Original article

Hepatotoxic effect of potassium bromate on the liver of wistar rats

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Abstract

Introduction: Potassium bromate ($KBrO_3$) is an oxidizing agent that has been used as a food additive mainly in the bread-making process as well as a dough conditioner for flour. It is generated as a contaminant in drinking water due to conversion of bromide found naturally in water to bromate by ozone which is used as disinfectant. **Materials and Methods**: Thirty animals were randomly divided into six groups, five rats each. The treated groups received potassium bromate in drinking water for 21 days. *Control group* received distilled water and feed, *group one,* received 140 mg/L of $KBrO_3$ in drinking water for 3 week, *group two:* This group contained 10 rats which were divided into two group containing 5 rats each i.e. group A & B. The rats in Group 2A and 2B received 170 mg/L of $KBrO_3$ in drinking water, thereafter, $KBrO_3$ was withdrawn from the animals in group 2B for another 2 weeks, *group three* received 200 mg/L of $KBrO_3$ in drinking water for 3 weeks, *group four:* This group contained 5 rats which received $KBrO_3$ at dose level of 200mg/L in drinking water with co – administration of vitamin E through oral route for 3 weeks. **Results:** The histology results revealed distortion in tissue architecture, congestion of the central vein and sinusoidal dilatation as well as cell necrosis in all the treatment. **Conclusion**: The use of $KBrO_3$ in edibles may not be advisable as it is not liver friendly.

Keyword: histology, sinusoidal, necrosis, potassium bromate.

1 Introduction

Potassium bromate ($KBrO_3$) is an oxidizing agent that has been used as a food additive mainly in the bread-making process (KUROKAWA, MAEKAWA, TAKAHASHI et al., 1990) and primarily as a dough conditioner for flour (DIACHENKO and WARNER 2002). 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 (ABUELGASIM, OMER and ELMAHDI, 2008).

Potassium bromate is generated as a contaminant in drinking water due to conversion of bromide found naturally in water to bromate by ozone which is used as disinfectant (UENO, OISHI, SAYATO et al., 2000). Studies have shown that potassium bromate has harmful effects on the nutritional qualities of bread by lowering vitamins A1, B1, B2, E and niacin, the main vitamins in bread (LABA, 2003). Studies have also shown that it possess the potential of inducing cancer, kidney failure, deafness, redness and pains of the eye and skin (MACK, 1988; DE ANGELO, GEORGE, KILBURN et al.,1998). Its toxicity has led to its ban in most countries

Vitamin E (a-tocopherols) are multifaceted antioxidants, that scavenge oxygen free radicals, lipid peroxides and singlet oxygen (DIPLOCK, MacHLIN, PACKER et al., 1989). They act as membrane stabilizers by their positive influence on membrane lipid organization (OYEWOLE, 2011).

The oral lethal dose (LD50) of potassium bromate has been established in wistar rat as 160-190 mg/kg (KUROKAWA, MAEKAWA, TAKAHASHI et al., 1990). Bromate is reduced to bromide in body tissues (FUJII, OIKAWA, SAITO et al., 1984). The aim of this study is to evaluate some effects of potassium bromate on the liver as well as determine if the co-administration of vitamin E will have an ameliorating importance on the effect produced on the histology of the liver.

2 Materials and Methods

2.1 Animals

Thirty (30) adult wistar rats were housed in ventilated cages in the Animal House of Physiology Department, Ladoke Akintola University, Ogbomoso, Nigeria. Wood shavings was collected from sawmill and used for beddings. The beddings were changed at least twice per week throughout the period of the experiment. The rats were left for a week as an adaptation period and they were allowed free access to distilled water and growers feed. The pellets were given to the animals in the morning and in the evening. The rats were weighed to assess their growth. They were housed in the Laboratory at 27 ± 2 °C, relative humidity 50 ± 15% and normal photo period (12h dark/12h light).

2.2 Feeds

The rats were fed with pelletized growers mash and water. The feed was bought from Bova–Jay Nigeria Enterprises, Apake, ogbomoso. The Pelletized growers mash is composed of the following- maize, soya, groundnut cake, corn brown,

palm kernel cake (PKC), fish meal, bone meal, oyster shell, vitamins and mineral, methionine, lysine, salt and blood meal. The rats were fed twice daily. The body weight of the rats were taken weekly and documented.

