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Toxicological Evaluation of Aqueous Extract of *Khaya senegalensis* Stem Bark on Liver function Indices in Albino Rats

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ABSTRACT

Toxicological evaluation of aqueous extract of Khaya senegalensis stem bark on some liver function parameters of normal rats (100-140g) were critically examined. The albino rats (16) were randomly assigned into four (I-IV) groups each of which contains four rats. They were acclimatised for a week and Khaya senegalensis stem bark extract was administered for three weeks after which they were sacrificed. Group I (Control) received equivalent volume of distilled water while group II, III and IV received 11.62 mg/kg bwt, 13.95 mg/kg bwt and 16.28 mg/kg bwt of the extract respectively. The activities of ALT, AST and ALP in serum at all doses of the extract was significantly ($p<0.05$) increased compared with the control. Also, the concentration of total protein and globulin in the serum was significantly ($p<0.05$) increased while the concentration of albumin in the serum was significantly ($p<0.05$) decreased when compared with the control. Overall, the results indicated that oral administration of aqueous extract of Khaya senegalensis stem bark once daily for three weeks at the doses of 11.62, 13.95 and 16.28 mg/kg body weight caused hepatocellular toxicity and could hamper normal functioning of the liver of the animals. Therefore, the aqueous extract of Khaya senegalensis stem bark is not safe as an oral remedy at the doses investigated in the present study.

Key words: *Khaya senegalensis, Stem bark, Liver function parameters, Medicinal herbs.*

INTRODUCTION

The use of medicinal herbs in traditional system of medicine is a common practice in many cultures around the world, especially in African society. This practice has gained widespread acceptance in developing as well as in developed nations. Researchers are also beginning to appreciate the role of medicinal plants in health care delivery. This is as a result of the effectiveness, low cost and the availability of these herbal medicines[1]. It is noteworthy that some orthodox medicines in use today were developed from the biochemical templates obtained from medicinal plants. However, the widespread use and popularity of herbal medicines do not guarantee their efficacy and safety[2]. Therefore, there is need for detailed scientific analyses and adequate information on the toxicity of commonly used herbal drugs[3]. They way to determine the safe or unsafe use of a medicinal plant is the assessment of how it affects hematological and biochemical parameters[4,5]. Changes from normal physiological levels of these parameters after administration of a chemical agent to the experimental animals is an indication of adverse effects of such agent on living organisms[6].

Khaya senegalensis (Ders.) A. Juss is a large and sturdy tree (up to 35m high with a diameter of 1 to 3m) of Meliaceae family. Also named Senegal mahogany, it is a forestry species well known and exploited by Africans[7]. Phytochemical screening of trunk bark allowed Lompo[8] to highlight the main chemical groups

in *K. Senegalensis*: fatty acids, carotenoids, coumarins, emodols, tannins, compounds reducers, anthracenosides, steroidal glycosides, flavonosides, carbohydrates, saponins, sterols and triterpenes, anthocyanins. Recently, Yuan[9] and Bickii[10] reported the isolation of some limonoids named Khayalenoids from the stem and bark. Yuan[9] elucidated the structures of those molecules based on spectroscopicanalysis. The stem bark extract is used for treating jaundice, malaria, dermatoses and hookworm infections[11]. Limonoids isolated from other one species of *Khaya* (*Khaya grandifoliola*) is declared highly effective against the causative agent of malaria, *Plasmodium falciparum*[10]. Also, It has been reported that the plant is used in the treatment of Diarrhoea[12], Bacterial Infections[13], Cancer[14,15], Helminthosis[16,17], Trypanosomosis[18,] Diabetes[19,20,21,22], mental illness[23]. Many of the indigenous plants are used by man without the actual knowledge of their toxic potentials in an attempt to cure diseases and relief physical suffering [24]. The present study was therefore undertaken to determine the effect of aqueous extract of *Khaya senegalensis* stem bark on liver function parameters in normal rats.

MATERIALS AND METHOD

Plant Material

The stem barks of *Khaya senegalensis* were obtained from Bayero University Kano, old Campus and was authenticated at the Herbarium of the Department of Plant Biology, Bayero University Kano, Nigeria, where a voucher specimen was deposited at the Herbarium of the Institute.

Experimental Animals

Wister male and female adult albino rats (16) weighing between 100-140g were obtained from National Veterinary Research Institute, Vom, Jos, Nigeria. The animals were housed in aluminum cages under standard conditions. They were maintained on standard animal pellets and water *ad libitum*. The animals were acclimatized for two weeks before the commencement of the experiment.

