



## 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<sub>3</sub>) 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<sub>3</sub> 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<sub>3</sub> (50 mg/kg b.wt.) orally. The experiment continued for five successive weeks. Results showed that the treatment with KBrO<sub>3</sub> 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<sub>3</sub> treated group comparing with control group. The treatment with VE+KBrO<sub>3</sub> ameliorated all the hematological, renal, and hepatic parameters tested. It is clear from the present results that VE reduced the severity of KBrO<sub>3</sub>. This could be mediated by its potent antioxidant effects.*

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

### INTRODUCTION

Potassium bromate (KBrO<sub>3</sub>) 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<sub>3</sub> is found in the samples of drinking water as a byproduct of ozone disinfection<sup>1</sup>. Several research had been executed in different parts of the world to prove that KBrO<sub>3</sub> is dangerous to health if consumed in water or food. It has been proven to be nephrotoxic in both experimental animals and man<sup>2</sup>. Furthermore, it induces renal cell tumors, follicular cell tumors of the thyroid, and mesotheliomas of the peritoneum<sup>3</sup>.

The nephrotoxicity caused by KBrO<sub>3</sub> 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<sub>3</sub> 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<sup>4</sup>.

International Agency for Research on Cancer (IARC) has labeled KBrO<sub>3</sub> as a possible human carcinogen (group 2B) and its using in food processing was confined. Indeed, many previous reports has documented that KBrO<sub>3</sub> can induce numerous organ toxicity in experimental animals and humans<sup>5</sup> and the kidney is the primary target organ of these dangerous compound<sup>6</sup>. KBrO<sub>3</sub> 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<sup>7</sup>. Therefore,

KBrO<sub>3</sub> has been banned in several countries including the United Kingdom in 1990, Nigeria in 1993 and Canada in 1994<sup>8</sup>. Toxicological studies have found out that KBrO<sub>3</sub> influences the nutritional quality of bread as the main vitamins present in bread are degraded<sup>9</sup>. It is known that KBrO<sub>3</sub> induces the oxidative stress of the tissues<sup>10</sup> that may be the basis of bromate-induced carcinogenesis<sup>11</sup>. 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<sup>12</sup>. 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<sup>13</sup>.

The present work attempts to study the effect of administration of KBrO<sub>3</sub> on hematological parameters, renal and hepatic functions of male rats and the attenuating effect of vitamin E on the deleterious consequences of KBrO<sub>3</sub>.

## MATERIALS AND METHODS

### Chemicals

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

Potassium Bromate (KBrO<sub>3</sub>) 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 KBrO<sub>3</sub> and VE for rats were calculated according to the method of Paget and Barnes<sup>14</sup>. The dose was estimated according to the factor's human-rat therapeutic

dose. The dose of KBrO<sub>3</sub> (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 KBrO<sub>3</sub> 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 (KBrO<sub>3</sub>) rats were received 50 mg/kg b.wt. of KBrO<sub>3</sub> 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+KBrO<sub>3</sub>) rats were received 30 mg/kg b.wt. of VE orally an hour before administration of KBrO<sub>3</sub> (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<sup>15</sup>. Measurement of hematocrit value (Hct) was determined according to the method of Rodak<sup>16</sup> 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<sup>17</sup>, the activity of alkaline phosphatase (ALP) was measured according to Englehardt<sup>18</sup>.

Urea and uric acid were estimated according to Young<sup>19</sup>. Creatinine was determined according to the method described by Bartels and Bohmer method<sup>20</sup>.

## Statistical analysis

Data were expressed as means  $\pm$  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 of Glantz<sup>21</sup> by post hoc test using 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, KBrO<sub>3</sub> (50 mg/kg b.wt.), vitamin E (30 mg/kg b.wt.) and vitamin E + KBrO<sub>3</sub> groups. The data in table (1) showed a non-significant change in the initial body weight between all groups.

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

Body weight	Control	KBrO <sub>3</sub>	% D	VE	% D	VE+KBrO <sub>3</sub>	% D	P-value
Initial weight (gram)	111.3 $\pm$ 3.2 <sup>a</sup>	112.8 <sup>a</sup> $\pm$ 2.70	1.35	106 $\pm$ 2.84 <sup>a</sup>	-4.8	115 $\pm$ 3.28 <sup>a</sup>	3.3	-
Final weight (gram)	177.3 $\pm$ 2.73 <sup>a</sup>	138.17 <sup>b</sup> $\pm$ 2.09	-22.06	170 $\pm$ 4.28 <sup>ac</sup>	-4.12	162.17 $\pm$ 2.59 <sup>c</sup>	-8.5	*

- Values represent the mean  $\pm$  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

Whereas the final body weight revealed a significant decrease in KBrO<sub>3</sub> 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+ KBrO<sub>3</sub>) 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 KBrO<sub>3</sub>, VE and the combination between VE and KBrO<sub>3</sub> 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, KBrO<sub>3</sub> treated rats, VE treated rats, and VE+ KBrO<sub>3</sub> 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 KBrO<sub>3</sub> 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 KBrO<sub>3</sub> restored RBCs and WBCs counts. Whereas the treatment with the VE+KBrO<sub>3</sub> failed to restore the decrease in PLTs, HB and HCT to control values, but it showed an increase comparing with the KBrO<sub>3</sub> group.

