Asian Journal of Advanced Research and Reports

9(4): 1-10, 2020; Article no.AJARR.55654
ISSN: 2582-3248

Ameliorative Effect of *Citrullus lanatus* (Water Melon) Seeds on Alloxan Induced Hepato and Nephro Toxicity

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Authors' contributions

This work was carried out in collaboration among all authors. Authors HEO, DEP and MOM designed the study. Author HEO performed the statistical analysis, wrote the protocol, wrote the first draft of the manuscript, managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJARR/2020/v9i430223
Editor(s):
(1) Dr. Longan Shang, Zhejiang University, China.
Reviewers:
(1) Shigeki Matsubara, Jichi Medical University, Japan.
(2) Aman Upaganlawar, Savitribai Phule Pune University, India.
Complete Peer review History: http://www.sdiarticle4.com/review-history/55654

Original Research Article

Received 18 February 2020
Accepted 24 April 2020
Published 02 May 2020

ABSTRACT

Some data suggested that the seeds of water melon may have therapeutic benefits. We here attempted to determine ameliorative effects of aqueous extract of *Citrullus lanatus* (water melon) seeds on alloxan-induced hepato- and nephrotoxicity on wistar rats. Rats were divided into 11 groups, with each group consisting of 3 rats. Groups 2-11 received single dose of 120 mg/kg b.wt. of alloxan monohydrate intraperitoneally. Groups 4 and 5 orally received a dose of 100 mg/kg b.w. of metformin for 7 & 21 days. Groups 6, 8 and 10 orally received 200 mg/kg b.w., 400 mg/kg b.w., and 600 mg/kg b.w. of the extract respectively for 7 days while groups 7, 9 and 11 orally received same doses respectively for 21 days. The most abundant phytochemicals present in the seeds sample were flavonoids mainly catechin (70.88 ± 0.21) and anthocyanin (42.11 ± 0.89). Blood samples were collected 24 hours after 7 and 21 days of treatment. Biochemical analyses were conducted on liver-injury, kidney-injury, and oxidative-stress markers. Liver/kidney histopathology were examined. Result revealed significant ($p \leq 0.05$) reduction in liver enzyme activities, creatinine and urea and malondialdehyde levels, while the electrolyte concentrations significantly increased in the extract treated groups on day 7 and 21 when measured against group 1. The histopathological

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examination revealed regeneration of the liver/kidney tissues in the extract treated groups mostly in 10 and 11. Thus, aqueous extract of water melon seeds ameliorated alloxan induced hepato-/nephron-toxicity in diabetic rats.

Keywords: Water melon seeds; hepatotoxicity; nephrotoxicity; diabetes.

1. INTRODUCTION

Phytomedicine is the application of plant's seeds, leaves, bark, berries, roots or flowers for production of drugs; presently, herbal medicine has being playing a major part in the treatment of diabetes mellitus mostly in countries where there is no link to synthetic antidiabetes drugs [1]. *Citrullus lanatus* also known as water melon is a well known fruit in several areas of the globe and has high therapeutic benefits. The fruit has different, sizes, shapes and rind pattern [2] and is made up of black and white seeds; the black seeds are mature and fertile while the white seeds are immature, these seeds are loaded with nutrients such as anti-inflammatory, antidiabetic, antifungal and antibacterial [3-5]. Watermelon seeds have not been given much importance in the diets of many Nigerians and are often thrown away discarded due to ignorance of the nutritive value and their curative advantages [6]. On this basis, this research was undertaken to ascertain the phytochemical and biochemical effects of water melon seeds.