Chemicals and reagents

The assay kits for alkaline phosphatase, aspartate and alanine transaminases were products of Randox Laboratories, United Kingdom. All other reagents used were of analytical grade and were prepared in glass distilled water.

Preparation of Plant Extract

The stem barks of *Khaya senegalensis* were oven dried at 40°C for 72 hours to a constant weight. The dried stem barks were then pulverized using Beltone Luinohun Blender (model MS-223, Taipei, Taiwan). The powdered material was stocked in a plastic container from which 100 g was extracted in 1000 ml of cold distilled water for 48 hours at 37^0C. This was then filtered with Whatman No. 1 filter paper. The filtrate was concentrated on a steam bath. The extract was reconstituted in distilled water to give the required doses of 11.62, 13.95 and 16.28 mg/kg body weight as used in this study. The reconstituted aqueous extract was administered orally using cannula to all the animals in different groups[25].

Experimental Design

The albino rats were divided into four groups of four rats each. The normal dose of *Khaya senegalensis* for average weight human being is 8140 mg/70kg body weight which is equivalent to 116.3 mg/kg body weight. Group I served as control, group II, III, IV were treated with 11.62, 13.95 and 16.28 mg/kg body weight of aqueous extract of *K. senegalensis* for three weeks.

Collection of blood sample and Preparation of serum

The rats were placed under diethyl ether anaesthesia; the neck area was quickly shaved to expose the jugular veins. The veins after being slightly displaced (to avoid contamination with interstitial fluid) were then cut with a sterile scalpel blade. Blood samples were then collected into clean dry centrifuge tubes and were allowed to clot for 30 minutes. This was then centrifuged at 33.5 g for 15 minutes using a Uniscope Laboratory Centrifuge (model SM800B). The sera were aspirated with Pasteur pipettes and stored frozen overnight at -20^0C before being used for the biochemical analyses[25].

Determination of biochemical parameters

Total protein was determined using the Biuret method of Henry *et al.*[26] Activities of aspartate transaminase (AST) (E.C.2.6.1.1) and alanine transaminase (ALT) (2E.C.2.6.1.2) were determined based

on the method described by Schmidt and Schmidt[27] while alkaline phosphatise (ALP) (E.C.3.1.3.1) activity was determined as described by Wright *et al*.[28] The concentration of albumin was determined as described by Grant and Kacchman[29]. All measurements were done using Spectronic 21 spectrophotometer (Bausch and Lomb, NY).

Statistical analysis

The data were expressed as mean ± standard deviation (SD). Statistical analysis was performed using analysis of variance (ANOVA) and Duncan multiple range test at 5% level of confidence ($p<0.05$).

RESULTS

Table 1 shows the activities of aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP) in the serum of rats administered with aqueous extract of *khaya senegalensis* stem bark. There was a significant ($p<0.05$) increase in the serum activities of ALT, AST and ALP at all doses of the aqueous extract of *khaya senegaalensis* when compared with the control group. Also, the increase was shown to be dose dependent at all treated groups when compared with the control (Table 1).

Table 2 shows the concentration of total protein, albumin and globulins in the serum of rats administered with aqueous extract of *khaya senegalensis* stem bark. There was a significant ($p<0.05$) increase in the serum concentration of total protein and globulins at all doses of the extract while there was a significant ($p<0.05$) decrease in the concentration of serum albumin when compared with the control. Also, the increase in the concentration of serum total protein, globulins and decrease in the concentration of serum albumin was shown to be dose dependent (Table 2).

Table 1: Activity of ALT, AST and ALP in serum of rats administered with aqueous extract of *Khaya senegalensis* stem bark

Group	ALT (U/L)	AST(U/L)	ALP (U/L)
Control	2.00 ± 0.00^{a}	13.00 ± 2.69^{a}	27.75 ± 2.25^{a}
11.52 mg/kg bwt	5.00 ± 0.00^{d}	15.25 ± 5.89^{d}	29.50 ± 1.66^{d}
13.95 mg/kg bwt	6.50 ± 0.87^{c}	18.50 ± 3.57^{c}	33.54 ± 5.89^{c}
16.28 mg/kg bwt	8.75 ± 1.09^{b}	20.25 ± 4.09^{b}	45.00 ± 3.67^{b}

