



## HEPATOTOXICITY STUDIES OF SUB-CHRONIC ADMINISTRATION OF AQUEOUS STEM BARK OF *KHAYA SENEGALENSIS* IN ALBINO RATS

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### ABSTRACT

The effect of oral daily administration for twenty eight (28) days of stem bark aqueous extract of *Khaya senegalensis* on alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT) activities and on the level of serum total bilirubin and total protein were investigated using Albino rats in three dose levels (10, 20, and 40 mg/kg body weight) plus a group serving as control. The result obtained indicated significant ( $p < 0.05$ ) increase in ALT, AST, ALP, and total bilirubin level in comparison with control. However, significant ( $p < 0.05$ ) decrease was observed in the level of total protein in comparison to control. The result indicated that the aqueous stem bark extract of *Khaya senegalensis* may possess toxic potential, at the dose levels studied.

**Keywords:** *Khaya senegalensis*, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, bilirubin.

### INTRODUCTION

Many of indigenous plants are used by man without the actual knowledge of their toxic potentials (Musa *et al.*, 2005). In Nigeria, one of such plants used by many localities is *Khaya senegalensis* (Desv) A. Juss [Family-Maliaceae] otherwise known as dry zone Mahogany (English), *Aganwo* (Yaruba), *Ono* (Igbo) and *Madaci* (Hausa). It is highly reputed for its numerous medicinal uses and is known to be used indigenously in the treatment of ailments by the Nupes of Niger State, Nigeria.

The decoction of the stem bark is given as remedy for malaria (Gill, 1992). The stem bark contains scopoletin, scoparone, limonoid, bitter principle, tannins, saponins and sterols (Gbile, 1986). The stem bark and leaves have been reported to be effective against *Plasmodium falciparum* *in vitro* (Egwim *et al.*, 2002). The stem and root bark have also been reported to have antisickling, antimicrobial and anthelmintic properties (Gill, 1992; Full *et al.*, 1999). The growing interest in herbal medicine demands information on the various plant preparations used. In the light of this, the present study is set out to provide information on the safety/toxicity risk potential of long-term administration of stem of *Khaya senegalensis* in albino rats.

### MATERIAL AND METHODS

#### Collection of plant material

Fresh samples of stem bark of *Khaya senegalensis* were cut from trees located within the University near the General Biology Laboratory, Usmanu Danfodiyo University, Sokoto – Nigeria. The stem bark was open-air-dried under the shade and pulverised into a coarse powder using pestle and mortar (Onoruvwe and Olorumfemi, 1998). Two hundred grams (200g) portion of the powdered sample was steeped in water (1000cm<sup>3</sup>) for 24 hours after which it was filtered with Whatman's No 1 filter paper and evaporated at 45 –

50° C using drying cabinets to yield 5% (w/v) to the concentrations of 10, 20, and 40mg/kg body weights were then made in distilled water before oral administration to the rats.

#### Animals

Twenty (20) albino rats of an inbred outrageous strain (wistar strain) weighing between 150-314g were used for this study. They were purchased from the animal house of the University of Jos, Nigeria and kept for one week at the botanical garden, Usmanu Danfodiyo University, Sokoto for acclimatization before commencement of the experiment.

#### Experimental procedure

The twenty (20) rats were randomly distributed into four groups of five rats each. Rats in group one served as control and were administered orally with distilled water (1cm<sup>3</sup>) on daily basis for 28 days. Groups 2, 3, and 4 received 10, 20 and 40mg/kg body weight respectively of the extract on daily basis for 28 days. The weights of all the rats were also taken pre and post treatment. The animals were sacrificed 24 hours after their 28 day dose. The blood sample was collected into separate, clean, and dry centrifuge tubes for biochemical analysis. The serum was later collected for used in the analysis. The biochemical parameters evaluated include transaminases activities determined as described by Reitman and Frankel (1957), alkaline phosphatase as described by Rec (1972), total protein by Biuret method of Henry *et al.* (1974) and total bilirubin as described by Jendrassik and Grof (1938).

#### Statistical analysis

Data were presented as means of 5 replicates ± standard deviation (SD); the multiple comparisons of the mean values were carried out using one-way ANOVA.

