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Original article

Study of Histological Changes in the Liver and Kidneys of Albino Mice Caused by Administration of Potassium Bromate

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ABSTRACT

Aims*. This study aims to elucidate the effect of potassium bromate (KBrO3) on vital tissues of the liver and the kidney by investigating the histopathological changes induced by their administration in experimental animals.* ***Methods****. White Swiss Albino mice were divided into two groups: group 1 served as a control; group 2 received KBrO3 for 42 days. Mice were euthanized, and samples of the liver and kidney were subjected to histopathologic analysis. Histopathologic changes in these tissues were assessed and compared to control cases under the light microscope.* ***Results****. Significant pathologic changes were observed specifically in samples from KBrO3-exposed mice. Mice treated with KBrO3 had pathologic changes present in the form of congestion and hemorrhage in both liver and kidney tissues. Necrotic changes and cirrhosis appeared in hepatocytes. Renal capsules appeared swollen, leaving little area remaining for the capsular space.* ***Conclusion****. The results demonstrated that KBrO3 produces adverse pathological effects on both liver and kidney tissues. Hence, it should be strictly prohibited in human consumption.*

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INTRODUCTION

Potassium bromate ($KBrO_3$) is a colorless, odorless, tasteless white crystal, granule, or powder [1]. frequently used as an oxidizing agent in the cosmetics and food industries, but with no medicinal value [2]. $KBrO_3$ first came into use as an oxidizing agent [3], and then later as a food enhancer and in the treatment of flour in the context of baking [4].
$KBrO_3$ decomposes at 370ºC and emits oxygen and toxic fumes [5]. The administration of $KBrO_3$ to rats causes increased hydrogen peroxide levels and decreased glutathione (GSH) content, indicating oxidative stress in the blood. $KBrO_3$ is also responsible for increasing lipid peroxidation and protein oxidation. Bromates also dramatically reduce the total antioxidant power in the blood and decrease vitamin C concentration [6]. Bromates administered in drinking water are tumorigenic and nephrotoxic in rats and mice [7], and are associated with multiple organ toxicity in experimental animals and humans [8-9].
In humans, the lethal dose of bromates has been estimated at 5-500 mg/kg of body weight, which can kill an adult human within 3-5 days after ingestion [10]. In cases of acute poisoning, bromates cause intense gastric mucosa irritation and abdominal symptoms, including pain, vomiting, and diarrhea. Sub-severe manifestations have included oliguria, anuria, deafness, thrombocytopenia, hypotension, vertigo, and depression of the central nervous system. In children and adults, acute bromate toxicity causes renal failure and hemolytic uremia [11]. When ingested, $KBrO_3$ is rapidly absorbed, reduced to bromide in the tissues, and then partly excreted in the urine as a bromide ion. Since the kidneys are the

primary target organ of $KBrO_3$, the toxic effects of this compound in cases of acute poisoning in humans arise from renal failure [12].

Lichtenberg and colleagues have reported that $KBrO_3$ is excreted by the kidneys [13], while another group has demonstrated that $KBrO_3$ is reduced to bromide in the gastrointestinal tract by the effect of sulfhydryl containing cysteine and glutathione compounds [14]. A recent study by Salami et al. (2020) has reported that $KBrO_3$ induces gastric ulcers in experimental animals [15]. Ahmad et al. (2016) reported adverse effects on the intestine caused by potassium bromates [16].

Despite its known benefits in the food industry as a maturing agent and flour improver, at least one study (Alli *et al.*, 2013) has reported that potassium bromates affect bread's nutritional qualities by lowering the main vitamins in the bread, such as A1, B1, B2, E, and niacin[17]. This report has also found that human consumption of potassium bromates can result in gastrointestinal distress, diarrhea, nausea, vomiting, kidney failure, hearing loss, and ophthalmic and bronchial issues [17]. At the cellular level, $KBrO_3$ induces chromatin and nuclear condensation of rat kidney cells, leading to cell damage and necrosis. $KBrO_3$ also reportedly can induce severe neurological disorders [14].

