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Effect of G*uiera senegalensis* and Natron on Serum Indices of Cardiac Function of Postpartum Rats

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Peripartum cardiomyopathy (PPCM) is a rare but devastating cardiac failure of indeterminate etiology occurring in late pregnancy or early puerperium. The prevalence of PPCM in Northern Nigeria could be attributed to the unique customary puerperal practices of prolonged consumption of large quantities of *Guiera senegalensis* and Natron. This study investigated the effect of decoction of *G. senegalensis* with and without Natron on cardiac markers, lipid profile and histology of the heart in postpartum female albino rats using standard methods. Thirty-five (35) female albino rats of body weights 190-200 g of five month were randomly grouped into seven (7) of five rats each. Group 2, 3 and 4 were orally administered with 100, 200 and 300 mg/kg body weight of *G. senegalensis*. Group 5, 6 and 7 were orally administered with 100, 200 and 300 mg/kg body weight (1:1) of *G. senegalensis* and Natron by gavage, whereas group 1 received distilled water. The study revealed significant ($p< 0.05$) decrease in triglyceride (TG) in group 2 to VII, high density lipoprotein cholesterol (HDL-c) in group 2, 5 and 6, very low density lipoprotein- cholesterol (VLDL-c) in group 3 to V, couples with significant ($p< 0.05$) increase in low density lipoprotein cholesterol (LDL-c) in group 2, 3, 5 and 7, and for (AIX) in group 2, total cholesterol (TC) in group 2, 3 and 7 when

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compared with control. Significant (p< 0.05) increase in lactate dehydrogenase (LDH) in group 3 to 7, and myoglobin (MB) in group 3 was observed. Significant decrease (p< 0.05) in Troponin I (TnI) in group 2 and 4 was detected. There were no significant (p>0.05) changes in troponin T (Tn T), aspartate amino transferase (AST) and Creatine Kinase **(**CK-NAC) of the treatment group when compared to control group. Histopathological examination of section of the heart revealed ventricular dilatation, hypertrophied with enlarged nuclei, stretched, and irregular and mural thrombi in group 2 to 4 and 7. Inflammation in group 5 and 7, Pigment deposited in group 4 to 7 and mild fibrosis in group 3 were observed. The study demonstrates that consumption of *G. senegalensis* and Natron for 28 days induces dyslipidemia and causes changes in the heart of postpartum rats and thus may contribute to the pathogenesis of PPCM.

Keywords: Guiera senegalensis; natron; peripartum cardiomyopathy (PPCM); serum indices; histopathological parameters; and postpartum rats.

1. INTRODUCTION

Guiera senegalensis is a widely distributed shrub in West and Central Africa. The plant is widely used for the folkloric treatment of infectious diseases, and management of several metabolic diseases [1]. Reports indicate that the plant parts are effective against stomach upset/pains, dysentery and diarrhea [2,3]. More so, the plant is active against cough, arthritis, enteritis, abdominal pain, joints problems, constipation, kidney diseases, jaundice, diabetes mellitus, hypertension and diarrhea [4]. Reprots by Sombie et al. [4] suggest that the plant possess antioxidant, anti-inflammatory activities. It is also believed to have acaricidal effects. Despite it wide usage as antibiotics, boiled extracts of *G. senegalensis*are increasingly used by women in Northern Nigeria for promoting milk production and milk flow during postpartum/postnatal period [5-7]. Thus, these have drawn the interest of researcher to study both the toxicological and biochemical effect of the plants.

Natron is a naturally occurring sodium rich composite material. It's majorly composed of sodium carbonate decahydrate and sodium bicarbonate, as well as minute quantities of both sodium chloride and sodium sulfate. This substance is widely available in parts of Northern Nigeria (especially within Kano state and Borno states), and some neighbouring countries including Chad and Niger Republic [8-10]. Aside the common table salt, natron is the most widely used salt in Nigeria [11]. Natron is traditionally used for as tenderizer, thickener, seasoning and as culinary agent. It also a potentiating adjunct, a preservative, flavour enhancer and additive [9,12-14]. It is commonly taken as an additive in guinea corn or millet porridge, thereby increasing the quality and quantity of breast milk, and the general health of nursing mothers [11,15]. Furthermore, this substance is believed to heal skin infection, respiratory problem, infertility and endocrine disturbances. It promotes uterine contractility and motility, as it may act as an abortifacient agent [16]. Additionally, it acts as an antacid and stomachic for the relief of constipation and flatulence [12].

The postpartum use of natron containing concoctions and hot water bath is widely prevalent in Northern Nigeria. This traditional attitude is suspected to be the basis for an increasing prevalence of peripartum cardiomyopathy (PPCM) amongst women in the region [17-18]. In northern Nigeria, the prevalence is 1 in 102 live births [18], as against 1 in 300 live births in Haiti [19], 1 in 1000 live births in South Africa [20], 1 in 4000 live births in the USA and an incidence of 1 in 6,000 live births in Japan [21]. Thus, investigating the effect of *G. senegalensis* and natron concoction vis-a-vis PPCM is significant. The aim of the present study was to evaluate the effect of aqueous *G. senegalensis* leaves extract, in combination with and without natron on the biochemical indices and histopathological parameters of postpartum rats' heart tissue.

2. MATERIALS AND METHODS

2.1 Chemicals and Reagents

All chemicals and reagents used in this study are of analytical grades. Assay kits were purchased from Randox Company, USA.

2.2 Sample Collection and Identification

Natron and fresh leaves of *G. senegalensis* were purchased from Sokoto Central Market, Sokoto State, Nigeria. The plant was identified and authenticated at the Herbarium unit of the

Taxonomy Unit, Department of Biological Sciences, Usmanu Danfodiyo University Sokoto (voucher number: UDUH/ANS/0144). The fresh leaves were rinsed and shed dried. The samples were pulverized and then sieved.

