STUDY THE PROTECTIVE EFFECT OF VITAMIN E AGAINST POTASSIUM BROMATE TOXICITY ON SOME HEMATOLOGICAL, RENAL, AND HEPATIC FUNCTIONS IN MALE RATS

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The current investigation was carried out to study the protective effect of vitamin E (VE) on the associated disturbances of hematological, renal, and hepatic functions in male rats produced in potassium bromate (KBrO_3) treated rats. Twenty-four rats were divided randomly into four groups: First group: served as control group. Second group: rats were received 50 mg/kg b.wt. of KBrO_3 orally. Third group: rats were received 30 mg/kg b.wt. of VE orally. Fourth group: rats were received 30 mg/kg b.wt. of VE orally an hour before administration of KBrO_3 (50 mg/kg b.wt.) orally. The experiment continued for five successive weeks. Results showed that the treatment with KBrO_3 revealed a significantly decrease in the mean of the body weight, red blood corpuscles (RBCs), white blood cells (WBCs), blood platelets (PLTs), hemoglobin (HB), hematocrit value (HCT) comparing to the control group. Whereas, the serum activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) enzymes, urea, uric acid, creatinine, were obviously elevated in KBrO_3 treated group comparing with control group. The treatment with VE+KBrO_3 ameliorated all the hematological, renal, and hepatic parameters tested. It is clear from the present results that VE reduced the severity of KBrO_3. This could be mediated by its potent antioxidant effects.

Keywords: Potassium bromate – Vitamin E – Hematological – Renal – Hepatic functions

INTRODUCTION

Potassium bromate (KBrO_3) commonly used as food additive in cheese production, beer making, and is added to fish paste products. It is likewise vital in pharmaceutical, cosmetic industries and is a constituent of cold wave hair solutions. In addition, KBrO_3 is found in the samples of drinking water as a byproduct of ozone disinfection. Several research had been executed in different parts of the world to prove that KBrO_3 is dangerous to health if consumed in water or food. It has been proven to be nephrotoxic in both experimental animals and man. Furthermore, it induces renal cell tumors, follicular cell tumors of the thyroid, and mesotheliomas of the peritoneum.

The nephrotoxicity caused by KBrO_3 has been attributed to its ability to stimulate the production of lipid peroxidation (LPO), reactive oxygen species (ROS), also, it triggers primary DNA oxidative damage and increased 8-hydroxydeoxyguanosine (8-OHDG) DNA adduct levels, a representative marker of oxidative DNA modification, in vivo and in vitro. The oxidative stress caused by KBrO_3 a long way exceeds the antioxidative defense capacity of the cells leading to marked nephrotoxicity in animals and human beings as well as the carcinogenicity in experimental animals.

International Agency for Research on Cancer (IARC) has labeled KBrO_3 as a possible human carcinogen (group 2B) and its using in food processing was confined. Indeed, many previous reports has documented that KBrO_3 can induce numerous organ toxicity in experimental animals and humans and the kidney is the primary target organ of these dangerous compound. KBrO_3 is highly injurious and irritating to tissues mainly those of the kidneys and the central nervous system (CNS). The pathological findings included hemolysis and renal tissue damage. Therefore,
KBrO₃ has been banned in several countries including the United Kingdom in 1990, Nigeria in 1993 and Canada in 1994. Toxicological studies have found out that KBrO₃ influences the nutritional quality of bread as the main vitamins present in bread are degraded. It is known that KBrO₃ induces the oxidative stress of the tissues that may be the basis of bromate-induced carcinogenesis. There have not been many reviews on the effect of potassium bromate on hematological indices, consequently this research was designed to check out the impact of potassium bromate on some blood parameters using male albino rats.

Vitamins are antioxidants that protect cells and tissues against oxidative stress. Among the most important antioxidant vitamins for tissue protection is vitamin E (VE). For proper physiological function, there is a balance between the amount of free radicals generated in the body and the antioxidants necessary for protection against them. This balance can be shifted resulting in oxidative stress when there are extra of free radicals and absence of antioxidant safety. The dietary and tissue balance of nutrients including vitamins are essential in protecting tissues in opposition to oxidative stress.

The present work attempts to study the effect of administration of KBrO₃ on hematological parameters, renal and hepatic functions of male rats and the attenuating effect of vitamin E on the deleterious consequences of KBrO₃.

**MATERIALS AND METHODS**

**Chemicals**

There are two types of chemical materials that used in the present study:

Potassium Bromate (KBrO₃) was obtained from El-Gomhouria Chemicals Company (Cairo, Egypt). It was dissolved in distilled water to form therapeutic doses for rats.

Vitamin E (VE) Alpha-tocopheryl acetate as a form of tablets for oral administration, its concentration 1000 mg and purchased from Safe pharms for pharco medical. It was dissolved in olive oil to form therapeutic doses for rats.

In the present study the equivalent therapeutic dose of KBrO₃ and VE for rats were calculated according to the method of Paget and Barnes. The dose was estimated according to the factor’s human-rat therapeutic dose. The dose of KBrO₃ (50 mg/kg b.wt.) was diluted in distilled water. Whereas the dose of VE (30 mg/kg b.wt.) was diluted in olive oil.