2.3 Drug

Potassium bromate salt, a product of British drug home limited, Poole England was supplied in its white crystalline form by SAVIDEB chemicals (Nigeria) enterprise, Farida Adeleke market, Dada Estate, Osogbo. It was administerd in drinking water. Eviol vitamin E (dl-alpha-tocopheryl acetate), a product of G.A. Pharmaceutical S.A Greece was obtained from JOPAT pharmaceutical, Ogbomoso, Oyo state. Vitamin E was administered by oral gavage route in dose 30mg/100g rats.

2.4 Experiment design

After acclimatization, the animals were randomly divided into six (6) groups, 5 rats each with five treated groups and one control. The treated groups received potassium bromate in drinking water for 21 days. The groups are as follows:

Control Group: This group contained 5 rats which received distilled water and feed for 3 weeks.

Group One: This group contained 5 rats which received 140 mg/L of $KBrO_3$ in drinking water for 3 weeks.

Group Two: This group contained 10 rats which were divided into two group containing 5 rats each i.e. group A & B. The rats in Group 2A and 2B received 170 mg/L of $KBrO_3$ in drinking water for 3 weeks. Thereafter, $KBrO_3$ was withdrawn from the animals in group 2B for another 2 weeks.

Group Three: This group contained 5 rats which received 200 mg/L of $KBrO_3$ in drinking water for 3 weeks.

Group Four: This group contained 5 rats which received $KBrO_3$ at dose level of 200 mg/L in drinking water with co – administration of vitamin E through oral gavage route for 3 weeks.

2.5 Administration of drug

The rats were weighed prior to the commencement of administration and in subsequent weeks during the research period. Potassium bromate salt was dissolved in distilled water to make a stock solution containing 140 mg/L $KBrO_3$, 170 mg/L $KBrO_3$, and 200 mg/L $KBrO_3$ from which the animals were fed during the experiment.

Capsules of vitamin E (Eviol di-alpha-tocopheryl acetate, G.A. Pharmaceutical S.A Greece) were cut open and emptied into a clean container. Vegetable oil was added to prepare a suspension solution containing a 34 mg of vitamin E in 0.1 mL. The suspension solution was kept from sunlight to avoid degradation, by stocking in a dark air-tight jar.

At the end of administration, the rats were sacrificed by cervical dislocation. The rats in the control group and those in groups 1, 2A, 3, 4, were sacrificed on the 21st day of administration while those in group 2B were sacrificed 14 days after. The animals were dissected and the livers were excised. Thereafter, the tissues were fix in 10% formal saline for histological studies.

2.6 Statistical analysis

The results were expressed as a mean value ±S.E.M. and data were analyzed statistically. Comparison was done using one-way analysis of variance (ANOVA). P values of <0.05 were considered statistically significant. Bar charts were used for graphical representation.

3 Results

3.1 Observation

There were no abnormal activities observed in the control group throughout the period of study. In the treatment groups there was reduction in physical activities when compared with the control group, although for group 2B the physical activity was restored to minimal (Figure 1).

Relative liver weights were examined and all the treatment groups showed significant increase ($p<0.05$) when compared with the control. Table 2 and Figure 2.

3.2 Histological plate

The histology results revealed distortion in tissue architecture, congestion of the central vein and sinusoidal dilatation as well as cell necrosis in all the treatment. Plates 1-6.

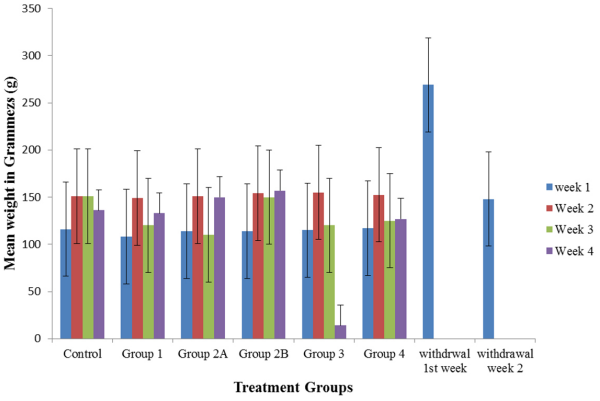

Figure 1. Average Body Weight.

Table 1. Effect of potassium on the body weight.

