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Original Research Article

THE EFFECT OF ETHANOL EXTRACT OF RIPE *DENETTIA TRIPETALA* FRUITS ON INDICES OF LIVER AND KIDNEY FUNCTION IN MALE ALBINO WISTAR RATS.

ABSTRACT

Aim: To investigate the effect of oral administration of ethanolic extract of ripe *Denettia tripetala (DT)* fruits some on indices of kidney and liver function in male albino rats.

Study design: Twenty (20) male albino rats weighing between 160 – 210 g were used for the study and randomly assigned into four groups of five animals each. Group 4 served as control while Groups 1, 2, and 3 received orally the ethanol extracts of *Denettia tripetala* at doses of 262.20 mg/kg, 524.40mg/kg and 786.61mg/kg respectively for 30 days.

Place and duration of study: the study was carried out at Department of Pharmacology and Toxicology Laboratory, University of Uyo between May 2016 and June 2016.

Methodology: Serum creatinine, urea, electrolytes, albumin, aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP) levels were measured using Randox kits, USA.

Results: The result showed a dose dependent increase in the level of potassium in Group 1 (6.10 ± 0.28), Group 2 (6.90 ±1.64) and Group 3 (7.58 ± 0.39) compared to control (6.32 ± 0.20). However, only Group 3 compared to control was significantly increased at (P =0.05). There was no significant difference (P = 0.05) in the level of creatinine, urea, sodium and chloride when compared to control. There was a significant increase (P =0.05) in the level of ALP in Group 2 when compared to control. There was no significant difference (P =0.05) in total bilirubin, albumin, ALT and AST levels in the treated groups when compared to control.

Conclusion: The study suggests that ethanol extract of ripe *Denettia tripetala* fruit was not toxic to the liver and kidney. However further work is needed to validate the results of the study.

Key words: *Denettia tripetala*, kidney and liver function, Potassium, Alkaline phosphatase.

INTRODUCTION

The World Health Organization survey estimated that 80% of the world population use medicinal plants in the treatment of disease; in African countries this rate is said to be much higher (1). According to Hammer *et al.,*(2), plants are the richest resource of drugs for traditional system of medicine, nutraceuticals, food supplements, folk medicines, pharmaceutical intermediates and chemical entities for synthetic drugs. Phytochemicals—the bioactive non-nutrient plant compounds in fruit, vegetables, grains, and other plant foods(3)—have been linked to reductions in the risk of major chronic diseases

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including cardiovascular disease, diabetes, cancers as well as neurodegenerative disorders(4). Therefore people who consume high quantities of vegetables and fruits may be at reduced risk for some of the diseases caused by biochemical dysfunction (5). Since most plants have medicinal properties, it is of utmost importance that their efficacy and toxicity risks are evaluated.

Denettia tripetala (DT-pepper fruit) is an indigenous fruit tree of the family Annonaceae (6). It is known in Nigeria by the following names: Ako (Edo), Mmimi (Ibo), Ata Igbere (Yoruba) and Nkarika (Ibibio/Efik). It's widely distributed and consumed by the inhabitants of Western Cameroons, Ivory Coast and Southern Nigeria. It is also used in traditional medicine as a remedy for cough, fever, toothache, diarrhea, diabetes, and nausea in pregnant women (6). Particularly, the rural dwellers consume it together with local gin (kaikai or ufofop) as snacks.

DT have received only minimal scientific attention throughout the past years. Phytochemical screening of the ethanolic extract revealed the presence of tannins, alkaloids, steroids, flavonoids, cardiac glycosides, saponins, and terpenoids (7). These constituents suggest the scientific basis for the use of DT in traditional medicine. Ikpi and Nku (8) investigated the effect of the ethanolic extract of DT on hematological parameters in normal healthy rats, the study showed that DT may be hematotoxic to rats at low to moderate dose, but the toxicity was relieved at administration of high dose of the extract. Due to dearth of literature on *in vivo* toxicity of *Denettia tripetala* fruits. It was therefore pertinent to examine the effect of ethanol extract of DT on indices of kidney and liver function.

MATERIALS AND METHODS

Denettia tripetala fruits

Mature ripe fruits of *Denettia tripetala* gotten from Oboh market in Etim Ekpo L.G.A Akwa Ibom State. It was washed, sun dried and grounded into powder with mortar and pistle. It was then taken to the lab for extraction. *Denettia tripetala* was macerated in 80% of ethanol for 3 days and was filtered, the filtrate was placed on the water bath for complete evaporation. The concentrated extract was stored in the freezer at -4 degrees Celsius until further analysis.