Values are expressed as Mean ± SD (n = 4). Values in each column with different superscript (a-d) are significantly different ($P<0.05$). ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 2: Concentration of Total protein, Albumin and Globulins in rats administered with aqueous extract of *Khaya senegalensis* stem bark

Group	Total protein (g/L)	Albumin (g/L)	Globulins (g/L)
Control	63.25 ± 2.04^{a}	38.25 ± 1.48^{a}	25.75 ± 1.48^{a}
11.52 mg/kg bwt	67.00 ± 1.00^{c}	34.75 ± 0.43^{a}	29.25 ± 1.30^{c}
13.95 mg/kg bwt	70.75 ± 2.68^{c}	33.50 ± 1.69^{a}	33.25 ± 3.24^{d}
16.28 mg/kg bwt	73.00 ± 2.45^{b}	30.25 ± 3.83^{a}	36.75 ± 1.30^{b}

Values are expressed as Mean ± SD (n = 4). Values in each column with different superscript (a-d) are significantly different ($P<0.05$).

DISCUSSION

Most reports on toxic effects as a result of the use of herbal medicines and dietary supplements are associated with hepatotoxicity, although untoward effects on other organs such as kidney, skin, brain and the heart have been published[30,31].

The aminotransferases (ALT and AST) are 'markers' of liver damage and can thus be used to assess liver cytolysis with ALT being a more sensitive biomarker of hepatotoxicity than AST[32]. The increase in the activity of serum ALT and AST as observed in this study might be a sign of hepatocellular damage[33,34,35].

ALT and AST are located in the cytoplasm and mitochondria of liver cells in high concentrations but low in blood. However, ALT is more liver-specific[36]. It is known that increased activities of these enzymes in serum are due to increased membrane permeability and leakage into the blood circulation when there is damage to liver cells[35]. Thus, rise in the activities of ALT and AST in the serum due to hepatic necrosis may be noticed several days before clinical signs are manifested[37].

Alkaline phosphatase (ALP) is a 'marker' enzyme of damage for the plasma membrane and endoplasmic reticulum[38,39]. It is frequently used to assess the integrity of the plasma membrane[40]. In this study, there was an increase in the activity of ALP in the serum at all doses of the extract. This may be an indicative of intra-hepatic cholestasis and pathological condition[41]. Also, alkaline phosphatase is a marker of obstructive jaundice or intra-hepatic cholestasis[42]. The bile duct obstruction induces synthesis of this enzyme by biliary tract epithelial cells, leading to very high level of the enzyme in blood circulation[41]. The response of the liver to any form of biliary tract obstruction is to induce synthesis of ALP and drugs have been known to cause intra-hepatic obstruction of bile flow[37,33]. Furthermore, mild elevation of ALP is seen in parenchymal diseases of the liver caused by infectious or toxic hepatitis, due to the effect of drugs or xenobiotics[43].

Total protein is composed of albumin and globulin and reflects the balance of protein biosynthesis and catabolism[44]. The increase in serum total protein concentration following the administration of the aqueous extract of *Khaya senegalensis* stem bark could be as a result of tissue damage[45]. Adedapo *et al*[46] find out that the effect of *K. senegalensis* alteration on the total protein is usually due to decrease in quantity of albumin which may be accompanied by an increase in level of globulin.

The concentration of serum albumin showed a dose dependent decrease when compared with the control. Albumin is preferred to assay for the synthetic function of liver[47]. The decrease in albumin may lead to loss of the integrity of plasma membrane and endoplasmic reticulum[40]. Also, the decrease in the level of albumin is a sign of progressive liver failure and may result in the alteration of total protein and as well as increase level of globulin[46]. The decrease level of albumin will lead to lowering of albumin/globulin ratio (A/G ratio).

The level of globulin was found to show a significant increase at all doses of the extract when compared with the control. The increase in level of globulin may suggest that the extract has the potential to boost the immune system by promotion production and immunoglobulins[48]. The increase in globulin will lead to lowering of albumin/globulin ration (A/G ratio). This increase in globulin will lead to decrease in albumin which will lead to reduced synthetic capacity of the liver.

CONCLUSION

The administration of aqueous extract of *Khaya senegalensis* stem bark has adverse effects on some parameters of liver function of the animals at the doses investigated in this study. Further studies are required for long-term and multiple organs should be involved to examine the effect of dose and duration of consumption of aqueous extract of *Khaya senegalensis* bark stem on the biological system.

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