	CONTROL	GROUP 1	GROUP 2A	GROUP 2B	GROUP 3	GROUP 4
1	116.00 ± 4.85	108.00 ± 3.39	114.00 ± 6.21	114.00 ± 6.21	115.00 ± 4.47	117.00 ± 4.64
2	115.00 ± 9.93	149.00 ± 3.67	151.00 ± 10.17	154.00 ± 11.45	155.00 ± 12.25	152.50 ± 9.68
3	167.00 ± 11.02	158.00 ± 8.16	170.00 ± 7.58	116.00 ± 10.17	173.00 ± 9.43	167.00 ± 6.26
4	136.00 ± 9.14	133.00 ± 6.04	150.00 ± 4.18	157.00 ± 6.25	148.00 ± 12.61	127.00 ± 7.84
5	—	—	—	269.00 ± 50.04	—	—
6	—	—	—	148.00 ± 1.14	—	—

4 Discussion

The result of this present study reveals that the intake of potassium bromate caused some characteristic physical changes in adult wistar rat as evident in the reduction of physical activity and feebleness

There was no significant difference in the body weight of animals administered with potassium bromate when compared with control; this finding is consistent with the research carried out by Abuelgasim, Omer and Elmahdi (2008). However group 2B animals showed some weight gain at the end of two weeks of withdrawal. Table 1.

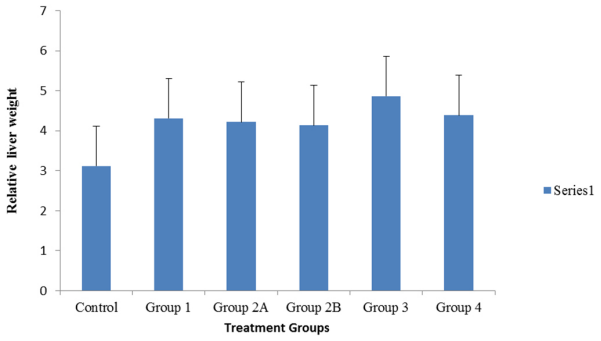

Figure 2. Effects of Potassium Bromate on Liver Weight.

Table 2. Effects of potassium bromate on liver weight.

Groups	Mean ± SEM
Control	3.12 ± 0.34
1	4.31 ± 0.37*
2A	4.22 ± 0.24*
2B	4.13 ± 0.06
3	4.87 ± 0.33***
4	4.39 ± 0.19*

Each value represents the mean ± SEM (n = 5), values are statistically different from control at $p < 0.05$* and 0.001*** one-way analysis of variance (ANOVA) + Tukey –Kramer Multiple Comparison Test.

This present study also showed a significant ($p < 0.05$) increase in the organ weight of the experimental animals when compared with the control group, which is in line with the previous work of Kawana, Nakaoka, Horiguchi et al. (1991), who reported increase in kidney, lungs and liver weight above the control organ weights.

The administration of potassium bromate caused intense damage to liver tissue architecture, as seen in the photomicrograph of the sections, distortion in tissue architecture, congestion of the central vein and sinusoidal dilatation as well as cell necrosis were recorded in all the treatment. This study is similar to the work carried out my Abuelgasim, Omer and Elmahdi (2008), where they reported 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. The present research is also supported by Akanji, Nafiu and Yakubu (2008) where Potassium bromate caused congestion of the central vein with blood cells in the hepatocytes, infiltration of the interstitial cells accompanied with acute nephritis in the nephrons and mild mucosal dysfunction in the small intestine. The finding contradicts that of Umemura, Sai, Takagi et al. (1995) where there were no pathological change in the liver.

However, the less intense liver damage seen in the photomicrograph of the sections of group 4 may be related to the ameliorating importance of vitamin E as an antioxidant in combating the free radical damage mechanism of potassium bromate. This agrees with the earlier work of Sai, Hayashi, Takagi et al. (1992) where he studied the suppression of potassium bromate – induced micronuclei formation by antioxidants. Moreover, the withdrawal of $KBrO_3$ may likely not reverse the effect of potassium bromate on the liver.