2. MATERIALS AND METHODS

2.1 Drugs, Chemicals and Reagents

Metformin (SKG-PHARMA, NAFDAC NO. A4-6597,0-7-18 to 0-7-23), Chloroform (Riedel-de Haen, England), Acetone, (LobaChemie, India), Xylene (LobaChemie, India), Ether (LobaChemie, India), Normal saline(Kermel, china), Alcohol, Haematoxylin-eosin, 100% formalin (JHD China), Alloxan monohydrate (sigma-aldrich, Germany), ALP kit (Randox, united Kingdom), ALT kit (Randox, united Kingdom)), AST KIT (Randox, united Kingdom), Cholesterol kits (Randox, united Kingdom), Triglycerides kit (Randox, united Kingdom), Pancreatic Amylase Elisa Kit was obtained from Abnova GmbH (Germany).

2.1.1 Experimental plants

Water melon fruits *(Citrullus lanatus)* were purchased from Choba Market, and Dr. E. Chimeze of Plant Science Biotechnology department identified and authenticated the plant seeds, with herbarium number UPH/P/183 and the specimen deposited in herbarium.

2.1.2 Experimental animals

All experimental protocol aligned with stipulations of World Medical Association Declaration of Helsinki regarding ethical conduct of research involving animals, and appropriated by the Department of Biochemistry, Imo State University Ethics Committee (IMSU/BCM/ETS/20190405).

Eighty-three rats weighing 125-200 g were purchased for this research. They were weighed and seventy seven rats were equally distributed into eleven groups, the females were separated from the male rats and were caged and left under suitable laboratory conditions for fourteen days for them to adapt to the new environment before commencing the experiment. The animals were given feed and water *ad libitum* and their body weights were recorded at the beginning and before the commencement of treatment.

2.2 Aqueous Extraction of *Citrullus lanatus* Seeds

Ripe water melon fruits were collected and cut open; the seeds were washed, dried and blended in a blender, four hundred grams of *Citrullus lanatus* seeds sample was soaked in 4000 ml of distilled water for one day in a macerating jar. Thereafter the impurities were removed from the sample using Whatman No. 1 sieving paper and were finally dried in a thermostat water bath at 60°C for use [7].

2.3 Acute Toxicity of *Citrullus lanatus* Seeds Extract

According to the report of Varghese et al. [7], the toxicity study showed that no death occur even up to a dose of 2000 mg/kg body weight of the extract after administration orally.

2.4 Induction of Diabetes Mellitus in Wistar Rats

This was done using alloxan monohydrate which was prepared by dissolving 0.9 g of alloxan

monohydrate in 6 ml of distilled water to form a solution. Then 120 mg/kg b.w. of the alloxan monohydrate solution was administered to the rats intraperitoneally after they were made to fast overnight and diabetes induction was confirmed using active glucometer 3 days after alloxan administration [8,9].

2.5 Experimental Design

The rats were divided into 11 groups of 3 rats in each and were handled as such for 21 days.

Group 1 : Normal rats which received distilled water for 21 days
Group 2 : Untreated diabetic rats for 7 days
Group 3 : Untreated diabetic rats for 21 days
Group 4 : Diabetic rats treated with 100 mg/kg b.wt of metformin for 7 days
Group 5 : Diabetic rats treated with 100 mg/kg b.wt of metformin for 21 days
Group 6 : Diabetic rats treated with 200 mg/kg b.wt of the extract for 7 days
Group 7 : Diabetic rats treated with 200 mg/kg b.wt of the extract for 21 days
Group 8 : Diabetic rats treated with 400 mg/kg b.wt of the extract for 7 days
Group 9 : Diabetic rats treated with 400 mg/kg b.wt of the extract for 21 days
Group 10 : Diabetic rats treated with 600 mg/kg b.wt of the extract for 7 days
Group 11 : Diabetic rats treated with 600 mg/kg b.wt of the extract for 21 days

Note: all treatments were done orally and alloxan administration was through intraperitoneal route.

2.6 Phytochemical Screening

2.6.1 Determination of saponin content

The technique of AOAC [10] was applied to estimate saponin.

2.6.2 Determination of alkaloid content

Harborne [11] technique was applied to get the amount of alkaloid in the seeds sample.

2.6.3 Determination of flavonoid content

The technique of Millongo-Kone et al. [12] applied for estimation of flavonoid.

