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Protective Effect of Methanolic Extract of *Allium cepa* on Potassium Bromate-Induced Nephrotoxicity in Rats

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Abstract
Potassium bromate is an oxidizing agent that has been implicated in nephrotoxicity. In this study, the phytochemical constituents of *Allium cepa* methanolic extract were determined followed by its protective effect on potassium bromate-induced nephrotoxicity in rats. Forty-two (42) male Wistar rats were randomized into 7 groups of 6 animals. Group 1 represents the control comprising untreated animals that received distilled water. Those in Groups 2, 3, 4 and 5 received 20, 50, 100 and 200 mg/kg body weight of potassium bromate respectively. Rats in Group 6 received 200 mg/kg body weight of the standard drug (Vitamin C) while those in Group 7 received 200 mg/kg body of *Allium cepa* extract. Administration was carefully done for 4 weeks via stomach injection twice a week during which experimental animals were kept on rat chow and portable water *ad libitum.* At the expiration of the experimental period, biochemical indices including bilirubin, urobilinogen, creatinine, serum total protein, urinary RBC and WBC were evaluated followed by histopathological examination of the kidney. The experimental rats exhibited partial paralysis upon potassium bromate injection. The 50 and 100 mg/kg bw doses of methanolic extract of *Allium cepa* significantly ($p<0.05$) restored the concentrations of bilirubin and creatinine, but not urobilinogen and serum protein concentrations at 50 mg/kg bw. At 200 mg/kg bw, the extract effectively prevented bromate-induced nephrotoxicity. This study showed that methanolic extract of *Allium cepa* has a protective effect against potassium bromate-induced nephrotoxicity in rats with maximum potency at 200 mg/kg bw when administered for four weeks.

Keywords: Potassium bromate, Nephrotoxicity, Kidney, *Allium cepa,* Histopathology

1. Introduction

Potassium bromate is a strong oxidizing agent that occurs as white crystals or powder and has been used as a dough improver in bakeries [1]. It is also known to be a byproduct of ozone disinfection of water containing bromide [2] and in drinking water that has been treated with hypochlorite [3]. The cosmetic industries have also used bromate as a neutralizing agent for permanent wave hair styling products [4]. Bromate salts are currently being used and permitted as dough bread conditioners at a maximum concentration of 75 ppm in flour and 20 ppb in finished dough [5, 6]. Although it is a group 2B possible human carcinogen, its use as a food additive is still permitted in raw flour [7]. Routes of exposure include oral consumption, dermal application and inhalation [8]. As revealed by toxicological studies, potassium bromate causes hepatotoxicity, nephrotoxicity, thyroid toxicity and induces the development of mesothelioma tumors in rats and carcinoma of kidney in humans [9, 10].

A single dose of 100 mg/kg bw generated nephrotoxic effects, produced reactive oxygen species and induced oxidative stress in male Wistar rats [11]. Occurrence of oxidative stress has been attributed to increased levels of 8-oxodeoxyguanosine (8-oxodG) (a representative marker of oxidative DNA damage) levels in the kidney [12]. Previous studies in Kaduna and Gwagwalada area of Abuja have reported the presence of potassium bromate in bread samples at very high concentrations in most bakeries. [13, 14]. Bromate has been reported to have adverse effects on liver and kidney functions of rats fed with diets formulated with bread containing potassium bromate [15]. It is associated with neurotoxicity [16], ototoxicity [17] and it reduces the nutritional quality of bread.

There are several treatment options for bromate toxicity including the use of synthetic antioxidants. However, their use has been discouraged due to toxicological uncertainties [18]. Naturally occurring agents like taurine, quercetin and rutin have been shown to be effective in combating potassium bromate-induced oxidative stress due to their protective properties [19-21]. It has been reported that *Allium cepa* possesses a high amount of phytochemical and elemental components [22, 23] which are responsible for its several pharmacological properties, including antioxidant, anticarcinogenic, antimicrobial and cytoprotective activities [24]. Hence, this study focused on evaluating the *in vivo* protective effect of methanolic extract of *Allium cepa* on potassium bromate-induced nephrotoxicity in rats.

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2. Materials and methods

2.1 Experimental animals, materials, chemicals and reagents

The male Wistar rats used for this study were obtained from the Animal House of Biochemistry Department, University of Ilorin, Nigeria. *Allium cepa* and rat chow (Purina) were purchased from a local market in Ilorin, Nigeria. All chemicals and reagents used are products of Randox Laboratory Co-Antrim, United Kingdom.

2.2 Preparation of methanolic extract of Allium cepa

Methanol (2.3 L) was used to soak 1,475 g of peeled and macerated *Allim cepa* for 72 hours followed by filtration using Whatman No. 1 filter paper. The resulting filtrate was concentrated by evaporation using a water bath at 65˚C. The resultant honey-like, brownish-black paste (93.66 g representing 6.35% percentage yield) was stored at 4˚C in a refrigerator until needed.

2.3 Determination of total phenolic and flavonoid contents

The total phenolic and flavonoid contents of the methanolic extract of *Allium cepa* was determined according to standard methods [25, 26].

2.4 Animal groupings

Forty-two (42) male Wistar rats that weighed between 100 g and 120 g were randomized into seven (7) groups as follows:

- Group 1 (positive control): received only distilled water.
- Group 2 (negative control): received 20 mg/kg body weight of potassium bromate (intragastric) twice a week (Mondays and Thursdays) for the last three (3) weeks.
- Group 3: received daily oral administration of 50 mg/kg body weight of the extract from *Allium cepa* for one week after which 50 mg/kg body weight of the extract and 20 mg/kg body weight of potassium bromate (intragastric; 3 hours after extract administration) was administered for the last three (3) weeks.
- Group 4: received daily oral administration of 100 mg/kg body weight of the extract from *Allium cepa* for one week after which 100 mg/kg body weight of the extract and 20 mg/kg body weight of potassium bromate (intragastric; 3 hours after extract administration) was administered for the last (3) weeks.
- Group 5: received daily oral administration of 200 mg/kg body weight of the extract from *Allium cepa* for one week after which 200 mg/kg body weight of the extract and 20 mg/kg body weight of potassium bromate (intragastric; 3 hours after extract administration) was administered for the last three weeks.
- Group 6: received daily oral administration of 200 mg/kg body weight of the standard drug (Vitamin C) for the one week, after which 200 mg/kg body weight of the standard drug and 20 mg/kg body weight of potassium bromate (intragastric; 3 hours after administration of standard drug) was administered for the last three weeks of experiment.
- Group 7: received only 200 mg/kg body weight of extract.