The dosage of KBrO₃ for rat was calculated to be equivalent 6.4 mg each rat depending on the factor’s human-mouse therapeutic dose. In the same manner, the dosage of VE for rat also was estimated to be equivalent 3.9 mg each rat according to the previous method.

**Animals for the experiment**

In this study, a total twenty-four male albino rats were used. The animals were housed in cages where they had ad libitum rat chow and water in an air-conditioned room with a 12-h light/12-h dark cycle and were randomly divided into four groups (six rats in each group). The first group was used as a control without any treatment, the second group potassium bromate (KBrO₃) rats were received 50 mg/kg b.wt. of KBrO₃ orally, the third group vitamin E (VE) rats were received 30 mg/kg b.wt. of VE orally, and the fourth group potassium bromate and vitamin E (VE+KBrO₃) rats were received 30 mg/kg b.wt. of VE orally an hour before administration of KBrO₃ (50 mg/kg b.wt.) orally. These treatments were continued for five successive weeks.

**The body weight gain**

All rats were weighted at the beginning (initial weight) and on the end (final weight) of the experiment, then the body weight gain for each group were calculated.

The percentage of body weight was calculated as follow:

$$\frac{\text{Mean of final body weight} - \text{Mean of initial body weight}}{\text{Mean of initial body weight}} \times 100$$

**Collection of the blood and serum samples**

At the end of the experimental period, the rats were fasted overnight and anesthetized using chloroform and then each experimental rat was decapitating, and the blood samples were collected. Blood samples were collected in EDTA bottle for hematological analysis and plain bottles for biochemical analysis. Samples for biochemical analysis were centrifuged at 4000 rpm for 20 min at 4 °C and immediately stored at -20 °C till time of analysis.
Hematological studies

Red and white blood cells count, hemoglobin content, mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC) and platelets count (PLTs) were performed according to Dacie and Lewis. Measurement of hematocrit value (Hct) was determined according to the method of Rodak by using heparinized capillary tube.

Analysis of biochemical indices of liver and kidney functions

Serum aspartate transaminase (AST) and alanine transaminase (ALT) activities were measured according to King, the activity of alkaline phosphatase (ALP) was measured according to Englehardt.

Urea and uric acid were estimated according to Young. Creatinine was determined according to the method described by Bartels and Bohmer method.

Statistical analysis

Data were expressed as means ± S.E. Statistical analysis was performed using SPSS program (Version 16). Significant differences among groups were determined by one-way analysis of variance (ANOVA) according to the method described by Duncan. Different letters were considered significant (p < 0.05).

RESULTS AND DISCUSSION

Results

Body weight

In the present study, the mean of body weight was recorded at the beginning (initial weight per gram) and the end of the experiment (final weight per gram) for the control, KBrO3 (50 mg/kg b.wt.), vitamin E (30 mg/kg b.wt.) and vitamin E + KBrO3 groups. The data in table (1) showed a non-significant change in the initial body weight between all groups.

Whereas the final body weight revealed a significant decrease in KBrO3 treated group comparing with control group with percent of change (-22.06 %) from the control value. Vitamin E (VE) group exhibits a non-significant change from the control group. In the same table (1), VE in the combined group (VE+ KBrO3) ameliorated the body weight to some extent, but it still lower than the control group recording (-8.5%).

Hematological results

The data represented in table (2) summarize the effects of KBrO3, VE and the combination between VE and KBrO3 on the hematological findings: Red blood Corpuscles (RBCs) count, White blood cells (WBCs) count, blood platelets (PLTs), hemoglobin content (HB), hematocrit value (HCT), Mean corpuscular volume (MCV), Mean corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC). A significant change in RBCs count, WBCs count, PLTs, HB content and HCT value were observed between control rats, KBrO3 treated rats, VE treated rats, and VE+ KBrO3 treated rats.

Table (2) revealed a significant decrease in the RBCs, WBCs, PLTs, HB content and HCT value recording -24.4%, -22.9%, -25.5%, -40.3% and -12.52 %, respectively in comparison to control values was observed in KBrO3 treated rats.

The treatment with VE showed a non-significant change in all the previous parameters comparing with control values. The treatment with the combination between VE and KBrO3 restored RBCs and WBCs counts. Whereas the treatment with the VE+KBrO3 failed to restore the decrease in PLTs, HB and HCT to control values, but it showed an increase comparing with the KBrO3 group.

The data in the same table (2), statically showed a non-significant change between all groups in MCV, MCH and MCHC values.

Table 1: Initial and final body weight in control and treated groups.

| Body weight (gram) | Control | KBrO3 | % D | VE | % D | VE+KBrO3 | % D | P-value |
|--------------------|---------|-------|-----|----|-----|-----------|-----|---------|
| Initial weight     | 111.3 ± 3.2  | 112.8± 2.70 | 1.35 | 106 ± 2.84  | 4.8 | 115 ± 3.28 | 3.3 | -       |
| Final weight       | 177.3 ± 2.73  | 138.17± 2.09  | -22.06 | 170 ± 4.28  | -12.52 | 162.17± 2.59 | -8.5 | *       |

* Values represent the mean ± S.E.
* Significance between groups at (p-value < 0.05)
* Statistically significant means (p-value < 0.05) are given different letters and statistically non-significant means are given the same letter.
* % D: Percentage difference [(Treated value – Control Value) / Control Value] x 100
The toxicity that induced by KBrO₃, VE and VE+KBrO₃ on the activities of liver enzymes AST, ALT and ALP enzymes, are shown in table (3). Also, the effects of VE and the combination between VE and KBrO₃ on the changes of AST, ALT and ALP activities are shown in table (3).