2.6.4 Determination of tannin content

The technique of Schofield et al., [13] was applied to analyze the total phenolic compounds.

2.6.5 Determination of phytic acid content

The procedure of Ayoola et al. [14] was applied to estimate phytic acid composition.

2.6.6 Determination of cyanogenic glycoside

Cyanogenic glycoside concentration was determined using alkaline picrate [15].

2.7 Determination of Liver Enzyme Markers

2.7.1 Determination of plasma aspartate transaminase activity

AST activity was assayed by the method reported by Amadi et al., [16].

2.7.2 Determination of plasma alanine transaminase activity

ALT activity was estimated by the procedure reported by Amadi et al., [16].

2.7.3 Determination of plasma alkaline phosphate activity

The plasma Alkaline phosphatase (ALP) was assayed using the method of Amadi et al., [16].

2.8 Determination of Plasma Kidney Function Markers

2.8.1 Assay of plasma creatinine concentration

The plasma creatinine concentration was assayed by applying the technique of Agomuo et al., [17].

2.8.2 Determination of plasma urea concentration

Agomuo et al., [17] technique was applied to get the urea level in plasma.

2.8.3 Determination of plasma sodium concentration

Omigie and Agoreyo, [4] technique was used to get the amount of plasma sodium ion.

2.8.4 Determination of plasma chloride concentration

Tiez [18] technique was adopted to get the amount of plasma chloride ion.

2.8.5 Determination of plasma potassium concentration

The technique of Tiez [18] was applied to get the amount of plasma potassium ion (K^+).

2.8.6 Determination of plasma bicarbonate concentration

Plasma bicarbonate was determined by the method of Omigie and Agoreyo [19].

2.9 Determination of Oxidative Stress Markers

2.9.1 Determination of catalase Activity

Catalase was assayed as described by Scott et al. [19].

2.9.2 Determination of Superoxide Dismutase Activity

Superoxide Dismutase activity was estimated as described by Ogbeifun et al., [20].

2.9.3 Determination of Malondialdehyde

Malondialdehyde assay was used to quantify lipid peroxidation by measuring the formation of MDA produced as described by Tripathi et al. [21].

2.10 Statistical Analysis

All figures are shown as means $\pm$ standard error of triplicate values, and were analysed statistically by ANOVA at 95% confidence with SPSS package version 24, using Tukey HSD multiple comparisons test to compare mean and determine statistical difference. The results were considered significant when P figures are below 0.05 ($P<0.05$) and non-significant when p figures are greater than 0.05 ($P>0.05$).

3. RESULTS

Quantitative analysis in Table 1 showed the presence of different flavonoids with catechin having the highest value (70.88 ± 0.21) and anthocyanidines being the lowest (1.91 ± 0.02). Alkaloids shown the presence of spartein, lunamarin and quinine with lunamarin having the highest value (13.23 ± 0.15) followed by spartein (12.98 ± 0.05) and quinine (8.66 ± 0.26) having the least value as shown in Table 2. Table 3 showed the plasma AST, ALT and ALP concentrations of the rats. The levels in the diabetic control groups (groups 2 and 3) were significantly ($p\leq0.05$) increased when compared to those in the normal control group (group 1). In the groups treated with the extract (group 6, 7, 8, 9, 10 and 11) there was a significant ($p\leq0.05$) decreased when compared to group 2 and 3.