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

**Table 2:** The effects of KBrO<sub>3</sub>, VE and VE+ KBrO<sub>3</sub> on the hematological parameters.

Blood Parameters	Control	KBrO <sub>3</sub>	% D	VE	% D	VE+KBrO <sub>3</sub>	% D	p-value
RBCs (10 <sup>6</sup> xmm <sup>3</sup> )	5 ± 0.28 <sup>a</sup>	3.78 ± 0.21 <sup>b</sup>	-24.4	5.03 ± 0.38 <sup>a</sup>	0.6	4.55 ± 0.29 <sup>ab</sup>	-9	*
WBCs (10 <sup>3</sup> xmm <sup>3</sup> )	6.32 ± 0.44 <sup>a</sup>	4.87 ± 0.15 <sup>b</sup>	-22.9	6.17 ± 0.44 <sup>a</sup>	-2.37	5.25 ± 0.35 <sup>ab</sup>	-16.93	*
PLTs(10 <sup>9</sup> /L)	224 ± 7.6 <sup>a</sup>	166.83±5.52 <sup>b</sup>	-25.5	222 ± 9.06 <sup>a</sup>	-0.89	184.33±13.49 <sup>b</sup>	-17.7	*
HB (g/dl)	16.25 ± 0.44 <sup>a</sup>	9.7 ± 0.41 <sup>b</sup>	-40.3	15.5 ± 0.52 <sup>a</sup>	-4.6	12.78 ± 0.78 <sup>c</sup>	-21.4	*
HCT(%)	30.67 ± 0.67 <sup>a</sup>	26.83± 1.33 <sup>b</sup>	-12.52	31 ± 0.63 <sup>a</sup>	1.07	27.67 ± 0.76 <sup>b</sup>	-9.78	*
MCV (fI)	88.7 ± 1.69 <sup>a</sup>	89.37 ± 2.21 <sup>a</sup>	0.755	88.25± 2.24 <sup>a</sup>	-0.51	86.48 ± 2.38 <sup>a</sup>	-2.5	-
MCH (Pg)	29.35 ± 0.30 <sup>a</sup>	29.52 ± 0.31 <sup>a</sup>	0.58	29.68± 0.15 <sup>a</sup>	1.12	29.35 ± 0.30 <sup>a</sup>	0	-
MCHC (%)	31.57 ± 0.82 <sup>a</sup>	30 ± 0.55 <sup>a</sup>	-4.97	31.9 ± 0.8 <sup>a</sup>	1.05	31.15 ± 0.84 <sup>a</sup>	-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

### Liver enzymes

The toxicity that induced by KBrO<sub>3</sub> on the activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) enzymes, are shown in table (3). Also, the effects of VE and the combination between VE and KBrO<sub>3</sub> 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 KBrO<sub>3</sub> 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 + KBrO<sub>3</sub> 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+KBrO<sub>3</sub> comparing with KBrO<sub>3</sub> treated group, but it still higher than the control group.

### Kidney function

Table (4) illustrate the effects of KBrO<sub>3</sub> (50 mg/kg b.wt.), VE (30mg /kg b.wt.) and VE administration an hour before KBrO<sub>3</sub> 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 KBrO<sub>3</sub> 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+ KBrO<sub>3</sub> group but the creatinine and blood urea not similar to control values recording 36.36% and 26.19%, respectively.

**Table 3:** The effects of KBrO<sub>3</sub>, VE and VE+KBrO<sub>3</sub> on the activities of liver enzymes AST, ALT and ALP.

Liver Enzymes	Control	KBrO <sub>3</sub>	% D	VE	% D	VE+KBrO <sub>3</sub>	% D	P-value
AST (IU/L)	125.1 ± 7.2 <sup>a</sup>	504.68 ± 88.6 <sup>b</sup>	303.58	120.9 ± 79.1 <sup>a</sup>	-3.4	147.31 ± 6.13 <sup>a</sup>	17.80	*
ALT (IU/L)	138.2 ± 0.4 <sup>a</sup>	435.12 ± 76.379 <sup>b</sup>	214.83	127 ± 5.3 <sup>a</sup>	-8.1	158.97 ± 18.12 <sup>a</sup>	15.02	*
ALP (IU/L)	92.7 ± 3.3 <sup>a</sup>	195.3 ± 15.4 <sup>b</sup>	110.7	90.7 ± 3.1 <sup>a</sup>	-2.2	143.1 ± 13.2 <sup>c</sup>	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 KBrO<sub>3</sub>, VE and KBrO<sub>3</sub>+ VE on the serum creatinine, urea and uric acid levels.