Twenty male albino rats were bought from University of Calabar and kept in animal house of Department of Biochemistry, Faculty of Basic Medical Science, University of Uyo, Akwa

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Ibom state. The animals were allowed to acclimatize for 30 days under standard laboratory with free access to commercial food and water.

Experimental design

Twenty male albino wistar rats weighing 160-210g were obtained from the animal house of Faculty of Basic Medical Sciences, University of Calabar, Cross River State, Nigeria, and was transported to the animal house, Department of Pharmacology and Toxicology, University of Uyo, Akwa Ibom State, Nigeria. They were allowed to acclimatize for two weeks under standard conditions with free access to water and feed. They were randomly selected into four groups, five animals per group. Group 4 served as control. Groups 1, 2, and 3 received orally the ethanol extract of *Denettia tripetala* fruits at doses of 262.20 mg/kg, 524.40mg/kg and 786.60mg/kg respectively for 30 days.

After the last administration, the animals were fasted overnight and then sacrificed under chloroform anesthesia. Blood was obtained by cardiac puncture into a sterilized sample bottles. The blood collected was allowed to clot by standing at room temperature for one hour and centrifuge at 2500g for ten minutes. The serum (supernatant) was isolated and stored at -4 degree Celsius.

Biochemical analysis

Creatinine, urea, sodium, potassium, chloride, total protein and albumin concentrations as well as aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP), activities were assayed using their respective Randox kits, USA, according to manufacturer's instructions.

Statistical analysis

Data are presented as mean ± standard error of the mean and were analyzed using one-way analysis of variance (ANOVA) followed with a *post-hoc* test (least significance difference) using SPSS version 15.0 (SPSS Inc. Chicago, IL 60606-9653, Nov. 2006) and Excel for windows (Microsoft Corporation 2010, Washington.). P =.05 was declared as statistically significant.

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RESULTS

The effect of ethanol extracts of ripe *Denettia tripetala* fruits on kidney function parameters, total protein and albumin in male albino Wistar rats are presented in Table 1. There was a dose dependent increase in the level of potassium in Group 1 (6.10 ± 0.28), Group 2 (6.90 ± 1.64) and Group 3 (7.58 ± 0.39) compared to control (6.32 ± 0.20). However, only Group 3 compared to control group was significantly increased at (P =.05). There was no significant difference (P =.05) in the level of creatinine, urea, sodium and chloride, total protein and albumin when compared to control.

The effect of ethanol extract of ripe *Denettia tripetala* fruits on some indices of liver function in male albino Wistar rats are presented in figure 1. There was a significant increase in the level of ALP in Group 2 (60 ± 3.91) when compared to control (46.2 ± 3.83). There was no significant difference in total bilirubin, ALT and AST levels in the treated groups compared to control.

Table 1: Effect of ethanol extracts of ripe *Denettia tripetala* fruits on indices of kidney function, total protein and albumin in male albino Wistar rats.

Groups/ Parameters	Urea (mg/dl)	Creatinine (mg/dl)	Sodium (mg/l)	Potassium (mg/l)	Chloride (mg/l)	Total Protein (g/l)	Albumin (g/l)
Group 1 (262.20mg/kg)	5.80 ± 0.57	84.80 ± 3.99	145.00 ± 1.62	6.10 ± 0.28	100.80 ± 0.49	72.20 ± 2.29	38.20 ± 1.69
Group 2 (524.40mg/kg)	6.00 ± 0.61	84.40 ± 4.53	147.60 ± 3.43	6.90 ± 0.36	101.00 ± 1.64	77.80 ± 5.03	40.60 ± 2.94
Group 3 (786.61mg/kg)	4.70 ± 0.30	90.60 ± 3.35	147.00 ± 1.48	7.58 ± 0.34a,c	102.40 ± 1.29	72.00 ± 4.01	38.80 ± 2.89
Group 4 (control)	4.76 ± 0.23	84.00 ± 1.82	145.90 ± 1.28	6.32 ± 0.20	99.80 ± 2.63	73.20 ± 2.31	39.80 ± 1.02

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Values presented as Mean ± SEM; a = significantly different at P = 0.005 when compared to Group I; b = significantly different at P =0.05 when compared to Group 2. c = significantly different at P = 0.05 when compared to Group 4 (control).