Table 1. Qualitative phytochemicals composition of *Citrullus lanatus* seeds sample

Parameters	Observation	Remark
Flavonoids	+ + +	Very high concentration
Alkaloids	+ +	High concentration
Saponin	+ +	High concentration
Tannin	+	Low concentration
Oxalate	+	Low concentration
Phytate	+	Low concentration

Note: + + + represent very high, + + represent high, and + represent very low

Table 2. Quantitative phytochemicals composition of *Citrullus lanatus* seeds sample

Parameter	Composition (ug/g)
Kaempferol	3.10 ± 0.00
Epicatechin	26.79 ± 0.19
Catechin	70.88 ± 0.21
Anthocyanin	42.11 ± 0.89
Sapogenin	9.15 ± 0.11
Ribalindine	9.22 ± 0.07
Rutin	4.14 ± 0.03
Tannin	8.95 ± 0.09
Anthcyanidines	1.91 ± 0.02
Spartein	12.98 ± 0.05
Lunamarin	13.23 ± 0.15
Quinine	8.66 ± 0.26
Oxalate	6.75 ± 0.06
Naringin	11.17 ± 0.04
Flavones	3.43 ± 0.05
Phytates	1.45 ± 0.09
Naringenin	4.12 ± 0.06

Values represent Mean ± SEM of triplicate sample

Table 3. Effect of varying concentrations of aqueous extract of *Citrullus lanatus* seeds on the activities of liver enzymes parameters in alloxan induced-diabetic wistar rats treated for 7 & 21 days

GRP	AST (µ/l)	ALT (µ/l)	ALP (µ/l)
1	69.67 ± 2.60^{bc}	23.67 ± 0.33	31.67 ± 2.60^{c}
2	130.00 ± 2.30^{a}	69.00 ± 0.58^{ac}	84.00 ± 0.58^{c}
3	136.67 ± 6.64^{a}	69.67 ± 1.45^{c}	85.67 ± 0.33
4	110.67 ± 14.15^{a}	40.67 ± 2.03	38.67 ± 0.88
5	110.00 ± 11.55^{a}	37.67 ± 1.45^{ab}	36.00 ± 2.31^{ab}
6	116.67 ± 0.33^{a}	33.67 ± 0.88^{c}	26.00 ± 0.58
7	70.67 ± 2.60^{bc}	28.67 ± 1.45	24.00 ± 1.73^{ab}
8	106.00 ± 2.31^{a}	38.00 ± 0.58	35.00 ± 0.58^{a}
9	61.00 ± 0.58^{bc}	30.67 ± 0.88	19.00 ± 0.58^{ab}
10	98.00 ± 6.93^{b}	40.67 ± 5.49^{c}	23.67 ± 0.88^{abc}
11	56.67 ± 4.91^{bc}	28.00 ± 0.58^{c}	16.00 ± 0.58^{abc}

Values are represented as Mean ± Standard error of mean (M±SEM); n =3 per group. Figures in same column with superscript (a, b, c) are significant different at p ≤ 0.05

Superscript (a) represent significant difference when group 1 is compared to other groups at p ≤ 0.05.
Superscript (b)represent significant difference when group 3 is compared to other groups at p ≤ 0.05.
Superscript (c) represent significant difference when group 5 is compared to other groups at p ≤ 0.05.
Figures that does not have superscript shown no significant difference when group 1, 3 and 5 were compared to the remaining groups at p ≤ 0.05

Table 4. Effect of varying concentrations of aqueous extract of *Citrullus lanatus* seeds on kidney function markers in alloxan induced-diabetic wistar rats treated for 7 & 21 days

Group	Na (meq/L)	K (meq/L)	Cl (meq/L)
1	125.00±0.58^{bc}	4.50±0.06^{bc}	42.00±1.15^{bc}
2	110.67±4.33	1.37±0.78^{c}	20.50±0.87^{ac}
3	112.00±2.89^{ac}	1.50±0.46^{ac}	21.50±0.29^{a}
4	115.00±1.73^{a}	2.67±0.55^{b}	28.50±0.29^{ab}
5	120.00±1.15^{ab}	2.90±0.35^{a}	30.50±0.87^{a}
6	116.00±3.46	2.97±0.32^{abc}	29.50±0.29^{ab}
7	122.67±0.88^{ab}	3.80±0.06^{abc}	28.00±0.58^{abc}
8	118.67±3.18^{abc}	3.50±0.58^{c}	33.50±0.29^{bc}
9	124.67±0.88^{abc}	4.27±0.15^{abc}	35.67±0.33^{ac}
10	117.67±0.88^{abc}	3.07±0.09^{abc}	30.50±0.29^{b}
11	123.67±0.88^{ab}	4.27±0.15^{abc}	30.67±1.45^{abc}

Values are represented as Mean ± Standard error of mean (M±SEM); n =3 per group. Figures in same column with superscript (a, b, c) are significant different at p ≤ 0.05.