Kidney parameters	Control	KBrO <sub>3</sub>	% D	VE	% D	VE+KBrO <sub>3</sub>	% D	p-values
Creatinine (mg/dl)	0.88 ± 0.054 <sup>a</sup>	1.54 ± 0.07 <sup>b</sup>	75	1.10 ± 0.29 <sup>ac</sup>	25	1.2 ± 0.037 <sup>c</sup>	36.36	*
Urea (mg/dl)	34.17 ± 1.65 <sup>a</sup>	51.78 ± 1.52 <sup>b</sup>	51.54	37.36 ± 1.56 <sup>a</sup>	9.34	43.12 ± 2.31 <sup>c</sup>	26.19	*
Uric acid (mg/dl)	1.9 ± 0.16 <sup>a</sup>	3.6 ± 0.4 <sup>b</sup>	89.5	2.2 ± 0.16 <sup>a</sup>	15.79	2.4 ± 0.34 <sup>a</sup>	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<sup>22</sup>. In the current study, the data revealed that the body weight decreased significantly in KBrO<sub>3</sub> treated group (50 mg/kg b.wt.), on the end of experimental period. This result was agreeing with the results that recorded by Rezaq<sup>23</sup>, who reported that the administration of KBrO<sub>3</sub> 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.*<sup>24</sup>. Vitamin E administration an hour before KBrO<sub>3</sub> treatment, caused a marked regain in body weight. These findings were in accordance with previous studies that carried by Hassan<sup>25</sup>, who stated that VE gain the body weight that reduced by KBrO<sub>3</sub> treatment. The reduction of the body weight in KBrO<sub>3</sub> treated group may be due to binding of KBrO<sub>3</sub> 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<sup>26</sup>. Similar studies also indicated that EDCs decrease the pubertal body weight<sup>27</sup>. Also, the decrease in the body weight that following KBrO<sub>3</sub> 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<sup>28</sup>. 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 KBrO<sub>3</sub> because of

its antioxidant properties that scavenge free radicals which resulting from KBrO<sub>3</sub> toxicity<sup>29</sup>.

The identification of blood disorders considered as an indicator of many pathological conditions<sup>30</sup>. In the present study, some hematological parameters were measured to throw the light on the effect of administration KBrO<sub>3</sub>, VE and the combination between them in rats. The results clearly demonstrated that KBrO<sub>3</sub> 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 doesn't have significant changes comparing with control values. The previous study carried out by Abd Elhalim<sup>31</sup>, revealed that the administration of 100, 200 mg/kg b.wt. KBrO<sub>3</sub> 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, KBrO<sub>3</sub> 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<sup>32</sup>. 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<sup>33</sup>. Ahmad *et al.*<sup>34</sup> hypothesized that

KBrO<sub>3</sub> 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<sup>35</sup>. 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 KBrO<sub>3</sub> 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+KBrO<sub>3</sub>), 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<sup>36</sup>. Counteracting the effects of KBrO<sub>3</sub> toxicity on the above parameters by VE could be attributed to inhibition of hemolysis of RBCs and/or toxic effects of KBrO<sub>3</sub> 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<sup>37</sup>. It is known that the activities of serum aminotransferases are considered as markers of toxicity in the liver induced by chemicals<sup>38</sup>. The most sensitive biomarkers used in the diagnosis of liver disorders are AST and ALT activities<sup>39</sup>, and their activities indicate the type and extent of damage inflicted that displays a state of hepatocyte injury<sup>40</sup>. It is clear from the present results that the rats consumed KBrO<sub>3</sub> 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.*<sup>41</sup>, who reported that KBrO<sub>3</sub> induced a significant rise in serum levels of AST and ALT in liver tissues. Also, it was reported previously that, KBrO<sub>3</sub> treatment in wister rats have hepatotoxic effects<sup>42</sup>. 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<sup>43</sup>. 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<sup>44</sup>. 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 KBrO<sub>3</sub> can induce hepatic impairment<sup>45</sup>. Herein, we found that VE treatment together with KBrO<sub>3</sub> alleviated the elevated activities of the markers of hepatocellular injury AST, ALT and ALP comparing with KBrO<sub>3</sub> treated rats. Various experimental research on the animal species showed that VE treatment ameliorated liver damage induced by carbon tetrachloride<sup>46</sup>, doxorubicin, anthracycline antibiotic<sup>47</sup>, and pesticides such as malathion<sup>48</sup>. Similar observation was reported in mice where VE ameliorated organophosphorus insecticide (diazinon) induced oxidative stress in mice liver<sup>49</sup>. The hepatoprotective effect of VE was also observed in melathion induced hepatotoxicity in rats. Al-Othman *et al.*<sup>50</sup>, 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 KBrO<sub>3</sub>. 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 KBrO<sub>3</sub>.

