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Evaluation of the hepatotoxic potential of methanol seed kernel extract of *Mangifera indica* (Mango) using rat model

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Abstract

The aim of this study was to evaluate the hepato-toxic potential of methanol seed kernel extract of *Mangifera indica* (mango). Dry mango seeds were broken to release the kernels which were subsequently dried at room temperature prior to grinding to fine powder. 500 g of powdered plant sample was developed into extract with the aid of a standard analytical procedure. Twenty (20) adult male albino rats divided into four (4) groups of five rats each. Group I (normal control) which was fed normal rat chow and water *ad-libitum*. Group II, III and IV were administered 100, 200 and 300 mg/kg of extract respectively for 21 days after which rats were sacrificed and blood sample collected and analysed for the activity of serum hepatomarkers ; Aspartate aminotransferase (AST), Alkaline phosphatase (ALP) and Alanine aminotransferase (ALT) was evaluated using standard procedures. Result obtained from the study showed that administration of 100 and 200 mg/kg bw did not increase the activity of the serum hepatomarkers. However, a contrary observation was made on the activity of serum hepatomarkers in rats administered with 400 mg/kg of MSKE inferring that methanol seed kernel extract of *Mangifera indica* (mango) could contain a hepatotoxic agent which can only elicit damage in large doses.

Keywords: *Mangifera indica*; Seed kernel; Hepatomarkers; Alanine aminotransferase; Alkaline phosphatase; Mango

1. Introduction

Mangos botanically referred to as *Mangifera indica* L and a member of *Anacardiaceae* family is widely cultivated in the tropical as well as the subtropical regions and their components are commonly employed in folk medicine as therapeutic options for diverse human diseases [1].The impressive acceptability of mango fruit in the making of diverse arrays of products of nutritional and health benefits such as nectar, leather, puree, canned slice, chutney and juices, etc translates to huge amount of seed as waste [2] which can be transformed into valuable products with the help of in depth research on resulting products. The seed kernel which is the portion of interest to researchers constitutes 45-85% of the seed [3; 4]. Research efforts have revealed the mango seed kernel is richly endowed with minerals such as potassium, calcium, copper, and zinc along with phytosterols, ascorbic acid, carotenoid, polyphenol, and has shown impressive antioxidant and antimicrobial activities [5].

The liver is an essential organ saddled with the task of metabolism and detoxification of xenobiotics [6] which hitherto predisposes it to damage resulting from extremely toxic substances some of which are very toxic phytochemicals among several other hepatotoxic agents and consequent debilitating disorders [7].

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Despite being the major byproduct of the mango processing industry with immense nutritional and health benefits, commercial exploration is negligible for health safety reasons [8; 9]. Therefore, it is imperative to investigate the hepato-toxic effect of the mango seed kernel.

2. Material and Methods

2.1. Collection and processing of mango seed kernel

Mango seed kernels obtained from mature, dry mango seed were dried at room temperature and were subsequently ground to fine powder. Precisely 500 g of powdered sample of *Mangifera indica* seed kernel held in a thimble and introduced into a 500 cm^3 Soxhlet extractor for extraction in methanol for 72 h. The resulting extract was evaporated to a paste at 40^0C for 8 h and was subsequently preserved in the refrigerator [10].

2.2. Animals

Albino rats which weighed 180-200 g were gotten from the Animal House of the Department of Science Laboratory Department, Akanu Ibiam Federal Polytechnic Afikpo and were housed in adequately ventilated transparent plastic cages and were fed rat chow and water ad-libitum. They rats were acclimatized for three weeks prior to commencement of experiment.

2.3. Median Lethal Dose 50% (LD50)

The Median Lethal Dose 50% was determined on extract by administering 10, 100 and 1000 g/kg bw separately to three groups of three wistar rats orally. The rats were subsequently observed for signs of toxicity for 24 hr. Being that mortality was not recorded on the groups, The second phase was initiated and another three groups of one rat each was each administered with 1600, 2900 and 5000 mg/kg of extract separately. The animals were observed for 48 hr for signs of toxicity [11].

