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Effects of Aqueous Extracts of *Cola millenii* K. Schum Seed on Toxicological Indices of White Male Albino Rats

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Abstract

The study investigated the acute toxicity and the effect of aqueous extracts of *C. millenii* seed on toxicological indices of wistar albino rats. A total of thirty (30) albino rats were used in this study. The rats were randomly divided into five groups, each group containing six (6) rats. The weights of the rats were between 100 - 300 g. Determination of LD_{50} was carried out by oral administration of 312.5, 625, 1250, 2500, 5000 mg of the *C. millenii* seed extracts per kilogram body weight of the rats for group 1, 2, 3, 4 and 5 respectively. Chronic toxicity test was also carried out. Group 1 served as control group, group 2, 3, 4 and 5 received 62.5, 125, 250 and 500 mg/kg of aqueous extracts of *C. millenii* respectively. The rats were sacrificed after twenty one days of oral administration of the extracts. Result indicated an LD_{50} of 1250 mg/kg. There were significant increases in the activities of alanine aminotransferase, aspartate aminotransferase and alkaline phosphate. The result suggests a dose dependent hepatotoxic effect of the aqueous seed extracts of *C. millenii* in wistar rats.

Keywords: *Cola milleni*; ALT; AST; ALP.

INTRODUCTION

There has been focus on the use of medicinal plants and their bioactive agents in drug design and development in recent decades which is the current trend in western world. Medicinal plants are plants with known medical applications as a result of characteristic phytochemicals that are competent alone or in synergy to prevent, heal or manage disease conditions [1].

Numerous reports on the drug effects of herbal medicines from all parts of the world are scattered in various literature [2]. Research contributions are also available on the chemical composition of some lesser-known tropical plants that may have long been used in traditional medicine [3]. The search for new therapeutic agents of plant origin in disease management is therefore a global concern. There is increasing need to explore plant materials for pharmacological and biochemical activities, with the aim of developing drugs and therapeutic agents [4]. Historically, they are many sources of new chemical substances with potential therapeutic effect apart from medicinal plants. It is believed that medicinal plants have been used in the prevention and/or management of many diseases such as cancer, convulsion, skin infections, hypertension, diabetes, sexually transmitted infections, and cardiovascular diseases among others with little or no side effect [1]. In view of these, medicinal plants offer opportunities for disease management, especially where current orthodox treatment methods have often been unsuccessful. Most times the medicinal chemical substances tend to present acute toxic effect, devastating side effects even sometimes future chronic side effects.

All medicinal plants including *Cola milleni* are toxic depending on the dosage administered, also, many therapeutic medications can be acutely toxic, but are beneficial when used at the appropriate concentrations.

Cola millenii is a tree plant with branches and edible fruits found in deciduous, closed and transition forest of SouthWestern Nigeria. It belongs to family of *Sterculiaceae.* It is commonly referred to as monkey kola in English, Obi-edun in Yoruba (Nigeria), mba utung-ita in Ibiobio (Nigeria) etc [5]. The plant is one of the most popular genera in the family of about 70 genera, totaling around 1,500 species of tropical trees and shrubs. The leaves, flowers, fruits and bark of the plant have been reported for use as a remedy for dysentery, diarrhoea, vomiting and cough [5,6].

In the work of Ubon *et al*. [5], the effect of ethanolic extracts of *C. millenii* seed on biochemical and toxicological indices of male wistar rats were reported. However, aqueous extracts of the seed are used in folk medicine as remedy for many disease conditions. We have therefore, investigated and reported the effect of aqueous

extracts of the *C. millenii* seed on toxicological indices in wistar albino rats.

(Odugbemi, 2006)

MATERIALS AND METHODS

Animals and treatment

A total number of 30 male wistar rats weighing 100g-300g were obtained from the Animal House of the Department of Chemical Sciences, Achievers University, Owo.

The animals were housed on individual steel cage, and were acclimatized for the period of two weeks before the commencement of the experiment. The animals were fed with pellet growers feed and with free access to clean drinking water. For LD_{50}, 30 male wistar rats were randomly divided into five groups of six per group. The animals were administered widely spread doses of 312.5mg/kg, 625mg/kg, 1250mg/kg, 2500mg/kg and 5000mg/kg body weight of *C. milleni* seed extract. The behaviors of the rat were examined for about 24 hours for signs of toxicity and the (LD_{50}) value was determined. For the Chronic toxicity test, 30 male wistar rats were divided randomly into five groups of six animals per group. Group 1 which served as control was administered with distilled water only, Group 2 to 5 received 62.5mg/kg, 125mg/kg, 250mg/kg and 500mg/kg of *cola milleni* seed extract respectively. The rats were weighed at the end of the experiment. The study was conducted based on the University guidelines for care and use of experimental animal resources.