This growing body of evidence has motivated some countries to revoke the approval of potassium bromate for use as a bread conditioner, however, its use continues in other parts of the world. In Libya, $KBrO_3$ has been banned by the General People's Committee for Economy and Trade since 2005, yet it continues to be mixed with food and flour its products are still being consumed.

In August 2022, the Ministry of Higher Education reported that potassium bromates rose by 1300 times in products from local bakeries. National and international laboratories have confirmed these estimates. Unfortunately, the national authorities have not yet taken action in response to these findings to reduce the dangers posed by potassium bromate in human food. This project aims to study whether the oral administration of potassium bromates has adverse pathologic effects on experimental animals and applying these findings to human health.

METHODS

Experimental animals

Five adult male albino mice (*Mus musculus*) with an average weight of 27 ± 4.24 g were obtained from the animal house at the College of Veterinary Medicine, Omar Al-Mukhtar University, and maintained and monitored in a specific pathogen-free environment.

Potassium bromates preparation and dosing schedule

Potassium bromate salt, a product of British Drug Home Limited, England, was obtained in its white crystalline form from the Al-Qemma laboratory. It was then dissolved in water to prepare the 200 mg/kg dose.

Administration of the drug

Animals were divided into two groups as follows: Group (I) was the control group (administered distilled water); Group (II) was the experimental group (administered 200 mg/kg $KBrO_3$). $KBrO_3$ was orally administered in a daily dose of 1 ml/mouse through oral intubation for 42 days. Daily water consumption was monitored, and animals were weighed before the administration and in subsequent weeks during the experiment. At the end of the administration, mice were euthanized with chloroform and sacrificed by cervical dislocation.

Histological examination

For the histological preparation, tissue samples from the kidney and liver from both control and treated mice were collected for histopathologic analysis. Samples were fixed in a 10% formalin solution and embedded in paraffin. The paravermis was then sectioned in the sagittal plane (5 µm thick) and stained with hematoxylin-eosin [18].

Ethical approval

This study was performed under the regulations of The National Committee for Biosafety and Bioethics. Ethical approval was obtained under Ref. No: NBC:000.A.22.1

RESULTS AND DISCUSSION

The results supported previous study on the adverse effects of administration of potassium bromates on experimental animals [4]. Administration of potassium bromate with drinking water exerts an adverse effect on mice; 3 mice died during the period of administration of potassium bromate. Postmortem examination showed severe gastric and intestinal bleeding, which might be related to the ability of potassium bromate to induce gastric ulcer and ulcerative colitis. We

observed signs of hyperactivity and movement disturbance, which might be described as neurological signs caused by the action of bromates.

Histopathologic findings within kidney and liver samples confirmed that administering $KBrO_3$ with drinking water results in adverse pathologic changes in these sites. Treated mice suffered from renal and liver failure compared with the control samples. Remarkable changes in the morphological structure of the liver and kidney cells are apparent in the complete picture of inflammation and hemorrhage.

The examined sections from the liver show that $KBrO_3$ induced severe damage to the hepatic tissue pattern. Narrow blood sinusoids with vacuolated hepatocytes were among the remarkable observations. The liver tissues were infiltrated with inflammatory cells, especially around the central vein, which was dilated. Histopathologic examination of the liver samples shows changes in the shape of the liver and severe deformity leading to cirrhosis in cells, bleeding in the central vein (Figure 1). As a result of $KBrO_3$ administration, hepatic tissue sections of $KBrO_3$-treated mice show congestion of the central vein with a relative increase in Kupffer cells (KCs), as an inflammatory indicator, in comparison to the control group.

