

Synthesis, Characterization and Toxicology Studies of the Copper (II) Complex of Sodium Barbitone

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Abstract

Complexation of sodium barbitone with Cu(II) has been studied. The complex formed was characterized using physical and spectroscopy studies. In the structural characterized complex, Infrared spectra suggest bidentate coordination of the ligand through one carbonyl oxygen, NaO⁺ oxygen and two carbonyl oxygen of acetate. Electronic spectra revealed octahedral geometry of the complex. Toxicology study was carried out by investigating the effect of the ligand and its complex on cardiac muscle, kidney, liver and lung of Sprague dawly rats.

Keywords: Sodium barbitone, metal complex, toxicology study, Sprague dawly rats, Cardial muscle

1. Introduction

The coordination chemistry of metal with biologically active ligands has attracted enormous interest over the years. Barbituric acid derivatives exert important action on the central nervous system and recently have been found totally new biomedical applications in fields such as cancer and AIDS therapy¹. Barbiturates are also used as anesthetics and sleeping agents, and are used for the treatment of anxiety, epilepsy and other psychiatric disorder, and possess effect on the motor and sensory functions². The relationship between structure and drug action of barbiturates was investigated and the structures, physical and chemical properties and pharmacological activity of a large amount of barbiturates were reviewed by *Doran*³. In this report, the Cu²⁺ complex of sodium barbitone has been synthesized and toxicology studies of the ligand and its complex have been carried out on Sprague dawly rats .

2. Materials and Method

Sodium barbitone is the ligand used while the metal salt used is Cu(CH₃COO)₂.H₂O The reagents and solvents used were of analytical grade; they were used without further purification. The infrared spectra of the complex were recorded as KBr discs on a pye-unicam SP3-300 spectrophotometer in the range 500-4000cm⁻¹. The electronic spectra of the sodium barbitone and its complex in methanol were recorded on a Lambda 3B UV/visible spectrophotometer.

2.1 Preparation of [Cu(Na-barb)₂(CH₃COO)₂]

1.9g of metal acetate Cu(CH₃COO)₂.H₂O in 50ml of distilled was added to clear colourless solution 4g of sodium barbitone in 30ml of distilled water. The resulting solution was stirred for an hour after which the precipitates formed were filtered, washed with methanol and dried over CaCl₂ in dessicator.

2.2 Toxicology studies

The sodium barbitone and its complex were dissolved in distilled water and administered orally to the male and female Sprague dawly rats in proportion to their body weight by means of disposable feeding needles. The control groups were fed with only feed and distilled water. The test solutions were prepared based on therapeutic dose as follows: Sodium barbitone – 0.5ml mg, per 50g body weight, once daily for two weeks and after which they were sacrificed. The toxicity was measured by comparing the weight taken of the experimental rats with that of the control rat⁴, and the physical state of cardiac muscle, kidney, lung and liver of the experimental rat with that of the control rat

3. Result and Discussion

The complex was characterized on the basis of metal analysis, melting point, Infrared and electronic spectra. Metal analysis along with other data was presented in the table one. The infrared spectra and electronic spectra are given in Table 2 and Table 3.

In the spectrum of free sodium barbitone, the absorption at 1565cm⁻¹, 1267cm⁻¹ and 3437cm⁻¹ were assigned to ν_{C=O} of ketone, ν_{C-O} and ν_{N-H} of amine. The bands 1565cm⁻¹ and 1267cm⁻¹ experienced lower shifts in the spectra of the metal complex with the appearance of the band 1658cm⁻¹ suggesting coordination through

carbonyl oxygen of acetate to the metal. The band that appeared at 538 cm^{-1} and 496 cm^{-1} were tentatively assigned to vibration of M-O=C and M-C-O respectively which gave the evidence of coordinating through the groups.

The electronic spectra data for the ligand and its metal complex are shown in Table 3. The two bands in the spectrum of sodium barbitone are attributed to $\pi \rightarrow \pi^*$ intraligand transition⁵. The spectrum of $\text{Cu}(\text{Na-barb})_2(\text{CH}_3\text{COO})_2$ showed absorption band at 11364 cm^{-1} which is consistent with six coordinate octahedral geometry and is assigned to ${}^2\text{E}_g \rightarrow {}^2\text{T}_{2g}$ transitions^{6,7}.

