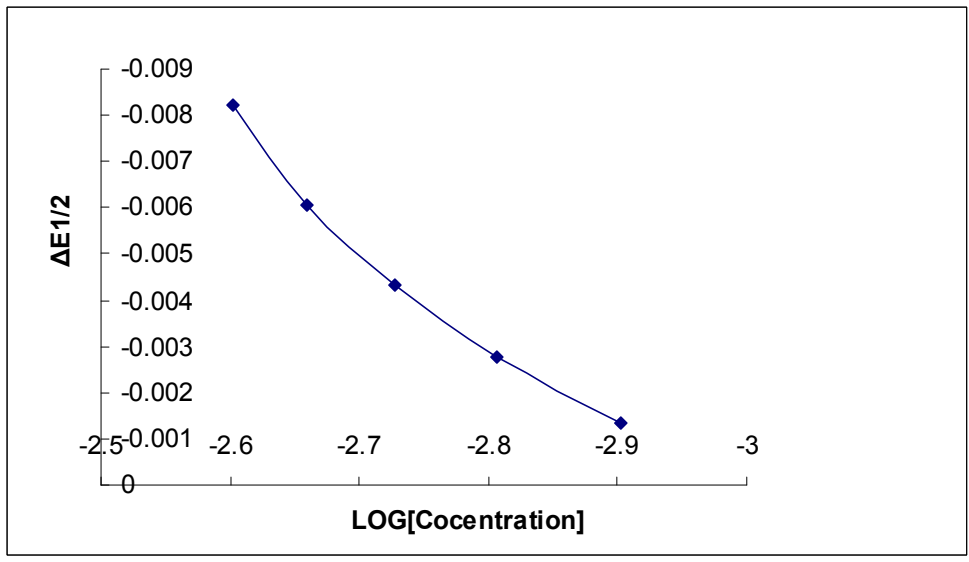


Fig 5. plot $-\Delta E_{1/2}$ vs. $\log[\text{concentration}]$ at 20⁰C.

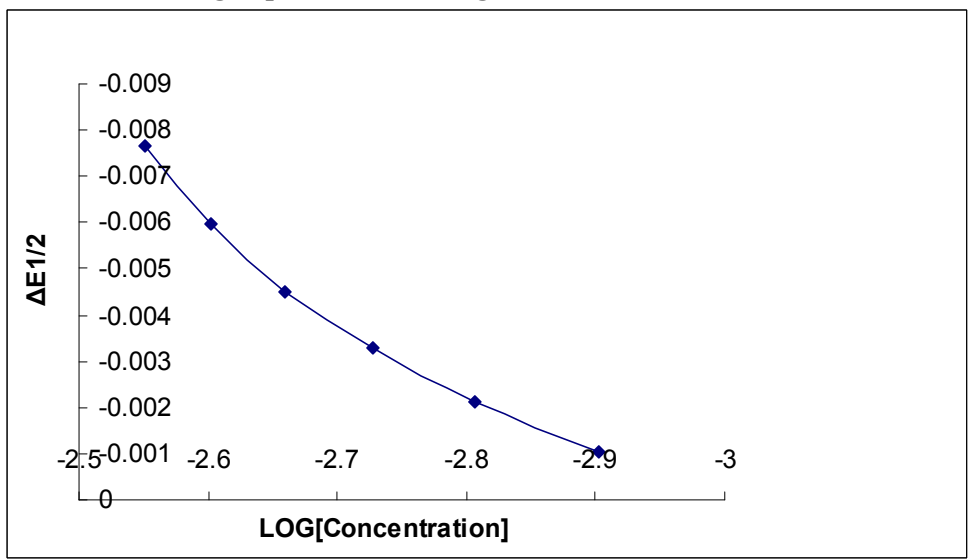


Fig 6. plot $-\Delta E_{1/2}$ vs. $\log[\text{concentration}]$ at 30⁰C.