2.3 Preparation of Extract

Two hundred grams of *G. senegalensis* powder in one liters of distilled water was shaken every six hours for 72 hours. The solution was filtered with a muslin cloth and then re-filtered using Whatman's number 1 paper (11 µm). The extract was evaporated to dryness at 25°C, and then cooled on an aluminum tray. Appropriate measurement of 100, 200 and 300 mg/kg body weight (b.w.) of plant extract, and 100, 200 and 300 mg/kg b.w. of plant extract + natron (1:1) were dissolve in distilled water. The extract and formulated concoction was administration once daily for a period of 28 days.

2.4 Experimental Animals

Three month old female albino rats having a body weight of 190-200 g were used in this study. The rats were purchased from the Nigerian Institute for Trypanosomiasis Research, Kaduna state. The experimental rats were housed in cages and kept in ventilated rooms at 12 hour light/dark cycle, with free access to pelleted feed (Vital feeds Nigeria Plc., Jos, Nigeria) and tap water *ad libitum*. The rats were grown into maturity and co-habited with male rats, then separated after pregnancy. After delivery, the rats were thereafter randomly divided into 7 groups grouped as follows: Group 1 were control animals administered distilled water; Group 2 were treated with 100 mg/kg b.w. of *G. senegalensis* extract; Group 3 were administered 200 mg/kg b.w. of *G. senegalensis* extract; Group 4 received 300 mg/kg b.w. of *G. senegalensis* extract; Group 5 were treated with 100 mg/kg b.w. (1:1) of *G. senegalensis* + natron; Group 6 were given 200 mg/kg b.w. (1:1) of *G. senegalensis* + natron; and Group 7 received 300 mg/kg b.w. (1:1) of *G. senegalensis* + natron. The treatments were orally administered daily, for a period of 28 days. Weight changes were monitored throughout the experimental period.

2.5 Acute Toxicity Study

Acute toxicity study was conducted using the method of Lorke [22] in two phases. In the first phase, 9 rats weighing 180 – 200 g were divided into three groups of three rats each. After overnight starvation, *G. senegalensis* aqueous extract was administered at a doses 10, 100 and 1000 mg/kg b.w. (body weight) respectively. The animals were observed for 24 h for signs of toxicity. In the second phase, 9 rats were administered the extract at a doses of 1600, 2900, and 5000 mg/kg b.w. respectively.

2.6 Blood Collection and Biochemical Analysis

Blood sampled were collected from jugular veins of anesthetized animals, allowed to clot and then centrifuged at 4000 rpm for 10 minutes. The serum was then used to analyse biochemical indices of cardiac function (parameters) and lipid profile. ELISA test kits were employed for determination of both cardiac specific troponin I (cTn-I), cardiac specific troponin T and myoglobin (MB) using the method of Apple et al. [23]. Creatine kinase (CK), lactate dehydrogenase (LDH) and aspartate amino transferase (AST) activities were determined [24-25].

Serum total cholesterol (TC) was estimated by cholesterol oxidase peroxidase (CHO-POD) method [26]. Triglyceride levels were assayed by the method [27], while serum HDL-C was estimated by enzymatic method [28]. The method of Friedewald et al. [29] was used for the estimation of both serum LDL-C, and serum VLDL–C, while atherogenic index (AIX) was calculated as the ratio of LDL-cholesterol to HDL-cholesterol [30]. Histopathological analysis was conducted using standard method [31].

2.7 Statistical Analysis

The results are expressed as mean ± standard error of mean (SEM). The differences variables were compared using one-way ANOVA, followed by Duncan's multiple comparison tests using GraphPad InStat software (Version 3.0, San Diego, USA). *P*-values of < 0.05 were considered statistically significant.

3. RESULTS

3.1 Acute Toxicity of Aqueous Extract of *G. senegalensis*

Table 1 shows the acute toxicity study *G. senegalensis* aqueous extract administered to rats. There were neither deaths nor any sign of toxicity after administration of 5000 mg/kg b.w.

single oral dose of *G. senegalensis* aqueous extracts.

3.2 Body Weight of Postpartum Rats Treated with *G. senegalensis* and Natron

The body weight of postpartum rats after 28 days administration of *G*. *senegalensis* aqueous extract with and without natron is presented in Table 2. The administration of 100 and 300 mg/kg b.w. aqueous extract of *G. senegalensis* + natron resulted in a significant ($p<0.05$) decrease in body weight in third and fourth week when compared to the control group. More so, significant ($p<0.05$) decrease were observed in the second, third and fourth weeks in animals treated with 200 mg/kg b.w. of *G. senegalensis* + natron.

3.3 Lipid Profile of Postpartum Rats Treated with *G. senegalensis* and Natron

Table 3 shows the lipid profile of postpartum rats administered aqueous extract of *G. senegalensis* with and without natron. There was significant increase ($p< 0.01$) in LDL and TC in groups treated with 100 and 200 mg/kg b.w. aqueous extract of *G. senegalensis* when compared to the control group. More so, a significant increase ($p< 0.01$) of AIX was observed among animals that received 100 mg/kg b.w. of aqueous *G. Senegalensis* as well as TC for animals treated with 300 mg/kg b.w., and LDL for 100 and 300 mg/kg b.w. *G. senegalensis* + natron. A significant ($p<0.01$) decline of TAG levels was observed amongst animals treated with 100 to 300 mg/kg b.w. of G*. senegalensis* + natron, when compared with the control group. A significant decrease ($p<0.01$) in HDL levels was observed in animals treated with 100 mg/kg b.w. of *G. senegalensis* + natron, while VLDL levels weresignificant decreased ($p < 0.05$) in animals treated with 300 mg/kg b.w.*G. senegalensis*, as well as in animals administered 100 mg/kg b.w. *G. senegalensis*, and 200 mg/kg b.w.*G. senegalensis* + natron.