As shown in table (3) a significant difference ($P < 0.005$) in the activities of AST, ALT and ALP were detected by using ANOVA analysis between control and KBrO₃ treated rats reaching 303.58%, 214.83% and 110.7%, respectively. However, the treatment with VE resulted in a non-significant change in the activities of these enzymes compared to the control group.

The treatment with VE+KBrO₃ revealed a significant reduction and restored the activities of AST and ALT to control like values reaching percent of change 17.80% and 15.02%, respectively. ALP enzyme showed improvement in its activity by the treatment with VE+KBrO₃ comparing with KBrO₃ treated group, but it still higher than the control group.

### Kidney function

Table (4) illustrate the effects of KBrO₃ (50 mg/kg b.wt.), VE (30 mg/kg b.wt.) and VE administration an hour before KBrO₃ treatment on the serum levels of creatinine (mg/dl), blood urea (mg/dl) and uric acid (mg/dl) on adult rats. The data in Table (4) revealed that the serum creatinine, blood urea and uric acid levels in KBrO₃ treated rats recorded a significant change ($P < 0.05$) reaching 75%, 51.54% and 89.5%, respectively compared to control group. However, the treatment with VE resulted in a non-significant change in serum creatinine, blood urea and uric acid levels as compared to control group. Whereas they were ameliorated in VE+KBrO₃ group but the creatinine and blood urea not similar to control values recording 36.36% and 26.19%, respectively.

### Table 2: The effects of KBrO₃, VE and VE+ KBrO₃ on the hematological parameters.

| Blood Parameters | Control | KBrO₃ | % D | VE | % D | VE+KBrO₃ | % D | p-value |
|------------------|---------|-------|-----|----|-----|-----------|-----|---------|
| RBCs (10¹²/mm³)  | 5 ± 0.28 a | 3.78 ± 0.21 b | -24.4 | 5.03 ± 0.38 a | 0.6 | 4.55 ± 0.29 ab | -9 | * |
| WBCs (10⁹/mm³)   | 6.32 ± 0.44 a | 4.87 ± 0.15 b | -22.9 | 6.17 ± 0.44 a | -2.37 | 5.25 ± 0.35 ab | -16.93 | * |
| PLTs (10⁹/L)     | 224 ± 7.6 a | 166.83 ± 5.52 b | -25.5 | 222 ± 9.06 a | -0.89 | 184.33 ± 13.49 b | -17.7 | * |
| HB (g/dl)        | 16.25 ± 0.44 a | 9.7 ± 0.41 b | -40.3 | 15.5 ± 0.52 a | -4.6 | 12.78 ± 0.78 b | -21.4 | * |
| HCT (%)          | 30.67 ± 0.67 a | 26.83 ± 1.33 b | -12.52 | 31 ± 0.63 a | 1.07 | 27.67 ± 0.76 b | -9.78 | * |
| MCV (Fl)         | 88.7 ± 1.69 a | 89.37 ± 2.21 b | 0.755 | 88.25 ± 2.24 a | -0.51 | 86.48 ± 2.38 b | -2.5 | - |
| MCH (Pg)         | 29.35 ± 0.30 a | 29.52 ± 0.31 b | 0.58 | 29.68 ± 0.15 a | 1.12 | 29.35 ± 0.30 b | 0 | - |
| MCHC (%)         | 31.57 ± 0.82 a | 30 ± 0.55 b | -4.97 | 31.9 ± 0.8 a | 1.05 | 31.15 ± 0.84 b | -1.33 | - |

- Values represent the mean ± S.E.
- Significance between groups at (p-value < 0.05)
- Statistically significant means (p-value < 0.05) are given different letters and statistically non-significant means are given the same letter.
- % D: Percentage difference [(Treated value – Control Value) / Control Value] x 100

### Table 3: The effects of KBrO₃, VE and VE+KBrO₃ on the activities of liver enzymes AST, ALT and ALP.

| Liver Enzymes | Control | KBrO₃ | % D | VE | % D | VE+KBrO₃ | % D | p-value |
|---------------|---------|-------|-----|----|-----|-----------|-----|---------|
| AST (IU/L)    | 125.1 ± 7.2 a | 504.68 ± 88.6 b | 303.58 | 120.9 ± 79.1 a | -3.4 | 147.31 ± 6.13 b | 17.80 | * |
| ALT (IU/L)    | 138.2 ± 0.4 a | 435.12 ± 76.37 b | 214.83 | 127 ± 5.3 a | -8.1 | 158.97 ± 18.12 b | 15.02 | * |
| ALP (IU/L)    | 92.7 ± 3.3 a | 195.3 ± 154 b | 110.7 | 90.7 ± 3.1 a | -2.2 | 143.1 ± 13.2 b | 54.37 | * |