2.5 Collection of urine, blood and kidney

After four weeks, the animals were kept in individual metabolic cages for 24 hours at room temperature during which rat chow was withdrawn and urine samples were collected. Thereafter, the animals were sacrificed by placing them in a jar containing cotton wool soaked in diethyl-ether. After they were unconscious, the jugular vein was sharply cut with a clean sterile scalpel blade for blood collection. The blood sample collected was allowed to clot and then centrifuged at 300 *g* for 5 minutes to collect the serum which was used to assay for marker enzymes. The rats were dissected, and the two kidneys were excised and weighed relative to the body weight of the animals.

2.6 Analysis of urine sample

Urine samples were assayed for pH, specific gravity, nitrate, creatinine, protein, urobilinogen, glucose, bilirubin, red blood cells and white blood cells count by using standard diagnostic kits (MediScreen Urine Strips, Orgenics, France) and standard AMP diagnostic kits (Stattogger Strasse 31b 8045 Graz, Austria). Urinary creatinine clearance (CrCl) was estimated by using the formula:

$$CrCl = \frac{UV}{PT}$$

Where U is concentration of creatinine in urine; V is the volume of urine collected after 24 hours; P is concentration of creatinine in plasma; and T is time in minutes.
The glomerular filtration rate (GFR) was calculated using the formula:

$$GFR = \frac{UV}{P}$$

Where U is concentration of creatinine in urine, V is the volume of urine collected after 24 hours and P is concentration of creatinine in plasma.

2.7 Biochemical analysis
Protein concentration in the serum was determined using Biuret method [27] while albumin and globulin levels in the serum were also determined [28, 29]. The method described by Wright *et al*. [30] was employed to determine the activity of alkaline phosphatase (ALP) while the concentration of urea was determined based on the enzymatic endpoint as described in the Randox assay kit.

2.8 Histological examination of the kidney
Histological study was carried out on the kidney as described by Krause [31]. The kidneys were carefully removed and fixed in 10% (v/v) formalin. Then, dehydrated through ascending grades of ethanol (70%, 90% and 95% v/v), cleaned in xylene and embedded in paraffin wax (melting point 56ºC). Tissue sections were prepared and then stained with haematoxylin/eosin (H&E). The processed histological slides were read with a light microscope. Then, the photomicrographs of the lung tissues were captured at x100 magnification.

2.9 Statistical analysis
Experimental data are presented as Mean ± Standard error of mean (SEM). Statistical analysis was implemented using computer software SPSS 20.0 version statistical package program (SPSS, Chicago, IL). One-way analysis of variance was used to compare variables among the different groups. Level of significance (Post hoc comparisons) among the various treatments was determined by Duncan's Multiple Range Test. The values were considered statistically significant at $P<0.05$.

3. Results
The total phenolic and flavonoid contents of the methanolic extract of *Allium cepa* were 394.70 mg GAE/g and 180 mg QE/g respectively. The percentage increase in body weight of the treated groups was not significantly different ($p< 0.05$) from the control group after the first week. However, there were significant decreases ($p< 0.05$) throughout the remaining three weeks except for the 200 mg/kg bw and vitamin C treated groups. A similar trend of result was obtained for the absolute kidney weight. The relative kidney weights though showed a rather irregular result. The negative control group and the 100 mg/kg bw as well as the 200 mg/kg bw groups were not significantly different ($p<0.05$) from each other. However, the group 200 mg/kg bw and Vitamin C showed values that were significantly different ($p< 0.05$) from the potassium bromate treated groups but were not significantly different ($p< 0.05$) from the control (non-induced) group (Table 1).

Specific activity of alkaline phosphatase and concentration of creatinine in the serum was significantly increased ($p<0.05$) by potassium bromate. Treatment with 200 mg/kg bw and Vitamin C showed no significant difference ($p<0.05$) from the control group, but lower doses (50 mg/kg bw and 100 mg/kg bw) did not appear as potent (Figures 1 and 2). Total protein, albumin and globulin concentrations were significantly lowered ($p< 0.05$) compared to the control group when potassium bromate was administered. However, methanolic extract of *Allium cepa* at 200 mg/kg bw and vitamin C restored normalcy. However, lower doses of the extract did not appear as effective (Figures 3, 4 and 5).

Results in Figure 6 showed that potassium bromate significantly increased ($p< 0.05$) the level of urea in the serum of the rats. Methanolic extract of *Allium cepa* significantly reversed ($p< 0.05$) the increase at 200 mg/kg bw dose. Also, at 100 mg/kg bw dose, urea concentration was significantly reversed but value was as well significant from the control group.

Table 1: Body weight and kidney-body weight ratio of potassium bromate-induced rats administered with methanolic extract of *Allium cepa*

Treatment	% increase in body weight (g) after				Absolute Kidney Weight	Relative Kidney Weight
	1st week	2nd week	3rd week	4th week		
Control	5.03±0.6[b]	3.73±0.3[bc]	5.09±0.5[c]	5.72±0.4[c]	1.06±0.0[a]	0.50±0.6[a]
$KBrO_3$	4.73±0.1[b]	0.88±0.2[a]	0.81±1.7[a]	1.04±0.2[a]	1.26±0.1[c]	0.68±0.7[c]
$KBrO_3$ + (50 mg/kg BW)	4.80±0.2[b]	0.95±0.6[a]	1.29±0.3[ab]	1.54±0.2[ab]	1.30±0.1[c]	0.58±0.2[b]
$KBrO_3$ + (100 mg/kg BW)	6.32±0.6[b]	2.25±1.2[ab]	2.65±0.5[b]	3.09±0.4[b]	1.19±0.4[b]	0.67±0.1[c]
$KBrO_3$ + (200 mg/kg BW)	6.29±0.7[b]	4.87±2.0[c]	4.61±0.3[c]	5.85±0.3[c]	1.09±0.0[a]	0.62±0.1[b]
$KBrO_3$ + Vitamin C	5.21±1.4[b]	4.26±0.9[bc]	5.27±0.4[c]	5.63±0.5[c]	1.08±0.0[a]	0.51±0.0[a]
200 mg/kg BW	4.72±0.4[b]	4.26±1.8[bc]	4.90±0.5[c]	4.76±0.5[c]	1.09±0.6[a]	0.50±0.0[a]

Values are expressed as Mean ± SEM (n = 6). Row values with different alphabets are significantly different from the control group at p<0.05.