3.1 Result of Toxicology study

From Table 4, it is shown that the administration of sodium barbitone and its metal complex on rat lead to decrease in the weight of the rats compare to control rat. The observed reduction in body weight caused by Sodium barbitone and its metal complexes suggests that the drugs may inhibit some metabolic processes (e.g. the synthesis of DNA), which are needed for normal cell growth and proliferation⁸. However, Figure 1-4 show effects of sodium barbitone and its Cu^{2+} complex on cardiac muscle, lung, liver, and kidney of rats. Therefore, both sodium barbitone and its complex are considered to be toxic.

5. Conclusion

The synthesized metal(II) complexes of sodium barbitone is blue in colour. Infrared spectra of complexes of sodium barbitone showed that sodium barbitone coordinated in bidentate fashion through one carbonyl and Na^+O^- oxygen atoms together with carbonyl oxygen of acetate to give tentatively octahedral geometry for Cu(II). From the toxicological studies of barbitone and its complex in rats, the result showed that both sodium barbitone and its complex affect the cardiac muscle, lung, liver and kidney. Therefore, prolonged administration of sodium barbitone and its complexes should be avoided.

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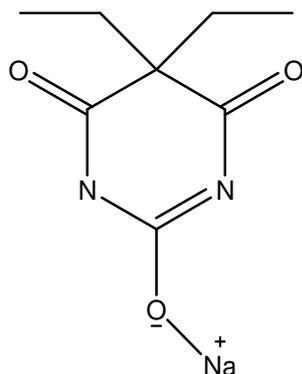


Fig.1 Structure of sodium barbitone

Table 1: Physical and Analytical measurements

| Complex | Colour | % yield | Melting point °C | % metal (Cal) found |
|---|--------|---------|------------------|---------------------|
| [Cu(Na-barb) ₂ (CH ₃ COO) ₂].H ₂ O | Blue | 48 | 300 | 15.83 |

Table 2: Infrared spectra data(cm⁻¹) for sodiumbarbitone and its metal complex

| Sodiumbarbitone | Cu(Na-barb) ₂ (CH ₃ COO) ₂ | Tentative assignment |
|-----------------|---|---------------------------------|
| 3437m | - | ν _{N-H} str. of amine |
| 1565s | 1554m | ν _{C=O} str. of ketone |
| 1266s | 1256w | ν _{C-O} str. |
| - | 1658w | ν _{C=O} str. of |
| - | 538s | M-O=C |
| - | 496m | M-C-O |

Key: s=strong, m=medium, w=weak

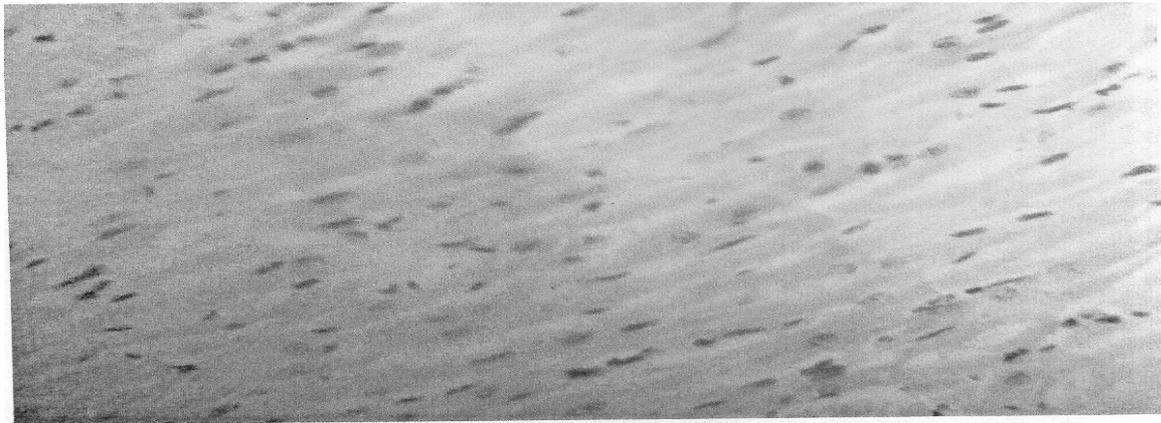
Table 3: Electronic spectra data for the compounds

