

Polarography and Pharmacological Study of Atropine Fe Complex for Its Increased Anesthetic Potency

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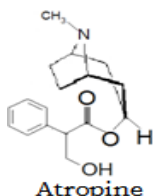
Abstract Atropine is an anesthetic drug used in anesthesia. Though the drug is being used as anesthetic but its potency may be increased by modifying the drug by way of molecular modification, in the present study, the drug has been modified by its complex formation with Fe. The drug-metal compound interaction has been studied using differential pulse polarography (DPP). The results of pharmacological study indicated increased potency of complex of atropine and metal as compared to the parent drug that is atropine.

Keywords: atropine, DCP, DPP, anesthetic drug

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1. Introduction

Atropine is a tropane alkaloid extracted from deadly nightshade (*Atropa belladonna*), jimsonweed (*Datura stramonium*), mandrake (*Mandragora officinarum*) and other plants of the family Solanaceae. It is a competitive antagonist of muscarinic cholinergic receptors. It is absorbed from the gastro-intestinal tract, and is excreted in the urine. It is a secondary metabolite of plants and serves as a drug with a wide variety of effects. It is a competitive antagonist for the muscarinic acetylcholine receptor. It is classified as an anticholinergic drug. Being potentially deadly, it derives its name from Atropos, one of the three Fates which, according to Greek mythology, chose how a person was to die. Atropine is a *core* medicine in the World Health Organization's "Essential Drugs List", which is a list of minimum medical needs for a basic health care system. Atropine undergoes hepatic metabolism and has a plasma half-life of 2-3 hours. Atropine ampoules should be stored away from light and never be frozen. Atropine is found in many members of the Solanaceae family. The most commonly-found sources are *Atropa belladonna*, *Datura innoxia*, *D. metel*, and *D. stramonium*. Other sources include members of the *Brugmansia* and *Hyoscyamus* genera. The *Nicotiana* genus (including the tobacco plant, *N. tabacum*) is also found in the Solanaceae family, but these plants do not contain atropine or other tropane alkaloids.



The IUPAC name of Atropine is benzeneacetic acid, alpha-(hydroxymethyl)-8-methyl- 8-azabicyclo{3.2.1}oct-3-yl ester endo -(±)-, its structure is depicted above. Atropine sublimates under high vacuum at 93 to 110 °C and has a melting point of 114 to 116°C. Atropine has low solubility in water (approximately 1g atropine in 455ml water and 1 g atropine in 90ml water at 80°C). One gram is soluble in 2 ml alcohol, 2.5ml alcohol at 60°C, 27 ml of glycerol, 25ml ether and 1 ml chloroform. Atropine is optically inactive. There is evidence that Intralipid, a commonly available intravenous lipid emulsion, can be effective in treating severe cardiotoxicity secondary to local anesthetic overdose, including human case reports of successful use in this way ('lipid rescue') [1,2,3,4,5].

A drug obtained from belladonna that is administered via injection, eye drops, or in oral form to relax muscles by inhibiting nerve responses. Used to dilate the pupils and as an antispasmodic. atropine, alkaloid drug derived from belladonna and other plants of the family *Solanaceae* (*nightshade family*). Available either as the tincture or extract of *belladonna*, or as the pure substance atropine sulfate, it is a depressant of the parasympathetic nervous system. It has some chemical similarity to the body substance acetylcholine and interferes with nerve impulses transmitted by that substance. Atropine produces rapid heart rate, dilated pupils, dry skin, and anesthetizes the nerve endings in the skin. Because it relaxes smooth muscle and suppresses gland and mucous secretions, it has been used to treat peptic ulcer by reducing the production of stomach acid. Atropine is given before general anesthesia to keep the air passages clear and is an ingredient in various preparations for symptomatic relief of colds and asthma. It also acts as an antidote in poisoning from such agents as mushrooms, morphine, prussic acid, and nerve gas, but overdosage causes delirium, convulsions, and coma. A related alkaloid, scopolamine, is used mainly as a sedative.

Atropine is a racemic mixture of D-hyoscyamine and L-hyoscyamine, with most of its physiological effects due to L-hyoscyamine. Its pharmacological effects are due to binding to muscarinic acetylcholine receptors. It is an antimuscarinic agent.

The most common atropine compound used in medicine is atropine sulfate ($C_{17}H_{23}N$ HYPERLINK "/wiki/Oxygen"O₃)₂·H₂SO₄·H₂O, the full chemical name is 1 α H, 5 α H-Tropan-3- α ol (\pm)-tropate(ester), sulfate monohydrate.

