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Ethanolic Extract of *Myristica fragrans (Houtt*) seeds ameliorates cadmium-induced hepatotoxicity and nephrotoxicity in female wistar rats

***Bamidele O.[1], Orti D.[1], Babatunde L. D.[1], Adedeji G. T.[1], Akinnuga A. M.[2] and Arokoyo D. S.[1]**

[1]*Department of Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, Bowen University, Iwo, Osun State, Nigeria*
[2]*Department of Human Physiology, Cross River University of Technology, Okuku Campus, Yala, Cross River State, Nigeria*

ABSTRACT

The effects of Myristica fragrans on cadmium-induced hepatotoxicity and nephrotoxicity was studied in female Wistar rats. Thirty rats were randomly divided into five groups of six rats per group. Group I was given normal saline (10ml/kg) for five weeks. Group II was given cadmium sulphate at a dose of 1.5mg/100kg body weight for three weeks. Group III received cadmium and Myristica fragrans extract at doses of 1.5mg/100kg body weight and 150mg/kg body weight respectively. Group IV received Myristica fragrans extract at a dose of 150mg/kg body weight for two weeks followed by cadmium at a dose of 1.5mg/100kg body weight from the third to the fifth week. Group V was given cadmium for the first three weeks followed by Myristica fragrans for the fourth and fifth weeks. Both cadmium sulphate and Myristica frangrans extract were administered orally. The levels of the liver enzymes in the serum and some markers to assay for kidney functions were measured. The results showed that cadmium sulphate significantly increased liver enzymes, Creatinine and Urea serum levels. There was also a significant decrease in Glutathione and Total protein serum levels compared with the healthy control group $p < 0.05$. Myristica fragrans extract showed significant reduction ($p<0.05$) in the levels of Alkaline Phosphatase, Alanine transaminase, Aspartate transaminase, Creatinine and Urea while it significantly increased ($p<0.05$) levels of Glutathione and Total protein when compared to the cadmium control group.Myristica fragrans seed has protective and therapeutic potentials against cadmium-induced hepatotoxicity and nephrotoxicity in female albino rats.

Key words: *Myristica fragrans* , Cadmium sulphate, Hepatotoxicity, Nephrotoxicity Liver enzymes, Albino rat.

INTRODUCTION

Pollution of the ecosystem with industrial, traffic, agricultural and sewage effluents results in contamination of air, food and water with toxic agents such as heavy metals which constitute a major public health hazard [1]. Humans are exposed to various types of environmental contaminants at different stages of their life span; the majority of these are harmful. Lead and cadmium are recognized as the most toxic environmental pollutants and exposure to it seems to be unavoidable for those who live in industrialized countries [2].

Cadmium (Cd) is considered to be one of the most toxic heavy metals. Cadmium has been found to produce wide range of biochemical and physiological dysfunctions in humans and laboratory animals [3]. Exposure to Cadmium

as a result of industrial and environmental pollution leads to dangerous health hazards [4]. Exposure to cadmium occurs primarily through ingestion of contaminated water, food and to a significant extent through inhalation and cigarette smoking. Cadmium poisoning came into prominence with the infamous itai-itai disease of the 1960s in Japan after ingestion of cadmium-contaminated rice. Cadmium has a long biological half life (20 yrs) and primarily affects the kidneys, liver and intestine, and a prolonged exposure has proven to be carcinogenic to liver, kidney, lung, prostate, hematopoietic and other systems [5].

Cadmium is a by-product of the mining and smelting of lead and zinc. It is used in nickel-cadmium batteries, dyes, plastics, electrochemistry and paint pigments. It can be found in soils because of insecticides, fungicides, sludge and commercial fertilizers containing Cadmium that are used in agriculture [6]. In addition, Cadmium is a carcinogenic metal to which humans are exposed through contaminated foods, water or air. Chronic cadmium poisoning can result in nephrotoxicity, osteoporosis, cardiovascular diseases, testicular necrosis, prostatic and testicular cancers, renal failure and neurodegenerative conditions [7].

One of the major concepts regarding the toxicity of heavy metals is attributed to their ability to generate reactive oxygen species, which cause oxidative stress [8]. Information on the underlying molecular mechanisms of Cadmium-induced pathologies is rather fragmentary, however multiple studies indicate that Cadmium exposure induces oxidative stress at the cellular level [9].