- Values represent the mean ± S.E.
- Significance between groups at (p-value < 0.05)
- Statistically significant means (p-value < 0.05) are given different letters and statistically non-significant means are given the same letter.
- % D: Percentage difference [(Treated value – Control Value) / Control Value] x 100
Table 4: The effects of KBrO₃, VE and KBrO₃+ VE on the serum creatinine, urea and uric acid levels.

| Kidney parameters | Control | KBrO₃ | % D | VE | % D | VE+KBrO₃ | % D | p-values |
|-------------------|---------|-------|-----|----|-----|----------|-----|---------|
| Creatinine (mg/dl) | 0.88 ± 0.054¹ | 1.54 ± 0.07³ | 75 | 1.10 ± 0.29⁶ | 25 | 1.2 ± 0.03⁷ | 36.36 | * |
| Urea (mg/dl)      | 34.17 ± 1.65² | 51.78 ± 1.52² | 51.54 | 37.36 ± 1.56⁶ | 9.34 | 43.12 ± 2.31⁷ | 26.19 | * |
| Uric acid (mg/dl) | 1.9 ± 0.16⁴ | 3.6 ± 0.4² | 89.5 | 2.2 ± 0.16² | 15.79 | 2.4 ± 0.34⁴ | 26.32 | * |

- Values represent the mean ± S.E.
- Significance between groups at (p-value < 0.05)
- Statistically significant means (p-value < 0.05) are given different letters and statistically non-significant means are given the same letter.
- % D: Percentage difference [(Treated value – Control Value) / Control Value] x 100

Discussion

The body weight considered as a sensitive indicator of toxic chemical effects. In the current study, the data revealed that the body weight decreased significantly in KBrO₃ treated group (50 mg/kg b.wt.), on the end of experimental period. This result was agreeing with the results that recorded by Rezq, who reported that the administration of KBrO₃ caused a significant reduction in body weight of swiss mice. Whereas, vitamin E (VE) showed a non-significant change in the body weight comparing with the control group, a result in accordance with that of Yin et al. Vitamin E administration an hour before KBrO₃ treatment, caused a marked regain in body weight. These findings were in accordance with previous studies that carried by Hassan, who stated that VE gain the body weight that reduced by KBrO₃ treatment. The reduction of the body weight in KBrO₃ treated group may be due to binding of KBrO₃ to iodine receptors, bromide and iodine are a member of halide group and they are similar in their receptors and the bromide considered as endocrine disrupting chemicals (EDCs) that interfere or mimic with endocrine hormone and leading to high risks. Similar studies also indicated that EDCs decrease the pubertal body weight. Also, the decrease in the body weight that following KBrO₃ treatment may probable be ascribed to the injured renal tubules because of oxidative stress, and the following loss of the tubular cells to reabsorb water, leading to dehydration and decrease in body weight. The above action leading to polyuria might be the reasons for the loss of body weight. Regain of the body weight in the present study by the VE may be due to the enhancement effect of VE on the toxicity that induced by KBrO₃ because of its antioxidant properties that scavenge free radicals which resulting from KBrO₃ toxicity.

The identification of blood disorders considered as an indicator of many pathological conditions. In the present study, some hematological parameters were measured to throw the light on the effect of administration KBrO₃, VE and the combination between them in rats. The results clearly demonstrated that KBrO₃ treatment for 5 weeks caused a significant reduction in the red blood corpuscles count (RBCs), white blood cells (WBCs), hemoglobin content (HB), hematocrit value (HCT) and platelets, but the Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC) values don't have significant changes comparing with control values. The previous study carried out by Abd Elhalim, revealed that the administration of 100, 200 mg/kg b.wt. KBrO₃ for 3 weeks showed a significant decrease in HB, HCT and MCHC content and a non-significant reduction in WBCs and RBCs, but MCV has a non-significant change. The outcome of the present investigation shows that, KBrO₃ causes a significant impact on the different hematological parameters compared to the control group. RBCs have antioxidant defense system that includes enzymatic and non-Enzymatic pathways. Oxidative stress causes damage for RBCs membrane by hemolysis and RBCs don't have the ability to repair these damages because mature RBCs without nucleus. So, the reduction in RBCs count may be because of oxidative stress; excessive amount of malondialdehyde (MDA) as a product of lipid peroxidation cause breaking down of RBCs membrane double bonds of polyunsaturated fatty acid (PUFA) of RBCs membrane. Ahmad et al. hypothesized that
KBrO₃ affected on the cellular antioxidant defense system by generating ROS inducing oxidative stress in the erythrocytes. The exposure of erythrocytes to chemical has been associated with erythrocytes distraction and hemolytic anemia. So, the depression in the hematological parameters recorded in the current study could be due to disturbed hematopoiesis, destruction of erythrocytes, the reduction in the rate of erythropoiesis and their removal from circulation as a consequence of the toxic effect of KBrO₃ toxicity on bone marrow, spleen and liver. In the rats treated with VE, we did not observe any changes in hematological parameters comparing with control animals. Whereas, the combined group (VE+KBrO₃), showed improvement in all hematological parameters that may be because of eating normally again and weight regains in addition to antioxidant properties of VE against the free radicals, VE inhibits the production of new free radicals. Counteracting the effects of KBrO₃ toxicity on the above parameters by VE could be attributed to inhibition of hemolysis of RBCs and/or toxic effects of KBrO₃ on the hematopoietic organs.