3.4 Cardiac Markers of Postpartum Rats Treated with Aqueous Extract of *G. senegalensis* with and without Natron

The effect of aqueous extract of *G. senegalensis* with and without natron on cardiac biomarkers of postpartum rats is presented in Table 4. The outcomes revealed that no significant difference ($p>0.05$) between the TnT, CK-NAC and AST of treatment group when compared with the control. A significant decrease in levels of TnI was observed amongst animals that received 100 mg/kg b.w. and 300 mg/kg b.w. of *G. senegalensis* aqueous extract ($p<0.05$ and $p<0.01$ respectively). Likewise, LDH decreased significant ($p<0.01$) amongst animals of 100 mg/kg b.w. *G. senegalensis.* Contrary, LDH activity increased significantly ($p<0.01$) in the 200 and 300 mg/kg b.w. of *G. senegalensis* extracts administered groups, and also for all *G. senegalensis* aqueous extract + natron groups.

3.5 Histopathological Finding of the Heart of Postpartum Rats

The histopathology of the heart of postpartum rats administered with *G. senegalensis* or in combination with natron is presented in Figs 1 to 7. Normal histological structure of the heart cellswere observed amongst control animals (Fig. 1). Severe ventricular dilatation, hypertrophy, stretched, mural thrombi and inflammatory cells in cardiac muscle were observed amongst animals that received 100 mg/kg b.w. *G. senegalensis* extract (Fig. 2). As seen in Figs. 3 and 4, animals given 200 or 300 mg/kg b.w. *G. senegalensis* extract had hypertrophy, ventricular dilatation, fibrosis, mural thrombi, with a stretched and pigmented cardiac muscle. In addition to inflammatory cells, similar deformities were observed amongs animal given different doses of *G. senegalensis* and natrond (Figs. 5, 6 and 7).

Table 1. Lethal Dose (LD_{50}) of aqueous extract of *G. senegalensis* on rats in 24 hours

Treatment	Number of rats	Mortality recorded	Mortality rate	Observation
Phase 1				
10mg/kg b.w.	3	Nil	__	No visible sign of toxicity
100mg/kg b.w.	3	Nil	__	No visible sign of toxicity
1000mg/kg b.w.	3	Nil	__	No visible sign of toxicity
Phase 2				
1600mg/kg b.w.	3	Nil	__	No visible sign of toxicity
2900mg/kg b.w.	3	Nil	__	No visible sign of toxicity
5000mg/kg b.w.	3	Nil	__	No visible sign of toxicity

Table 2. Effect of *G. senegalensis* extract and natron concoction on the body weight of postpartum albino rats

Weeks	Control (H_2O ml/kgb.w.)	*G. senegalensis*(mg/kg b.w.)			*G. senegalensis* + Natron (mg/kg b.w.)		
	10	100	200	300	100	200	300
0	191.20 ± 1.39	192.40 ± 2.58	191.80 ± 3.77	193.00± 2.39	192.40 ± 2.56	192.00 ± 2.19	192.40 ± 2.56
1	198.00 ± 1.82	196.40 ± 2.29	201.80 ± 3.12	204.60 ± 2.23	197.00 ± 2.98	196.00 ± 2.20	190.80 ± 2.46
2	206.80 ± 2.04	200.00 ± 2.35	199.80 ± 3.00	209.60 ± 0.86	205.00 ± 4.03	191.80 ± 2.20*	198.00 ± 3.52
3	211.60 ± 1.99	208.80 ± 1.66	209.00 ± 2.03	214.40 ± 1.50	200.40 ± 2.50*	201.40 ± 2.50*	200.00 ± 3.02*
4	223.60 ± 4.06	217.40 ± 2.18	220.00 ± 1.87	221.80 ± 1.99	212.80 ± 2.52*	209.00 ± 1.87*	202.00 ± 2.15*

*Result are express as mean ± SEM (n=5). Values with asterisk are significant (*p< 0.05) different when compared with normal control group.*

Table 3. Effect of aqueous extract of *G. senegalensis* and natron concoction on lipid profile of postpartum albino rats

Parameters	Control (H_2O ml/kg b.w.)	*G. senegalensis* (mg/kg b.w.)			*G. senegalensis* + Natron (mg/kg b.w.)		
	10	100	200	300	100	200	300
TC (mg/dl)	57.78 ± 1.31	77.77 ± 0.68*	65.56 ± 1.58*	53.33 ± 2.22	57.78 ± 0.72	53.33 ± 1.38	69.99 ± 1.12*
TG(mg/dl)	52.22 ± 0.95	36.66 ± 1.22*	27.77 ± 1.66*	19.99 ± 0.85*	28.88 ± 1.46*	38.88 ± 1.82*	46.67 ± 0.78*
HDL(mg/dl)	37.05 ± 2.62	25.18 ± 1.21*	33.33 ± 1.76	39.26 ± 1.40	23.70 ± 1.82*	30.37 ± 1.03*	37.04 ± 1.07
LDL(mg/dl)	10.30 ± 1.02	45.23 ± 1.92*	25.32 ± 0.99*	10.08 ± 1.15	28.29 ± 2.13*	15.32 ± 1.84	23.63 ± 1.55*
VLDL(mg/dl)	10.44 ± 1.78	7.33 ±1.03	5.55 ± 1.27*	3.68 ± 0.42*	5.78 ± 0.96*	7.78 ± 0.78	9.33 ± 1.34
AIX(mg/dl)	0.31 ± 0.15	2.84 ± 1.11*	0.85 ± 0.25	0.29 ± 0.12	1.73 ± 0.68	0.56 ± 0.11	0.63 ± 0.18

*Result are express as mean ± SEM (n=5). Values with asterisk are significant (*p< 0.05) different when compared with control group. TC-Total Cholesterol, TG-Triglyceride, HDL-High density lipoprotein, LDL- Low density lipoproteins, VLDL- very low density lipoproteins, AIX- Atherogenic Index.*