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 KBrO<sub>3</sub>. It is clear from the present results that there is an impairment in the kidney function of KBrO<sub>3</sub> treated rats. The levels of creatinine, blood urea and uric acid significantly increased in KBrO<sub>3</sub> treated group as compared with the control group. Conversely, VE+KBrO<sub>3</sub> group manifested a significant decline in the levels of these parameters comparing with the KBrO<sub>3</sub> 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  $\text{KBrO}_3$  in different animals and at various doses induced a renal failure indicated by elevation of serum creatinine, blood urea and uric acid levels<sup>51&52</sup>. Also, it was recorded a significant increasing in the sera levels of creatinine and urea at dose of 20 mg/kg of  $\text{KBrO}_3$ <sup>53</sup>. Conversely, a little or no evidence of renal impairments in rats have been found<sup>31&54</sup>. The major mechanism of  $\text{KBrO}_3$ - 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<sup>55</sup>. Accordingly, the impairment in the kidney function reported in the present study in response to  $\text{KBrO}_3$  administration could be mediated by oxidative stress induced by  $\text{KBrO}_3$ . Also, these changes can be attributed to the damage of nephrons structural integrity<sup>56</sup>, 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<sup>57</sup>. 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<sup>58</sup>, who reported the enhancer effect of VE (150,300 and 450 mg/kg) against toxicity induced by  $\text{KBrO}_3$  (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  $\text{KBrO}_3$  treatment. These effects can be attributed to the recorded potent antioxidant effect of VE<sup>59</sup>.

### Conclusion

Based on the results reported here, the treatment with  $\text{KBrO}_3$  revealed deleterious effects on the body weight, hematological parameters, liver and kidney functions. However, the administration of vitamin E an hour before administration of  $\text{KBrO}_3$  has the ability to restore the changes in these parameters induced by  $\text{KBrO}_3$ .

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## نشرة العلوم الصيدلانية جامعة أسيوط



### دراسة التأثير الوقائي لفيتامين (هـ) ضد سمية برومات البوتاسيوم علي بعض وظائف الدم والكلي والكبد في ذكور الجرذان

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لقد أجريت الدراسة الحالية لدراسة التأثير الوقائي لفيتامين هـ على الاضطرابات المصاحبة لوظائف الدم والكبد والكلي في ذكور الجرذان المعالجة ببرومات البوتاسيوم. لقد تم تقسيم أربع وعشرون جرذا الي أربع مجموعات: المجموعة الأولى تمثل المجموعة الضابطة. المجموعة الثانية: تم معالجة الجرذان بـ ٥٠ ملجم/ كجم من وزن الجسم من برومات البوتاسيوم عن طريق الفم. المجموعة الثالثة: تلقت الجرذان ٣٠ ملجم/ كجم من وزن الجسم من فيتامين هـ عن طريق الفم. المجموعة الرابعة: تلقت الجرذان ٣٠ ملجم/ كجم من وزن الجسم من فيتامين هـ عن طريق الفم قبل معالجتها بـ ٥٠ ملجم/ كجم من وزن الجسم من برومات البوتاسيوم بساعة عن طريق الفم. استمرت التجربة لمدة خمس أسابيع متتالية. ولقد أظهرت المعاملة ببرومات البوتاسيوم انخفاضا معنويا في متوسط وزن الجسم، كريات الدم الحمراء (RBCs)، خلايا الدم البيضاء (WBCs)، الصفائح الدموية (PLTs)، الهيموجلوبين (HB)، الهيماتوكريت (HCT) وزيادة نشاط انزيم ناقلة أمين أسبارتات (AST)، انزيم ناقلة أمين الألانين (ALT)، انزيم الفوسفاتاز القلوي (ALP) ومستوي اليوريا وحمض البوليك والكرياتينين عند المقارنة بالمجموعة الضابطة. بينما أدى العلاج بكلا من برومات البوتاسيوم وفيتامين هـ الي تحسن جميع فحوصات الدم والكبد والكلي التي تم قياسها. وبذلك أظهرت النتائج الحالية أن فيتامين هـ له القدرة علي التقليل من خطورة برومات البوتاسيوم وذلك من خلال التأثير المضاد للأكسدة ل فيتامين هـ.