Medicinal plants have played and continue to play an invaluable role in the drug discovery process [10]. Nutmeg (*Myristica fragrans*), whose seed is widely used as a spice, is a tropical, dioeciously evergreen tree native to the Moluccas or Spice Island of Indonesia. Nutmeg has a characteristic pleasant fragrance and is slightly warm feel in the mouth [11]. Nutmeg is popular as a spice and also possesses various therapeutic properties. It is used for both culinary and medicinal purposes [12]. It has aromatic, stimulant, narcotic, carminative, astringent, aphrodisiac, hypolipidemic, anti-platelet aggregation, antifungal, antidysenteric, anti-inflammatory activities, and also as a remedy for stomach ache, rheumatism and vomiting in pregnancy [13,14].

As a part of the growing consciousness of dietary habits, herbs and spices are becoming an important source of natural antioxidants [15]. A study conducted by Olaleye et al. [11] shows that nutmeg popularly consumed as food and for various medicinal purposes may contain some bioactive components with antioxidant properties. Cadmium-induced hepatotoxicity and nephrotoxicity has been established to result from oxidative stress at the cellular level. *Myristica fragrans* has been found to possess antioxidant properties. However, it has not yet been proven whether or not *Myristica fragrans*, has ameliorative effects on Cadmium-induced hepatotoxicity and nephrotoxicity. Hence, this present study was conducted to scientifically investigate the effect of ethanolic extract of *Myristica fragrans houtt*. seed (nutmeg) on cadmium-induced hepatotoxicity and nephrotoxicity in female wistar rats.

MATERIALS AND METHODS

PLANT MATERIAL

The *Myristica fragrans* seeds were obtained from Sango local market in Ibadan, Nigeria. The seeds were identified and authenticated by Dr Ayanbamiji of the Department of Biological Sciences, Bowen University, Iwo (Voucher number BUI 065).The seeds were dried after which they were ground with a blender to reduce it to fine powder. Ethanol (70% v/v, BDH) was used as solvent for extraction of the seed material. 2 kg of the ground seed was soaked in 4L (4000ml) of ethanol (70% v/v, BDH) for 72 hours. Thereafter, the mixture was filtered with Whatman no.1 filter paper to separate the filtrate from the residue. The filtrate was obtained and dried to constant weight using a Rotatory evaporator. About 32g of extract was obtained. A stock solution of 50mg/ml was then prepared and kept in capped sample bottles in a refrigerator until the time of experiment.

EXPERIMENTAL ANIMALS

Thirty (30) female Wistar rats weighing between 200g-250g were obtained from Animal holding of Ladoke Akintola University of Technology, Ogbomoso, Oyo State. They were housed in animal cages with suitable temperature and humidity in the Animal House of Department of Physiology, Bowen University, Iwo, Osun state, Nigeria. The animals were fed with rat pellet and water ad libitum. The rats were acclimatized for 2 weeks before the start of the experiment. All procedures involving the use of animals in this study complied with the guiding

principles for research involving animals as recommended by the declaration of Helsinki and the Guiding principles in the care and use of animals [16].

EXPERIMENTAL DESIGN
Thirty (30) female Wistar rats were distributed into five (5) groups of six (6) rats per group.
Group 1: Control group, received normal saline for 5 weeks by oral gavage.
Group 2: Cadmium control group, received Cadmium sulphate daily for 3 weeks by oral gavage.
Group 3: Cadmium and *Myristica fragrans* simultaneous treatment group, received Cadmium sulphate and *Myristica fragrans* daily for 3 weeks by oral gavage.
Group 4: *Myristica fragrans* pre-treatment group, received *Myristica fragrans* for the first 2 weeks followed by Cadmium sulphate for 3 weeks by oral gavage.
Group 5: *Myristica fragrans* post-treatment group, received Cadmium sulphate for the first 3 weeks followed by *Myristica fragrans* for 2 weeks by oral gavage.

BODY WEIGHT MEASUREMENT
The body weights of the rats were taken before the start of the experiment and at the end of each week throughout the period of the experiment. The measurements were taken using a sensitive weighing balance.

SERUM ANALYSIS
Blood was collected from the rats by cardiac puncture after anaesthesia with Chloroform. The blood was left to clot in plain bottles after which it was centrifuged at 5000 rpm for 5 minutes and then the serum was collected into plain serum bottles. The serum was used for the following analyses:

a. Tests of Liver function: Alanine transaminase (ALT), Aspartate transaminase (AST), Alkanine phosphatase (ALP), Glutathione (GSH)
b. Tests of Kidney function: Total protein, Creatinine, Urea

LIVER FUNCTION ANALYSIS:
Activities of ALT and AST were assayed by the method of Reitman and Frankel [17]. ALP activity was determined by Rec. GSCC method [18] while GSH was assayed according to the method described by Ellman [19].