Table 4. Effect of *G. senegalensis* aqueous extract and natron concoction on serum heart function biomarkers of postpartum albino rats

Parameters	Control (H_2O ml/kg b.w.)	*G. senegalensis* (mg/kg b.w.)			*G. senegalensis* + Natron (mg/kg b.w.)		
	10	100	200	300	100	200	300
TnT(µg/l)	6.91 ± 1.43	10.89 ± 1.46	5.28 ± 0.96	4.71 ± 0.53	11.60 ± 2.21	4.72 ± 0.89	7.09 ± 1.31
TnI(µg/l)	8.26 ± 0.51	5.07 ± 0.33*	6.92 ± 0.69	3.92 ± 1.15*	5.74 ± 0.81	6.75 ± 0.93	6.90 ± 0.21
MY(µg/l)	2.74 ± 0.29	2.96 ± 0.40	6.47 ± 1.06*	4.36 ± 0.54	2.54 ± 0.45	2.98 ± 0.84	4.99 ± 1.58
CK -NAC(µKat/l)	1.03 ± 0.45	1.11 ± 0.46	0.66 ± 0.25	0.41 ± 0.12	0.82 ± 0.29	0.36 ± 0.09	0.92 ± 0.55
LDH(µKat/l)	2.18 ± 0.75	1.63 ± 0.21*	9.00 ± 1.11*	66.76 ± 0.94*	31.50 ± 0.91*	19.51 ± 1.47*	17.87 ± 1.28*
AST(µKat/l)	18.07 ± 2.65	14.25 ± 3.00	13.26 ± 1.66	22.07 ± 2.38	18.58 ± 2.41	18.51 ± 3.54	13.51 ± 2.60

*Result are express as mean ± SEM (n=5). Values with asterisk are significant (*p< 0.05) different when compared with control group. TnT–Troponin T, TnI-Troponin I, MY-Myoglobin, CK-NAC-Creatine kinase (N-Acetyle cysteine), LDH- Lactate dehydrogenase, AST-Aspartate amino transferase.*

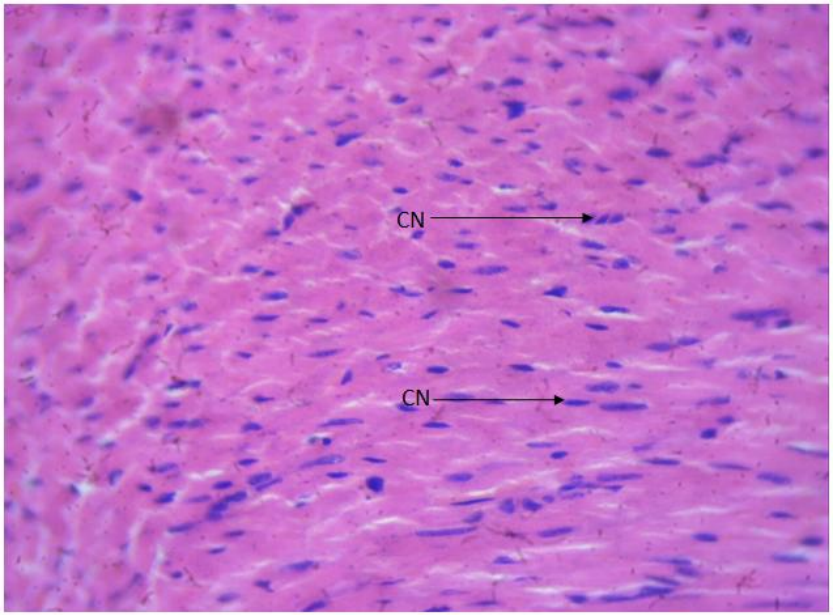


Fig. 1. Micrograph of heart of rats (control group) showing normal histological structure of the heart: cell nucleus (CN) and abundant cytoplasm (CY) Hematoxylin & Eosin X400. Group 1: Control animals administered distilled water