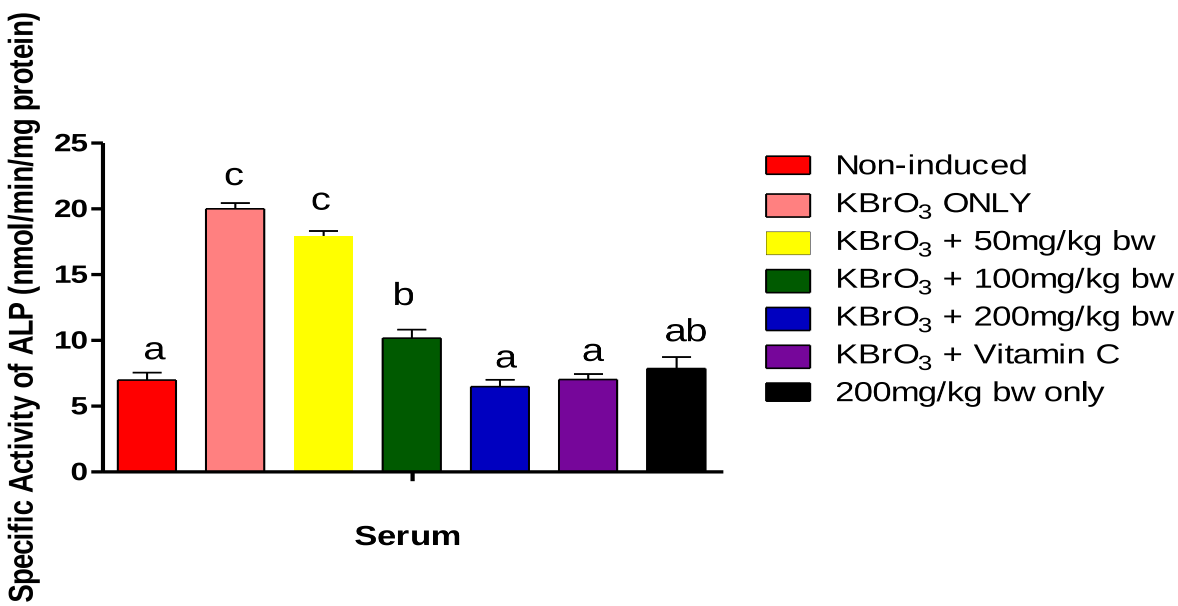


Figure 1: Specific activity of alkaline phosphatase (ALP) in the serum of potassium bromate-intoxicated rats administered with methanolic extract of *Allium cepa*. Values are expressed as Means of six determinations ± SEM. Bars with different letters are significantly different at p<0.05

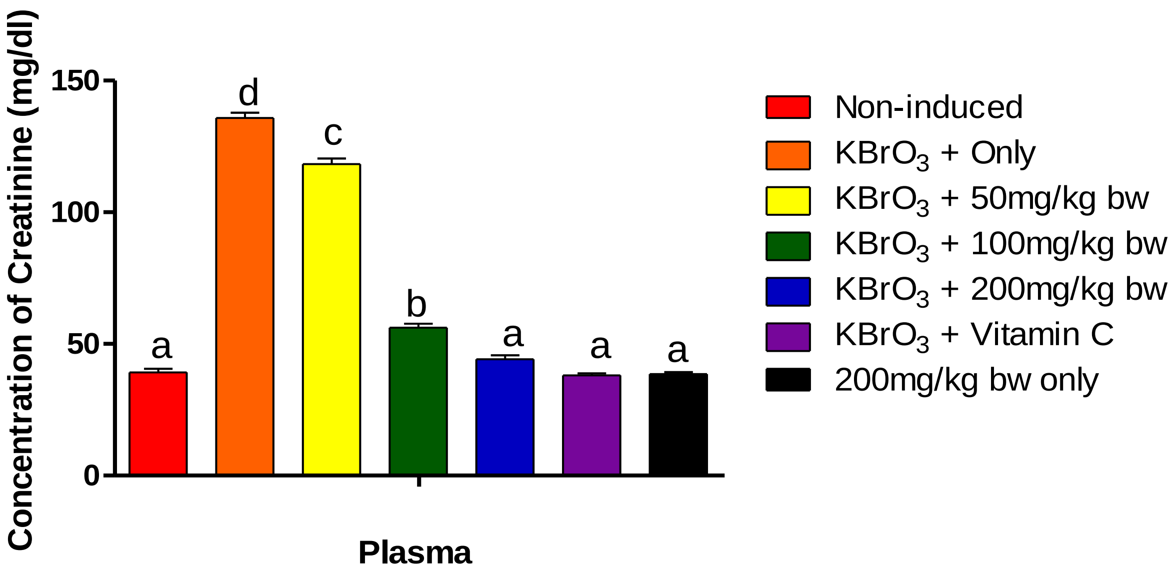


Figure 2: Concentration of creatinine in the plasma of potassium bromate-intoxicated rats administered with methanolic extract of *Allium cepa*. Values are expressed as means of six determinations ± SEM. Bars with different letters are significantly different at $p<0.05$

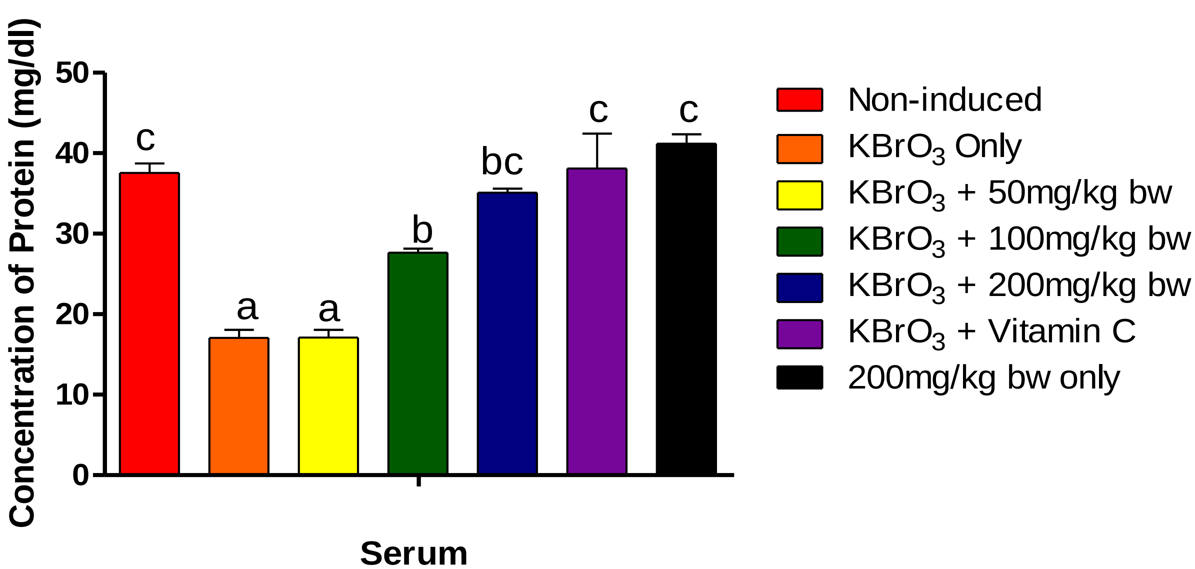


Figure 3: Total protein concentration in the serum of potassium bromate-intoxicated rats administered with methanolic extract of *Allium cepa*. Values are expressed as Means of six determinations ± SEM. Bars with different letters are significantly different at $p<0.05$