KIDNEY FUNCTION ANALYSIS:
Total protein levels in the serum of the animals were assayed by Biuret method [20]. The concentrations of creatinine and urea in serum were evaluated with commercially available kits from Randox Laboratories Limited (United Kingdom) via spectrophotometry.

STATISTICAL ANALYSIS
The results were expressed as Mean ± Standard Error of the Mean (SEM). The one way ANOVA method was used to analyze the data, followed by a post-hoc test (Newman-Keuls) using the GraphPad Prism® 6 statistical software. The results were considered significant at $p < 0.05$ and $p< 0.01$.

RESULTS

Effect of Cadmium and *Myristica fragrans* on Body Weights in Cadmium-Treated Wistar Rats
The body weights of the rats were expressed in Mean ± Standard Error of the Mean (Mean ± SEM). The rats were weighed at the start of the experiment (week 0), and at the end of each week throughout the experiment (weeks 1-5). .When the mean body weights of cadmium control group (Group II) were compared with the healthy control group (Group I) over the weeks at a p-value of 0.05 and 0.01, there was a progressive weight loss that was not statistically significant.

In the cadmium and *Myristica fragrans* simultaneous treatment group (Group III), when the mean body weights were compared with Cadmium control group (Group II) over the weeks at a p-value of 0.05 and 0.01, there was progressive weight loss that was not statistically significant.

There were weight losses in *Myristica fragrans* pre-treatment and post treatment groups (Group IV and V), when the mean body weights were compared with healthy control (Group I) over the weeks. The weight losses were statistically significant in both groups at week 5 ($p < 0.05$ and $p < 0.01$ respectively).

TABLE1: Effect of *Myristica fragrans* extract on body weights of cadmium sulphate-treated female wistar rats (n=5)
a = significantly different from the healthy control group (Group I) at p < 0.05

GROUPS	BODY WEIGHT(g)					
	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4	WEEK 5
GROUP I (Normal Control)	244.33±8.353	229.33±7.424	231.67±1.856	226.33±2.963	228.33±1.856	233.33±6.333
GROUP II (Cadmium control)	228.33±4.178	226.67±3.180	230.67±15.815	235.00±4.163	225.33±3.930	217.00±2.000
GROUP III (Cadmium + M. fragrans)	237.00±9.166	249.00±8.000	252.00±7.506	239.33±1.202	227.33±2.963	240.67±5.333
GROUP IV (M. fragrans pre-treatment)	250.00±5.196	224.00±5.508	212.67±3.383	205.67±10.990	212.67±3.390	203.33±16.333^{ap}
GROUP V (M. fragrans post-treatment)	231.33±2.667	227.33±3.930	228.33±3.844	202.00±10.408	204.00±8.000	199.00±13.000^{ap}

p = significantly different from the healthy control group (Group I) at p < 0.01

Effect of Cadmium and *Myristica fragrans* on Some Hepatic Biochemical Parameters

ALKALINE PHOSPHATASE (ALP)

The ALP levels of rats treated with Cadmium and *Myristica fragrans* is represented in Table 2.

Table 2: Effect of *Myristica fragrans* on Cadmium Sulphate Induced Changes in Some Hepatic Biochemical Parameters in Female Wistar Rats (n=5).

GROUPS	ALP (u/l)	AST(u/l)	ALT(u/l)	GSH(u/l)
GROUP I (Control)	107.55±1.519	17.17±1.934	11.61±3.448	29.33±7.688
GROUP II (Cadmium control)	220.800±19.386^{ap}	67.133±2.171^{apbq}	40.75±1.050^{ap}	10.00±5.000^{ap}
GROUP III (Cadmium + M. fragrans)	130.64±14.282^{bq}	50.34±1.729^{apbq}	29.43±4.119^{a}	35.50±2.500^{bq}
GROUP IV (M. fragrans pre-treatment)	146.28±19.320^{bq}	42.35±0.550^{apbq}	38.03±9.690^{ap}	38.00±4.723^{bq}
GROUP V (M. fragrans post-treatment)	143.52±19.320^{bq}	55.55±2.650^{apbq}	5.77±2.050^{bq}	63.00±1.000^{apbq}

ALP- Alkaline Phosphatase, AST- Aspartate Aminotransferase, ALT- Alanine Aminotransferase, GSH- Glutathione.
a = significantly different from the healthy control group (group 1) at p.0.05
b = significantly different from the cadmium control group (group 2) at p.0.05
p = significantly different from the healthy control group (group 1) at p.0.01
q = significantly different from the cadmium control group (group 2) at p.0.01

When the cadmium control group (Group II) was compared to the healthy control group (group I) at a p-value of 0.05 and 0.01, there was an increase in ALP level that was statistically significant. When the cadmium control group (Group II), the *Myristica fragrans* pre-treatment group (Group IV) and the *Myristica fragrans* post-treatment group (Group V) were compared to the healthy control group (Group I) at a p-value of 0.05 and 0.01 there was an increase in ALP levels that was not statistically significant.