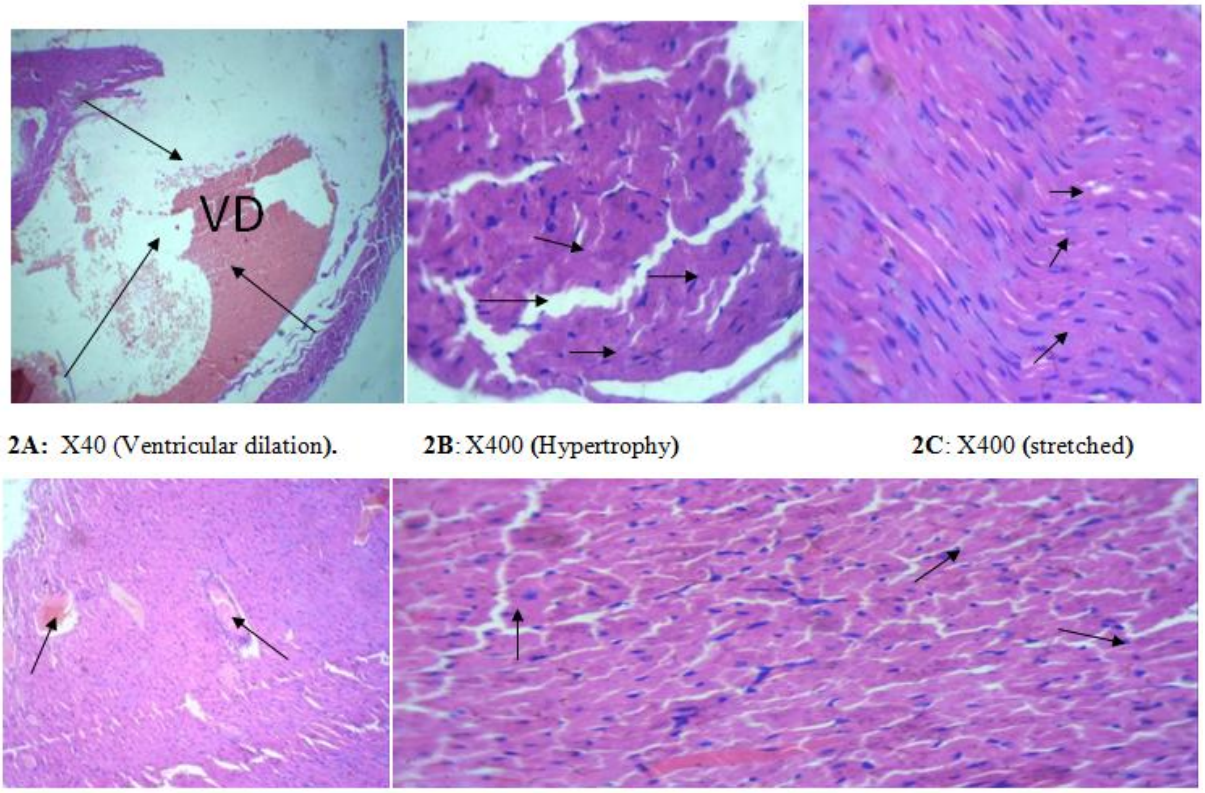


Fig. 2. Micrograph of rat heart (group 2) showing severe ventricular dilatation, hypertrophy, stretched, mural thrombi and inflammatory cells of cardiac muscle (Hematoxylin & Eosin). Group 2: Animals treated with 100 mg/kg b.w. of *G. senegalensis* aqueous extract

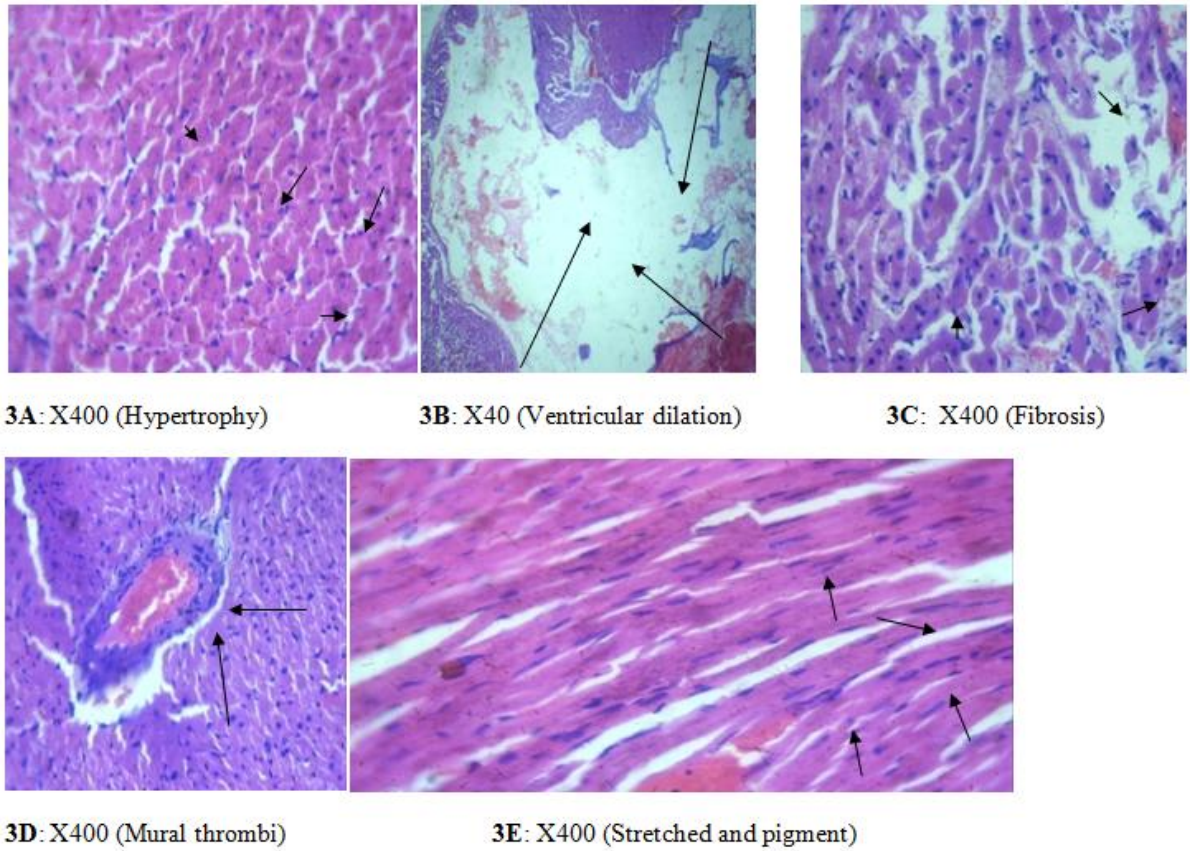


Fig. 3. Micrograph of rat heart of (group 3) showing hypertrophy, ventricular dilatation, fibrosis, mural thrombi, stretched and pigment in cardiac muscle (Hematoxylin & Eosin). Group 3: Rats treated with of 200 mg/kg b.w. of *G. senegalensis* aqueous extract

