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Serrobiochemical Effects of Potassium Bromate on Wistar Albino Rats

[1]Afaf I. Abuelgasim, [2]Rehab Omer and [1]B. ELmahdi
[1]Faculty of Veterinary Medicine,
University of Khartoum, Shambat, Sudan
[2]Faculty of Medicine, University of Dongola, Sudan

Abstract: The present study aimed to clarify the toxic effect of potassium bromate in Wistar albino rats. Thirty rats were divided into 5 groups. The first group severed as control and the other four groups received potassium bromate orally at doses 50, 100, 200 and 400 mg kg^{-1} body weight (b.wt.) for 21 days. Rats received 400 mg kg^{-1} b.wt. died within 3 days and those received 200 mg kg^{-1} b.wt. died on the 18th day post treatment. The body weights of rats treated with potassium bromate were not affected but the relative weights of the kidney and liver were significantly increased ($p<0.05$) in the group of rats received 100 mg kg^{-1} b.wt. potassium bromate compared to the control group. Clinically difficulty in breathing and depression occurred in those rats received 100 and 200 mg kg^{-1} b.wt. of potassium bromate. A significant ($p<0.05$) increase of urea, creatinine and potassium beside a decrease in Na level was evident in the groups received 100 and 200 mg kg^{-1} b.wt. of potassium bromate. Histopathological examination of the groups of rats received 100, 200 and 400 mg kg^{-1} b.wt. showed generalized congestion, haemorrhage and degenerative changes in the kidney and liver. Also increased intestinal goblet cells, stomach epithelium desquamation, pneumonia, haemorrhage, neuronal degeneration and vaculation of the brain were evident. The group of rats received 50 mg kg^{-1} b.wt. of potassium bromate was not affected compared to the control.

Key words: Potassium bromate, nephrotoxicity, nervous degeneration

INTRODUCTION

Food additives play a vital role in today's bountiful and nutritive food supply and are carefully regulated by various international organizations to ensure that additives introduced into food intended for human consumption are safe.

Potassium bromate has been used as food additive and was listed as flour treatment agent by FAO/WHO (1964). Later ondeleterious effects have been realized and was claimed to be carcinogenic. (Chipman *et al*., 1998).

Potassium bromate is rapidly absorbed from gastrointestinal tract and can be detected in the plasma within 15 min. It is very stable in the body and small amount was reduced to bromide by glutathione process in the liver and kidney (Kutom *et al*., 1990). It is excreted in urine either as bromate or bromide (Fujie *et al*. 1982).

Mark (1988) stated that 185-385 mg kg^{-1} b.wt. potassium bromate resulted in irreversible toxic effect mainly renal failure and deafness in human beside diarrhea, vomiting and abdominal pain. Exposure of mice to 1.2 mmol kg^{-1} b.wt. of potassium bromate for three hours resulted in elevation of serum uric acid, creatinine and xanthine oxidase activity (Watanabe *et al*., 2004).

Corresponding Author: Afaf I. Abuelgasim, Department of Pathology, Faculty of Veterinary of Medicine, University of Khartoum, Shambat, Sudan

Several safety evaluations for potassium bromate have been done and they were controversial. The present study was aimed to evaluate the toxic effects of potassium bromate in Wistar albino rats.

MATERIALS AND METHODS

Animals

Thirty apparently healthy Wistar albino rats of both sex weighing 60-70 g were used. They were housed in the premises of the Faculty of Veterinary Medicine, University of Khartoum under standard conditions and have free access to water and diet. They were acclimatized for a week. The experiment was conducted in 2005.

Experimental Design

The animals were divided randomly into five groups, 6 in each with similar mean body weights. Group A was left as a control received distilled water while the other groups (B, C, D, E) were orally administered with potassium bromate (Potassium bromate powder was obtained from Sudanese Consumer Protection Association at Khartoum, Sudan) using nasogastric tube daily at a concentration of 50, 100, 200 and 400 mg kg^{-1} b.wt. for 21 days, respectively.

Clinical signs and mortality were recorded. All animals were weighed weekly. Blood samples were collected by puncturing retro orbital plexus into clean dry tube and allowed to clot, then centrifuged at 3000 rpm for 5 min. Sera were separated and stored at -20°C until analyzed. Urea and creatinine were determined according to Monica (1992). The serum level of sodium and potassium were measured according to Varley (1980).

At the end of the experiment all animals were slaughtered. Livers and kidneys were weighed. The relative organ weights were calculated. Slices from kidneys, heart, lung, spleen, stomach intestine and brain were fixed in 10% neutral formalin embedded in paraffin wax, sectioned at 5 μm and stained by hematoxylin and eosin (Drury and Wallington, 1980).