The liver performs a significant role in the metabolic homeostasis, as it is responsible for the metabolism, synthesis, storage and redistribution of vitamins, carbohydrates, and fat. Importantly, it is the primary detoxifying organ of the body, which gets ride of wastes and xenobiotics by metabolic conversion and biliary excretion. It is known that the activities of serum aminotransferases are considered as markers of toxicity in the liver induced by chemicals. The most sensitive biomarkers used in the diagnosis of liver disorders are AST and ALT activities, and their activities indicate the type and extent of damage inflicted that displays a state of hepatocyte injury. It is clear from the present results that the rats consumed KBrO₃ revealed an impairment in the liver function. This was indicated from the significant increase in the activities of AST, ALT and ALP enzymes when compared to control rats. The current findings are in line with the previous results published by Bayomy et al., who reported that KBrO₃ induced a significant rise in serum levels of AST and ALT in liver tissues. Also, it was reported previously that, KBrO₃ treatment in wister rats have hepatotoxic effects. This may be attributed to the hyperlipidemia interferes with liver functions. Previous experimental researchers have proven that longstanding hyperlipidemia results in increased lipid oxidation and progression of liver impairment. Also, oxidative stress damages the integrity and stability of biological membranes and increases permeability, leading to the outflow of cytoplasm enzymes such as AST, ALT and ALP into the blood. So, the elevation of liver enzymes activities may be due to the failure of parenchymal cells of the liver under pathological conditions to ensure the vital functions, causing distribution of metabolism. As, it was shown that KBrO₃ can induce hepatic impairment. Herein, we found that VE treatment together with KBrO₃ alleviated the elevated activities of the markers of hepatocellular injury AST, ALT and ALP comparing with KBrO₃ treated rats. Various experimental research on the animal species showed that VE treatment ameliorated liver damage induced by carbon tetrachloride, doxorubicin, anthracycline antibiotic, and pesticides such as malathion. Similar observation was reported in mice where VE ameliorated organophosphorus insecticide (diazinon) induced oxidative stress in mice liver. The hepatoprotective effect of VE was also observed in melathion induced hepatotoxicity in rats. Al-Othman et al., evaluated the protective effect of VE in melathion induced oxidative injury in the liver and kidney of rats. He and co-workers observed that VE was effective in alleviating oxidative damage in liver of rats. Vitamin E was able to reverse melathion induced increase in AST and ALT activities in rats. It is clear from the present data in the combined treatment, VE reduced the hepatotoxic effect induced by KBrO₃. This was indicated from the decreased the activities of AST, ALT and ALP enzymes. So, the VE has protective effects on the liver function solely and in combination with KBrO₃.

Increasing creatinine, blood urea and uric acid levels considered as an indicator of kidney failure and were measured in the present study to evaluate the changes in the kidney function under the effect of KBrO₃. It is clear from the present results that there is an impairment in the kidney function of KBrO₃ treated rats. The levels of creatinine, blood urea and uric acid significantly increased in KBrO₃ treated group as compared with the control group. Conversely, VE+KBrO₃ group manifested a significant decline in the levels of these parameters comparing with the KBrO₃ group.
Vitamin E treatment solely did not show a significant difference in their levels comparing to the control animals. Consistent with the previous studies, the administration of KBrO₃ in different animals and at various doses induced a renal failure indicated by elevation of serum creatinine, blood urea and uric acid levels. Also, it was recorded a significant increasing in the sera levels of creatinine and urea at dose of 20 mg/kg of KBrO₃. Conversely, a little or no evidence of renal impairments in rats have been found. The major mechanism of KBrO₃-induced nephrotoxicity is by the production of ROS, which initiates lipid peroxidation and decreases the enzymatic and non-enzymatic antioxidants, an action that will finally culminate in oxidative stress. Accordingly, the impairment in the kidney function reported in the present study in response to KBrO₃ administration could be mediated by oxidative stress induced by KBrO₃. Also, these changes can be attributed to the damage of nephrons structural integrity, which is consistent with reports confirming that the level of serum creatinine increases only if at least half of the kidney nephrons are already damaged. The indices of kidney damages (creatinine, blood urea and uric acid) were restored to almost normal values by the supplementation with VE. These results like the results recorded out by Alahdal and Arafat, who reported the enhancer effect of VE (150,300 and 450 mg/kg) against toxicity induced by KBrO₃ (125 mg/kg) by reducing the levels of serum creatinine, blood urea and uric acid. These results confirm the efficacy of VE against the deterioration in renal function induced by KBrO₃ treatment. These effects can be attributed to the recorded potent antioxidant effect of VE.

Conclusion
Based on the results reported here, the treatment with KBrO₃ revealed deleterious effects on the body weight, hematological parameters, liver and kidney functions. However, the administration of vitamin E an hour before administration of KBrO₃ has the ability to restore the changes in these parameters induced by KBrO₃.