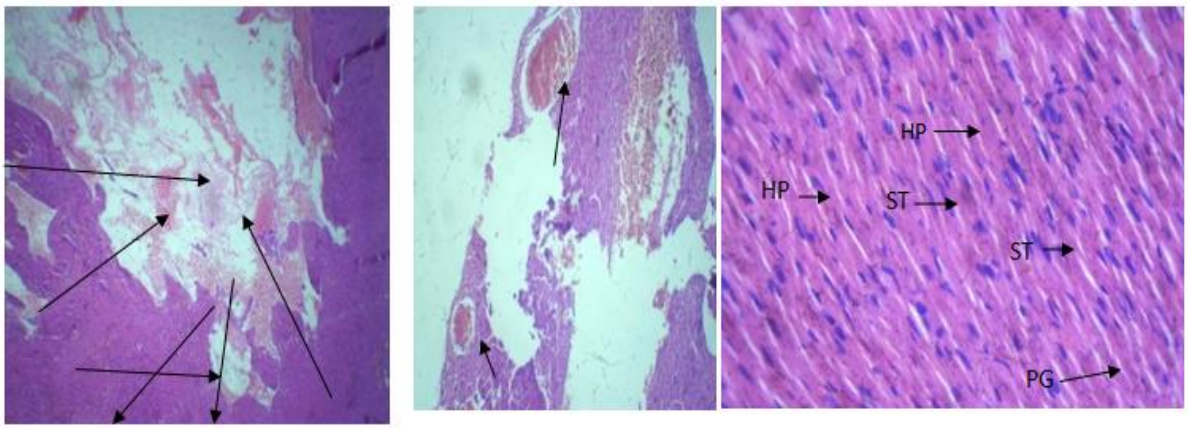
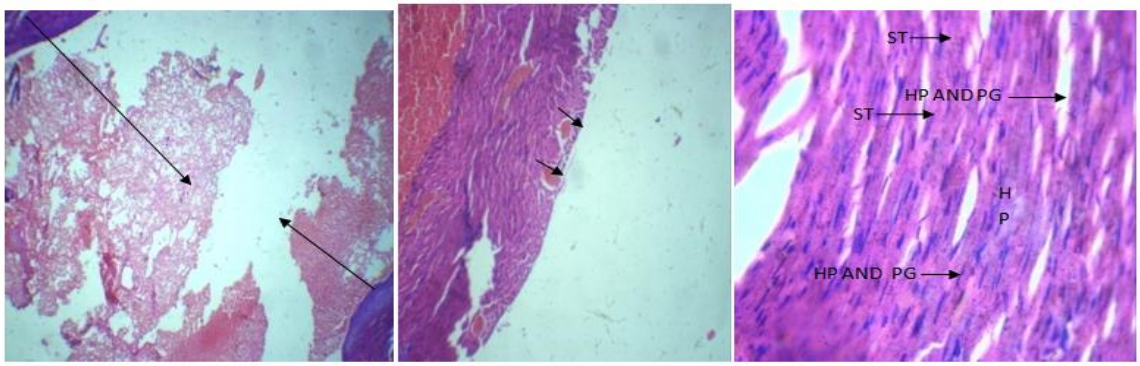
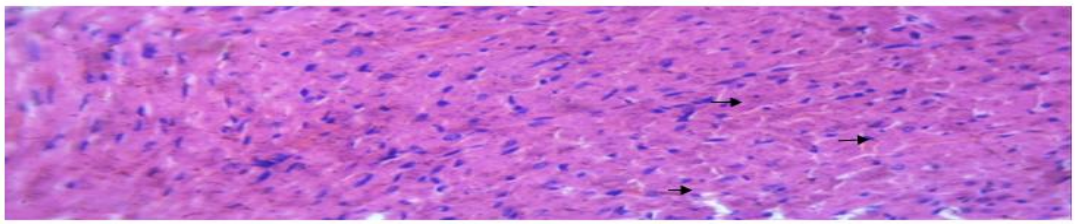


Fig. 4. Micrograph of rat heart of (group 4) showing ventricular dilatation, mural thrombi, hypertrophy, stretched and pigment in cardiac muscle (Hematoxylin& Eosin). Group 4: Experimental group given 300 mg/kg b.w. of *G. senegalensis* aqueous extract

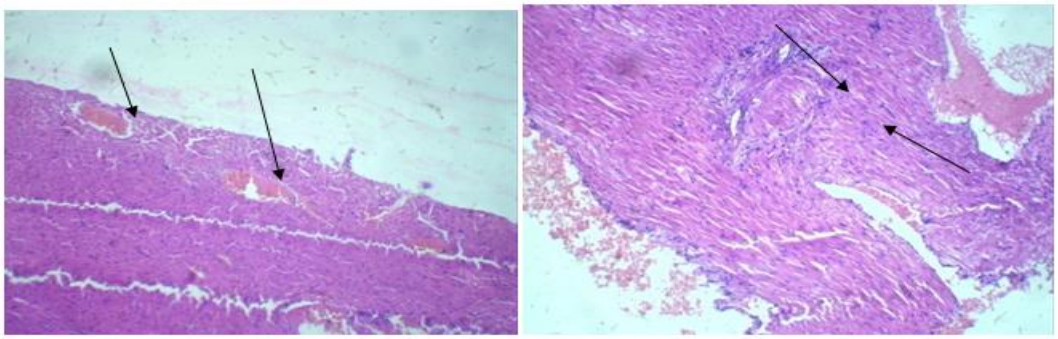


5A: X40 (ventricular dilatation) **5B**: X100 (mural thrombi) **5C**: X400 (streched, hypertropy and pigment)

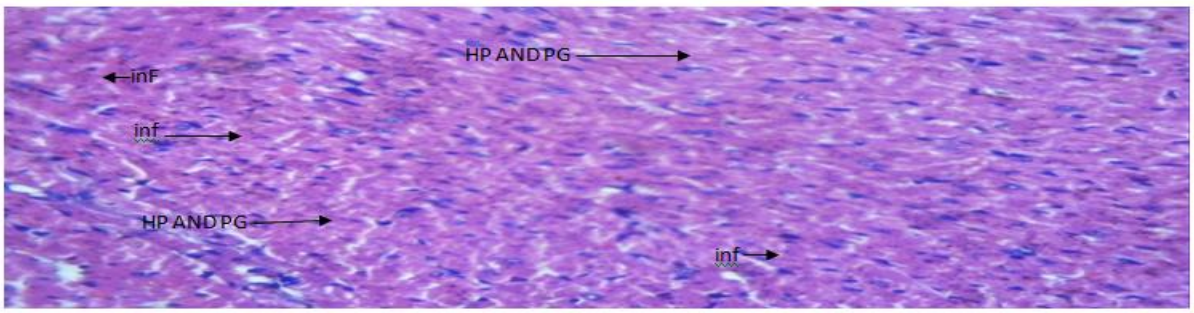


5D: X400 (Inflammatory cells)