Data were analyzed statistically by student t-test (Mendenhall, 1971).

RESULTS

The control rats as well as those received 50 mg kg^{-1} b.wt. potassium bromate showed no clinical signs. However, depression and difficulty in breathing were observed in rats which received 100 and 200 mg kg^{-1} b.wt. potassium bromate. Rats received 400 mg kg^{-1} b.wt. potassium bromate died within three days without obvious signs. All rats received 200 mg kg^{-1} b.wt. potassium bromate died within eighteen days. There were no significant differences in the body weights between rats treated with potassium bromate and the control (Table 1). However, the rate of increase in body weight at the end of the experiment was slow as 15% in rats received 100 mg kg^{-1} b.wt. compared to the controls (24.5%) and those received 50 mg kg^{-1} b.wt. was (23.9%). There was an increase in the relative weights of the livers and kidneys in rats received 100 mg kg^{-1} b.wt. compared to the control rats (Table 1). The relative weight of liver and kidney in the rats treated with 50 mg kg^{-1} b.wt. were not affected compared to the control.

The effects of various doses of potassium bromate on serum constituents were showed in (Table 2). The urea and creatinine levels were significantly elevated after treatment with 100 and 200 mg kg^{-1} b.wt. of potassium bromate as compared with the control group. Meanwhile the significant reduction in sodium levels were observed in groups treated with 100 and 200 mg kg^{-1} b.wt. of potassium bromate. However, the potassium level was increased after the second week at the dose 100 and 200 mg kg^{-1} b.wt. A dose of 50 mg kg^{-1} b.wt. of potassium bromate resulted in no significant differences in the concentration of urea, creatinine, Na and K compared to the control group.

Table 1: The body weight (g) and relative organ weights (%) of rats orally treated by potassium bromate

Doses	Body weights (g)			Relative organ weights (%)	
(mg kg^{-1} b.wt.)	Week 1	Week 2	Week 3	Liver	Kidney
0	69.5±7.2	79.0±8.3	86.5±9.4	3.0±0.09	0.72±0.08
50	67.0±3.1^{NS}	76.0±6.1^{NS}	83.0±6.1^{NS}	3.3±0.05^{NS}	0.82±0.07^{NS}
100	68.8±3.1^{NS}	77.3±4.6^{NS}	79.1±5.6^{NS}	3.8±0.04*	0.99±0.02*

Values are expressed mean±S D, NS : Not Significant, *p<0.05

Table 2: The mean changes in serum constituents of rats orally treated with various levels of potassium bromate

Duration (weeks)	Doses (mg kg^{-1} b.wt.)	Urea (mg dL^{-1})	Creatinine (mg dL^{-1})	Sodium (meq L^{-1})	Potassium (meq L^{-1})
1	50	28.6±4.2^{NS}	1.2±0.50^{NS}	134.8±2.9^{NS}	3.6±0.12^{NS}
	100	33.4±2.8*	2.4±0.48*	130.0±4.6^{NS}	3.9±0.50^{NS}
	200	41.7±5.0*	3.0±0.82*	123.0±3.5*	5.2±0.40*
2	50	34.0±4.7^{NS}	1.4±0.25^{NS}	136.0±7.5^{NS}	3.9±0.50^{NS}
	100	49.0±1.0*	2.8±0.96*	127.2±5.2*	4.4±0.30*
	200	57.0±2.9*	4.8±0.40*	117.3±4.3*	6.3±0.35*
3	50	39.3±4.5^{NS}	1.8±0.27^{NS}	139.0±2.5^{NS}	3.8±0.50^{NS}
	100	50.0±5.0*	3.8±0.63*	123.8±3.3*	5.7±0.50*

Values are expressed mean±S D; NS : Not Significant; *p<0.05

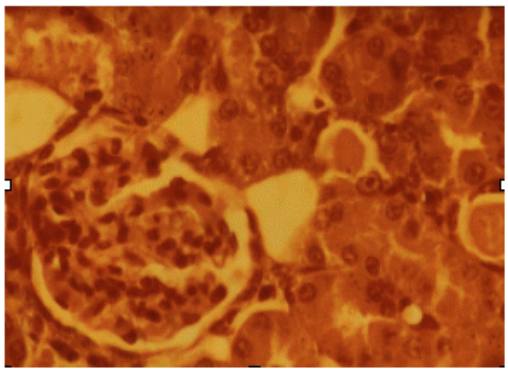

Fig. 1: Kidney of rat treated with 400 mg kg^{-1} potassium bromate. Note the homogenous material in the tubules. H and E x200