Superscript (a) represent significant difference when group 1 is compared to other groups at p ≤ 0.05.
Superscript (b)represent significant difference when group 3 is compared to other groups at p ≤ 0.05.
Superscript (c) represent significant difference when group 5 is compared to other groups at p ≤ 0.05.
Figures that does not have superscript shown no significant difference when group 1, 3 and 5 were compared to the remaining groups at p ≤ 0.05

Tables 4 and 5 showed the plasma sodium, potassium, chloride and bicarbonate concentrations of the rats in the diabetic control group significantly (P≤0.05) decreased when compared to those in the normal control group (group 1). In the groups treated with the extract (group 6, 7, 8, 9, 10 and 11) there was a significant (P≤0.05) increased when compared to group 2 and 3.

While in Table 5 showed the plasma urea and creatinine concentrations of the rats in the diabetic control groups (group 2 and 3) significantly (P≤0.05) increased when compared to those in the normal control group (group 1). In the groups treated with the extract (group 6, 7, 8, 9, 10 and 11) there was a significant (P≤0.05) decreased when compared to group 2 and 3.

Table 6 shows the plasma SOD and CAT activities of the rats in the diabetic control groups (group 2 and 3) significantly (P≤0.05) decreased when compared to those in the normal control group (group 1). In the groups treated with the

extract (group 6, 7, 8, 9, 10 and 11) there was a significant (P≤0.05) increased in the activities of the antioxidant enzymes when compared to groups 2 and 3. While in Table 6, MDA levels significantly (p≤0.05) increased in the diabetic control groups (groups 2 and 3) when compared to the normal control group. In the groups treated with the extract (group 6, 7, 8, 9, 10 and 11) there was a significant (p≤0.05) decreased in MDA levels when compared to group 2 and 3.

Table 5. Effect of varying concentrations of aqueous extract of *Citrullus lanatus* seeds on kidney function markers in alloxan induced-diabetic wistar rats treated for 7 & 21 days

GRP	Hco_3 (meq/L)	UREA(µmol/l)	Creatinine(µmol/l)
1	22.00 ± 0.58^{bc}	3.67 ± 0.033^{c}	94.00 ± 0.58^{bc}
2	14.00 ± 0.58^{abc}	14.87 ± 0.95^{a}	188.67 ± 3.76^{c}
3	15.00 ± 0.58^{c}	14.77 ± 0.72^{c}	190.00 ± 1.2^{ac}
4	18.40±1.15a	9.37 ± 0.03^{a}	132.67±1.45
5	20.00 ± 0.58^{ab}	6.70 ± 0.12^{ab}	120.67 ± 2.6^{ab}
6	18.20±1.15	9.60 ± 0.23^{ab}	130.67 ± 6.64^{c}
7	19.00 ± 1.15^{abc}	6.87 ± 0.15^{bc}	115.00 ± 2.3^{abc}
8	19.33±2.31	8.80 ± 0.06^{a}	123.67 ± 0.88^{bc}
9	21.00 ± 0.58^{abc}	5.20 ± 0.12^{abc}	105.67 ± 0.88^{abc}
10	19.00 ± 0.58^{c}	8.90 ± 0.81^{abc}	125.33 ± 1.83^{a}
11	20.00 ± 0.58^{abc}	5.80 ± 0.12^{abc}	113.00 ± 2.3^{abc}