Fig. 5. Micrograph of rat heart (group 5) showing ventricular dilatation, mural thrombi, hypertrophy, stretched, pigment and inflammatory cells of cardiac muscle (Hematoxylin & Eosin). Group 5: Animals administered 100 mg/kg b.w. of *G. senegalensis* saqueous extract + natron



6A: X100 (mural thrombi) **6B:** X100 (ventricular inflammation)



6B: X400 (Inflammatory cells, hypertrophy and pigment).

Fig. 6. Micrograph of rat heart of (group 6) showing mural thrombi, inflammatory cells, hypertrophy and pigment in cardiac muscle (Hematoxylin & Eosin). Group 6: Animals given a treatment of 200 mg/kg b.w. of *G. senegalensis* aqueous extract + natron

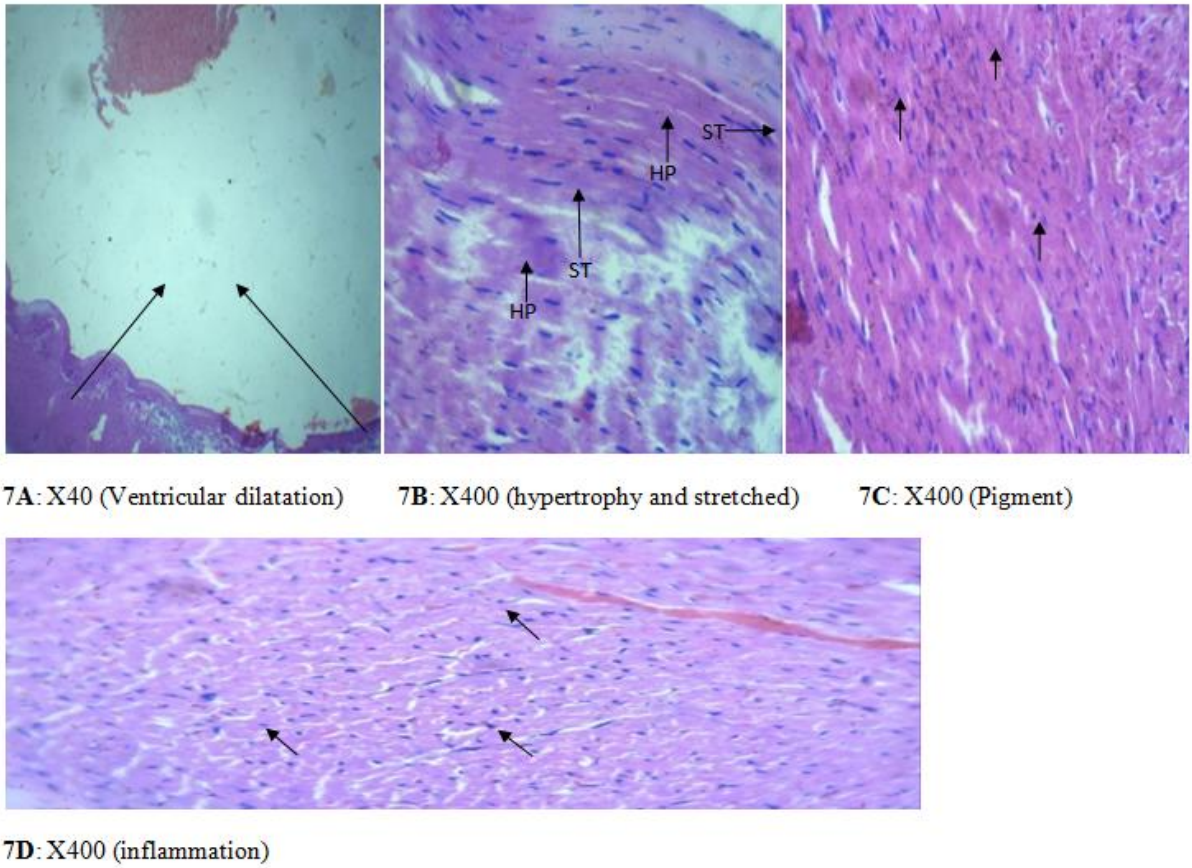


Fig. 7. Micrograph of rat heart of (group 7) showing ventricular dilatation, hypertrophy, pigment and inflammatory cells in cardiac muscle (Hematoxylin & Eosin). Group 7: Aminals given 300 mg/kg b.w. of *G. senegalensis* aqueous extract + natron

4. DISCUSSION

Peripartum cardiomyopathy is an uncommon life-threatening health condition. It is linked to heart failure mainly due to left ventricular systolic dysfunction [32]. It occurs within childbearing age in individuals (with no preexisting cardiac problem), during the last month of pregnancy or first five months after delivery [33]. In the present study, 28 days effect of *G. senegalensis* extract and *G. senegalensis* + natron on postpartum rats was evaluated. Acute toxicity studies LD_{50} showed that 5000 mg/kg b.w. of *G. senegalensis* leaves aqueous extracts resulted to zero motality after a 24 hour periods. Thus, the extract is relatively safe at low dosage upon short term exposure. Similarly it was reported that the LD50 of the extracts of the *G. senegalensis* was found to be above 5000 $mgkg^{-1}$ [34-35]. In other studies the signs of toxicity were observed when methanol extract of *G. senegalensis* leaves at 1000 mg/kg b.w. were administed to experimental animals. These differences in LD50 values could be as a result of varied geographic location. LD50 values may vary with age, sex, nutritional status and solvent used for the extractions. The toxicity symptoms include ruffle hair, transient anorexia, respiratory abnormalities, obstructed cardiac function, weakness/abrupt cessation of physical activities, depression, coma and death [36-37].