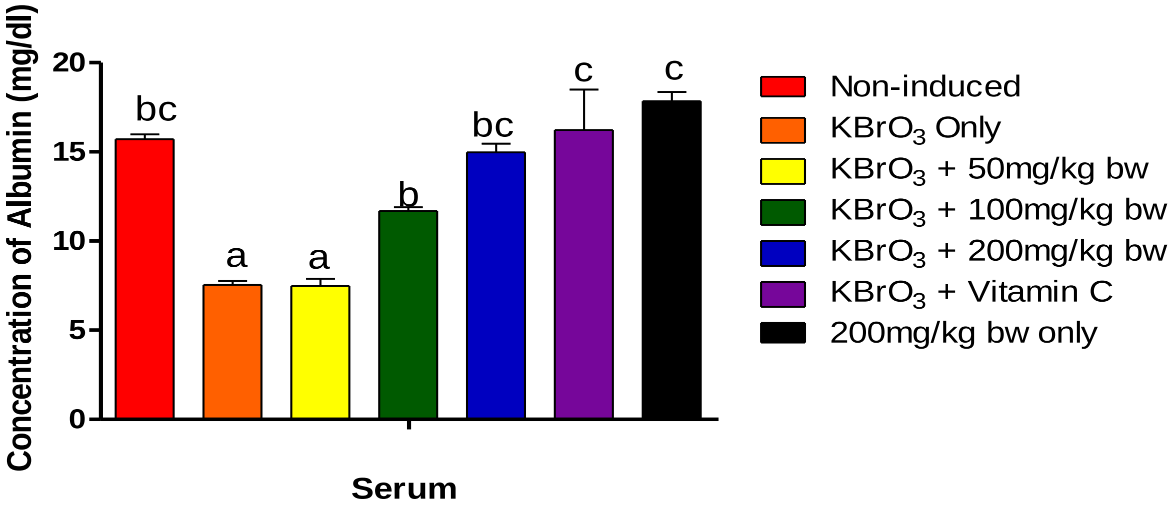


Figure 4: Concentration of albumin in the serum of potassium bromate-intoxicated rats administered with methanolic extract of *Allium cepa*. Values are expressed as Means of six determinations ± SEM. Bars with different letters are significantly different at $p<0.05$

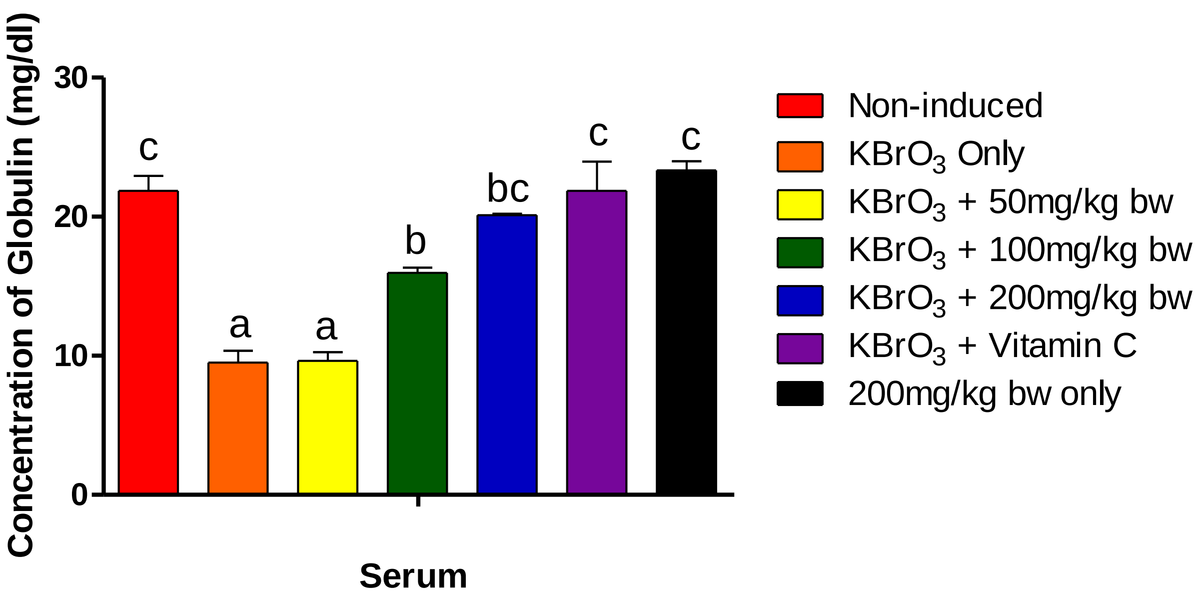


Figure 5: Concentration of globulin in the serum of potassium bromate-intoxicated rats administered with methanolic extract of *Allium cepa*. Values are expressed as means of six determinations ± SEM. Bars with different letters are significantly different at $p<0.05$

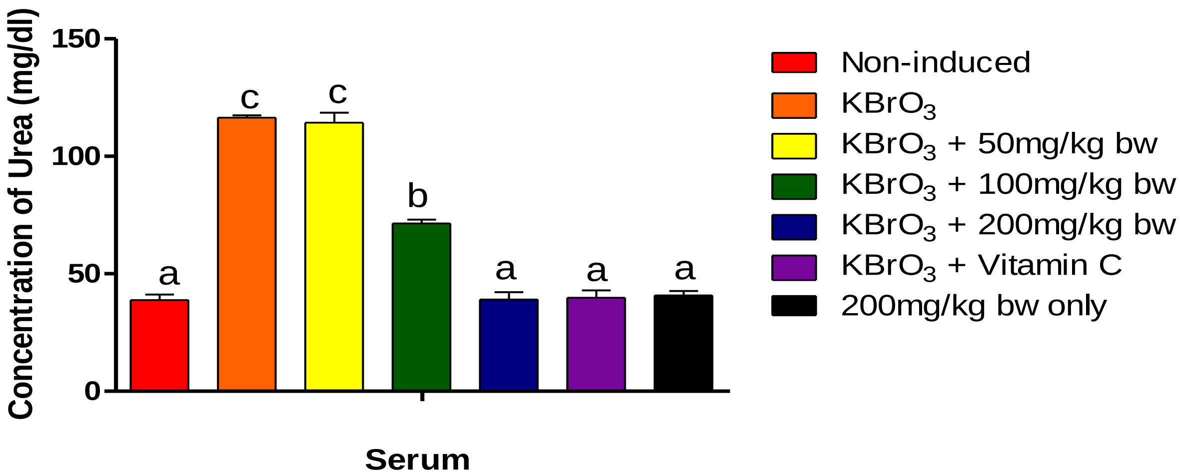


Figure 6: Concentration of urea in the serum of potassium bromate-intoxicated rats administered with methanolic extract of *Allium cepa.* Values are expressed as means of six determinations ± SEM. Bars with different letters are significantly different at p<0.05