Values are represented as Mean ± Standard error of mean (M±SEM); n =3 per group. Figures in same column with superscript (a, b, c) are significant different at p ≤ 0.05.
Superscript (a) represent significant difference when group 1 is compared to other groups at p ≤ 0.05.
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Superscript (c) represent significant difference when group 5 is compared to other groups at p ≤ 0.05.
Figures that does not have superscript shown no significant difference when group 1, 3 and 5 were compared to the remaining groups at p ≤ 0.05

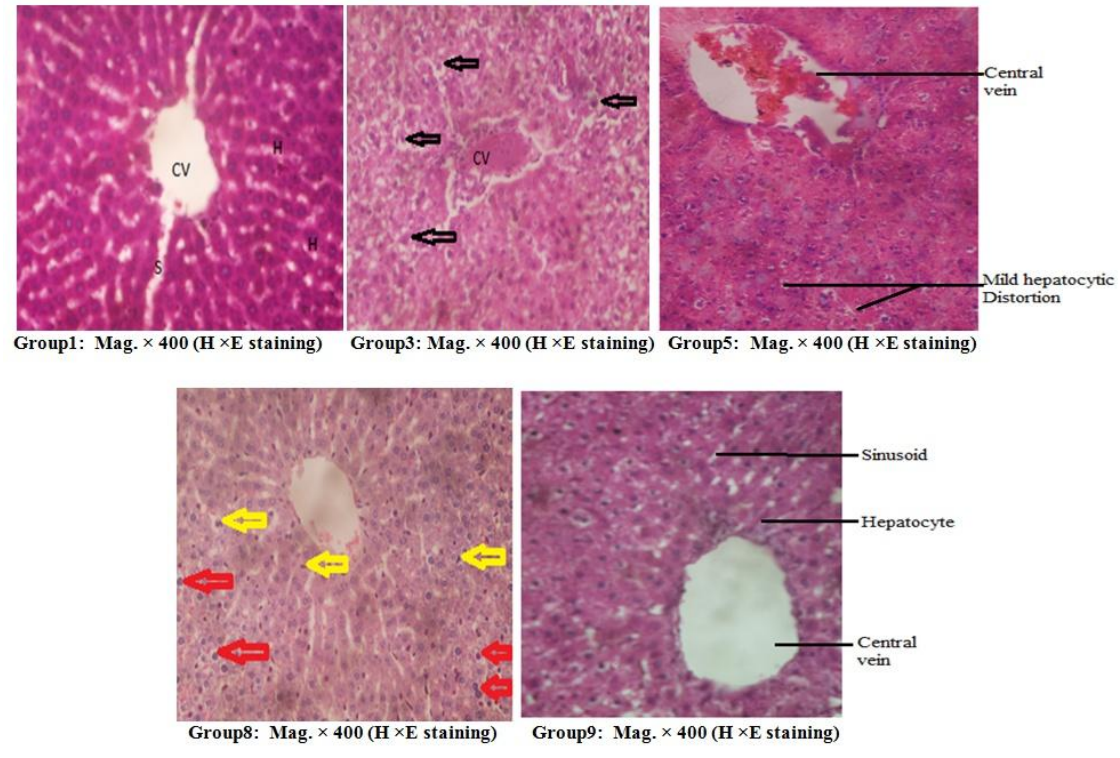

Fig. 1. Histopathology of the liver

Table 6. Effect of varying concentrations of aqueous extract of *Citrullus lanatus* seeds on oxidative stress markers in alloxan induced-diabetic wistar rats treated for 7 & 21 days