REFERENCES
1. M. L Urso and P. M Clarkin, "Oxidative stress, exercise, and antioxidant supplementation", Toxicology, 189(1-2), (2003) 41-54.
2. H. A. Uchida, H. Sugiyama, S. Kanehisa, K. Harada, K. Fujiwara, T. Ono, M. Yamakido and H. Makino, "An elderly patient with severe acute renal failure due to sodium bromate intoxication", Internal Medicine, 45(3), 151-154 (2006).
3. Y. Kurokawa, A. Maekawa, M. Takahashi and Y. Hayashi, "Toxicity and carcinogenicity of potassium bromate—a new renal carcinogen", Environmental Health Perspectives, 87, 309-335 (1990).
4. J. Ajarem, N. G. Altoom, A. A. Allam, S. N. Maodaa, M. A. Abdel-Maksoud and B. K. Chow, "Oral administration of potassium bromate induces neurobehavioral changes, alters cerebral neurotransmitters level and impairs brain tissue of swiss mice", Behavioral and Brain Functions, 12(1), 1-10 (2016).
5. M. K. Ahmad, A. A. Khan and R. Mahmood, "Taurine ameliorates potassium bromate-induced kidney damage in rats", Amino Acids, 45(5), 1109-1121 (2013).
6. I. A. Robert and B. C. William, "Carcinogenicity of potassium bromate in rabbit", Biology Education, 34, 114-120 (1996).
7. O. B. Oloyede and T. O. Sunmonu, "Potassium bromate content of selected bread samples in Ilorin, Central Nigeria and its effect on some enzymes of rat liver and kidney", Food and Chemical Toxicology, 47(8), 2067-2070 (2009).
8. K. Sai, S. Uchiyama, Y. Ohno, R. Hasegawa and Y. Kurokawa, "Generation of active oxygen species in vitro by the interaction of potassium bromate with rat kidney cell", Carcinogenesis, 13(3), 333-339 (1992).
9. J. L. Parsons and J. K. Chipman, "The role of glutathione in DNA damage by potassium bromate in vitro", Mutagenesis, 15(4), 311-316 (2000).
11. J. K. Chipman, J. L. Parsons and E. J. Beddowes, "The multiple influences of glutathione on bromate genotoxicity: implications for the dose–response relationship", *Toxicology*, 221(2-3), 187-189 (2006).

12. V. Lobo, A. Patil, A. Phatak and N. Chandra, "Free radicals, antioxidants and functional foods: Impact on human health", *Pharmacognosy Reviews*, 4(8), 118 (2010).

13. B. A. Alahmadi, S. H. El-Alfy, A. M. Hemaid and I. M. Abdel-Nabi, "The protective effects of vitamin E against selenium-induced oxidative damage and hepatotoxicity in rats", *Journal of Taibah University for Science*, 14(1), 709-720 (2020).

14. G. E. Paget and J. M. Barnes, "Toxicity tests", In D. R. Laurence, & A. L. Bachrach (Eds.), Evaluation of Drug Activities, *Pharmacometrics*, vol. 1, pp. 135–166 (1964). London: New York: Academic Press.

15. J. V. Dacie, and S. M. Lewis, "Practical hematology", 7th ed. London: Churchill, PP. 37-58 (1991).

16. L. C. Rodak, "Routine testing in haematology", In: *Diagnostic Haematology W B London, Toronto*. PP. 128-144 (1995).

17. J. King, "The transferases-alanine and aspartate transaminases", *Practical Clinical Enzymology*, (1965).

18. A. Englehardt, "Measurement of alkaline phosphatase", *Aerztl Labor*, 16, 42-51 (1970).

19. D. S. Young, "Effects of disease on Clinical Lab. Tests", 4th ed.AACC Press. 37 (2001).

20. H. Bartels and M. Bobmer, "*Clinica Chimica Acta*, 37, 193 (1972).

21. A. S. Glantz, "Primer of biostatistics", Mc Graw-Hill, Inc. U.S.A., PP.2-18 (1992).

22. H. Y. Kim, S. B. Lee, K. T. Lim, M. K. Kim and J. C. Kim, "Subchronic inhalation toxicity study of 1, 3-dichloro-2-propanol in rats", *Annals of Occupational Hygiene*, 51(7), 633-643 (2007).

23. A. A. Rezq, "Potential protective and ameliorate effects of sesame oil and jojoba oil against potassium bromate (Kbro3)-induced oxidative stress in rats", *Journal of Studies and Searches of Specific Education*, 3(1, Part 1), 155-189 (2019).

24. N. Yin, X. Yao, Q. Zhou, F. Faiola and G. Jiang, "Vitamin E attenuates silver nanoparticle-induced effects on body weight and neurotoxicity in rats", *Biochemical and Biophysical research communications*, 458(2), 405-410 (2015).

25. A. A. H. Hassan, "Effect of Potassium Bromate on the Liver of Wistar rats (Doctoral dissertation )", (unpublished thesis). *Graduate College Faculty of Medicine International University of Africa*, (2018).