When the cadmium and *Myristica fragrans* simultaneous treatment group (Group III), the *Myristica fragrans* pre-treatment group, the *Myristica fragrans* post-treatment group (Group V) were compared to the cadmium control group (Group II) at a p-value of 0.05 and 0.01, there was a significant decrease in ALP levels.

ASPARTATE TRANSAMINASE (AST)

The AST levels of rats treated with Cadmium and *Myristica fragrans* is represented in Table 2.
When the cadmium control group (group II) and the *Myristica fragrans* pre-treatment group (group IV) were compared to the healthy control group (group I) at a p value of 0.05 and 0.01, there was an increase in AST levels that was statistically significant. When the cadmium and *Myristica fragrans* simultaneous treatment group (group III) was compared with the healthy control group at a p value of 0.05, there was an increase in AST levels that was

statistically signicant, while at a p value of 0.01, increase in AST levels is not statistically significant. When the *Myristica fragrans* post-treatment group (group V) was compared to the healthy control group (group I) at a p-value of 0.05 and 0.01, there was a decrease in AST levels that was not statistically significant.

The result showed that *Myristica fragrans* post-treatment group (group V) significantly decrease AST levels when compared with the cadmium control group ($p< 0.05$). When the cadmium and *Myristica fragrans* simultaneous treatment group (group III) was compared with the cadmium control group (group II) at a p-value of 0.05 and 0.01, there was a decrease in AST levels that was not statistically significant. When the *Myristica fragrans* pre-treatment group (group IV) was compared with the cadmium control group (group II) at a p value of 0.05 and 0.01, there was an increase in AST levels that was not statistically significant.

ALANINE TRANSAMINASE (ALT)

The ALT levels of rats treated with Cadmium and *Myristica fragrans* is represented in Table 2.

When the cadmium control group (group II), the cadmium and *Myristica fragrans* simultaneous treatment group (group III), the *Myristica fragrans* pre-treatment and post-treatment (groups IV and V respectively) groups were compared with the healthy control group (group I) at a p value of 0.05 and 0.01, there was an increase in ALT levels that was statistically significant.

When the cadmium and *Myristica fragrans* simultaneous treatment group (group III), the *Myristica fragrans* pre-treatment and post-treatment (groups IV and V respectively) groups were compared with cadmium control group (group II) at a p value of 0.05 and 0.01, there was a decrease in ALT levels that was statistically significant.

GLUTATHIONE (GSH)

The GSH levels of rats treated with Cadmium and *Myristica fragrans* is represented in Table 2.

When the cadmium control group (group II) was compared with the healthy control group (group I) at a p value of 0.05 and 0.01, there was a decrease in GSH level that was statistically significant. When the *Myristica fragrans* post-treatment group (group V) was compared with the healthy control group (group I) at a p value of 0.05 and 0.01, there was an increase in GSH level that was statistically significant. When the cadmium and *Myristica fragrans* simultaneous treatment group (group III) and the *Myristica fragrans* pre-treatment group (group IV) was compared with the healthy control group (group I) and there was an increase in GSH level that was not statistically significant.

When the cadmium and *Myristica fragrans* simultaneous treatment group (group III), the *Myristica fragrans* pre-treatment and post-treatment groups (groups IV and V respectively) were compared with the cadmium control group (group II) at a p value of 0.05 and 0.01, there was an increase in GSH level that was statistically significant.

EFFECT OF CADMIUM AND *Myristica fragrans* ON SOME RENAL BIOCHEMICAL PARAMETERS

CREATININE

The blood serum Creatinine concentration of rats treated with Cadmium and *Myristica fragrans* is represented in Figure 1.

When the cadmium control group (group II), the *Myristica fragrans* pre-treatment and post-treatment group (groups IV and V respectively) were compared with the healthy control group (group I) at a p-value of 0.05 and 0.01, there was an increase in creatinine concentration that was statistically significant (p.0.05 and p.0.01 respectively). When the cadmium and *Myristica fragrans* simultaneous treatment group (group III) was compared to the healthy control group (group I) at a p-value of 0.05 and 0.01, there was an increase in creatinine concentration that was not statistically significant (p.0.05 and p.0.01 respectively).