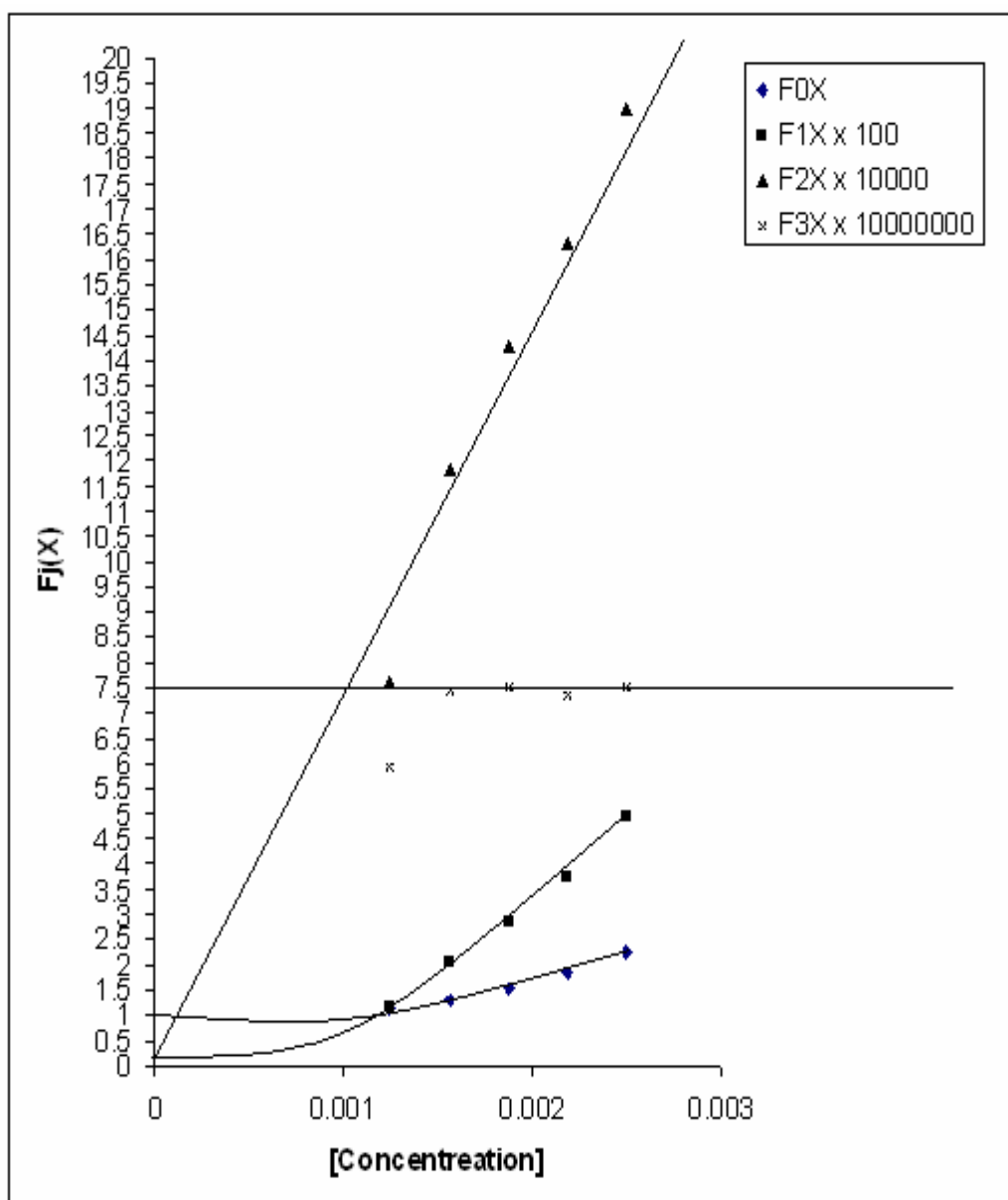


Fig. 7 Fj (X) values of Pb²⁺-Theophylline system at T = 20 °C

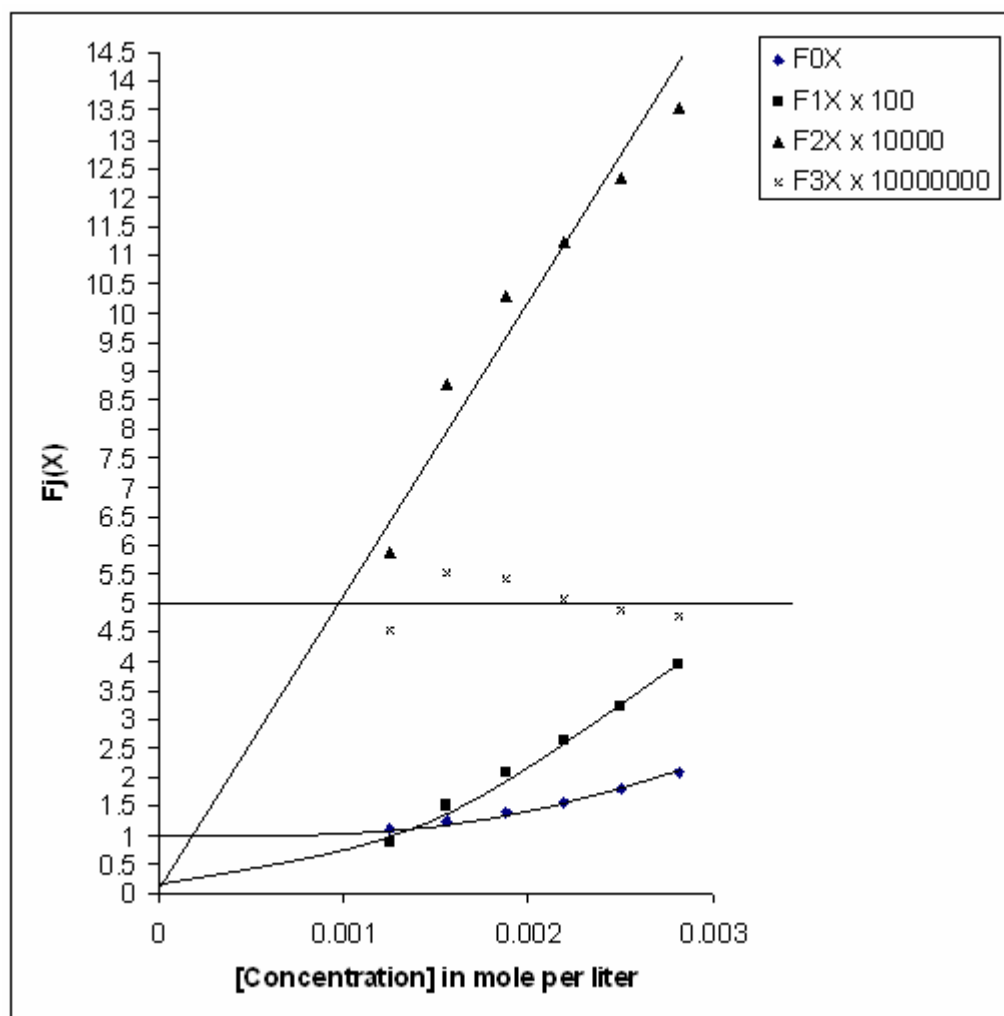


Fig. 8 $F_j(X)$ values of Pb^{2+} -Theophylline system at $T = 30\text{ }^\circ\text{C}$

Thermodynamic parameters

The thermodynamic parameters²⁸⁻²⁹ such as free energy change (ΔG), enthalpy change (ΔH), and entropy change (ΔS) of interaction are important to interpret the binding mode of metal-ligand complex.³⁰ The kind of complex species that can be measured with a dropping mercury electrode depends on thermodynamic aspect.³¹ Experiments were carried out at $20\text{ }^\circ\text{C}$ and $30\text{ }^\circ\text{C}$, since Theophylline does not undergo any gross structural change in this temperature range. The values of thermodynamic parameters of the complexes are given in Table 4.

In Table 4, it can be seen that the negative value for ΔG indicates the spontaneity of the binding of Theophylline with Pb^{2+} . The negative value for ΔG is

increases when we going to 1:1 to 1:3 complexes it shows that deriving tendency of complexation reaction increases from left to right and reaction tend to proceed more spontaneously.³² The negative value of ΔH suggests that Pb^{2+} -Theophylline system is exothermic i.e. in stepwise replacement of solvent molecule by ligand, more heat is released ongoing from 1:1 to 1:3 complex.