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ELECTROCHEMICAL AND PHARMACOLOGICAL ANALYSIS OF CU-ATROPINE COMPLEX

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ABSTRACT: The Cu-Atropine complex may have potential applications in medicinal chemistry, as atropine is used in the treatment of certain medical conditions such as bradycardia and as a pre-anesthetic to decrease salivation. Additionally, the complexation of atropine with copper could potentially enhance its therapeutic effects or alter its pharmacokinetic properties. In the present study, the drug has been modified by complex formation with absolute methanol and concentrated sulphuric acid following standard procedures to increase its potency. IR spectra of Cu- atropine complex has taken. The analytical data indicates that a complex form of the drug, Cu-Atropine, is formed in a 1:1 ratio. To study the interaction between drugs and metal complexes, differential pulse polarography (DPP) has been used. These techniques are simple and cost-effective, making them suitable for qualitative and quantitative determination of active drug compounds. In a pharmacological study, modified atropine showed more potency compared to its parent drug.

INTRODUCTION: In the modern age, an analytical chemists solve their chemical analysis problems quantitatively and qualitatively by making use of some instrumentation techniques, like polarography, pH metering, spectroscopy *etc*. Past three decades have witnessed a wider use of electroanalytical techniques for the study of metal complexes in solution. For metal ligand system it is possible to determine the degree of formation, distribution and stability constants of all species present.

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Polarography, finds an extensive use in the determination of various organic and inorganic depolarizers present even in micro to ultra micro quantity. For a current voltage curve, if the specific rate of the electrochemical reaction is very high, so that the current is controlled essentially by diffusion process, the calculation of the shape of the current-voltage curves is relatively very easy and such process is termed as the reversible electrode process.

In the last two-three decades, the technique has found increasing application as a means of identifying the stoichiometry and formation constants of coordination compounds. Looking at the usefulness of polarographic methods in the analysis of organic compounds, it has been used to study the chemistry of atropine (in the study of adsorption, complex formation, inhibition of chain

oxidations, and the mechanism of organic reactions).

EXPERIMENTAL: All the chemicals used were of Himedia/BDH/CDH grade. The sulphate of Cu^{2+} was used. Double distilled water was used to prepare all the solutions. Stock solution of 1M Borate buffer and .01M Atropine was prepared in double distilled water and alcohol.

Experimental sets were prepared by keeping overall metal ion and supporting electrolyte (borate buffer) concentrations fixed at 1.0mM and 1.0M respectively. The pH of the solution was adjusted to 8.2 ±0.1. The necessary amount of boric acid and sodium Hydroxide solution was used to adjust the pH of test solutions. The experimental set was prepared by taking 1ml of sample solution and 10ml of borate buffer as supporting electrolyte in a polarographic cell and the total volume was made is 50ml with distilled water. The pH of the test solution was adjusted to 8.2±0.1.

RESULTS AND DISCUSSION: Atropine and its complexes gave well-defined cathodic reduction wave at pH = 8.2±0.1 in 1M Borate buffer. The plots of i_d vs $\sqrt{h_{corr}}$ yielded straight lines in each case, passing through the origin confirming the diffusion controlled nature of the reduction process.

Effect of Ligand Concentration:-On increasing the ligand concentration in each set and subjecting these experimental set to polarography. It was observed that the half wave potential shifted to more electronegative value. The plot of change in half wave potential with logarithm of change in ligand concentration yielded a straight line, suggesting the formation of single complex species in case of Cu(II)-Atropine system, **Fig. 2**. Lingane's treatment of the observed polarographic data in case of Cu(II)-Atropine system, revealed the stoichiometry and formation constants of the complexes formed. The results have been tabulated **Table 1**.

TABLE 1: FORMATION CONSTANTS OF ATROPINE COMPLEXES

Complex	Stoichiometry	Formation Constant log β_1
Cu-(II)-Atropine	1:1	5.85

TABLE 2: POLAROGRAPHIC DATA ON CU(II) – ATROPINE COMPLEX SYSTEM. Cu(II)=1.0 mM, 1.0 M Borate buffer pH = 8.2±0.1,

Concentration of ligand	log Cx	$E_{1/2}$
0.0000	-	-1.37
0.0005	-3.301	-1.52
0.0010	-3.000	-1.537
0.0020	-2.698	-1.551
0.0030	-2.522	-1.568
0.0040	-2.397	-1.573

log β_1= 8.40

Polarograms of Cu(II)-Atropine Complex:

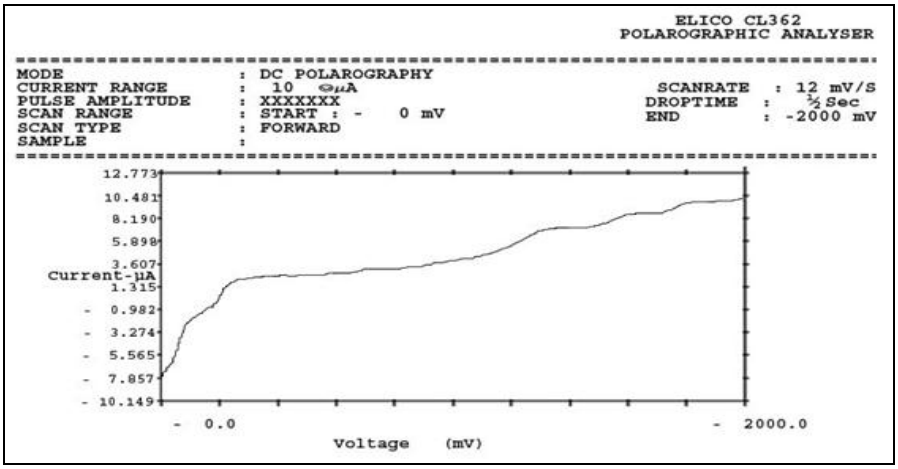


FIG. 1A: DIRECT CURRENT POLAROGRAM OF Cu(II)-ATROPINE COMPLEX IN BORATE BUFFER (0.2M) AT pH 8.2±0.1.

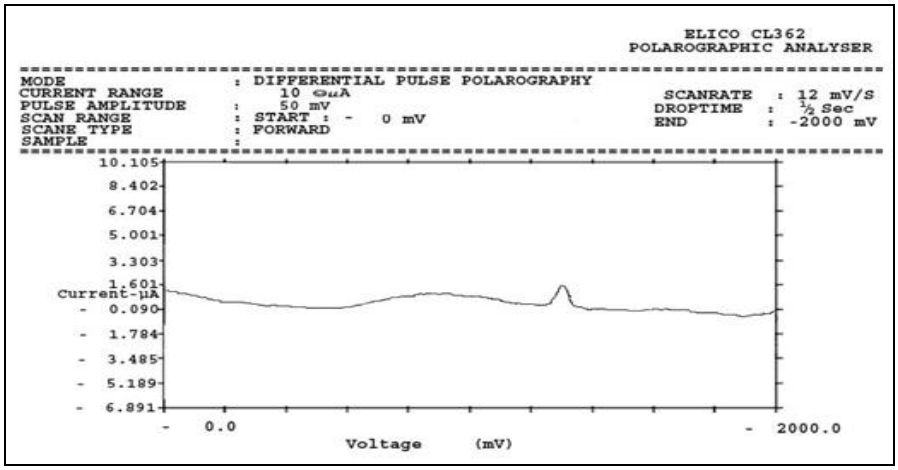


FIG. 1B: DIFFERENTIAL PULSE POLAROGRAM OF CU(II)- ATROPINE COMPLEX IN BORATE BUFFER (0.2M) AT pH 8.2±0.1.

Plot of $E_{1/2}$ vs log Cx:

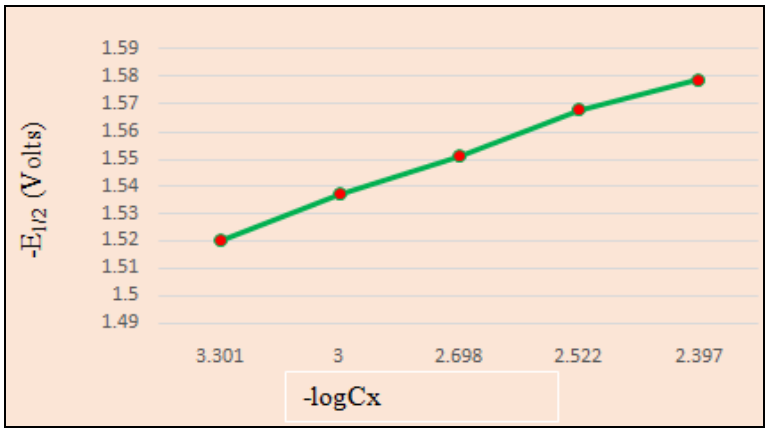
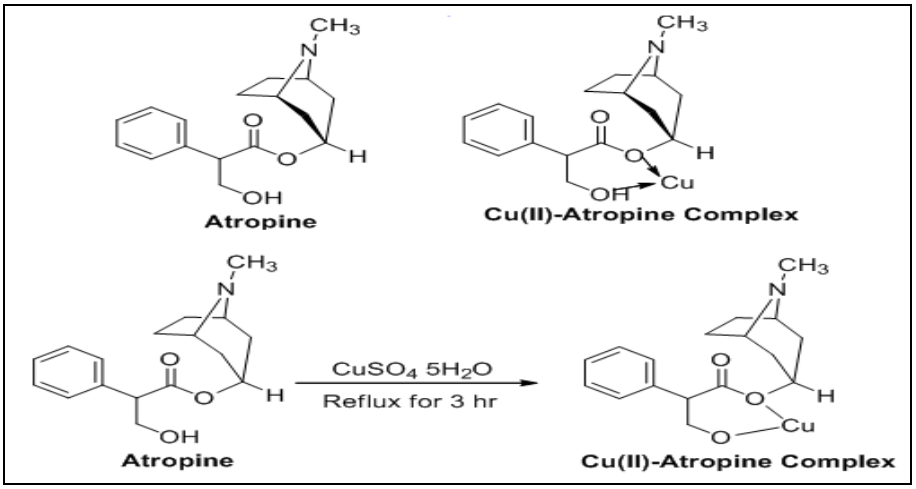