By the first century A.D., Dioscorides recognized wine of mandrake as an anaesthetic for treatment of pain or sleeplessness, to be given prior to surgery or cautery [6]. Atropine extracts from the Egyptian henbane were used by Cleopatra in the last century B.C. to dilate her pupils, in the hope that she would appear more alluring. In the Renaissance, women used the juice of the berries of *Atropa belladonna* to enlarge the pupils of their eyes, for cosmetic reasons; "bella donna" is Italian for "beautiful lady" [7]. This practice resumed briefly in the late nineteenth- and early twentieth-century in Paris.

2. Experimental

Polarograms of Fe(II)-Atropine complex

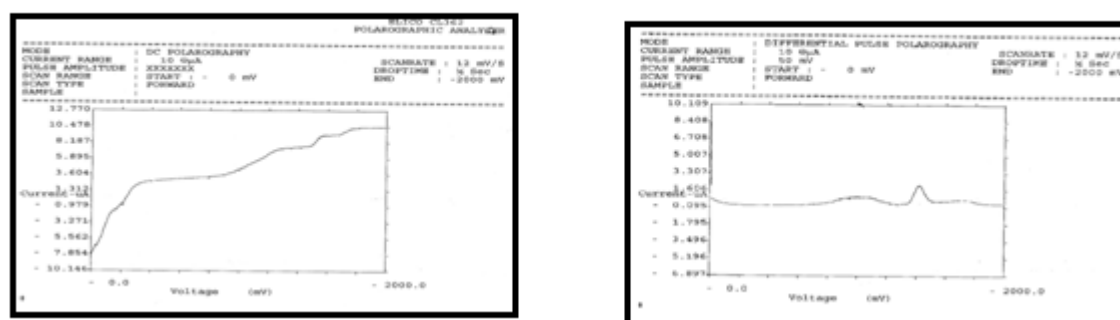


Figure 1. Direct current Polarogram and Differential pulse Polarogram of Fe(II)-atropine complex in borate buffer (0.2M) at pH 8.2 \pm 0.1

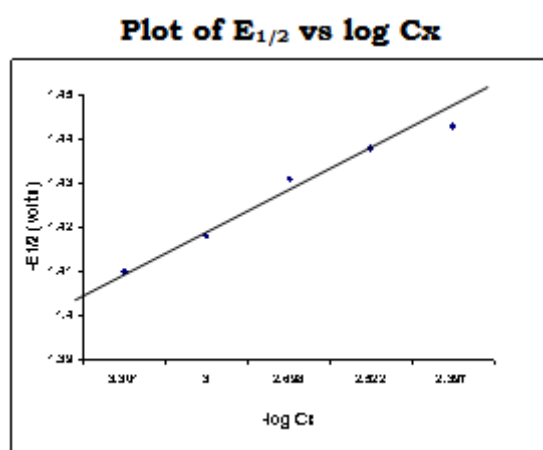


Figure 2. Fe(II)-Atropine Complex

4. IR Spectral Analysis of Fe(II)-Atropine Complex

On comparing the IR spectra of atropine and its Fe(II) complex, it was observed that the band at 1730 cm⁻¹ due to

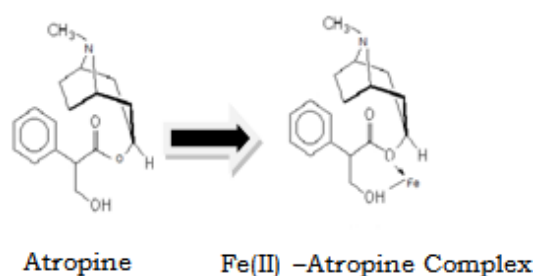
All the chemical used were of Himedia/BDH/CDH grade. The sulphates of Fe²⁺ was used. Double distilled water was used to prepare all the solutions. Stock solution of 1M Borate buffer and .01M Atropine was prepared in double distilled water and alcohol.

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 \pm 0.1. Necessary amount of boric acid and sodium Hydroxide solution was used to adjust the pH of test solutions. 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 \pm 0.1.

3. Results and Discussion

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

C=O group in the spectrum of pure drug disappeared in the spectrum of its Fe(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 Fe(II)-atropine complex, which confirms involvement of C=O and -OH in the complexation of the drug with Fe(II). Thus on the basis of polarographic and IR studies a tentative structure to 1:1, Fe(II)-atropine complex may be as under:



5. 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. The table shows that Fe(II)-Atropine complex is more potency anesthetic drug of the authentic drug under study.

Table Effect of Atropine and its complexes Fe (II) instillation on the pupillary size of experimental rabbit

S. No.	Time interval in (minutes)	Control	Standard drug Atropine	Complex with Fe
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

6. Conclusion

The observed analytical data clearly speaks the formation of complex of the drug in 1:1 ratio in each case.

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

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