| Compounds | λ(cm ⁻¹)/(ε(dm ³ mol ⁻¹ cm ⁻¹)) | Assignment | Tentative geometry |
|---|---|--|--------------------|
| Na-barb | 46728 (1591) | π→π* | |
| | 43103 (1542) | π→π* | |
| Cu(Na-barb) ₂ (CH ₃ COO) ₂ | 11364(64) | ² E _g → ² T _{2g} | Octahedral |

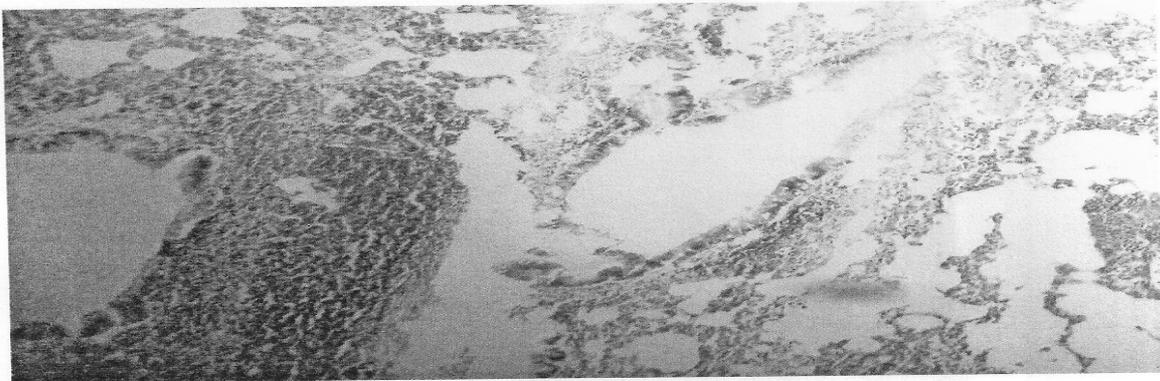
Table 4 :Toxicity studies on Sprague dawly rats

| Rats | Initial Weights(g) | Samples | Volume Administered(ml) | Final weights(g) after 2 weeks | Weight differences(g) |
|------|--------------------|---------|-------------------------|--------------------------------|-----------------------|
| A | 102.3 | D | 5.1 | 93.3 | -9 |
| B | 76.5 | E | 3.8 | 65.5 | -11 |
| C | 47.0 | - | 52.0 | +5 | |

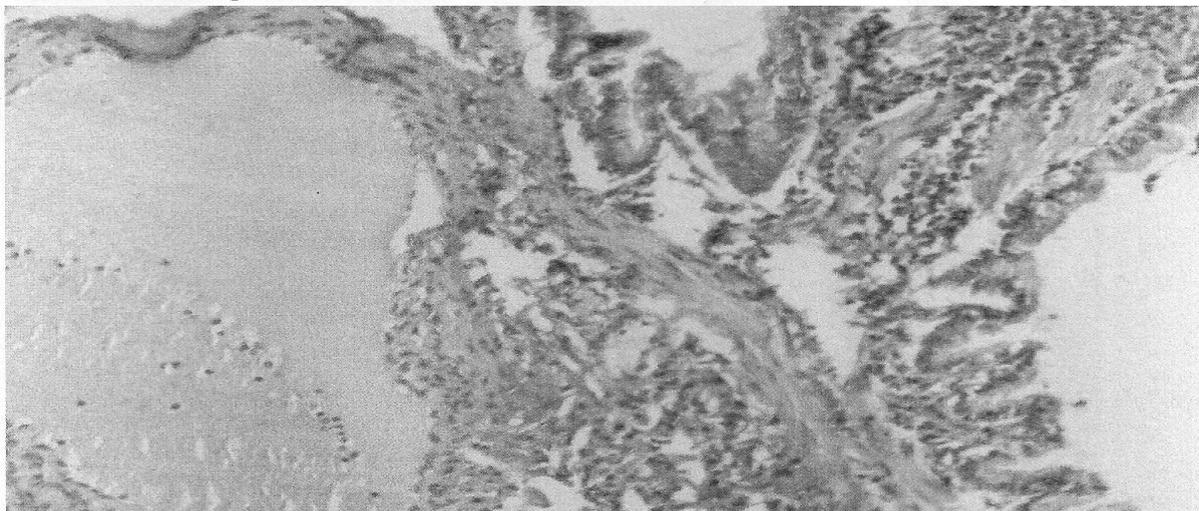
Key: - = indicates sample not added; D=sodium barbitone ; E= Cu(Na-barb)₂(CH₃COOH)₂