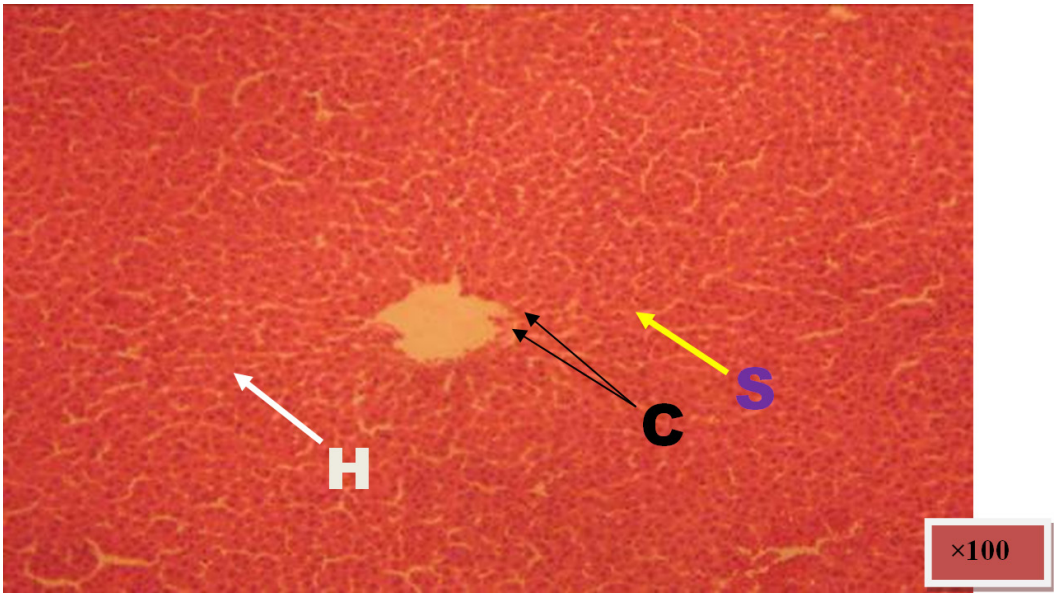

Plate 1A. Photomicrograph of a Liver section in the control group showing normal lobular architecture. Central vein (C), cords of hepatocytes (H) and sinusoidal spaces (S) (H and E).

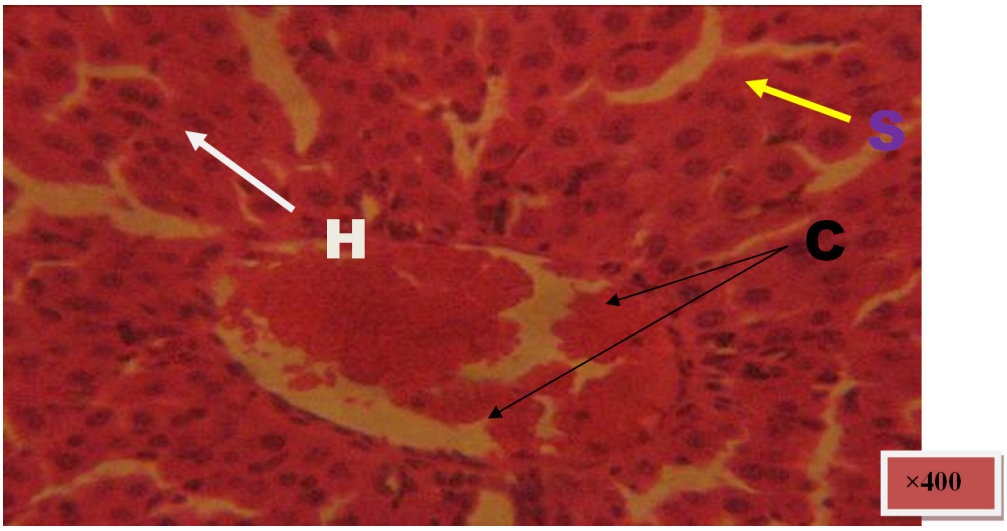

Plate 1B. Photomicrograph of a Liver section in the control group showing normal lobular architecture. Central vein (C) and cords of hepatocytes (H), sinusoidal spaces (S) (H and E ×400).

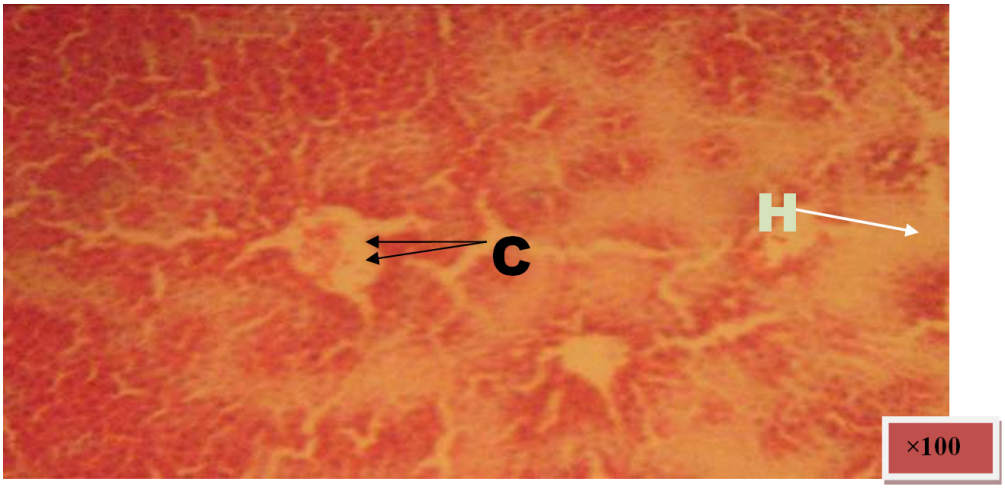

Plate 2A. (Group 1**)**: Photomicrograph of a Liver section in the group treated with 140mg/L $KBrO_3$ showing distortion of hepatic lobular architecture. There is mild congestion of the central vein (C). (H and E ×100).