When the cadmium and *Myristica fragrans* simultaneous treatment group (group III) was compared with the cadmium control group (group II) p-value of 0.05 and 0.01, there was a decrease in creatinine concentration that was statistically significant (p.0.05 and p.0.01 respectively). When the *Myristica fragrans* pre-treatment group (group IV) was compared to the cadmium control group at a p value of 0.05 and 0.01, there was an increase in creatinine concentration that was not statistically significant (p.0.05 and p.0.01 respectively). When the *Myristica fragrans* post-treatment group (group V) was compared to the cadmium control group (group II) at a p-value of 0.05 and 0.01, there was an increase in creatinine concentration that was not statistically significant (p.0.05 and p.0.01)

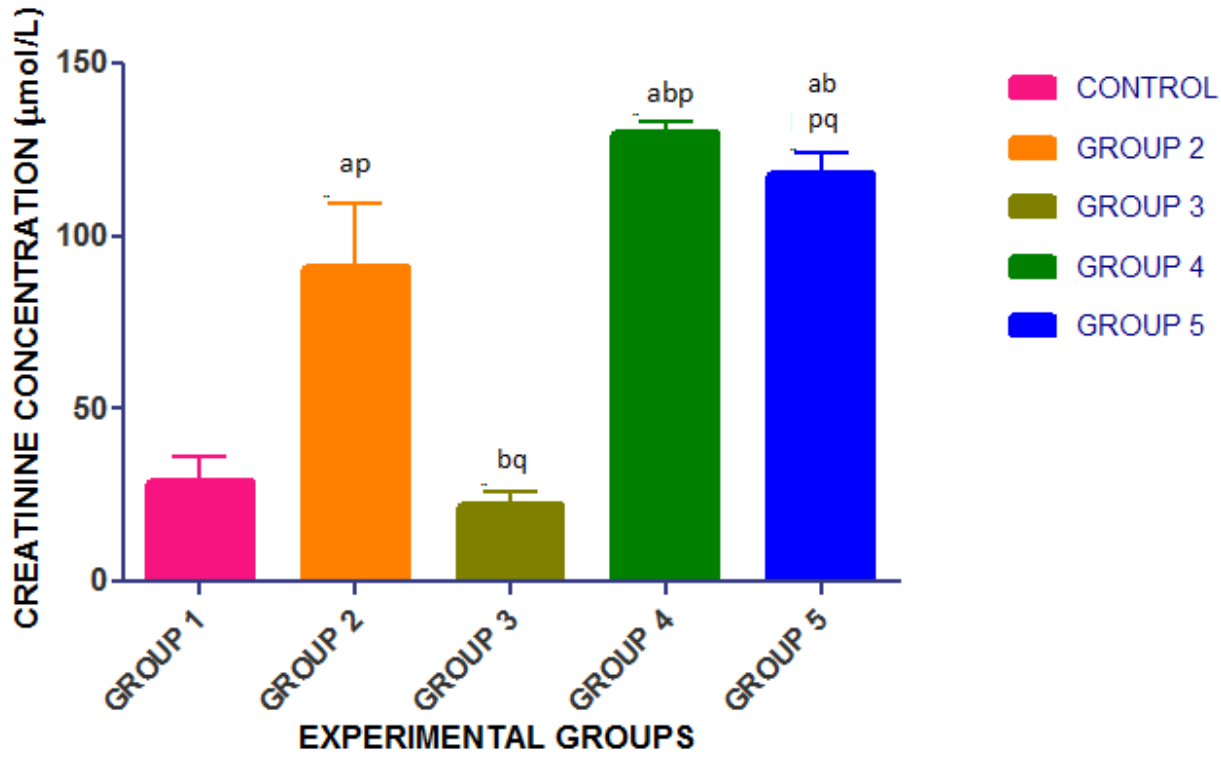

FIGURE 1: LEVELS OF CREATININE CONCENTRATION IN THE EXPERIMENTAL RATS.
a = significantly different from the healthy control group (group 1) at p.0.05
b = significantly different from the cadmium control group (group 2) at p.0.05
p = significantly different from the healthy control group (group 1) at p.0.01
q = significantly different from the cadmium control group (group 2) at p.0.01

UREA

The blood serum urea concentration of rats treated with Cadmium and *Myristica fragrans* is represented in Figure 2.

When the cadmium control group (group II) and the *Myristica fragrans* pre-treatment group (group IV) was compared to the healthy control group (group I) at a p value of 0.05 and 0.01, there was an increase in urea concentration that was statistically significant (p.0.05 and p.0.01 respectively). When the cadmium and *Myristica fragrans* simultaneous treatment group (group III) and the *Myristica fragrans* post-treatment group (group V) were compared with the healthy control group (group I) at a p value of 0.05 and 0.01, there was an increase in urea concentration that was not statistically significant (p.0.05 and p.0.01 respectively).