Exposure of postpartum rats to high dases *G. senegalensis* aqueous extract, and even moderate levels of *G. senegalensis* + natron resulted in pronounced decline of body weight on a long term bases, when conpared with the control group. The observed weight loss by moderate concentrations of *G. senegalensis* + natron suggest that natron had deleterious biological effects, either due to distortion of ion potentials, redox potential and/or dehydration. Consequently, chronic intack of the concoction is responsible for cardiomyopathy amongs women in Northern Nigeria. Previous studies suggest that potash resulted to reduced water and food

intake, and thus dehydration [38]. The anorexia effect of potash is closely related to its composite nature (i.e. calcite, hanksite, halite, pirssonite, borax, sodium sesquicarbonate, sodium carbonate, sodium sulphate) which have distinct biological effects [8]. More so, earlier report indicated that long term administration of high natron doses resulted in body weight loss [9-11].

A lower level of HDL and HDL-C, coupled with increasing levels of VLDL and TC suggested the potential risk of developing cardiomyopathy and other cardiac problems [39]. In the present study, a decreased level of HDL and an increasing level of TC were observed. This is a direct indication of an increased risk cardiovascular dysfunction. Saidu et al. [40] previously demonstrated that the administration of high doses of natron induces dyslipidemia in postpartum rats. More so, the administration of natron and related salts to postpartum rat negatively affect the level of HDL-C in a dose dependent manner [15,41]. Ultimately, the present finding and previous reports show characteristic dyslipidemia in the treated animals. These could accelerate atherosclerotic processes such as heart failure and coronary atherosclerosis. In addition, epidemiologic investigations attest that LDL-C and AI are strong marker of cardiovascular risk. High LDL and AI are linked to complications of peripartum cardiomyopathy. These are consistent with the findings of the present study where LDL and AI are found to increase upon treatment with G*. senegalensis* or *G. senegalensis* + natron.

Histopathological studies suggest that the consumption of dried lake salt affects the morphology of heart tissue muscles [41]. Lipid peroxidation of HDL-C and other lipids results to oxidative damage to cardiomyocytes, thereby affecting the functionality of the cardiac muscles due to dilation, stretched in cardiac muscles, mural thrombi and hypertrophy. Geoge et al. [42] indicated that oxidized LDL (a marker of oxidative stress) was elevated in PPCM.

The increased levels of LDH and MY in the present study suggested the poosible phytotoxicity of the extracts used. Several studies have reported toxicities of alkaloids and tannins in animals following a prolonged treatment. For instance, alkaloids derived from the bark of Yohimbe tree are reported to alter liver and kidney function parameters upon administration of 14 $mgkg^{-1}$ for 15 days [43]. Tannins are also reported to cause changes in liver enzymes activities of rats administered 2.5 $mgml^{-1}$ doses [44]. Bako et al. [45] observed no changes in LDH activities when experimental animals were administered aqueous extracts of *G. senegalensis.* Okoye et al. [11] reported anincreased LDH activity upon natron administration on rats. Previous finding demonstrated that patients with cardiac myocyte damaged and women with PPCM have increased myoglobin levels [46]. More specifically, LDH activity and MY levels are reported to increase when either *G. senegalensis* or *G. senegalensis* + natron was administered to postpartum rats [40]. The present findings suggest that elevated level of serum myoglobin and increased activity of LDH may be as a result of the cytotoxic effect of *G. senegalensis* or natron on the heart muscle as seen in histological.

Additionally, the alteration in the levels of TnI, TnT and CK-NAC to the experimental animals is a symptomatic indication of the cardiological effect of the administered treatments. However, a non significant change in the activities of AST is an indication of the non harmful effect of *G. senegalensis* and *G. senegalensis* + natron at low and moderate concentration to heart tissue. The present finding is in agreement with the previous reports [45,47]. Whereas, higher doses of the plant extract are shown to significantly increase AST activity [34,48]. Reports by Saidu et al. [40] shows that the consumption of 300 mg/kg b.w. natron by postpartum rats had no effect on AST activity and on pathological changes in different organs studied. These findings are not in agreement with other studies [9-10,14] where AST activities were significantly affected upon chronic administration of higher doses and on long-term exposure.

The histological finding of the present study shows that chronic administration of *G. senegalensis* and *G. senegalensis* + natron plays a significant role in the pathogenesis of PPCM. Mild to severe ventricular dilatation, moderately to severe hypertrophied with enlarged nuclei, as well as mural thrombi were found in group 2, 3, 4 and 7. In group 5 and 6, mild to severe inflammation were observed. More so, pigmentations were observed in 4, 5, 6 and 7, while mild fibrosis was observed in group 3. Group treated with only G. *senegalensis* aqueous extract exhibited higher histological toxicity scores than animals that received the plant extract + natron. The chronic administration of dried lake salt have been reported distort the

morphology of myocardial tissue, with defects such as dilation cardiac chamber, myocyte hypertrophy and focal atrophy, thus making patients more prone to developing PPCM [18,39-40].

5. CONCLUSION

In general, long term consumption of *G. senegalensis*, natron or *G. senegalensis* + natron could result in the distortion/disruption of the cytostructure of myocytes and myocardial tissue. Although the actual mechanism of these toxicities are unknown, the occuring dilation of the heart chamber and ventricular hypertrophy are closely related to the weakening of cardiac muscles, reduced ventricular compliance, cardiac remodeling, structural stress and increased oxygen demand by myoctes.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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