FIG. 2: CU(II)-ATROPINE COMPLEX

IR Spectral Analysis of Cu(II)-Atropine Complex: On comparing the IR spectra of atropine and its Cu(II) complex, it was observe that the band at 1730 cm^{-1} due to C=O group in the spectrum of pure drug disappeared in the spectrum of its Cu(II) complex and also the sharp –OH signal at 3608 cm^{-1} observed in atropine is shifted to 3650 cm^{-1} in the spectrum of Cu(II)-atropine complex, which confirms involvement of C=O and –OH in the complexation of the drug with Cu(II). Thus on the basis of polarographic and IR studies a tentative structure to 1:1, Cu(II)-atropine complex may be as under.



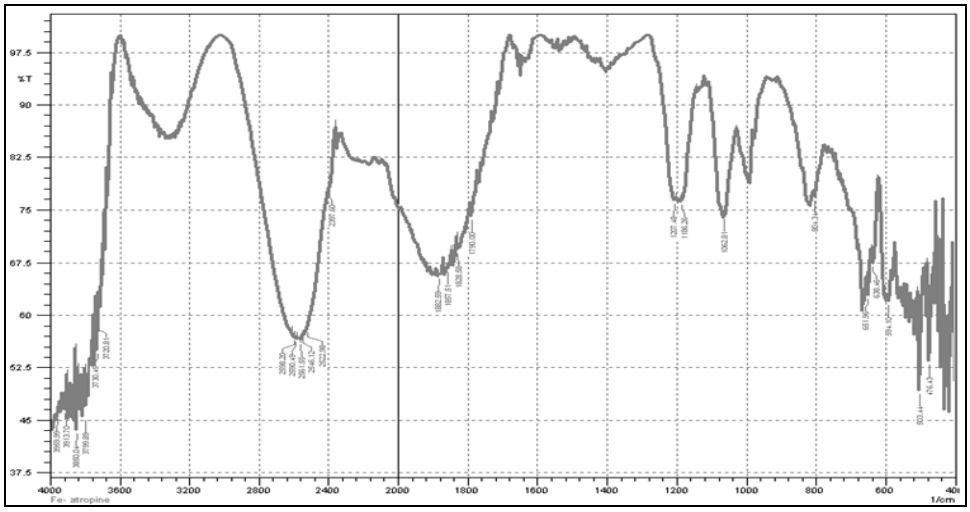


FIG. 3: IR SPECTRA OF CU- ATROPINE COMPLEX

Pharmacological Experiments: A rabbit was placed in a Rabbit holder (box) keeping the head out side. The size of the rabbit pupil of both eyes was observed. The effect of light reflex of the rabbit's eye to and fro was observed. The corneal reflex was examined by touching a side of the cornea with a cotton piece. A few drops of atropine were instilled in the conjunctiva (4-6 times) over a period of 8-10 minutes in the right eye of the rabbit. The left eye of the rabbit served as control. The pupillary size was recorded after 10 minutes of drug instillation and the data was tabulated. The experiment was repeated with atropine complexes. **Table 3** shows that Cu(II)-Atropine complex is more potency anesthetic drug of the two complexes under study.

TABLE 3: EFFECT OF ATROPINE AND ITS COMPLEXES CU (II) INSTILLATION ON THE PUPILLARY SIZE OF EXPERIMENTAL RABBIT

S. no.	Time interval in (minutes)	Control	Standard drug Atropine	Complex with Cu
1.	Initial	.7cm	.7cm	.7cm
2.	After 10 minutes	.7cm	.8cm	.8cm
3.	20 minutes	.7cm	.9cm	.9cm
4.	30 minutes	.7cm	1.3cm	1.4cm
5.	40 minutes	.7cm	1.0cm	1.6cm
6.	50 minutes	.7cm	.9cm	1.0cm
7.	60 minutes	.7cm	.8cm	.9cm
8.	70 minutes	.7cm	.7cm	.8cm
9.	80 minutes	.7cm	.7cm	.7cm
10.	90 minutes	.7cm	.7cm	.7cm

CONCLUSION: The observed analytical data clearly speaks the formation of complex form of the drug (Cu-Atropine) in 1:1 ratio in each case.

Results of pharmacological study on the anesthetic activities of above systems showed that the modified drug complex is found to be more potent than parent atropine drug.

On the basis of reported data and ongoing discussion it could be concluded that the proposed electroanalytical methods provide accurate and precise data on trace analysis of atropine and its modified forms. The techniques are best suited because of simplicity as well as economics of the procedure for the simultaneous qualitative and quantitative determination of traces of active principles of drugs and may be recommended for their possible use in medicinal industries. The author also recommends the modified drugs to the therapeutic experts to ascertain the possible use of the modified forms as more potent anesthetics in lieu of parent atropine drug.

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CONFLICTS OF INTEREST: The authors declare that there are no conflicts of interest.

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