When the cadmium and *Myristica fragrans* simultaneous treatment group (group III) and the *Myristica fragrans* post-treatment group (group V) were compared with the cadmium control group (group II) at a p value of 0.05 and 0.01, there was a decrease in urea concentration that was statistically significant (p.0.05 and p.0.01 respectively). When the *Myristica fragrans* pre-treatment group (group IV) was compared with the cadmium control group at a p value of 0.05 and 0.01, there was a decrease in urea concentration that was not statistically significant (p.0.05 and p.0.01 respectively).

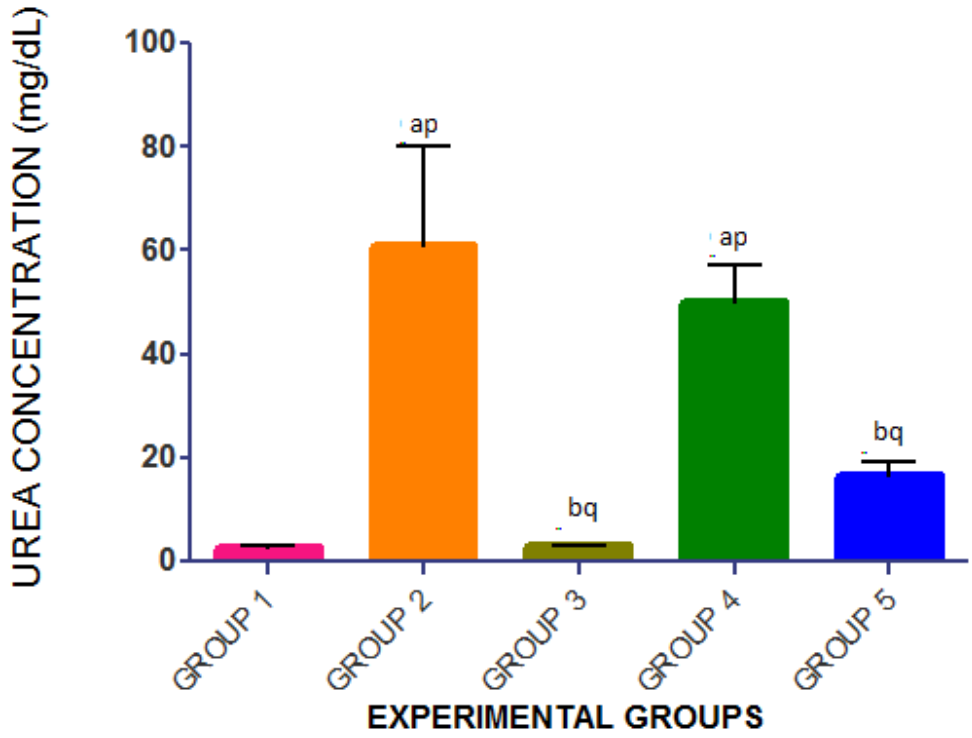

FIGURE 2: LEVELS OF UREA CONCENTRATION IN THE EXPERIMENTAL RATS
a = significantly different from the healthy control group (group 1) at p<0.05
b = significantly different from the cadmium control group (group 2) at p<0.05
p = significantly different from the healthy control group (group 1) at p<0.01
q = significantly different from the cadmium control group (group 2) at p<0.01

TOTAL PROTEIN

The blood serum total protein concentration of rats treated with Cadmium and *Myristica fragrans* is represented in Figure 3.

When the cadmium control group (group II), the cadmium and *Myristica fragrans* group (group III), the *Myristica fragrans* post-treatment group (groups V) were compared with the healthy control group (group I) at a p-value of 0.05 and 0.01, there was a decrease in total protein concentration that is statistically significant (p.0.05 and p.0.01 respectively). When the *Myristica fragrans* pre-treatment group (group IV) was compared with the healthy control group (group I) at a p-value of 0.05 and 0.01, there was an increase in total protein concentration that was statistically significant (p.0.05 and p.0.01 respectively).

When the cadmium and *Myristica fragrans* simultaneous treatment group (group III), the *Myristica fragrans* pre-treatment and post-treatment groups (groups IV and V respectively) were compared with the cadmium control group (group II) at a p-value of 0.05 and 0.01, there was an increase in total protein concentration that was statistically significant (p.0.05 and p.0.01 respectively).