Concentrations of bilirubin and creatinine in the urine of potassium bromate-induced rats were significantly increased ($p<0.05$) when values were compared with the control group. However, normalcy was restored at 200 mg/kg bw dose of the extract and with vitamin C. Although lower doses (50 mg/kg bw and 100 mg/kg bw) produced positive results, values obtained were still significantly higher ($p<0.05$) than the control group (Figures 7 and 8). Figure 9 shows that the concentration of nitrate in the urine of potassium bromate-intoxicated rats was significantly reduced. This was however significantly reversed ($p<0.05$) at 200 mg/kg bw of the extract and by vitamin C. The extract at 50 mg/kg bw and 100 mg/kg bw produced positive results, but values were still significantly different from the control group.

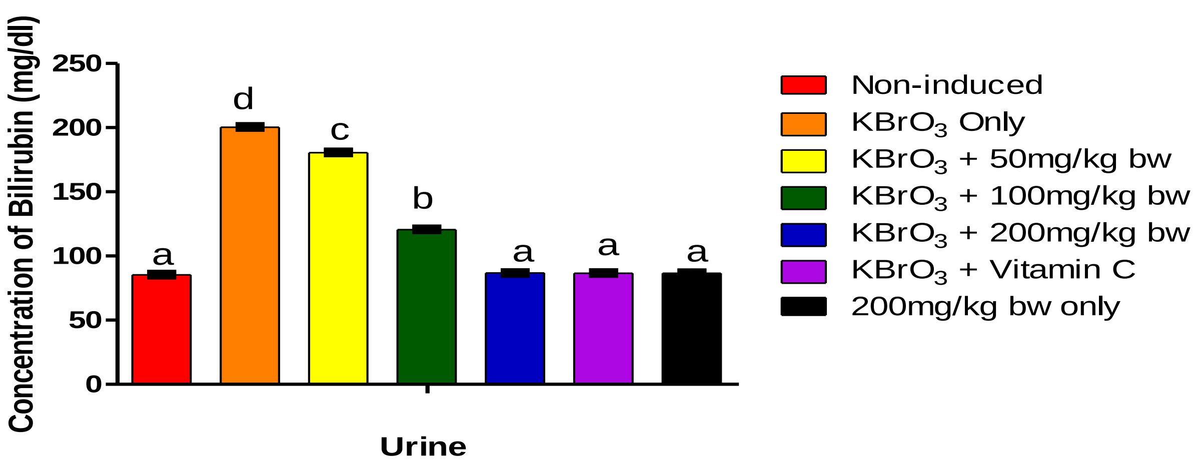


Figure 7: Concentration of bilirubin in the urine of potassium bromate-intoxicated rats administered with methanolic extract of *Allium cepa*. Values are expressed as means of six determinations ± SEM. Bars with different letters are significantly different at P<0.05

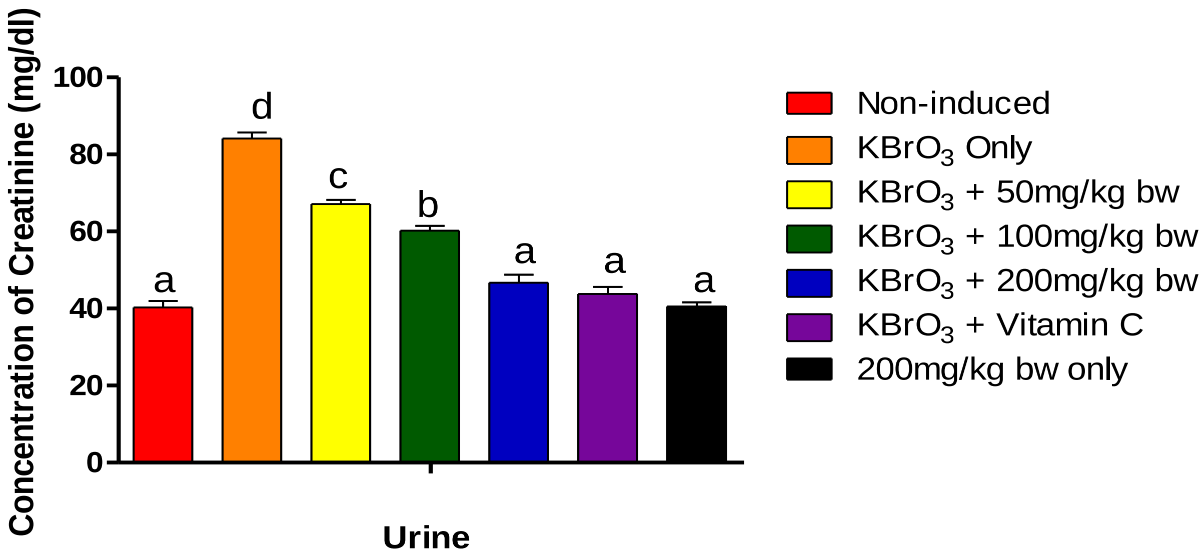


Figure 8: Concentration of creatinine in the urine of potassium bromate-intoxicated rats administered with methanolic extract of *Allium cepa*. Values are expressed as means of six determinations ± SEM. Bars with different letters are significantly different at $p<0.05$