Blood collection

Experimental period lasted for twenty-one days after which the rats were sacrificed and collection of blood sample was done by cardiac puncture. Fresh uncoagulated blood was centrifuged at 1000x*g* for 15min to obtain plasma. Tests which include; alanine transaminase, aspartate transaminase, alkaline phosphate were carried out on the blood sample.

Biochemical Analysis

Alanine aminotransferase and aspartate aminotransferase in the blood was determined using the kit leaflet (Randox laboratory, LTD.UK) according to the method described by Reitman and Frankel [7].

Statistical Analysis

All data were analyzed using analysis of variance (ANOVA) by employing the method of Steel and Torrire [8]. Significance difference between the treatment mean was also determined.

RESULTS

The summary of the results is as shown on Table 1 and Figure 1-3. Table 1 shows the result of the acute toxicity test on the rats, where the LD_{50} was determined. Figure 1 shows the specific activities of alanine aminotransferase in plasma of experimental rats at the end of the 21 days of treatment using *C. milleni* seed extract. The specific activities of aspartate aminotransferase in plasma of experimental rats at the end of the 21 days of treatment using *C. millenii* seed extract are represented in Figure 2. Also, Figure 3 shows the specific activities of alkaline phosphate in plasma of experimental rats at the end of the 21 days of treatment using *C. millenii* seed extract.

Table 1: Effect of Oral Administration of Aqueous Extract of *C. millenii* Seed on White Albino Rats

GROUPS	Conc. (mg/kg)	No. of animal in the group	No. of deaths per group
1	312.5	6	0
2	625	6	0
3	1250	6	3
4	2500	6	5
5	5000	6	6

Each value represent Mean± SD for each experimental group (n=6). (*) indicates mean value is significantly different (P=0.05) when compared to the control group.

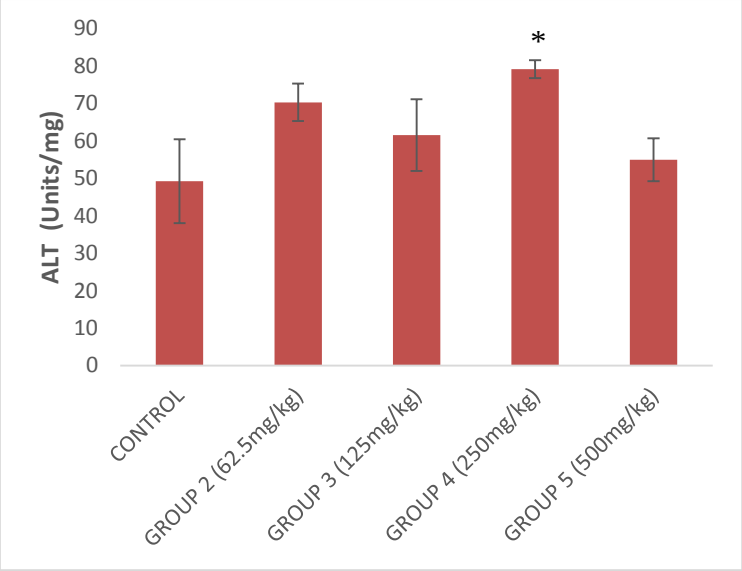

Figure 1: Level of alanine aminotransferase activity in plasma of experimental rats. Each value represent Mean ± SD for each experimental group (n=6). (*) indicates mean value is significantly different (P=0.05) when compared to the control group.

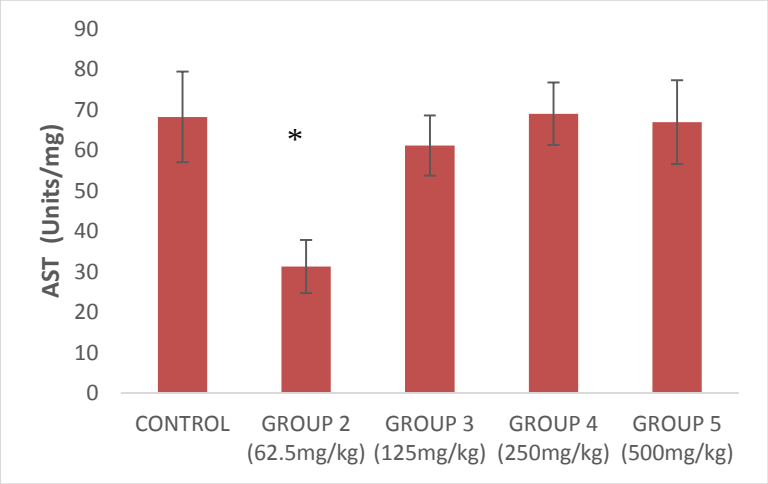

Figure 2: Level of aspartate aminotransferase activity in plasma of experimental rats. Each value represent Mean ± SD for each experimental group (n=6). (*) indicates mean value is significantly different (P=0.05) when compared to the control group.