Photomicrograph of cardiac muscle of rat (CONTROL) - The cells are normal as compared to the normal cells of Atlas of normal histology.

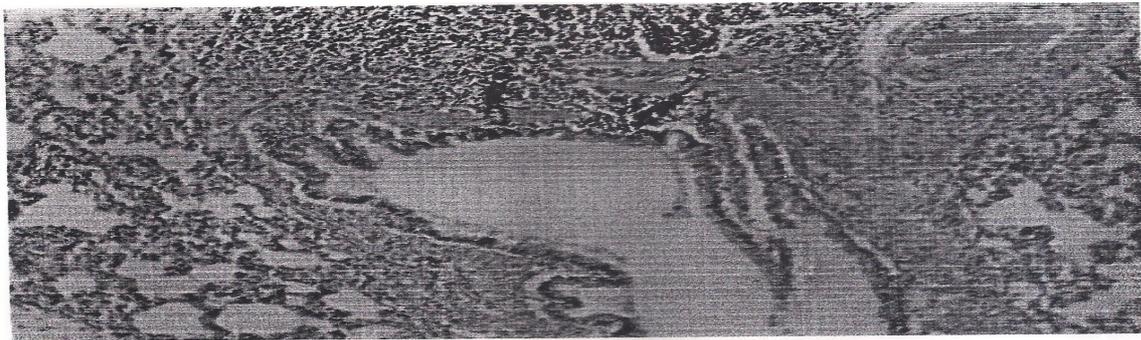


Photomicrograph of cardiac muscle of rat inoculated with sodium barbitone – There is cerum and enlargement of the cardiac muscle.

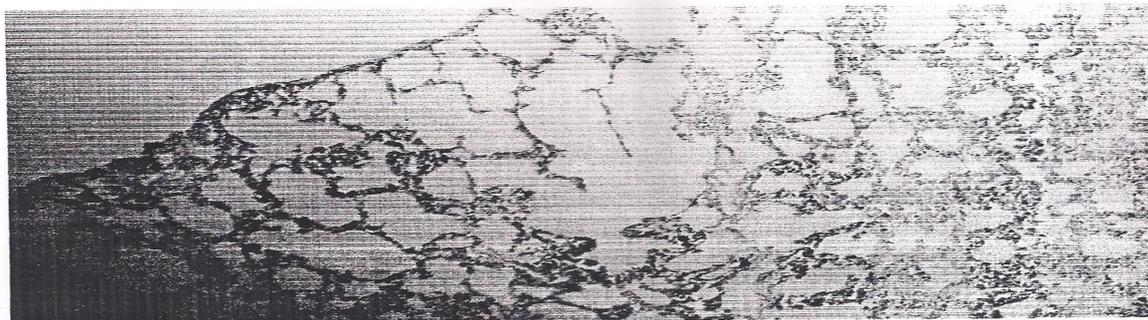


Photomicrograph of cardiac muscle of rat inoculated with copper barbitone – There is haemorrhage.

