



Effect of Oral Administration of the Leaf Extract of *Uvaria chamae* (Mmimi Ohia) in Albino Wistar Rats

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Authors' contributions

This work was carried out in collaboration among all authors. Author ISIO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors EOO and EIO managed the analyses of the study. Authors CCO, BNE, NJO and COU managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Uvariachamae (vernacular; *mmimiohia*) belongs to the family Annonaceae. It is a small tree that grows wild to about 4.5 meters in the savanna and rain forest regions of Nigeria and other African countries. It is known to possess various medicinal and therapeutic properties. The biochemical and toxicological effects of its ethanolic leaf extract on Wistar albino rats were assessed in this study. Twenty albino rats grouped into 4 (5 animals in each group) were used. Group A served as control while groups B, C, D received 250, 500 and 1 000mg/kg body weight of the extract for a period of 30 days. The mean alkaline phosphatase activity of the control was 350±11.0lu/l as against 490±38.00, 630±60, and 370±20 for groups B, C, and D (p =0.01, >0.05, 0,001)

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respectively. The mean serum urea concentration of the control was 5.00 ± 0.19 mg/dl as against 3.80 ± 0.31 , 3.30 ± 0.28 and 3.50 ± 0.18 mg/dl ($p=0.01$, 0.001 , 0.001) for groups B, C, D respectively. The extract had no significant effects on the liver enzymes, ALT and AST, serum sodium, potassium, chloride as well as creatinine of the rats. Serum bicarbonate was raised significantly, 26.00 ± 0.53 , 28.00 ± 0.60 , 27.00 ± 1.10 , 29.00 ± 1.10 for groups B, C, D ($p= 0.042$, >0.05 , 0.043) respectively. Histological studies showed no abnormality in the kidneys and mild peri-portal lymphocytic infiltration of the liver. Phytochemical analyses of the extract revealed the presence of alkaloids, flavonoids, resins, proteins terpenoids and reducing sugar. Hence, ethanolic extract of leaves of *Uvaria chamae* has no serious deleterious effects on Wistar albino rats and may be safely used in traditional medical practice.

Keywords: Leaf extract; *Uvaria chamae*; albino wistar rats; toxicity.

1. INTRODUCTION

Uvariachamae belongs to the family Annonaceae [1] is a small tree that grows to a height of about 4.5 meters. It is commonly found in the savanna and rain forest regions of Nigeria and other African countries. It is call *mmimiohia*, *kaskaifi*, and *akisan* among the Igbos, Hausas and Yorubas tribes of Nigeria respectively [2]. The fruits are yellow when ripe and have a sweet pulp which is consumed. The fruit carpels are in finger-like clusters and all parts of the plant are fragrant. The barks of the roots and stem as well as the leaves have wide traditional medicinal applications. In Nigeria *Uvaria chamae* is used for the treatment of diarrhea [3]; for the treatment of severe abdominal pains and as pomade in Ghana [1]; amenorrhoea and prevention of miscarriage in Senegal, [4] and in Togo it is given for pains of childbirth. The root extract is used to treat piles, menorrhagia, epistaxis, haematuria and haemolysis, and applied to wound and sores for quick and proper healing [5,1], Okwu, [6] reported that extract of *Uvaria chamae* can be used to treat gastroenteritis, vomiting, diarrhoea, dysentery, wounds, sore throat, inflamed gums and a number of other ailments.

Although numerous uses of *Uvaria chamae* in traditional medicines has been reported from Nigeria, but information regarding biochemical and toxicological properties of *Uvaria chamae* has been very much limited. Therefore, the present investigation aims at studying its effects on the liver, kidney and electrolyte metabolism by taking albino wistar rat as a test insect.

2. MATERIALS AND METHODS

The leaves of *Uvaria chamae* were collected from a farmland near the Staff Quarters of the University of Nigeria, Enugu Campus and were authenticated by a botanist in the Nsukka

Campus of the University. A specimen was kept in the University Herbarium with voucher number 95. The leaves were air-dried under a shade (500 g), grounded to fine powder and kept in leak-proof container. The entire powder was extracted into 5 liter of absolute ethanol over a period of 48 hours with intermittent agitations. The extract was filtered through a muslin cloth first and next through No 1 filter paper and the filtrate evaporated to dryness and gave a 12.6% yield, (w/w). A solution of 100mg/ml of the dried powder was made in tween 80 and utilized in the study. Rats were procured from the Anatomy Department of the University of Nigeria, Enugu Campus and acclimatized for 2 weeks before commencement of experiments. Handling of animals was according to international guidelines for the experiments involving use of vertebrates.

LD50 was determined with three groups of rats (3animals/group) that were given 1000mg, 2000mg and 2500mg/kg body weight respectively. The rats were constantly observed for the first 2 hours, intermittently for the next 4 hours and then overnight.

The experiment to evaluate changes in biochemical properties was performed with 4 groups of rats, (5 per group) which received orally 250, 500 and 1000 mg/kg body weight of the extract respectively for 30 days. Within this period they were given water and standard pellets (Guinea-feed[®]) *ad libitum*. They were observed daily for signs of physical and behavioral toxicity.

On day 31, 5 ml of blood was collected from each animal through the retro-orbital vein into plain bottles and the sera harvested for biochemical analyses. Two animals from each group were euthanized and sacrificed for collection of liver and kidneys excised and

preserved in 10% formal-saline for histological assessment.

The phyto-chemistry of the extract was carried out using standard methods for reducing sugars, terpenoids, alkaloids, anthraquinones, resins, saponins, tannins, proteins and carbohydrates.