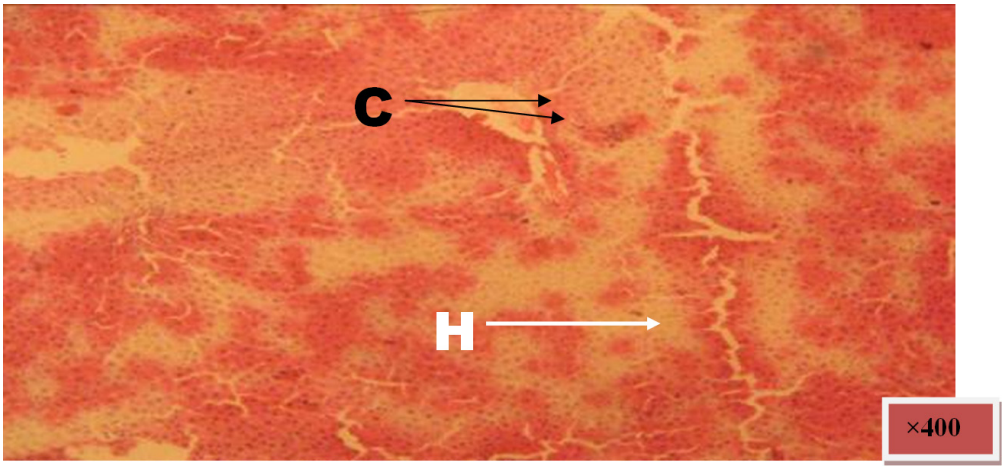

Plate 2B. (Group 1**)**: Photomicrograph of a Liver section in the group treated with 140mg/L $KBrO_3$ showing distortion of hepatic lobular architecture. Areas of hepatic cellular necrosis (H) are also visible. There is mild congestion of the central vein (C). (H and E ×400).

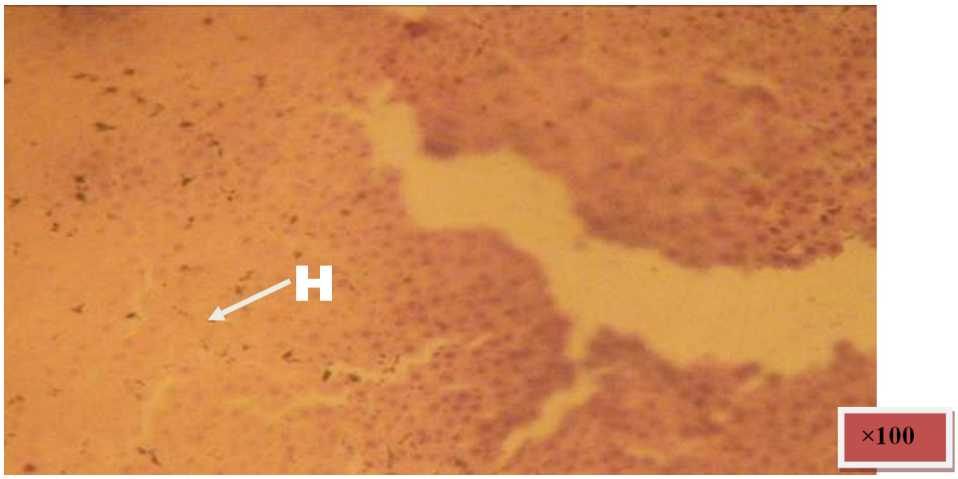

Plate 3A. (Group 2A): Photomicrograph of a Liver section in the group treated with 170mg/L potassium bromate showing distortion of lobular architecture. Hepatic cell necrosis (H) There is paucity of central vein. (H and E ×100).