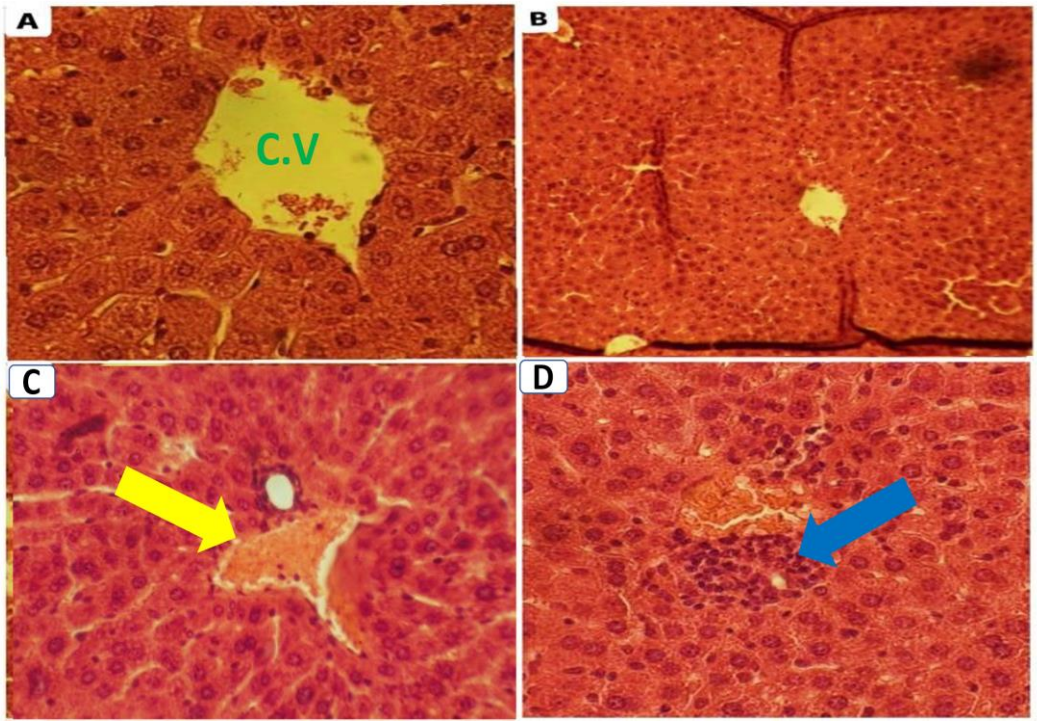

Figure 1. Effect of KBrO3 on the histology of the liver. (A, B) control group sections showing normal central vein (C.V) and intact lobular architecture. (C) KBrO3-treated sectionsa congested central vein (Yellow arrow). (D)Features of inflammation presented in inflammatory cells (blue arrow).

Histopathologic examination of the kidney shows congestion, tubular necrosis, and hemorrhage. Figure 2 shows glomerular injuries, kidney lumen dilation with intensive hemorrhage, and congestion in the capillaries. Narrowing in the capsular spaces is due to edematous degeneration. The glomeruli are disturbed by cellular distortion and some blood vessels in their collecting duct wall. Some glomeruli still appear shrunken, while some detectable hemorrhage is also observed. Severe bleeding and congestion can be observed in tissues with infiltration of immune cells