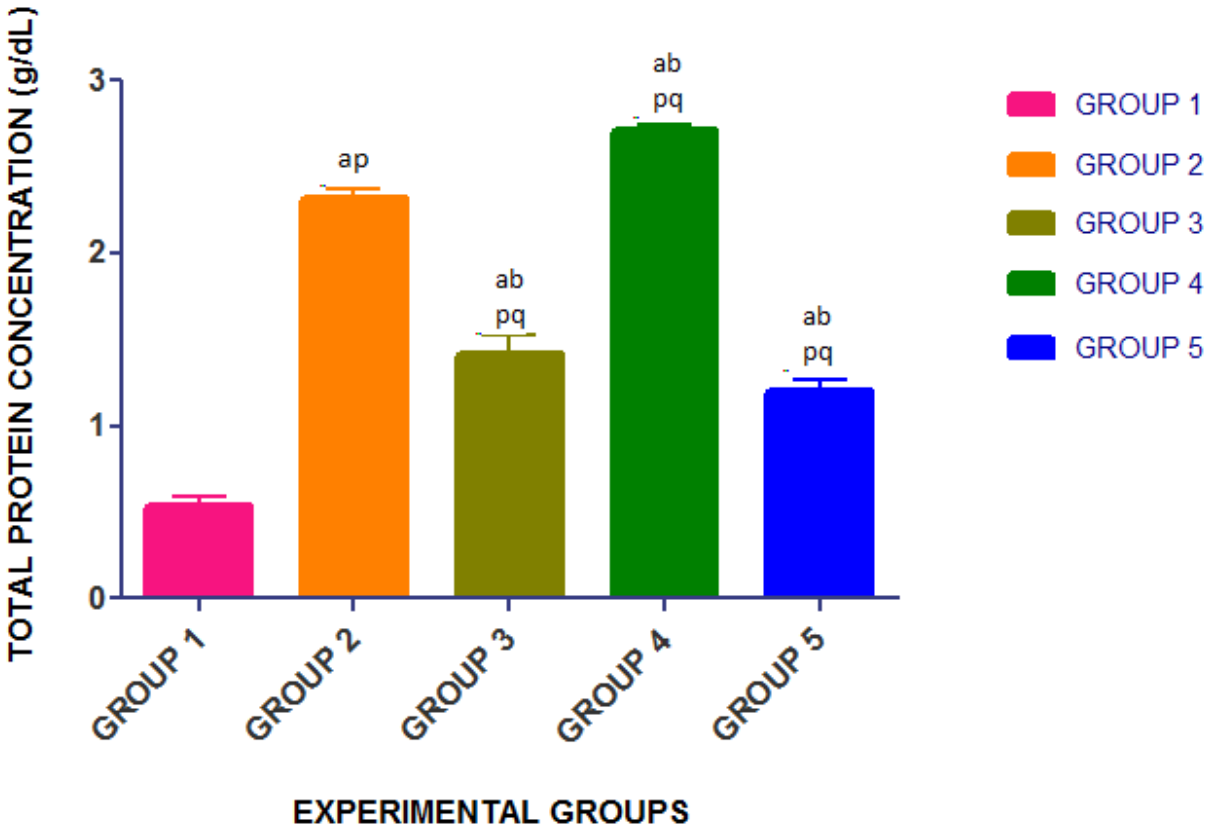

FIGURE 3: TOTAL SERUM PROTEIN LEVELS IN THE EXPERIMENTAL RATS.
a = significantly different from the healthy control group (group 1) at p.0.05
b = significantly different from the cadmium control group (group 2) at p.0.05
p = significantly different from the healthy control group (group 1) at p.0.01

DISCUSSION

The present study showed the effects of seed extract of *Myristica fragrans* , on cadmium-induced hepatotoxicity and nephrotoxicity in female wistar rasts. In this study, the cadmium control group experienced progressive weight loss throughout the experiment which was statistically significant in the third week. This is in accordance with the result of Nwokocha et al [21] in a study carried out on the comparative effect of palm oil in reducing cadmium and lead liver toxicity. The cadmium and *Myristica fragrans* simultaneous treatment group, the *Myristica fragrans* pre-treatment and post-treatment groups showed a non-significant progressive weight loss throughout the experiment. This is contradictory to the study carried out by Nivetha and Prasanna [22] where *Myristica fragrans* reversed weight loss caused by Gentamicin-induced toxicity. Also, the *Myristica fragrans* pre-treatment and post-treatment groups showed a significant weight loss when compared with the healthy control group while the cadmium and *Myristica fragrans* simultaneous treatment group showed a non-significant weight loss when compared with the healthy control group. This again is contradictory to the study carried out by Nivetha and Prasanna [22]. This may be due to the increased burden on the liver of both substances administered during the time period which was reflected as weight loss in the rats.