2.4. Animal Grouping

Twenty rats were divided into 4 groups of 5 rats each and treated as follows.

- Group 1:Normal control; fed only rat chow and water
- Group 2: Apparently healthy rats administered with 100 mg/kg of extract
- Group 3: Apparently healthy rats administered with 200 mg/kg of extract
- Group 4: Apparently healthy rats administered with 400 mg/kg of extract

2.5. Biochemical Analysis

Oral administration of extract lasted for three weeks after which rats were fasted overnight, anesthetized with chloroform before being sacrificed 24 hour after the last treatment. Blood sample was collected and used to determine the activity of AST, ALT and ALP.

2.6. Liver Function Test (LFT)

Blood sample was subjected to centrifugation at 3000 rpm for 10 min. The clear serum collected was used for evaluating ALT, AST, ALP activity with the aid appropriate test kits according to standard procedures [12].

2.7. Histopathology

A section of the liver was excise and processed for viewing under the light microscopy by paraffin embedding, 6-*m*m sectioning, and staining with hematoxylin and eosin (H&E) to allow for morphological examination.

2.8. Statistical Analysis

The data was analyzed using SPSS (Version 23). The differences in mean values among groups were compared using the Duncan Multiple Range Test. $P< 0.05$ was considered significant.

3. Results

Table 1 Activity of Liver Enzymes in Rats treated with Methanol Seed Extract of *Mangifera indica* (Mango)

Grouping	Treatment	AST (U/I)	ALT (U/I)	ALP (U/I)
Group I	Normal Control	7.98±0.78^{a}	7.12±3.04^{a}	128.77±0.8^{a}
Group II	100 mg/kg MSKE	8.00±1.15^{ab}	7.20±0.57^{a}	128.67±6.64^{a}
Group III	200 mg/kg MSKE	8.67±3.02^{ab}	7.33±2.88^{a}	130.67±6.54^{ab}
Group IV	300 mg/kg MSKE	10.47±0.33^{c}	13.00±0.58^{b}	136.67±5.69^{c}

Results are expressed as mean ± standard deviation of three determinations. Values with different superscript in a row are significantly (P<0.05) different

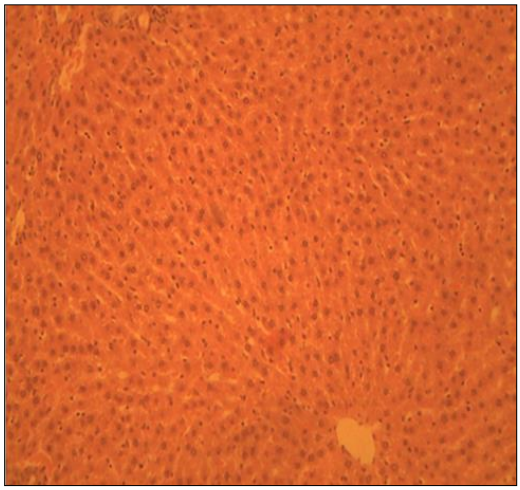

Figure 1 Photomicrograph of liver of the normal control group showing normal hepatocyte

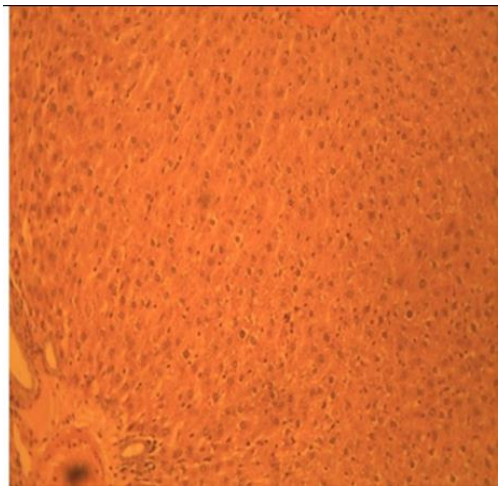

Figure 2 Photomicrograph of liver of rats administered with 100 mg/kg of MSKE showing healthy liver cells