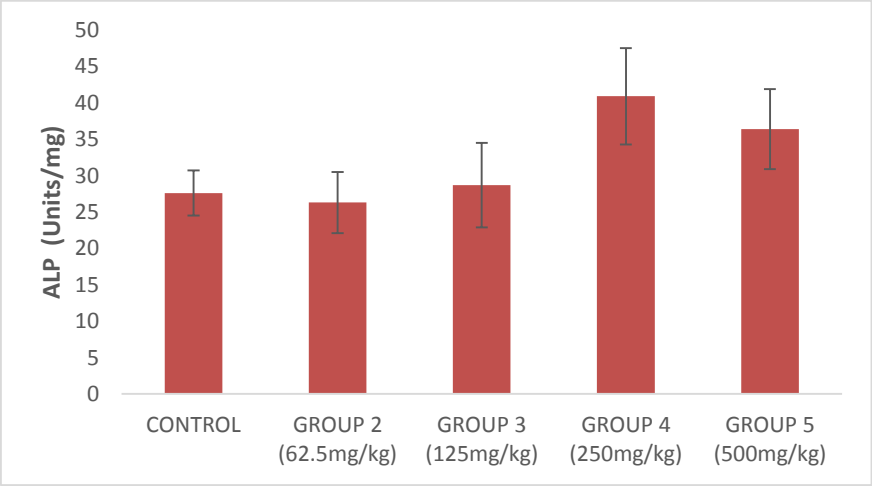

Figure 3: Level of alkaline phosphatase activity in plasma of experimental rats. Each value represent Mean ± SD for each experimental group (n=6). (*) indicates mean value is significantly different (P=0.05) when compared to the control group.

DISCUSSION

The study examined the toxicity of aqueous extracts of *C. milleni* seed extract on wistar rats. LD_{50} administration of doses up to 625 mg/kg *Cola milleni* caused no death or any observable signs of toxicity even beyond 48 hours. Signs of toxicity were observed at 1250 mg/kg and 5000 mg/kg extract administration. Such signs included corner sitting, drowsiness, convulsions, paralysis, heavy breathing and then death. From the result shown in *Table 1*, the LD_{50} was denoted to be 1250 mg/kg, this was

not in agreement with the study carried out by Giwa *et al*. [9].

In *Figure 1*, there is a significant increase in ALT concentration in the 62.5 mg/kg and 250 mg/kg group when compared to the control group. ALT is found in the blood and in various body tissues but is most common in the liver. Studies by Salauhdeen [10] indicated an increase in plasma ALT of rats treated with aqueous extract of *Cola milleni* , this implies that acute administration of this seed extract can cause little or no toxicity to the rats but prolonged administration of this seed extract can cause increase in the plasma ALT which is an indication that liver integrity is affected.

Result from *Figure 2*, shows no significant increase in serum AST concentration but rather it shows a significant decrease in 62.5 mg/kg group, this implies that decrease in the concentration of the administered seed extract will cause no effect but maintain the serum AST concentration. AST is an enzyme associated with liver parenchyma cells and it catalyzes the transfer of an amino group between aspartate and glutamate. Also prolong consumption of *Cola milleni* seed extract will not increase serum AST concentration.

From *Figure 3*, ALP concentration is increased in 250 mg/kg and 500 mg/kg dose group, but there is little or no significant increase in ALP concentration when administered with lower concentration of *Cola milleni* seed extract. This indicates that continuous administration of the *Cola milleni* seed extract to the rats at higher concentration can cause increase in the body ALP concentration. Burtis and Ashwood reported an increase in ALP concentration in blood plasma of rats administered with ethanolic extract of *Cola milleni* causing certain diseases such as hepatitis. This indicates that prolong consumption of *Cola milleni* could lead to hepatoxicity. ALP concentration is raised in acute liver damage, but is also present in red blood cells.

CONCLUSION

In conclusion, consumption of *C. millenii* seed is not harmful to the body and it's very medicinal though it must be taken in at concentrations not more than 62.5mg/ kg. It is of noteworthy that prolonged consumption of *Cola milleni* seed at certain high concentration more than 250mg/kg dose can be toxic and may lead to changes in the concentration of some marker enzymes in the body due to oxidative stress which can lead to minor health conditions. It is lethal to take more than 1250mg/ kg dose as it is the $LD_{50.}$ Users should not rule out completely the possibility of chronic toxicity developing with the continual usage of the aqueous extract of *Cola milleni* seed. It is recommended that more study should be conducted to determine the therapeutic dosage for clinical applications.

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