The commonest enzymes employed as indicators of hepatocellular damage are ALT, AST, and ALP. Damage to the liver results in increased plasma activities of these enzymes. Increases in these enzymes activities are proportional to the extent of the hepatic damage (Morgan et al, 1993). Serum activities of ALP, ALT and AST were increased significantly in the cadmium control group when compared with the healthy control group. This is similar to previous studies [23, 24]. *Myristica fragrans* ameliorated this effect as can be seen in the significant decrease in ALT activities of the Cadmium and *Myristica fragrans* simultaneous treatment group and *Myristica fragrans* pre-treatment and post-treatment groups and also the significant decrease in AST activities in the *Myristica fragrans*

post-treatment group when compared to the cadmium control group. This may be due to the antioxidant and hepatoprotective activities of *Myristica fragrans* [25] and is in accordance with the study carried out by Ige et al, [26] where Allium cepa was used to reverse Cadmium-induced hepatotoxicity.

Serum activitivity of ALP was increased in the cadmium control group significantly in comparison with the healthy control group. This is in accordance with the results of Obianime et al [27]. *Myristica fragrans* was found to alleviate this effect in the cadmium and *Myristica fragrans* simultaneous treatment group and the *Myristica fragrans* pre-treatment and post-treatment groups which showed a significant decrease in ALP levels when compared to the cadmium control group. This result reinforces the hepatoprotective effect of *Myristica fragrans* and is also in line with the results of Obianime et al [27] where vitamins C and E were shown to alleviate cadmium-induced hepatotoxicity in female guinea pigs.

Kidney GSH activity level was found to be significantly lower in the cadmium control group when compared with the healthy control group. This may be as a result of the cytotoxicity of cadmium which alters cellular GSH metabolism [28] and is in accordance with the results of Kaplan et al, [29] where GSH level was significantly lower in rats chronically exposed to Cadmium

chloride. *Myristica fragrans* caused significant increases in the GSH levels of the cadmium and *Myristica fragrans* simultaneous treatment group and the *Myristica fragrans* pre-treatment and post-treatment groups when compared with the cadmium control group. This may be due to the free radical scavenging activities of *Myristica fragrans* and the result is comparable also with that of Nivetha and Presanna [22] where *Myristica fragrans* restored serum GSH levels to near normalcy in Gentamicin-induced hepatotoxicity and it also demosnstrates the ability of *Myristica fragrans* in reversing cadmium hepatotoxicity.

The results also significant increase in creatinine and urea levels in the cadmium control group when compared to the healthy control group. This is in accordance with the results of El-Maraghy et al [30]. This may be due to the damage caused by cadmium in cellular membrane components especially, of the proximal tubular cells which leads to tubular dysfunction [31, 32]. There was a significant decrease (to near normal levels) in the both creatinine and urea levels in the cadmium and *Myristica fragrans* simultaneous treatment group when compared with the cadmium control group. The *Myristica fragrans* pre-treatment group showed non-significant decrease in urea levels when compared with the cadmium control group but significant increase when compared with the healthy control group urea level was also decreased significantly in the *Myristica fragrans* post-treatment group when compared to the cadmium control group. These results are in accordance with that of Nivetha and Presanna [22] where *Myristica fragrans* increased serum urea and creatinine levels in Gentamicin-induced nephrotoxic rats. This means that *Myristica fragrans* may have a protective ability against cadmium-induced nephrotoxicity.

There was a significant decrease in total serum protein level of the cadmium control group when compared with the healthy control group. This is in accordance with the research carried out by Ige et al [26] and may be due to cadmium-induced glomerular damage which leads to proteinuria, hence reduced serum total protein level [33]. The cadmium and *Myristica fragrans* simultaneous treatment group, the *Myristica fragrans* pre-treatment and post-treatment groups showed significant increase in the serum total protein level when compared with the cadmium control group. This is also in accordance with the results of Nivetha and Presanna [22] and also demonstrates the ability of *Myristica fragrans* to reverse cadmium-induced kidney damage.

CONCLUSION

Myristica fragrans is effective in alleviating cadmium-induced kidney and liver damage due to its antioxidant properties. This study showed that *Myristica fragrans* may act as an effective post-treatment (therapeutic effect) in cadmium-induced hepatotoxicity while in cadmium-induced nephrotoxicity, *Myristica fragrans* may have both protective and therapeutic effects. Hence, the inclusion of *Myristica fragrans* in the diet of human populations should be strongly advised and promoted, especially in populations at risk of cadmium poisoning due to prolonged environmental exposure.

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