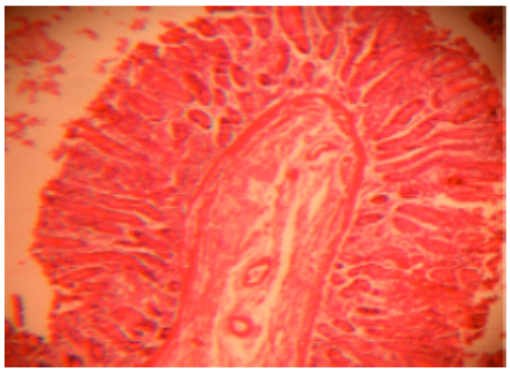

Fig. 2: Intestine of rat treated with 400 mg kg^{-1} potassium bromate. Note the haemorrhage and epithelial degeneration. H and E x100

Histopathological findings revealed congestion, haemorrhage and proteinaceous material in the tubules of the kidney of rats treated with 400 mg kg^{-1} b.wt. of potassium bromate (Fig. 1) beside haemorrhage and epithelial degeneration of the intestinal mucosa (Fig. 2). At the dose 100 and 200 mg kg^{-1} b.wt. similar lesions were seen including tubular epithelial degeneration and proteinaceous

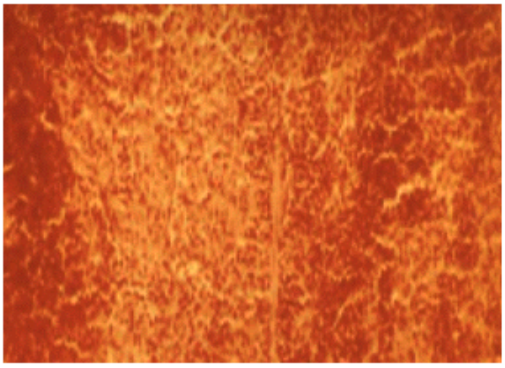

Fig. 3: Spleen of rat treated with 200 mg kg^{-1} potassium bromate. Note depletion of lymphocytes. H and E x100

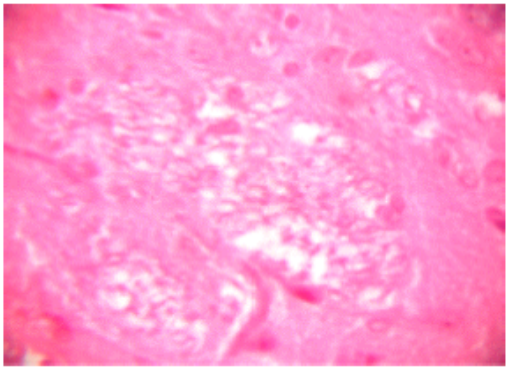

Fig. 4: Brain of rat treated with 200 mg kg^{-1} potassium bromate. Note vacuolation. H and E x100

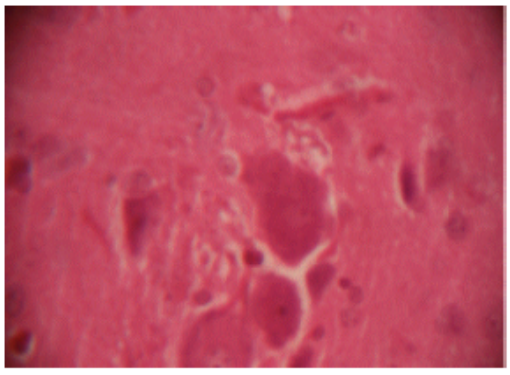

Fig. 5: Brain of rat treated with 100 mg kg^{-1} potassium bromate. Note neuronal degeneration. H and E x200

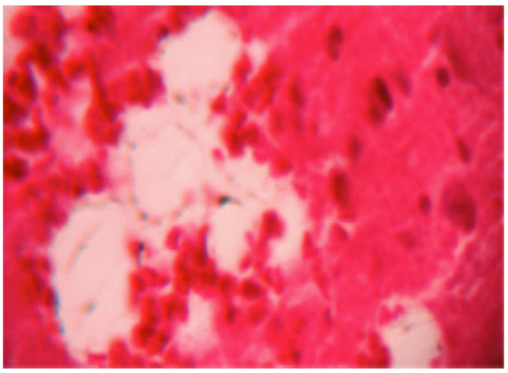

Fig. 6: Brain of rat treated with 200 mg kg^{-1} potassium bromate. Note haemorrhage. H and E x200