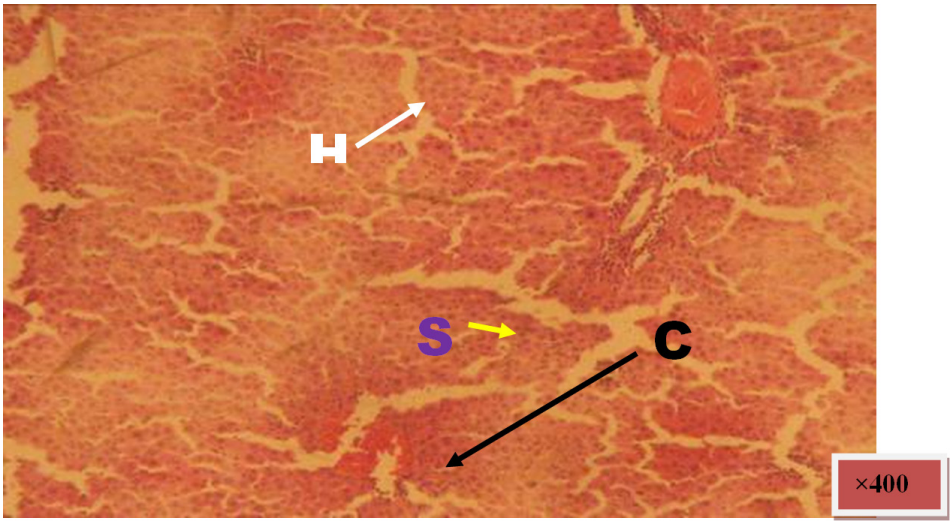

Plate 3B. (Group 2A): Photomicrograph of a Liver section in the group treated with 170mg/L $KBrO_3$ showing distortion in arrangement of hepatocytes (H) with areas of hepatic cell necrosis (H) and sinusoidal dilatation (S). The central vein is markedly congested (C). (H and E ×400).

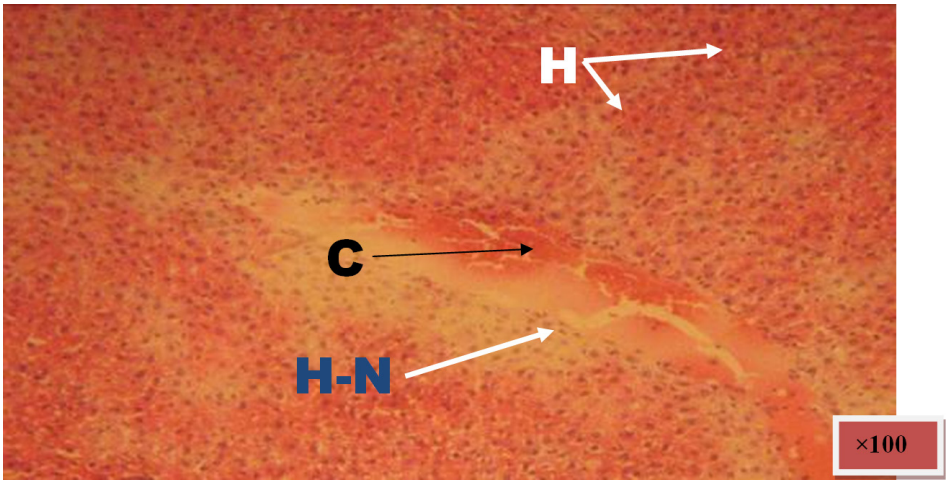

Plate 4A. (Group2B): Photomicrograph of a Liver section in the group treated with 170mg/L $kBrO_3$+ 2wks withdrawal showing distortion in arrangement of hepatocytes (H) with areas of hepatic cell necrosis (H-N). The central vein is congested (C). (H and E ×100).