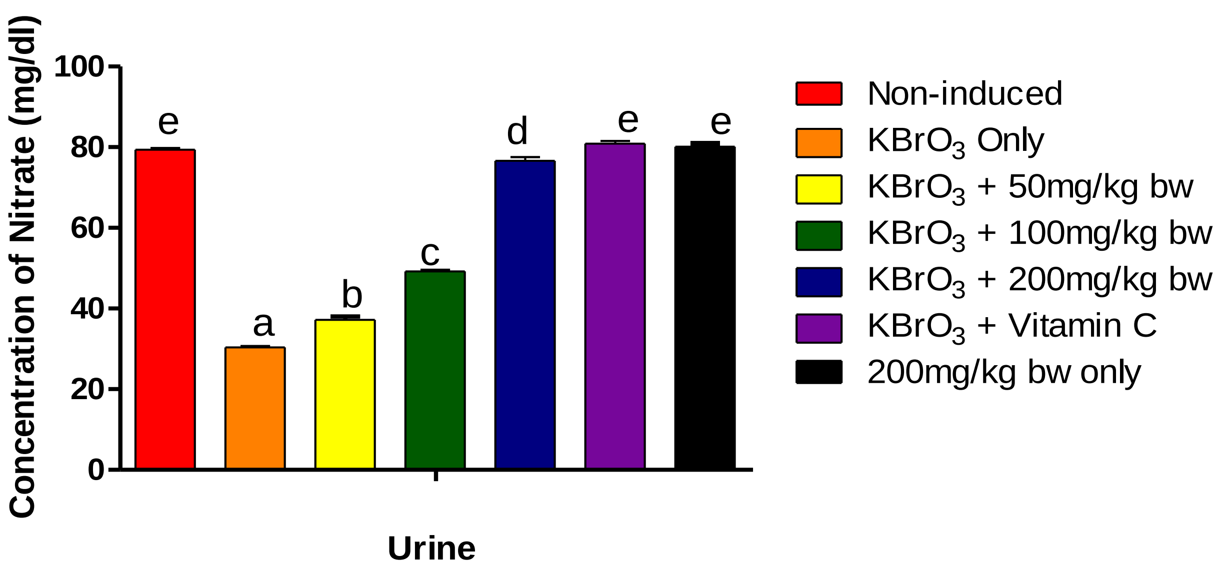


Figure 9: Concentration of nitrate in the urine of potassium bromate-intoxicated rats administered with methanolic extract of *Allium cepa*. Values are expressed as means of six determinations ± SEM. Bars with different letters are significantly different at $p<0.05$

Figures 10 and 11 revealed that concentrations of protein and urobilinogen in the urine of potassium bromate-intoxicated rats were significantly increased (p<0.05) when values were compared with the control group. Methanolic extract of *Allium cepa* and vitamin C significantly reduced (p<0.05) the observed increase to the level of the control group at all doses for protein with the exception of 50 mg/kg bw and 100 mg/kg bw for urobilinogen.

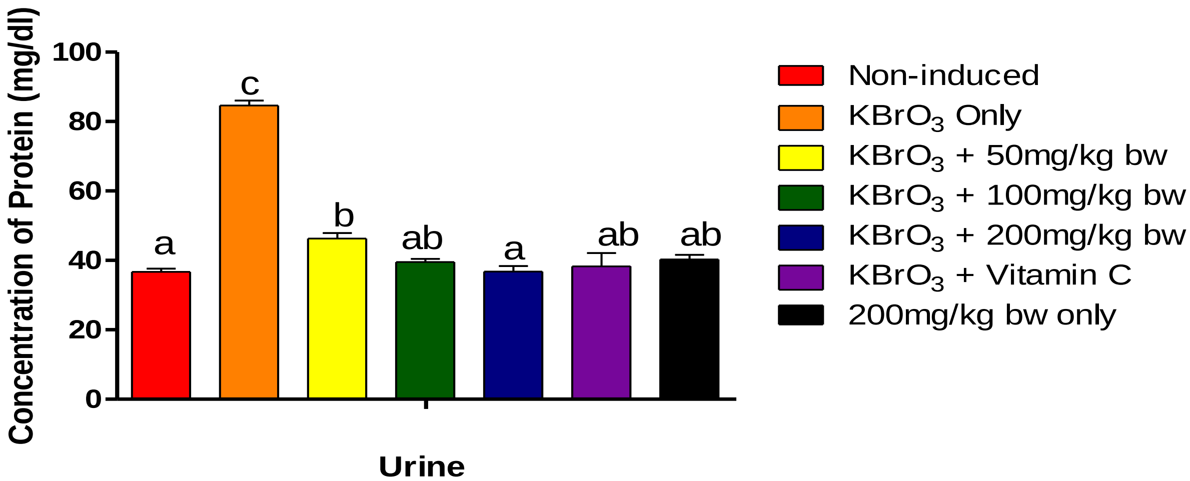


Figure 10: Total protein concentration in the urine of potassium bromate-intoxicated rats administered with methanolic extract of *Allium cepa*. Values are expressed as means of six determinations ± SEM. Bars with different letters are significantly different at p<0.05

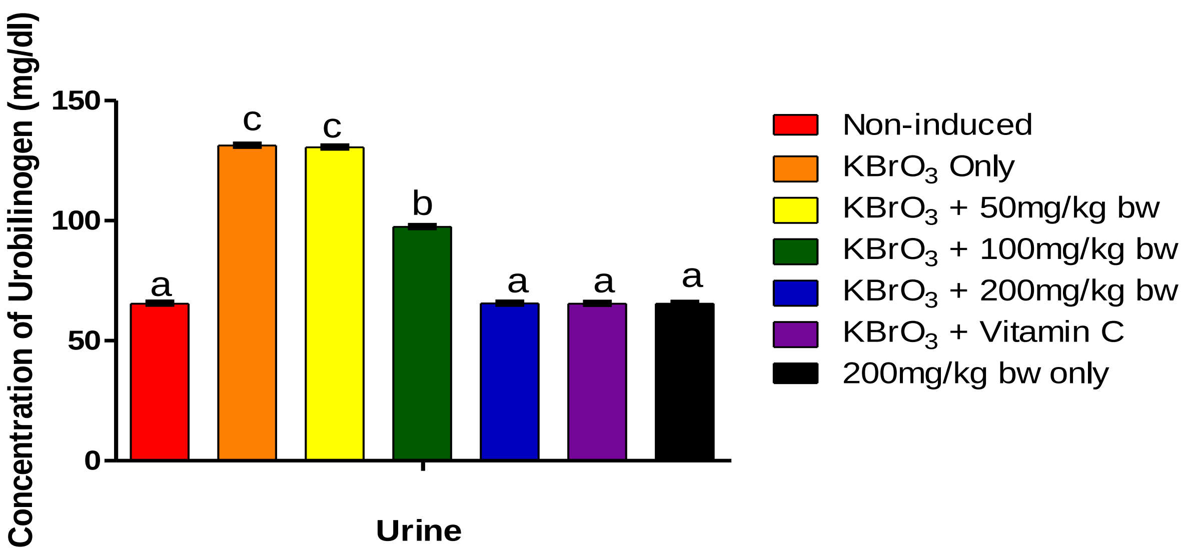


Figure 11: Concentration of urobilinogen in the urine of potassium bromate-intoxicated rats administered with methanolic extract of *Allium cepa*. Values are expressed as means of six determinations ± SEM. Bars with different letters are significantly different at p<0.05

Urinary levels of physical parameters (Table 2) including pH, GFR and creatinine clearance were significantly lowered ($p<0.05$) following potassium bromate intoxication. Values from vitamin C and 200mg/kg bw of the extract were not significantly different ($p<0.05$) from the control group with little deviation when the extract was administered alone. For the specific gravity, values were significantly increased ($p<0.05$) by potassium bromate. However, normalcy was restored by the extract in a dose-dependent manner.