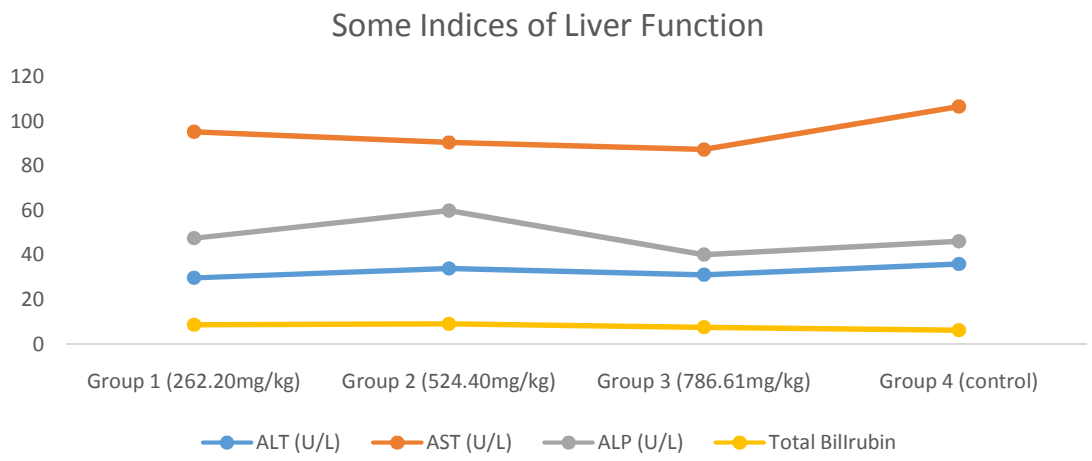

Figure 1: Graphical presentation of some indices of liver function following the administration of ethanolic extract of ripe *Denettia tripetala* to albino Wistar rats.

Discussion

Potassium ion (K^+) is found predominantly in the intracellular fluid and it functions in the regulation of neuromuscular excitability, contraction of heart muscles and maintenance of ICF volumes and hydrogen ion concentration. Kidneys are important in the regulation of K^+ balance by reabsorbing nearly all K^+ by the proximal tubules and then excreting the additional or excess potassium in the urine under the influence of aldosterone (9).

Hyperkalemia develops when there is excessive production (oral intake, tissue breakdown) or ineffective elimination of potassium (10). It is reported to arise in states characterized by excessive destruction of cells with redistribution of K^+ from the intracellular to extracellular compartment in massive hemolysis (11), renal insufficiency thereby decreasing the body's ability to regulate serum potassium via the kidneys (12) and exercise (13).

The dose dependent increase in the level of potassium in Group 1, Group 2 and Group 3 compared to control is not surprising because, Okaka and Okaka (14) reported that *Denettia tripetala* fruits extracts contain high amount of potassium (2.48%), calcium (1.80%), sodium (0.72%), while zinc, copper, manganese, cobalt, nickel and cadmium are available in trace quantities. However, only Group 3 compared to control group was significantly increased at (P = .05).

Severe hyperkalemia is rare in normal individuals, but when it occurs, it can lead to impairment of neuromuscular, cardiac and gastrointestinal organ system. This may be due to depolarization of membrane potentials of cells due to increase in the equilibrium potential of potassium ions; as a result, voltage-gated sodium channels are open and there is increase inactivation at the same time. Since the depolarization due to concentration change is slow,

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action potential is not generated resulting in accommodation. Above a certain level of potassium, the depolarization may inactivate sodium channels and open potassium channels rendering the cell refractory (15).

Consequently, ALP is one of the enzymes reflecting liver cell damage, it has widespread tissue distribution including liver, bone, placenta and gastro intestinal tract (16). Its precise function is unknown but it is released into plasma in cholestasis, extrahepatic biliary obstruction, primary biliary cirrhosis (17). Also, bone disease with increased osteoblastic activity shows increased ALP level in the serum as seen in Pagets disease (18). High level of ALP was seen to increase significantly in Group 2 when compared to control. There was no significant difference in the level of AST, ALT and bilirubin in all the groups when compared to the control.

The elevated level of potassium in Group 3 compared to control is not sufficient to conclude that ethanol extract of DT fruits was toxic to the kidneys since other kidney indices like urea and creatinine levels were not significantly raised. Similarly, the extract is not hepatotoxic since AST and ALT were not significantly raised; also ALP is not a specific marker for liver damage.

Conclusion/Recommendation

In conclusion, the study therefore suggests that the ethanol extract of *Denettia tripetala* was not toxic to liver and kidney. Further studies should be done to ascertain this effect.

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