³³ It means greater the amount of heat released in reaction, more stable are the reaction products. The negative value of ΔS in 1:1 and 1:2 ratios corresponds to a more ordered activated complex and this implies a small value of the steric factor. Positive value of entropy in ratio 1:3 reveals the formation of comparatively disordered complex.³⁴

Table -4: Thermodynamic parameters of Pb²⁺-Theophylline system at 20 °C and 30 °C.

System	Ratio	Thermodynamic parameters		
		ΔG	ΔH	ΔS
Pb(THP) ⁺²	1:1	-07298.92	-21237.90	-47.57
Pb(THP) ₂ ⁺²	1:2	-18519.10	-23740.60	-17.82
Pb(THP) ₃ ⁺²	1:3	-44180.00	-29933.10	48.62

Conclusion

It is clear from the study that the $E_{1/2}$ becomes more negative on increasing the concentration of Theophylline to Pb²⁺, which confirms complex formation. Pb²⁺ formed 1:1, 1:2 and 1: 3 complexes. The values of their stability constants have varied from 1.30 to 7.88. The stability constants (log β) and thermodynamic parameters such as free energy change (ΔG), enthalpy change (ΔH) and entropy change (ΔS)

of Pb²⁺ complexes with Theophylline were determined by employing the polarographic technique in (0.1M) Acetate buffer at pH- 5 at 20 °C and 30 °C.

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