Group	SOD (unit/mg)	CAT (unit/mg)	MDA (µmol/mg)
1	0.51 ± 0.01^{bc}	6.30 ± 0.06^{c}	0.13 ± 0.00^{bc}
2	0.11 ± 0.00^{ac}	0.73 ± 0.27^{a}	0.54 ± 0.01^{c}
3	0.11 ± 0.01^{a}	1.00 ± 0.06	0.53 ± 0.01^{a}
4	0.24 ± 0.01^{ab}	4.40 ± 0.29	0.22 ± 0.02
5	0.15 ± 0.02^{a}	4.30 ± 0.17^{a}	0.23 ± 0.03^{a}
6	0.20 ± 0.01^{a}	1.97 ± 0.09	0.33 ± 0.01^{c}
7	0.25 ± 0.02^{ab}	4.00 ± 0.17^{ab}	0.21 ± 0.03^{c}
8	0.14 ± 0.01^{a}	2.07 ± 0.15^{a}	0.39 ± 0.01^{bc}
9	0.29 ± 0.04^{abc}	5.10 ± 0.12	0.21 ± 0.04^{c}
10	0.25 ± 0.01^{ab}	2.17 ± 0.15^{abc}	0.23 ± 0.02^{bc}
11	0.39 ± 0.00^{a}	5.27 ± 0.72^{abc}	0.31 ± 0.01^{c}

Values are represented as Mean ± Standard error of mean (M±SEM); n =3 per group. Figures in same column with superscript (a, b, c) are significant different at p ≤ 0.05.
Superscript (a) represent significant difference when group 1 is compared to other groups at p ≤ 0.05.
Superscript (b) represent significant difference when group 3 is compared to other groups at p ≤ 0.05.
Superscript (c) represent significant difference when group 5 is compared to other groups at p ≤ 0.05.
Figures that does not have superscript shown no significant difference when group 1, 3 and 5 were compared to the remaining groups at p ≤ 0.05

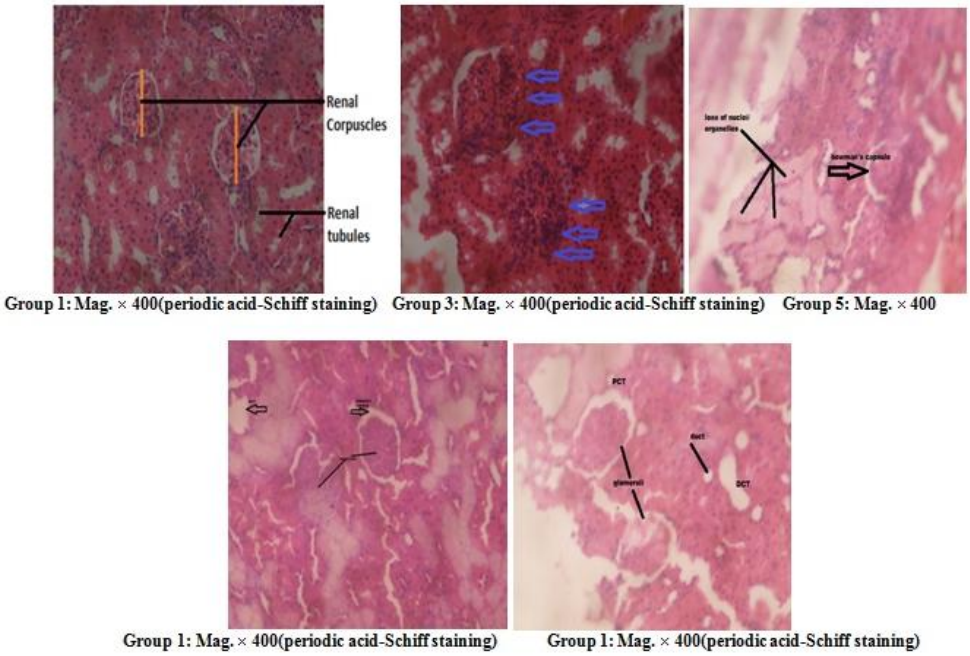

Fig. 2. Histopathology of the kidney

4. DISCUSSION

Lipid peroxidation is usually a marker of oxidative tissue damage which leads to free radical injuring membrane part of cell inducing cell necrosis and inflammation [22,23]. The increased in free radicals in diabetic condition may occur as a result of escalated lipid peroxidation [24] and injuring of antioxidant enzymes [25]. A decreased in antioxidant enzyme system in diabetes is connected to continuous glycation of the enzyme protein [26].The result of oxidative stress markers correlates with previous finding. Varghese et al., [7] demonstrated a valuable ($p \leq 0.05$) increased malondialdehyde (MDA) levels and at the same time decreased in SOD