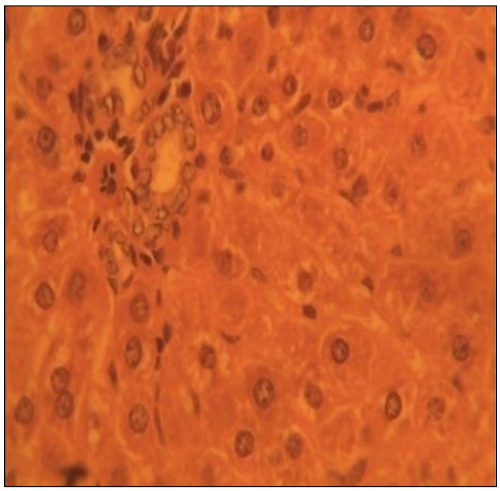

Figure 3 Photomicrograph of liver of rats administered with 200 mg/kg of MSKE showing slightly inflamed liver cells

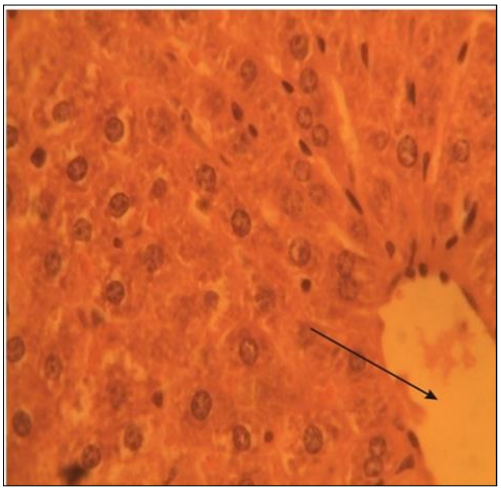

Figure 4 Photomicrograph of liver of rats administered with 400 mg/kg of MSKE showing damaged liver cells

4. Discussions

Liver plays a key role in metabolism and excretion of xenobiotics which makes it highly susceptible to toxicity resulting from some of their toxic components [13]. Table 1 shows the activity of liver enzymes in rats treated with methanol seed kernel extract of *Mangifera indica* showing that the activity of the serum hepatomarkers (aspartate transaminase (AST), Alanine aminotransferase (ALT) and alkaline phosphatase) treated with 100 and 200 mg/kg was not significantly ($P>0.05$) different from that reported for the control group. This could be attributed to the ability of MSKE to condition the hepatocytes in order to induce accelerated regeneration of parenchyma cells, thereby shielding against membrane fragility and reducing the leakage of marker enzymes into circulation. This is consistent with the findings of Nithitanakool et al. [14] Which established that the administration of 2000 mg/kg MSKE to rats treated with CCl4, for three weeks significantly reduced elevated activity of liver enzymes levels which were not significantly ($P>0.05$) different from those of a healthy controls (ALT 26 and AST 60 U/L). This effect is in tandem with the widely accepted fact that elevated serum levels of transaminases return to normal with the healing of the hepatic parenchyma and the regeneration of hepatocytes. However, a contrary observation was made on the activity of the serum hepatomarkers following the administration of 400 mg/kg MSKE. The observed increase in the activity of serum hepatomarkers following oral administration 400 mg/kg MSKE corroborates the opinion of Singh et al. [12] that certain medicinal agents in overdose and sometimes even within therapeutic ranges may injure the liver owing to the presence of different harmful phytoconstitutent.

5. Conclusion

Through this study, it is evident that mango seed kernel contains components which could be hepatotoxic. Therefore, research effort should be geared towards identifying and characterizing these compound(s) for documentation and referral purposes.

Compliance with ethical standards

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Disclosure of conflict of interest

Authors hereby declare that no conflict of interest exists.

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