The statistical significance was considered at  $p < 0.05$  and all analysis were performed using Istat3 software.

**RESULTS**

The results are presented in Table 1. There were significant ( $p < 0.05$ ) increase in the level of ALT, AST, ALP, and total bilirubin. However, significant ( $p < 0.05$ ) decrease were observed in the level of total protein.

**Table 1: Effect of Oral Administration of Aqueous Extract of *Khaya senegalensis* Stems Bark on Albino Rats**

Dose mg/kg Body weight	AST (U/L)	ALT(U/L)	ALP(U/L)	TB (mg/dl)	TP (g/dl)
0	32.44±3.69	23.10±0.82	155.7±3.36	0.070±0.01	6.28±0.53
10	33.32±3.74	24.20±1.57	155.7±4.33	0.074±0.01	6.20±0.73
20	47.60±2.10*	29.24±1.58*	151.2±7.59	0.160±0.02*	4.42±0.78*
40	55.00±3.1*	37.20±1.95*	181.2±8.94*	0.25±0.03*	3.42±0.70*

Values are mean ± standard deviation (SD) N = 5, (\*) significantly different ( $p < 0.05$ ) from control using one-way ANOVA

**DISCUSSION**

The enzymes considered in this study are important and play well-known role in diagnosis of liver cytolysis and damage to the plasma membrane of the liver cells (Schmidt and Schmidt, 1979; Shahjahan *et al.*, 2004). The measurement of the level of total protein and total bilirubin is use to assay for the synthetic and excretory function of the liver respectively. The result of this study showed significant increase in the level of serum ALT and AST in the rat treated with 20 mg of the extract. Their presence in high concentration in the serum as compared with control indicated liver cytolysis, through which they are release into circulation. The aminotransferases occupy a central position in the amino acid metabolism as they help in retaining amino groups (to form new amino acid) during the degradation of amino acids and are also involved in the biochemical regulation of intracellular amino acid pool. Also, when these enzymes are depleted in the liver, glutamate concentration also is affected (decrease to about 3%). Its depletion also might result in depletion of the level of some important biomolecules, for instance, glutathione, one third of which is formed from glutamate, and might become depleted when glutamate is insufficient (Stryer, 1995). Detoxification is the essential role of glutathione, and cells are exposed to attack by active metabolite when it is depleted. Also there was a significant increase in the level of total bilirubin in the experimental rats treated with 20 and 40 mg/kg. But there was no significant ( $p > 0.05$ ) increase in the group treated with 10 mg/kg. An increase in total bilirubin may indicate that the excretory function of the liver has been affected by damage caused to the liver by the plant extract. It could also indicate that a component of the plant extract might have competed

and displaced the binding of bilirubin on albumin or the uptake of bilirubin is inhibited by the plant extract, all these would lead to increase in total bilirubin in the serum.

Extract administration produce a significant decrease in the total protein concentration. Total protein is the sum of albumin (60%) and globulins in the serum, a decrease in the concentration of serum total protein might indicate inhibition of protein synthesis (Musa *et al.*, 2005). Hence the aqueous stem bark extract might inhibit the synthesis of some proteins, thereby resulting in decrease in the serum total protein. Low protein level results when there is extensive liver damage as seen in liver function (Wada and Snell, 1962), however, determination of serum albumin is preferred to assay for the synthetic function of the liver (Corless and Middleton, 1993). Also according to the result, there was a significant increase in the concentration or activity of serum alkaline phosphatase only in the rats treated with 40 mg/kg body weight of the extract. ALP is a marker enzyme for the plasma membrane and endoplasmic reticulum (Wright and Plummer, 1974). It is often employed to assess the integrity of plasma membrane of liver (Akanji *et al.*, 1993). The significant increase in the serum ALP following administration of the plant extracts may be due to disruption of liver plasma membrane. But ALP exits as isoenzymes so an elevation of ALP level may consist of a combination of various ALP isoenzymes (Corless and Middleton, 1993).

Results from this study have shown that oral daily administration of the aqueous stem bark extract of *Khaya senegalensis* for long period has side effect. Therefore, chronic usage of the stem of the plant should be avoided.

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