and CAT activities in diabetic rats when compared to the control rats. The extract significantly ($p \leq 0.05$) reduced MDA levels while SOD and CAT activities increased in all the extract treated groups. The antioxidant properties of the extract could be attributed to the presence of flavonoids predominantly catechin, alkaloids, oxalates and soponin in *Citrullus lanatus* seeds [7]. Flanovoids have been reported to act as powerful antioxidant that can protect the human body from free radicals and reactive oxygen species [27].

High quantities of the hepatic enzymes revealed cellular linkage and loss of functional integrity of cell membrane of the liver [28]. The significant ($p \leq 0.05$) increased in the activities of aspartate transaminase, alanine transaminase and alkaline phosphatase in the diabetic control groups when compared to the normal agrees with previous work by Nwanjo, [29] which reported that these enzymes increased in diabetic rats. The increased may be as a result of the production of these enzymes from cytoplasm into the blood circulation after injuring of plasma membrane and cells [30]. Treatment with aqueous extract of *Citrullus lanatus* seeds reduced the activities of these enzymes were observed in all the treated groups

The kidneys act to normalize electrolytes concentrations in the blood despite changes in the body [31]. Thus, plasma electrolyte values usually indicate renal function or dysfunction. In uncontrolled diabetes mellitus, kidney function is compromised. Glycosuria, a characteristic of diabetes, induces loss of water in the body through glucose osmotic diuretic. The loss of water in the body is followed by serious loss of electrolytes including sodium, potassium, chloride, bicarbonate, calcium and phosphates [32,33]. The result showed decreased in plasma electrolyte concentration of diabetes control compared against group 1. This is in line with other researchers findings [31,33,34]. Oral administration of aqueous extract of *Citrullus lanatus* seeds increased the plasma electrolyte levels of the alloxan rats. This could be due to the presence of phytochemicals such as alkaloids, flavonoids, oxalates and saponin in the seeds as reported by Manach et al., [27] that the seeds have antioxidant property and hence help to protect the body from free radicals and reactive species. Flavonoids mainly catechin are potent antioxidants which could protect the membrane lipids from oxidation [35] by scavenging free radicals through donation of hydrogen atoms or electrons which converts them to more stable products [36].

Significant increases in plasma creatinine and urea concentrations indicate damaged kidney [37,38]. The result revealed a significant ($P < 0.05$) increased in creatinine and urea in the diabetic control group when compared against group 1 is in line with other studies and showed that diabetes may cause inability of the kidney to function due to the stimulation of gluconeogenesis as alternative glucose supply route as a result of lack of insulin. Gluconeogenesis is sustained by rise proteolysis which produces glucogenic amino acids that are deaminated in the liver causing high urea levels [39].

Rise in amount of creatinine revealed damaged kidney function or kidney disorder. This disorder will cause the creatinine level in the blood to rise due to inability of the kidneys to clear creatinine [37]. Treatment with aqueous extract of *Citrullus lanatus* seeds significantly ($P < 0.05$) reduced urea and creatinine concentrations when compared to the diabetic control. The significant fall in urea concentration after treatment may be due to the strength of the extract to lower glucose quantity and increase insulin concentration thus causing a reduction in proteolysis [40]. The significant decreased in creatinine concentration after treatment may be due to the strength of the extract to ameriolarate the kidneys, thereby stimulating the rate of filtration by kidneys [41]. The histological study provides delicate proof of the potentiality of the extract to reduce the damage on the hepatocytes and kidney treated groups for 7 and 21 days.

5. CONCLUSION

The study reveals that *Citrullus* seeds extract exhibited ameliorative effect against alloxan induced hepato and nephro toxicity in wistar.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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