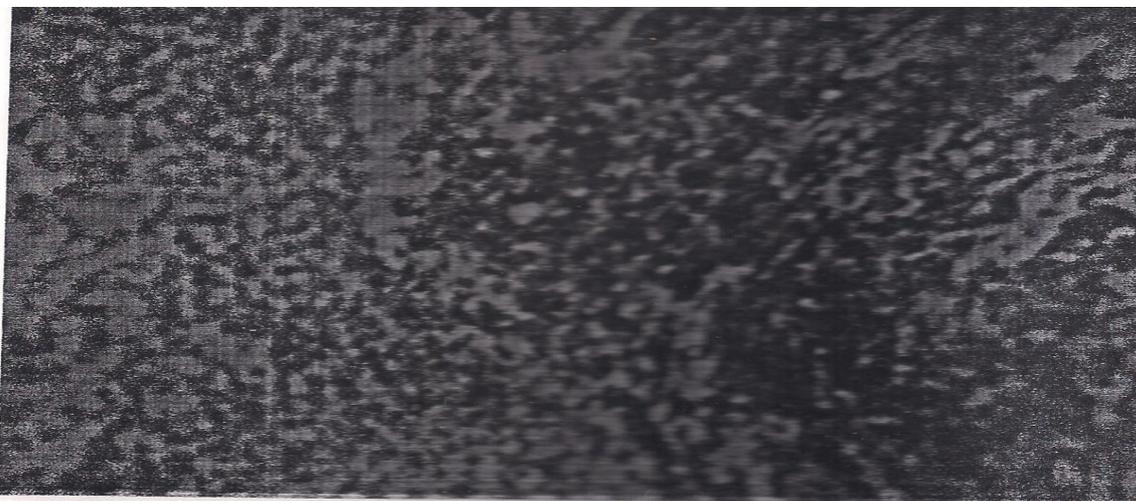
Figure 2



Photomicrography of lungs (CONTROL) – The cells are normal as compared to the normal cells of Atlas of normal histology.

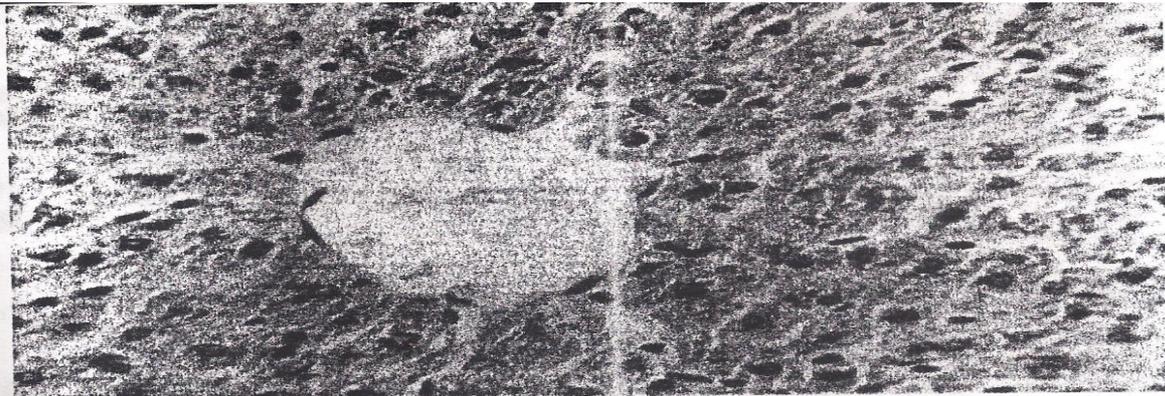


Photomicrography of lungs of rat inoculated with sodium barbitone – Lysis of the cell, breakages of the alveoli, the epithelial lining, the respiratory bronchi are also affected as it is indicated on the micrographs.