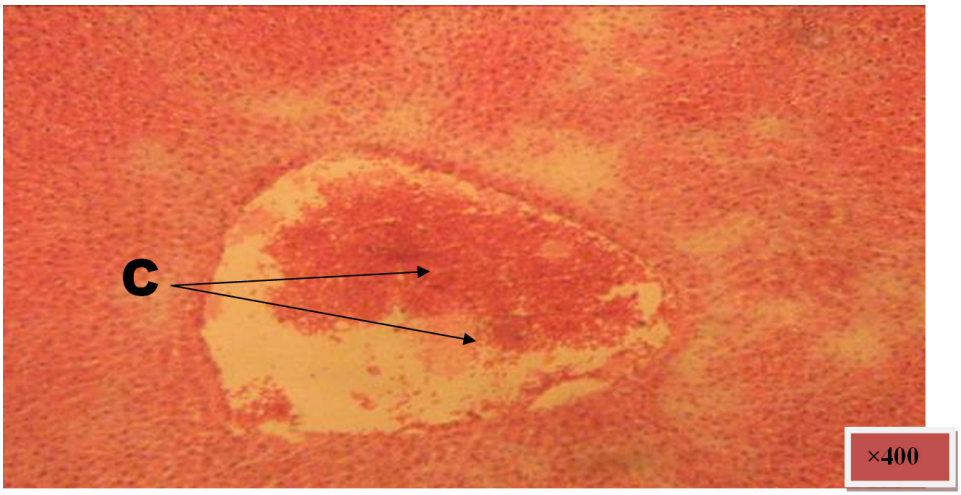

Plate 4B. (Group 2B): Photomicrograph of a Liver section in the group treated with 170mg/L $kBrO_3$+ 2wks withdrawal showing distortion in arrangement of hepatocytes with areas of hepatic cell necrosis. Central vein (C). (H and E ×400).

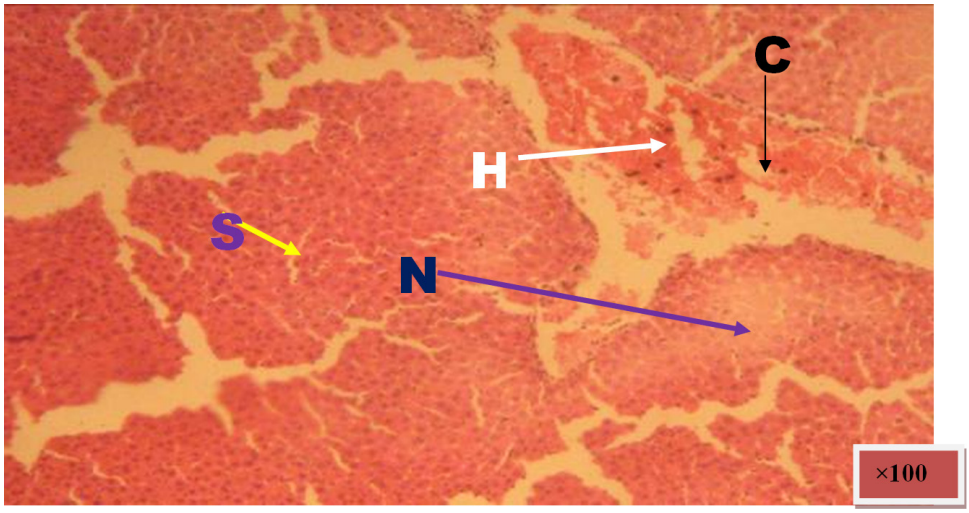

Plate 5A. (Group 3): Photomicrograph of a Liver section in the group treated with 200mg/L $KBrO_3$ showing of hepatic lobular architecture, hepatic cell necrosis (N). The central vein is congested (C). The sinusoidal dilation (S) (H and E).

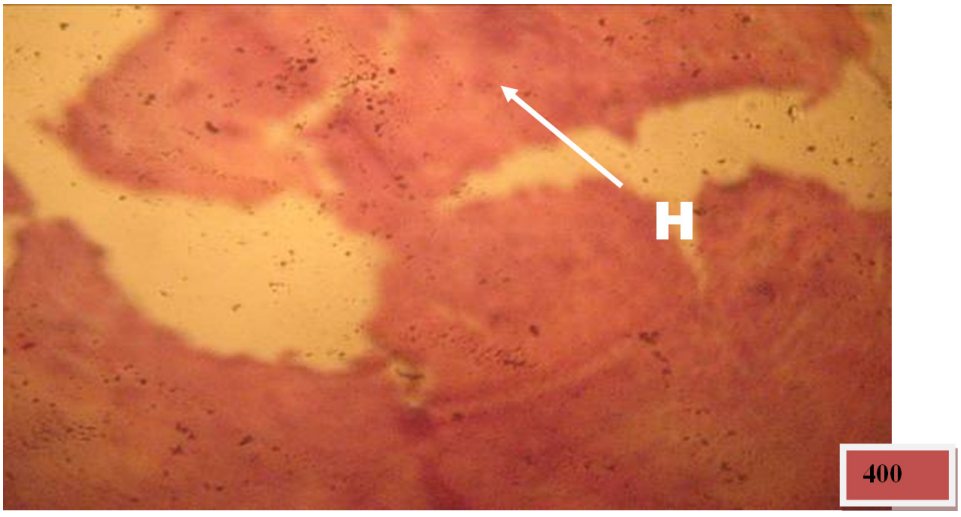

Plate 5B. (Group 3): Photomicrograph of a Liver section in the group treated with 200mg/L $KBrO_3$ showing distortion of hepatic lobular architecture. The section shows hepatic cell necrosis. (H and E).