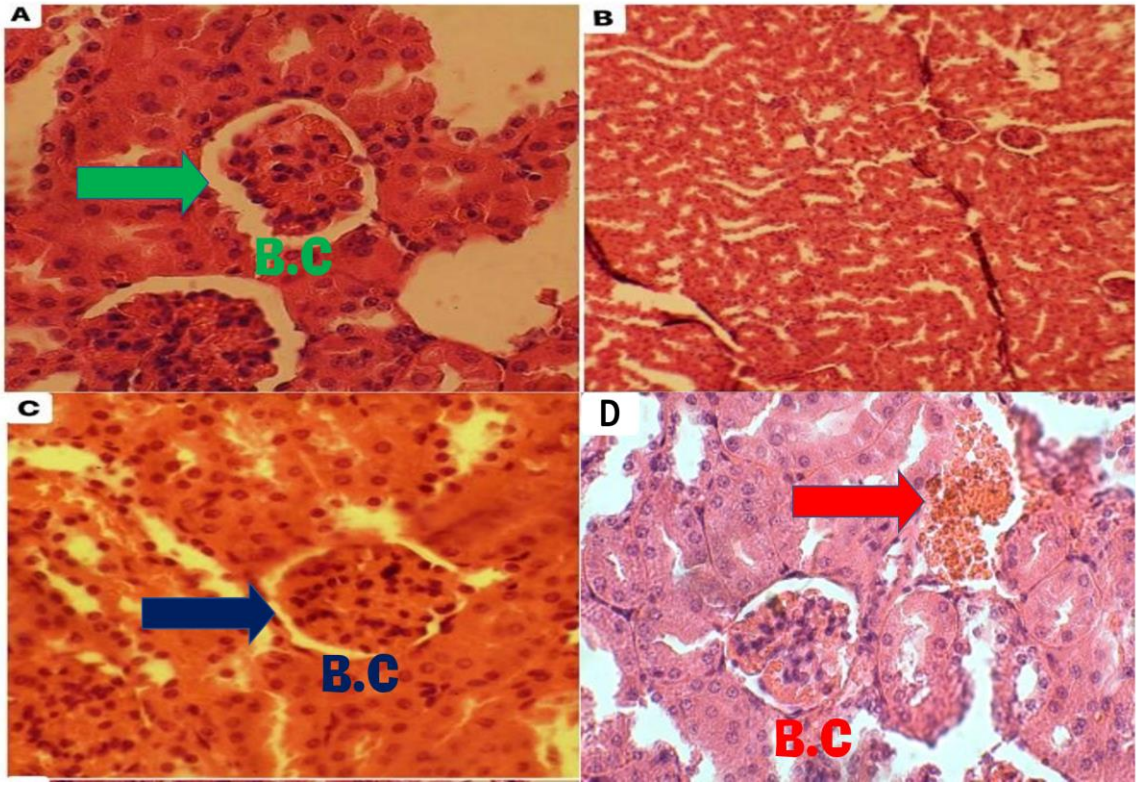

Figure 2. Histopathologic effects of KBrO3 on the kidney. (A, B) The control group sections show normal kidney tubules and normal Bowman's capsules (B.C) (Green arrow). (C) Kidney section treated with KBrO3 shows dilation and swelling in Bowman's capsule (blue arrow). (D)- Kidney hyperactivity, swelling in Bowman's capsule and hemorrhage indicated by the red arrow.

CONCLUSION

The results show that oral administration of potassium bromate significantly affects both liver and kidney tissues. Histopathologic changes included inflammatory figures, with aggregation of inflammatory cells such as neutrophils and monocytes. Some mice experienced hyperactivity after 15 days of oral administration of potassium bromate. Three mice died from digestive symptoms and intestinal hemorrhage caused by potassium bromate. This paper presents histological findings underlying the toxicity of KBrO3 introduced with drinking water to experimental mice.

Recommendations

Food additives and flavor enhancers should be subjected to closer evaluation, so that regulations of the national health authorities and food science agencies can take into account all of the possible health effects of adding any substance to human food.

$KBrO_3$ treatment of Swiss albino mice at 200 mg/kg body weight has several adverse consequences, including disturbance of renal and hepatic histopathology and decreasing antioxidant capacity. Due to these dangerous effects and the increasing prevalence of its use in the food industry, $KBrO_3$ use in human beings should be stopped. This study clearly shows that consuming potassium bromates has the potential to harm both liver and kidney tissues. Food additives and flavor enhancers should be subjected to strict monitoring by national health authorities and food science agencies to investigate all possible health adverse effects.

Disclosure statement

The authors declare no conflicts of interest. This manuscript has not been published or submitted elsewhere. This work complies with the Ethical Policies of the Journal and has been conducted under internationally accepted ethical standards following relevant ethical review.

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