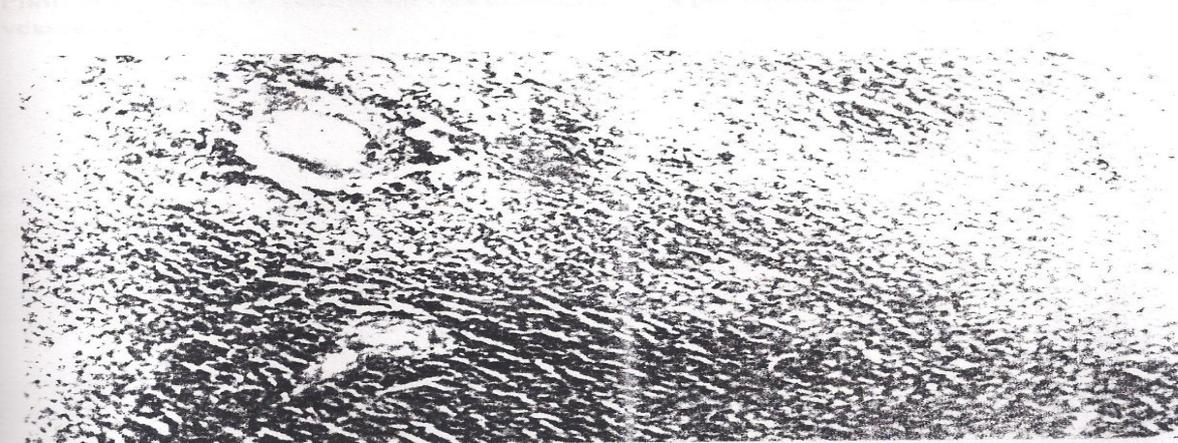


**Photomicrograph of lungs of rat inoculated with copper barbitone
Haemorrhage/cerum occurred.**

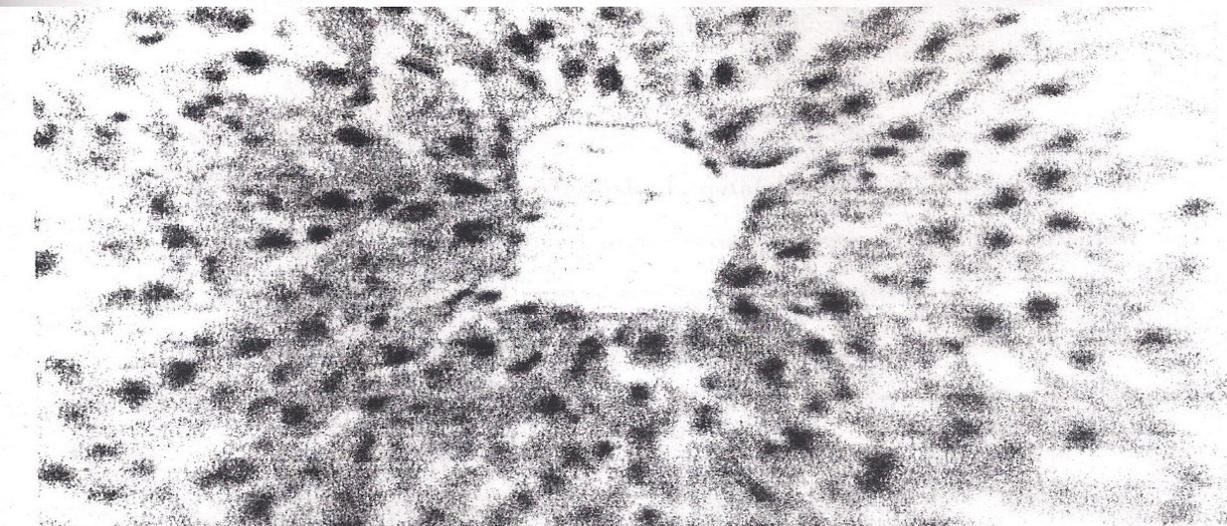
Figure 3



Photomicrograph of liver (CONTROL) – The cells are normal as compared to the normal cells of Atlas of normal histology.