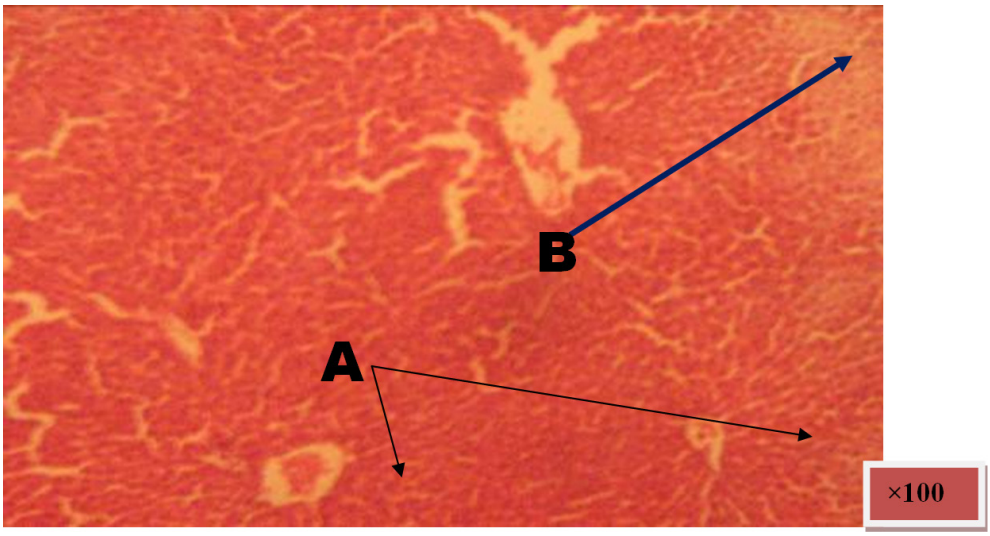

Plate 6A. (Group 4**)**: Photomicrograph of a Liver section in the group treated with 200mg/L $KBrO_3$+Vit.E showing mixed areas of normal (A) and distorted (B) lobular architecture and hepatic cell necrosis. The central veins are slightly congested (H and E).

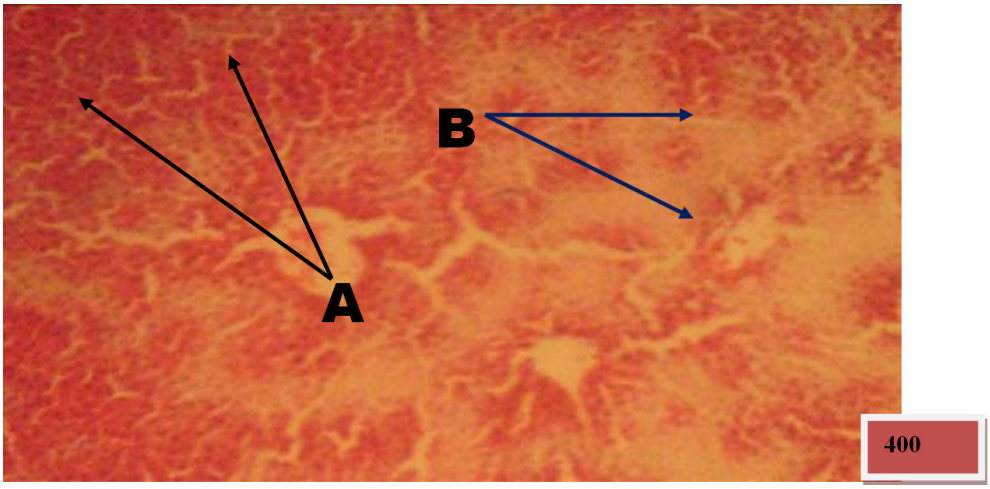

Plate 6B. (Group 4**)**: Photomicrograph of a Liver section in the group treated with 200mg/L $KBrO_3$+Vit.E showing mixed areas of normal (A) and distorted (B) lobular architecture and hepatic cell necrosis. The central veins are slightly congested (H and E).

5 Conclusion

This study had shown that potassium bromate ($KBrO_3$) altered the tissue architecture of the liver as well as physical activity rats; though vitamin E may be useful in lowering the toxic activity of potassium bromate the consumption of potassium bromate therefore should be discouraged.

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Received August 12, 2012
Accepted May 23, 2013