Table 2: Urinary concentrations of physical parameters in potassium bromate-intoxicated rats administered with methanolic extract of *Allium cepa*

Treatment	pH	Specific Gravity	GFR	Creatinine Clearance (*10^-3) (mL/min)
Control	7.6±0.0[d]	1.10±0.0[a]	2.06±0.04[b]	1.43±0.03[b]
$KBrO_3$	6.1±0.0[a]	1.90±0.0[e]	1.29±0.01[a]	0.89±0.01[a]
$KBrO_3$ + (50 mg/kg BW)	6.5±0.0[b]	1.40±0.0[d]	1.31±0.02[a]	0.91±0.02[a]
$KBrO_3$ + (100 mg/kg BW)	7.0±0.0[c]	1.30±0.0[c]	2.04±0.06[b]	1.41±0.03[b]
$KBrO_3$ + (200 mg/kg BW)	7.4±0.0[d]	1.20±0.0[b]	1.91±0.07[b]	1.32±0.05[b]
$KBrO_3$ + Vitamin C	7.6±0.0[d]	1.10±0.0[a]	2.11±0.06[b]	1.46±0.04[b]
200 mg/kg BW	7.7±0.0[d]	1.10±0.0[a]	2.43±0.11[c]	1.68±0.07[c]

Values are expressed as mean ± SEM (n = 6). Row values with different letters are significantly different from the control group at $p<0.05$.

Table 3 shows the levels of some biochemical parameters. RBC, WBC, glucose and ketone body levels were significantly increased ($p<0.05$) by potassium bromate. Values obtained after treatment with vitamin C and 200 mg/kg bw of extract were not significantly different ($p<0.05$) from the control group except for glucose. Lower doses of the extract gave positive results but did not appear to be as effective.

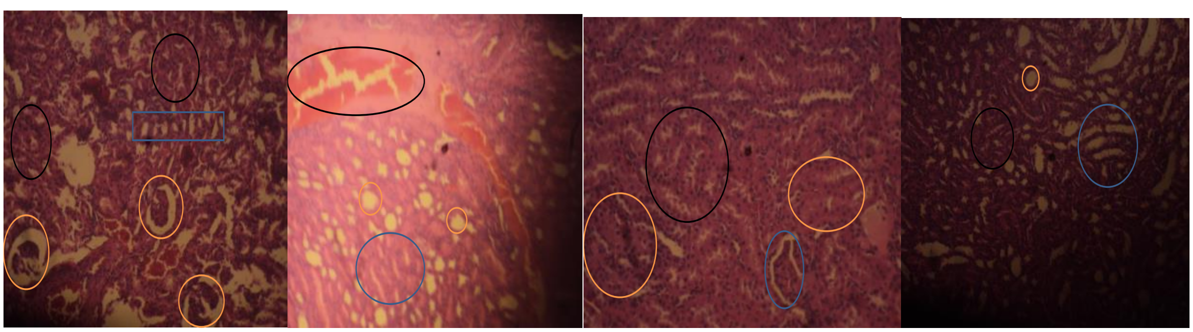
Table 3: Urinary biochemical parameters in potassium bromate-intoxicated rats administered with methanolic extract of *Allium cepa*

Treatment	RBC/µl	WBC/µl	Glucose (mg/dl)	Ketone Body (mg/dl)
Control	0.00±0.0[a]	10.67±0.8[a]	7.50±0.0[a]	10.46±0.2[a]
$KBrO_3$	40.00±0.0[d]	150.00±0.0[d]	166.67±21.1[a]	160.46±0.1[e]
$KBrO_3$ + (50 mg/kg BW)	19.83±0.9[c]	70.00±0.0[c]	100.00±0.0[b]	80.54±0.1[d]
$KBrO_3$ + (100 mg/kg BW)	10.00±0.0[b]	30.00±0.0[b]	52.00±0.0[c]	40.62±0.1[c]
$KBrO_3$ + (200 mg/kg BW)	0.50±0.3[a]	10.83±0.8[a]	10.00±0.0[d]	15.46±0.1[b]
$KBrO_3$ + Vitamin C	0.67±0.3[a]	10.33±0.4[a]	6.70±0.2[e]	10.35±0.1[a]
200 mg/kg BW	0.00±0.0[a]	10.33±0.8[a]	5.00±3.4[e]	10.46±0.1[a]

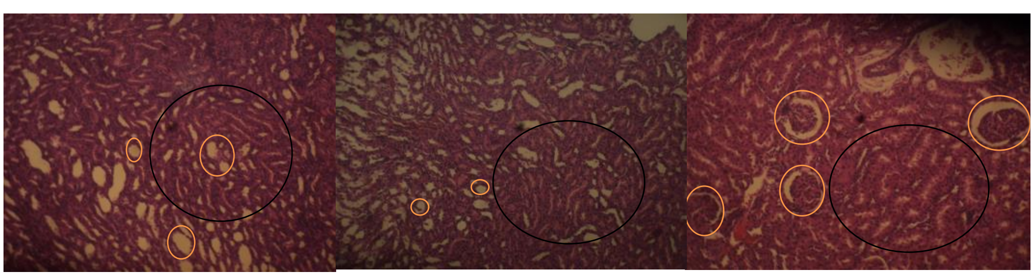
Values are expressed as mean ± SEM (n = 6). Row values with different letters are significantly different from the control group at $p<0.05$.