Alkaline phosphatase was estimated by the method of Kind and King [7] transaminases by the methods of Reitman and Frankel, [8], urea using the diacetylmonoxime method, (Rosenthal, 1980) and creatinine by Jaffe reaction, (1954); all of them determined with Randox kits. Serum chloride was estimated by the method of Schales and Schales and bicarbonate by the titrimetric method of Van Slyke, [9]. Sodium and potassium were estimated using Ion Selective Analyzer.

Histological assessments were done using paraffin sections stained by the hematoxylin and eosin method and observed using the Leitz DIALUX research microscope and photomicrographs produced in bright field at a magnification of x 400.

3. RESULTS

The result of the toxicity studies showed that the extract of the leaves of *Uvariachamae* had LD50 greater than 2500mg/kg body weight in rats. Phytochemical analyses revealed the presence of flavonoids, alkaloids, resins, proteins, reducing sugars and terpenoids.

Alkaline phosphatase activities were significantly raised in groups B 490 ± 38 iu/l ($p=0.01$) and C

630 ± 60 iu/l ($p = 0.001$); (control = 350 ± 11 iu/l) while Alanine transaminase and aspartate transaminase activities and mean value of serum creatinine showed no significant difference from the control. The mean values of urea decreased significantly with increase in the dose of extract, (B 3.8 ± 0.31 mg/dl; $p= 0.01$; C 3.3 ± 0.28 mg/dl; $p = 0.001$; D 3.5 ± 0.18 mg/dl; $p = 0.001$; Control 5.0 ± 0.19 mg/dl) (Table 1).

Of the electrolytes, only the mean value of bicarbonate in groups B (28.0 ± 0.60 mmol/l; $p= 0.01$) and D (29.0 ± 1.10 mmol/l; $p=0.01$) showed significant difference from the control (26.0 ± 0.53 mmol/l) (Table 1).

4. DISCUSSION

Herbal medicine is gaining popularity in developing countries as it has been estimated that 80% of the world population still depend mainly on traditional medicine and treatment involving the use of plant extracts [10]. Therefore, there is need to provide information on the safety or adverse effects of these medicinal plant. Few scientific studies have been undertaken to ascertain the safety of *Uvaria chamae* plant, which has been reported to be used extensively in traditional medicines from Nigeria.

The acute toxicity studies revealed no any adverse effects on the rats at different dosage since no death was observed among the experimental animals. The result of phytochemical analyses corroborates earlier studies by Egonyonmi et al. [11] with the exception of antraquinone and anthracene which were not detected.

Table 1. Showing the effects of ethanolic extract of *Uvariachamae* (EEUC) leaf on biochemical markers of liver and kidney functions in Wistar albino rats

Parameter	Groups (n=5)			
	A (Control)	B (250 mg/kg body weight)	C (500 mg/kg body weight)	D (1000 mg/kg body weight)
ALP (U/l)	350±11	490±38**	630±60***	370±20
ALT(U/l)	56±5.2	56±3.3	56±4.1	56±1.9
AST(U/l)	76±6.7	70±7.3	64±3.1	78±5.2
Urea(mg/dl)	5.0±0.19	3.8±0.31**	3.3±0.28***	3.5±0.18***
Creatinine(mg/dl)	77.0±4.3	71.0±5.8	81.0±4.2	64.0±6.7
Sodium(mmol/l)	140.0±2.0	140.0±0.68	140.0±0.85	140.0±1.5
Potassium(mmol/l)	6.10±0.48	5.80±0.14	6.40±0.09	6.10±0.20
Chloride(mmol/l)	110.0±2.9	110.0±0.31	110.0±0.52	110.0±1.6
Bicarbonate(mmol/l)	26.0±0.53	28.0±0.60*	27.0±1.10	29.0±1.10*

Results expressed as Mean ± SEM

*Compared with Control (Group A) * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Alkaloids are nerve stimulants, convulsants and muscle relaxants, [12]. The biological functions of flavonoids include protection against allergies, platelet aggregation, microbe invasion, ulcers, hepatotoxins, viruses and tumour[13,14]. However, some flavonoids behave as powerful protective agents against inflammatory disorders. They reduce oedema formation, and inhibit synthesis of prostaglandin E₂, prostaglandin F₂ and thromboxane B₂ [14].

The biochemical indices monitored in the liver and kidneys are useful markers for the assessment of organ function; if altered, indicate the impairment of organ function, [15]. The transaminases are useful markers for liver cytolysis [16] and the normal values observed indicate liver integrity.

Alkaline phosphatase activity may greatly increase in liver tumour or lesion and moderately in hepatitis. Treated rats have elevated ALP activity which may be due to inflammation resulting from lymphocytic infiltration of the peri-portal aspects of the liver as seen in histologic studies.

Serum urea levels decreased with increase in dose of extract. This can also be seen in severe liver diseases or malnutrition but are not diagnostic of these conditions. The creatinine levels remained normal indicating normal kidney function, [17]. This was supported by the normal results got for serum electrolytes, sodium, potassium and chloride except bicarbonate which increased slightly but significantly in a non-dose dependent fashion. This may suggest respiratory difficulties associated with collection of samples from small animals such as rats or other causes.

The mild peri-portal lymphocytic infiltration of the liver was not dose-dependent and may be due to metabolism of toxic materials contained in the extract.

5. CONCLUSION

In conclusion, *Uvaria chamae* leaf extract may be safe when consumed in low dose and its use in traditional medicine may not pose much, if any, danger to the patients.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Animal Ethic committee approval has been collected and preserved by the author(s)

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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