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SYNTHESIS AND TOXICOLOGICAL STUDIES OF COBALT (II) COMPLEXES OF ASPIRIN AND PARACETAMOL.

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ABSTRACT

Co(II) complexes of Aspirin and Paracetamol have been synthesized and the effect of administration of the novel complexes on activities of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in the liver of albino rats, have been evaluated. The result showed that there are significant difference ($P > 0.05$) between serum of the rats administered with the control and the synthetic compounds. It is therefore concluded that the synthetic compounds are non-toxic to the animals cellular system.

Keywords: Synthesis Toxicological evaluation studies Aspirin Paracetamol complexes.

INTRODUCTION

Metal ions play a vital roles in a vast number of widely differing biological processes. They have a considerable effect in biological processes and depending on their concentrations, they may either contribute towards the health of the organism or causes toxicity (1).

Toxicological studies of chemotherapeutic agents are usually carried out by examining some organs of the sacrificed experimental animals. Akanji and Nlumanze (2) carried out a toxicological study on the effect of repeated administration of suramin on the level of ALP activities in some rate tissues and organs investigated. The homogenate of the heart, kidney, liver, small itnetine and large intestines were analyzed for ALP activity by measuring the p-nitrophenol liberated from p-nitrophenyl

phosphate. However, in 2007, Obaleye and Lawal (3) reported the synthesis and antibacterial studies of some Aspirin and Paracetamol metal complexes. The complexes were found to have higher activities than the original Aspirin and Paracetamol.

As part of continuation of our studies on metal complexes of Aspirin and Paracetamol metal complexes, we have studied the toxicological studies of these metal complexes on Albino rats. We therefore reported the synthesis and toxicological studies Co(II) complexes of Aspirin and Paracetamol.

MATERIALS AND METHODS

Thirty white Albino rats (both sexes) weighing between 150-170 were obtained from the Biochemistry Department, University of Ilorin. The rats were fed for a week prior to their

usage. They were divided into five groups of six rat each. One of the groups served as the control. Other reagents used were of analytical grade and were prepared in all-glass distilled water.

Dose selection

The dosage level used was 5% w/v. The average weight of rats was 160g. 4.0g/550ml of Paracetamol per solvent and 2.4g/50ml of Aspirin were used. The solutions prepared were administered orally using syringe on a five hours intervals, three times daily for five days.

Preparation of tissue homogenates

The rats were sacrificed by anaesthetizing them in a glass jar containing cotton wool soaked in chloroform. The rats were quickly dissected. The blood sample was taken and the tissue required were removed and immersed in ice cold 0.25M sucrose solution. The homogenate of the liver was prepared by cutting a known weighted tissue with a clean scissors and homogenized with a leflon pestle. All operations were carried out at 0-4°C. The homogenase was stored in the freezer until it was needed.

Tissue dilution

Before the enzyme assay was carried out, the tissue homogenized was diluted. This was done by taking 1ml of the homogenate into 4ml of sucrose solution into different grouped test tubes.

Enzyme Assay

The tissue homogenates were all diluted in ratio 1:20 with saline water before the enzyme assay. All enzyme activity was determined using enzyme kits prepared by Randox laboratories limited (4).

Determination of Aspartate Aminotrasferase (AST)

Table 1: Results of Aspartate aminotransferase (AST)

Group	Serum	Liver	Kidney
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The homogenates were used based on the four groups of rats used for the toxicological studies. 1ml of homogenase was taken into 4ml of sucrose solution into different test tubes. 0.25ml of AST

buffer was added to 0.05ml of the homogenate. It was mixed and incubated for 30 minutes at 37°C 2,4-dinitrophenylhydrazine was added into a 0.25ml of the homogenate. It was mixed and allowed to stand for 20 minutes at 20-25°C. 2.5ml pf NaOH was added. The absorbance of the sample was taken 5 minutes later against a blank sample at a wavelength of 546 nm.

Calculation

The absorbance obtained for each sample was extrapolated from the standard graph by plotting absorbance against concentration to obtained the corresponding protein concentration.

$$\text{Protein concentration} = C * F$$

Where C=Concentration from the length
F = dilution factor

RESULTS AND DISCUSSION

The results of enzyme assay using Aspartate aminotransferase (AST) showed that there was no significance difference in the liver of the groups used compared with the control. It was concluded that the metal complexes are non-toxic. The results of the enzyme using alanine amino-transferase (ALT) showed that there was no significance difference in the livers of rats in the groups used compared with the control (5). Hence it was concluded that the synthetics complexes administration to the rats were non-toxic.

The results are presented in Tables 1 and 2 below

Control	12 ± 1.1	20 ± 2.3	25 ± 1.8
Aspirin	12 ±	25 ±	30 ± 1.2

	1.7	1.4	
Paracetamol	21 ± 2.2	27 ± 2.1	28 ± 2.5
Co (Asp) ₂ Cl ₂	26 ± 2.6	28 ± 2.0	30 ± 1.3
Co (Par) ₂ Cl ₂	25 ± 2.3	30 ± 1.8	37 ± 1.5

Table 2: Results of Alanine Aminotransferase (ALT)

Group	Serum	Liver	Kidney
Control	8 ± 1.0	14 ± 1.8	27 ± 2.6
Aspirin	16 ± 1.7	18 ± 2.1	31 ± 2.5
Paracetamol	19 ± 2.0	22 ± 2.0	32 ± 2.8
Co (Asp) ₂ Cl ₂	20 ± 2.3	24 ± 2.5	35 ± 3.0
Co (Par) ₂ Cl ₂	22 ± 2.5	26 ± 2.2	34 ± 2.0

4. Randox Laboratories Ltd, UK. Randox Enzyme assay manual: ACP, ALP, GOT, GTP (1997).

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CONCLUSION

The results of the effect of AST and ALT activity of the complexes of Aspirin and Paracetamol showed that they were non-toxic.

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