Figure 12 depicts the photomicrographs of the kidney of experimental rats intoxicated with potassium bromate and treated with different doses of *Allium cepa* methanolic extract. In the control group (non-treated rats), the renal tissue is composed of glomeruli (orange circle) at the cortex, numerous tubules and blood vessels (black circle). The tubules are lined back-to-back with scanty or unappreciable interstitial space (blue rectangle). The glomeruli show normal histology under light microscopy. For the potassium bromate-intoxicated but untreated rats (negative control group), the kidney section revealed renal tissues composed of cortex with numerous glomeruli (orange circle) which exhibit abnormal histology. The tubules are lined back-to-back by cuboidal epithelium with occasional area of hemorrhage (black circle) within the interstitial spaces. The medulla is composed of numerous tubules arranged in perpendicular array (blue circle). The photomicrograph of the kidney of potassium bromate-intoxicated rat treated with 50 mg/kg bw of *Allium cepa* methanolic extract shows cortex with numerous glomeruli (blue circle), renal tubule and vascular channels (black circle). The glomeruli are numerous with normal histology and the medulla is composed of numerous tubules arranged in perpendicular array. The tubules are lined by cuboidal epithelium (orange circle). In potassium bromate-intoxicated rats treated with 100 mg/kg bw of *Allium cepa* methanolic extract, the photomicrograph of the kidney revealed renal tissue composed of numerous glomeruli (orange circle), renal tubule, vascular channel (black circle) and scanty interstitial space. The glomeruli exhibited normal histology and non-obsolete tubules lined by cuboidal epithelium back-to-back (blue circle).

The kidney of rats intoxicated with potassium bromate and treated with 200 mg/kg bw developed cortex with normal numerous glomeruli (orange circle) with normal histology. The tubules are lined back-to-back by cuboidal epithelium. The medullar aspect is composed of numerous tubules arranged in perpendicular array (black circle). In rats administered Vitamin C, the kidney shows renal tissues composed of numerous glomeruli (orange circle) at the cortex admixed with numerous tubules and occasional area of vascular channels. The medullar aspect is composed of numerous tubules arranged in perpendicular array and lined by cuboidal epithelium (black circle). The photomicrograph of the kidney of rat treated with 200 mg/kg bw of *Allium cepa* methanolic extract revealed renal tissue composed of numerous glomeruli (orange circle) lined back-to-back and blood vessels. The glomeruli show normal histology and non-obsolete with renal tubules lined by cuboidal epithelium (black circle).



Positive Control **Negative Control** **$KBrO_3$ +50 mg/kg bw AC** **$KBrO_3$ + 100 mg/kg bw AC**



$KBrO_3$ + 200 mg/kg bw AC **$KBrO_3$ + Vitamin C** **200 mg/kg bw AC**

Figure 12: Photomicrograph of the kidney of potassium bromate-intoxicated rats treated with methanolic extract of *Allium cepa*. (AC means *Allium cepa*)

4. Discussion

Potassium bromate ($KBrO_3$) is used in most bakeries as dough improver [1] and the compound has been implicated in renal toxicity through the production of reactive oxygen species which are important agents of lipid peroxidation and DNA damage in the kidney [32]. It was previously reported that labialization of cell plasma membrane and loss of both cytosolic and membrane enzymes occur in rats exposed to chronic administration of potassium bromate Akanji [33]. *Allium cepa* bulbs have been shown to possess antioxidant, anti-diabetic, antihypertensive, anti-thrombic, hypoglycemic and anti-hyperlipidemic potential [34]. It is rich in phenolics, majorly quercetin which is used nutritionally as a supplement for its antioxidant and anti-inflammatory properties [35,36]. This study is therefore centered at investigating the possible protective effect of methanolic extract of *Allium cepa* on potassium bromate-induced nephrotoxicity in rats

The observed reduction in body weight but increased the absolute and relative kidney weight caused by potassium bromate administration was reversed by the *Allium cepa* extract. The effect on the kidney could be due to lipid peroxidation caused by the free radicals generated as a result of the potassium bromate administration. Similar results have been reported in previous studies [38-40]. However, the present study revealed the potency of *Allium cepa* extract at 200 mg/kg bw dose. The observed significant increase in the activity of ALP in the serum of the potassium bromate-intoxicated rats may be attributed to loss of membrane components such as ALP into the extracellular fluid, the serum [41], inactivation of the enzyme molecule in situ [42], or inhibition of the enzyme activity at the cellular or molecular level. It may also be caused by reduction in concentration or total absence of specific phospholipids required by this membrane-bound enzyme to express its full activity [43]. The observed reduction is in line with a previous report [33].

The observed marked increase in the serum concentrations of creatinine and urea following potassium bromate administration is in line with several earlier reports suggesting toxicity of potassium bromate and leakage of creatinine and urea into the serum [21,34,35]. However, marked improvement was observed upon treatment with *Allium cepa* extract at 200mg/kg bw as well as vitamin C. The significantly reduced serum concentrations of protein, albumin and globulin in the potassium bromate-treated groups agreed with an earlier report [21]. This might have resulted from considerable leakage due to injury to glomeruli and tubules. *Allium cepa* treatment at 200 mg/kg bw as well as vitamin C revealed significant prevention of toxicity.

Urinalysis provides important clues about acid-base balance and kidney function [46]. The significant increase in urine levels of bilirubin, creatinine, protein, urobilinogen, glucose, white blood cells (WBC), red blood cells (RBC), ketone bodies and specific gravity following potassium bromate intoxication are in line with previous reports [21,47,48]. These parameters reflect kidney dysfunction and renal injuries induced by potassium bromate [47, 48]. Increase in these indices is a symptom of dehydration, renal artery steatosis, necrosis and decreased blood flow to the kidneys [21]. Additionally, the observed increment in RBC and WBC counts may be an indication of severe injuries to renal tissues. Higher levels of protein, RBC and WBC concentration might have also contributed to the increased value of these parameters. The hematuria, proteinuria and glucosuria observed in the present study could be related to necrosis and kidney dysfunction [49]. It was found that the glomerular capillary wall is permeable to low molecular-weight (LMW) proteins [50]. Therefore, an appreciably high level of proteinuria indicates the leakage of LMW proteins. The oxidative stress induced by potassium bromate might promote the formation of various vasoactive mediators that can affect renal function directly by initiating renal vasoconstriction or decreasing the glomerular capillary ultrafiltration coefficient [21]. This action will reduce the glomerular filtration rate, leading to proteinuria [21]. Administration of extract of *Allium cepa* prevented toxicity in kidneys especially at 200 mg/kg bw. Overall, the present study clearly demonstrated that treatment of potassium bromate-intoxicated rats with methanolic extract of *Allium cepa* normalized the levels of urinary nitrate and the biophysical parameters in a dose-dependent fashion.

5. Conclusion

This study concluded that *Allium cepa* methanolic extract, up to 200 mg/kg body weight dose, has protective effect against potassium bromate-induced nephrotoxicity in rats. This may be attributed to the high contents of flavonoids in the extract. *Allium cepa* therefore represents a highly promising agent in protecting against the risk of chemical-induced nephrotoxicity.

6. References

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