26. J. Fisher and R. J. Bull, "Development of a rat dosimetry model for bromate", *Toxicology*, 221(2-3), 235-240 (2006).

27. G. R. Klinefelter, L. F. Strader, J. D. Suarez, N. L. Roberts, J. M. Goldman and A. S. Mur, "Continuous exposure to dibromoacetic acid delays pubertal development and compromises sperm quality in the rat", *Toxicological Sciences*, 81(2), 419-429 (2004).

28. A. Fathollahi, F. Daneshgari and A. T. Hanna-Mitchell, "Effect of polyuria on bladder function in diabetics versus non-diabetics" an article review, *Current Urology*, 8(3), 119-125 (2014).

29. S. Bharrhan, K. Chopra and P. Rishi, "Vitamin E supplementation modulates endotoxin-induced liver damage in a rat model", *American Journal of Biomedical Sciences*, 2(1), 51-62 (2010).

30. E. L. E. N. Abdullah and M. K. Turan, "Classifying white blood cells using machine learning algorithms", *International Journal of Engineering Research and Development*, 11(1), 141-152 (2019).

31. O. Abd Elhalim, "Biochemical Effect of Potassium Bromate on Wistar Albino Rats", MV Sc. Thesis, Faculty of Veterinary Medicine, University of Khartoum. p 1-38 (2006).

32. P. K. Maurya, P. Kumar and P. Chandra, "Biomarkers of oxidative stress in erythrocytes as a function of human age", *World Journal of Methodology*, 5(4), 216 (2015).

33. Y. Yawata, (2006), "Cell membrane: the red blood cell as a model", *John Wiley & Sons*.

34. M. K. Ahmad, S. Amani and R. Mahmood, "Potassium bromate causes cell
lysis and induces oxidative stress in human erythrocytes", *Environmental Toxicology*, 29(2), 138-145 (2014).
35. B. Beutler, "Autoimmunity and apoptosis: the Crohn's connection", *Immunity*, 15(1), 5-14 (2001).
36. J. M. Zingg, "Molecular and cellular activities of vitamin E analogues", *Mini Reviews in Medicinal Chemistry*, 7(5), 545-560 (2007).
37. J. Oliva, B. A. French, X. Qing and S. W. French, "The identification of stem cells in human liver diseases and hepatocellular carcinoma", *Experimental and Molecular Pathology*, 88(3), 331-340 (2010).
38. S. P. Govindwar and R. R. Dalvi, "Age-dependent toxicity of acorn extract in young and old male rats", *Veterinary and Human Toxicology*, 32(1), 23-26 (1990).
39. L. Pari and N. A. Kumar, "Hepatoprotective activity of Moringa oleifera on antitubercular drug-induced liver damage in rats", *Journal of Medicinal Food*, 5(3), 171-177 (2002).
40. L. Pari and P. Murugan, "Protective role of tetrahydrocurcumin against erythromycin estolate-induced hepatotoxicity", *Pharmacological Research*, 49(5), 481-486 (2004).
41. N. A. Bayomy, G. M. Soliman and E. Z. Abdelaziz, "Effect of potassium bromate on the liver of adult male albino rat and a possible protective role of vitamin C: histological, immunohistochemical, and biochemical study", *The Anatomical Record*, 299(9), 1256-1269 (2016).
42. O. O. Oyewo, F. M. Onyije and P. O. Awoniran, "Hepatotoxic effect of potassium bromate on the liver of wistar rats", *Journal of Morphological Sciences*, 30(2), 107-114 (2017).
43. S. H. Gou, H. F. Huang, X. Y. Chen, J. Liu, M. He, Y. Y. Ma, X. N. Zhao, Y. Zhang and J. M. Ni, "Lipid-lowering, hepatoprotective, and atheroprotective effects of the mixture Hong-Qu and gypenosides in hyperlipidemia with NAFLD rats", *Journal of the Chinese Medical Association*, 79(3), 111-121 (2016).
44. H. Ebaid, S. A. Bashandy, A. M. Abdel-Mageed, J. Al-Tamimi, I. Hassan and I. M. Alhazza, "Folic acid and melatonin mitigate diabetic nephropathy in rats via inhibition of oxidative stress", *Nutrition & Metabolism*, 17(1), 1-14 (2020).
45. I. Hassan, H. Ebaid, I. M. Alhazza and J. Al-Tamimi, "The alleviative effect of vitamin B2 on potassium bromate-induced hepatotoxicity in male rats", *BioMed. Research International*, (2020).
46. A. A. A. Khalaf, M. E. M. Mekawy, M. S. Moawad and A. M. Ahmed, "Comparative study on the protective effect of some antioxidants against CCl4 hepatotoxicity in rats", *Egyptian Journal of Natural Toxins*, 6(1), 59-82 (2009).
47. A. Gokçimen, A. Cim, H. T. Tola, D. Bayram, A. Kocak, F. Özgüner and A. Ayata, "Protective effect of N-acetylcysteine, caffecic acid and vitamin E on doxorubicin hepatotoxicity", *Human & Experimental Toxicology*, 26(6), 519-525 (2007).
48. S. Kalender, A. Ogutcu, M. Uzunhisarcıklı, F. Açıkgoz, D. Durak, Y. Ulusoy and Y. Kalender, "Diazinon-induced hepatotoxicity and protective effect of vitamin E on some biochemical indices and ultrastructural changes", *Toxicology*, 211(3), 197-206 (2005).
49. N. S. El-Shenawy, F. El-Salmy, R. A. Al-Eisa and B. El-Ahmary, "Amelioratory effect of vitamin E on organophosphorus insecticide diazinon-induced oxidative stress in mice liver", *Pesticide Biochemistry and Physiology*, 96(2), 101-107 (2010).
50. A. M. Al-Othman, K. S., Al-Numair, G. E. El-Desoky, K. Yusuf, Z. A. Al Othman, M. A. Aboul-Soud and J. P. Giesy, "Protection of tocopherol and selenium against acute effects of malathion on liver and kidney of rats", *African Journal of Pharmacy and Pharmacology*, 5(10), 1263-1271 (2011).
51. A. A Alwazzan, M. M. El Mahdy and S. S. Abdelgayed, "Dose and Time-Related Toxic and Carcinogenic Effects of Potassium Bromate on Kidneys in Albino Rats", *Journal of Veterinary Science* (Suwŏn-si, Korea) 8(4), 206-212 (2019).
52. I. M. Alhazza, I. Hassan, H. Ebaid, J. Al-Tamimi and S. H. Alwase, "Chemopreventive effect of riboflavin on the potassium bromate–induced renal toxicity in vivo", *Naunyn-Schmiedeberg's
53. R. A. Khan, M. R. Khan and S. Sahreen, "CCl 4-induced hepatotoxicity: protective effect of rutin on p53, CYP2E1 and the antioxidative status in rat", *BMC Complementary and Alternative Medicine*, 12(1), 1-6 (2012).