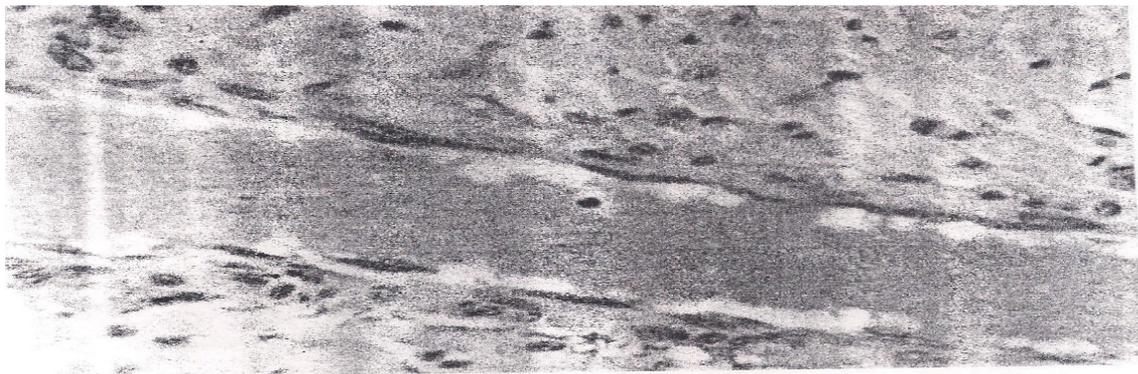


Photomicrograph of liver of rat inoculated with sodium barbitone – Cerum hepatitis is also recorded as well as odematus.



Photomicrograph of liver of rat inoculated with copper barbitone – Serum of the blood vessels and vein.

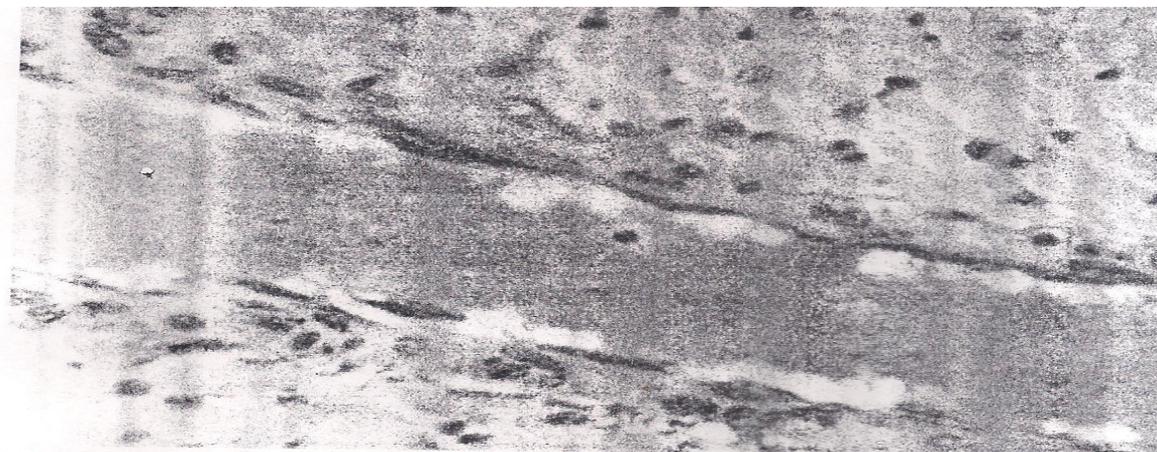
Figure 4



Photomicrograph of kidney of rat (CONTROL) – The cells are normal as compared to the normal cells of Atlas of normal histology.



Photomicrograph of kidney of rat inoculated with Barbitone sodium – There is cerum hepatitis and enlargement of the various veins of the tissue.



Photomicrograph of kidney of rat inoculated with Copper Barbitone – Cerum linings of lymphoid tissues edematus (enlargement of the cells).

Figure-5

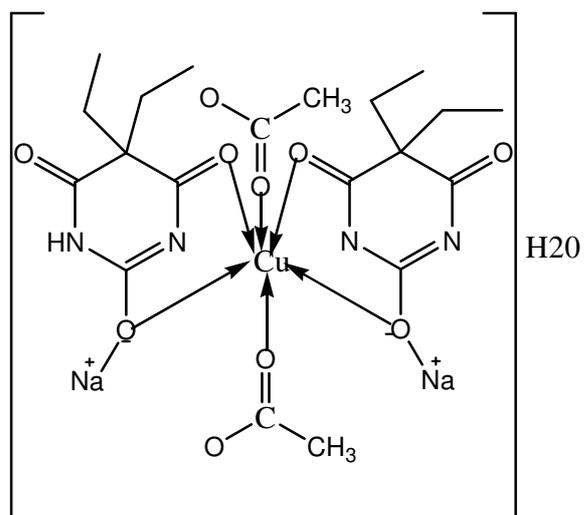


Fig 6 : Proposed structure of $[Cu(Na\text{-barb})_2(CH_3COO)_2]H_2O$

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