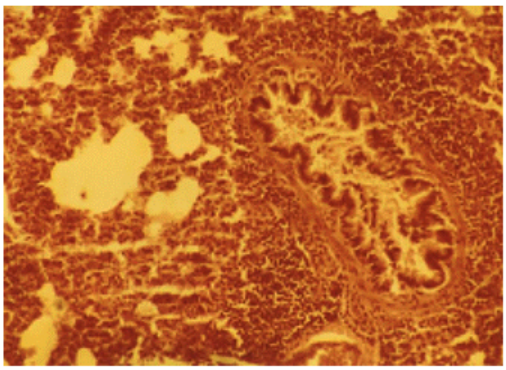

Fig. 7: Lung of rat treated with 100 mg kg^{-1} potassium bromate. Note Pneumonia cellular infiltration. H and E x200

material in the lumen of the tubules. Also there was an increase in goblet cells in the intestine, sloughing and necrosis of stomach epithelium. Heart muscles were degenerated with areas of haemorrhage. Lymphocytic depletion in the spleen was observed (Fig. 3). In the brain there were vacuolation (Fig. 4), neuronal degeneration (Fig. 5) and haemorrahage (Fig. 6). Pneumonia was also seen in the lungs of rats in these groups (Fig. 7). There were no pathological changes seen in the group of rats treated with 50 mg kg^{-1} b.wt.

DISCUSSION

The present study has shown that rapid death occurred within three and eighteen days when potassium bromate was administered to rats orally at a dose of 400 and 200 mg kg^{-1} b.wt., respectively. This probably due to renal damage as reflected by high level of urea and creatinine. This finding is similar to that reported by Kurokawa *et al*. (1990) who pointed out that lethal dose of potassium bromate in rats range between 280-495 mg kg^{-1} b.wt. However, rats dosed with 100 and 200 mg kg^{-1} b.wt. of potassium bromate exhibited signs of poisoning by difficulty in breathing and depression. This may be correlated with pneumonia and generalized congestion occurred as well as its direct effect on lesions in the brain.

Mark (1988) reported signs of renal failure and deafness in human at an oral dose of 185-385 mg kg^{-1} b.wt. orally of potassium bromate beside gastrointestinal disturbances.

Although there was no significant effect on the body weights in rats received potassium bromate compared to the controls, the rate of body weight gain was low in the group received more than 50 mg kg^{-1} b.wt. potassium bromate. Kurokawa *et al*. (1990) reported that rats exposed to 300 mg kg^{-1} b.wt. of potassium bromate in water for 15 month caused marked inhibition in body weight gain. Farombi *et al.* (2002) and Watanabe *et al.* (2004) reported absence of potassium bromate effect on the body weight; this is in agreement with the findings. In contrast, Okalie and Ikewuchi (2004) reported a significant reduction in bodyweight of rabbits received potassium bromate.

Farombi *et al*. (2002) reported significant increase in relative kidney weight while body weight and relative liver weight were not affected. In present finding the relative kidney and liver weights were increased in rats received 100 mg kg^{-1} b.wt. of potassium bromate. Similar result was obtained by Watanabe *et al*. (2004).

The increase in serum levels of urea and creatinine in this study are indication of renal toxicity. This was illustrated by pathological changes occurred in the kidney. This is in agreement with previous study by Khan *et al.* (2003) who stated that 125 mg kg^{-1} b.wt. of potassium bromate given intraperitoneally to rats resulted in marked elevation of BUN and ceatinine. Similar findings were also reported by Watanabe *et al*. (2004).

Sodium and potassium serum levels are regulated by the kidney. The reduction in serum level of sodium and together with elevation of serum potassium reflects the toxic effect of potassium bromate on the kidney tubules which change the permeability of tubular cell membrane. Okalie and Ikewuchi (2004) found a significant reduction in activities of Na-K ATPase which regulate the Na-K pump. These authors stated that the reactive oxygen species generated from potassium bromate might be a principle agent for that provoked oxidative stress. Chipman *et al.* (1998) and Watanabe *et al*. (2001) reported that potassium bromate produced a serious oxidative modification to protein, lipid and DNA.

El-Sokkary (2000) reported that potassium bromate caused degeneration and necrotic changes in the tubular epithelium of the kidney and presence of hyaline droplets. In the present finding similar lesions in the kidneys were observed. Umemura *et al.* (1993) reported cell proliferation in the proximal tubules while DeAgelo *et al*. (1998) stated that potassium bromate is carcinogenic to kidney. Such changes were not evident in the present study which may be due to duration of the experiment.

The histological changes occurred in stomach and intestine may be due to the irritation caused by contact of potassium bromate with the mucosal surface. The generalized haemorrhage and congestion may be due to the endotheliotoxic effect of potassium bromate.

The pathological changes observed in the heart in the present study were similar to those described by Paul (1966). In this study there was evident that potassium bromate had an effect on the brain. The lesions in the brain indicate that potassium bromate may cross the brain barrier and exert its effects on the endothelium permeability as well as brain tissues. This may lead to the believe that it has a neurotoxic effect. Contrary to present findings Crofton (2006) claimed that there were no nervous system malformation caused by potassium bromate.

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