54. D. E. Dodd, D. K. Layko, K. E. Cantwell, G. A. Willson and R. S. Thomas, "Subchronic toxicity evaluation of potassium bromate in Fischer 344 rats", *Environmental Toxicology and Pharmacology*, 36(3), 1227-1234 (2013).

55. M. A. Spassova, D. J. Miller and A. S. Nikolov, "Kinetic modeling reveals the roles of reactive oxygen species scavenging and DNA repair processes in shaping the dose-response curve of KBrO3-induced DNA damage", *Oxidative Medicine and Cellular Longevity*. ID 764375, 12 pages (2015).

56. R. A. Khan, M. R. Khan and S. Sahreen, "Evaluation of Launaea procumbens use in renal disorders: A rat model", *Journal of Ethnopharmacology*, 128 (2), 452-461 (2010).

57. H. Bhattacharya and L. Lun, "Biochemical effects to toxicity of CCl 4 on rosy barbs (Puntius conchonius) ", *Our Nature*, 3(1), 20-25 (2005).

58. A. T. Alahdal and R. A. Arafat, "The Antioxidant effects of Wheat Germ Oil Against Potassium bromate Induced Hepatorenal toxicity in Male Rats", *Life Science Journal*, 14(9), 71-80 (2017).

59. S. K. Agarwal, "chronic kidney disease and its prevention in India", *Kidney International*, 68, S41-S45 (2005).
دراسة التأثير الوقائي لفيتامين (E) ضد سمية برومات البوتاسيوم على بعض وظائف الدم والكلى والكبد في ذكور الجرذان

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لقد أجريت الدراسة الحالية لدراسة التأثير الوقائي لفيتامين E على الاضطرابات المصاحبة لوظائف الدم والكبد والكلى في ذكور الجرذان المعالجة ببروتام البوتاسيوم. لقد تم تقسيم أربع وعشرون جرذًا إلى أربع مجموعات: المجموعة الأولى تمثل المجموعة الضابطة. المجموعة الثانية: تم معالجة الجرذان ب 5 ملم/جم من وزن الجسم من برومات البوتاسيوم عن طريق الفم. المجموعة الثالثة: تلقى الجرذان 30 ملم/جم من وزن الجسم من فيتامين E عن طريق الفم. المجموعة الرابعة: تلقى الجرذان 30 ملم/جم من وزن الجسم من فيتامين E عن طريق الفم قبل معالجتها ب 5 ملم/جم/جم من وزن الجسم من برومات البوتاسيوم عن طريق الفم. استمرت التجربة لمدة خمس أسابيع متتالية. ولقد أظهرت المعاملة ببروتام البوتاسيوم انخفاضًا ملحوظًا في متوسط وزن الجسم، كربات الدم الحمراء (RBCs)، الصفيحات الدمية (WBCs)، الهيموجLOBين (HB)، الفوسفاتاز القلوي (ALP)، إنزيم ناقل أمين الأمينات (AST)، ونسبة البوليكالكريتينين عند المقارنة بالمجموعة الضابطة. بينما أدى العلاج بكلا من برومات البوتاسيوم وفيتامين E إلى تحسن جميع فحوصات الدم والكبد والكلى التي تم قياسها. وبذلك أظهرت النتائج الحالية أن فيتامين E له القدرة على التقليل من خطورة برومات البوتاسيوم وذلك من خلال التأثير المضاد للأكسدة لفيتامين E.