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Administration of Combined Exogenous L-arginine and Ascorbic Acid Attenuates Potassium Bromate-Induced Renal and Hepatic Toxicity

O.T. KOLAWOLE[1* A, D], S.O. BAKARE[2 B, C], A.A. AYANKUNLE[3 C, E], O.A. ADEYEBA[4 F]

[1]Department of Pharmacology and Therapeutics, Ladoke Akintola University of Technology, Ogbomoso, Nigeria
[2]UNIOSUN Teaching Hospital, Osogbo, Osun State, Nigeria
[3]Department of Pharmacology, Osun State University, Osogbo, Nigeria
[4]Department of Medical Microbiology and Parasitology, Ladoke Akintola University of Technology, Ogbomoso, Nigeria

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article.

Abstract

Background: The use of potassium bromate ($KBrO_3$) as food additive is still widespread and there is need to search for agents with protective effect against $KBrO_3$-induced toxicity.
Objective: In this study, the protective effects of L-arginine, ascorbic acid, and their combined regimen on $KBrO_3$-induced renal and hepatic toxicity were investigated in Wistar rats.
Methods: Five groups of male rats were used for the study. Group A was given distilled water (control), and group B was treated with $KBrO_3$ only. In addition to $KBrO_3$, groups C, D, and E were given L-arginine, ascorbic acid, and combined L-arginine and ascorbic acid respectively. After 28-day treatment, blood samples were taken for biochemical analysis; liver and kidney were harvested for histological examination.
Results: $KBrO_3$ significantly ($p < 0.05$) raised serum levels of creatinine, urea, ALT, and AST compared to distilled water-treated control. Levels of SOD, CAT, and GPx were also significantly reduced. No significant changes in these parameters were observed with ascorbic acid and L-arginine given separately. Treatment with combined regimen of L-arginine and ascorbic acid resulted in significant ($p < 0.05$) reduction in the serum levels of creatinine, AST and ALT, and significant increase in the serum levels of SOD, CAT and GPx compared to the control. The distortions induced by $KBrO_3$ in the structural architecture of renal and hepatic tissues were largely reduced in rats treated with combined ascorbic acid and L-arginine.
Conclusion: The study showed that L-arginine and ascorbic acid synergistically attenuate $KBrO_3$-induced renal and hepatic toxicity.
Keywords: Potassium bromate, L-arginine, ascorbic acid, liver, kidney

INTRODUCTION

Quality and enjoyable food is essential for humans to keep living. In the absence of good food, the body ceases to function properly, growth is retarded, and the ability of the body to fight infections and diseases is greatly compromised. There are various kinds of food that people enjoy, but one of the most popular foods consumed by young and old around the world is bread (Mode *et al*., 2023). Bread is produced from wheat flour. In order to improve the texture of bread and maximize profit, baking industry uses potassium bromate ($KBrO_3$) as an additive (Magomya *et al*., 2013). However, many studies have reported the negative impact of $KBrO_3$ on human health. Some manifestations of acute toxicity of $KBrO_3$ are diarrhea, vomiting, and abdominal discomfort. Multiple organ damage including liver, kidney, and the central nervous system have been reported. It has also been shown that $KBrO_3$ is carcinogenic in human and

experimental animals (Kurokawa *et al*., 1990; Ncheuveu *et al*., 2023). In view of these toxic effects, many countries including Canada, Nigeria, and India have banned the use of potassium bromate as food additive. Other countries like United States of America still allow its use in permissible limit. In spite of the negative effects of $KBrO_3$ on human health, bakers continue to use it. They believe that with the very high temperature of the baking oven, potassium bromate is converted to harmless potassium bromide. However, the possibility of some residue of $KBrO_3$ remaining in the final product cannot be ruled out (Oyekunle *et al*., 2014). For example, recent analysis of a number of Tunisian breads revealed that bromate concentrations ranged from 5.95 to 49.31µg/g (El Ati-Hellal *et al*., 2018). Even in countries where its use has been banned, bakers illegally continue to use $KBrO_3$ to attract more profit. In Nigeria for instance, despite the ban, the use of $KBrO_3$ in bread is still common. A study carried out in Ibadan, Oyo State, reported that all thirty samples of bread analyzed contain $KBrO_3$ with conce ntrations ranging between 1.24µg/g and 9.31µg/g.
These concentrations are above the safe level for human consumption (Airaodion et al., 2019). Bread consumers are thus at risk of all the aforementioned toxic and long-term health implications of the chemical. In view of the high probability of exposure to $KBrO_3$, there is need to find ways of minimizing its damaging effects in consumers. Since $KBrO_3$ is an oxidizing agent, antioxidants such as ascorbic acid and drugs that induce antioxidant response such as L-arginine might have protective effect against potassium bromate-induced toxicity. L-arginine is the precursor for the synthesis of nitric oxide (NO). Both L-arginine and its product NO regulate cellular redox status and play essential role against oxidative stress (Ranjbar *et al.*, 2016; Abu-Serie *et al*., 2015). Pathogenesis of many physiologic disorders has been linked to oxidative stress, and NO has been reported to be an effective antioxidant, capable of preventing the development or arresting the progression of many oxidative stress-induced disorders (Rolo *et al*., 2012). Administration of exogenous L-arginine has been demonstrated to enhance nitric oxide bioavailability which is a critical factor in the suppression of oxidative stress and induction of endogenous antioxidant response (Moreira *et al*., 2019). Ascorbic acid is a water-soluble vitamin and its role as antioxidant is also well documented. It has the ability to react with and scavenge superoxide and hydroxyl radicals (Shen *et al*., 2021). In this study, we investigated the effects of L-arginine and ascorbic acid on potassium bromate-induced renal and hepatic toxicity.

METHODOLOGY

Materials and methods

Experimental animals

Thirty male Wistar rats with an average weight of 180 g were used for the experiment. The rats were obtained from Animal House of College of Health Sciences, Ladoke Akintola University of Technology, Ogbomoso. The animals were maintained in a well-ventilated environment with the temperature ranging between 22-25 ^oC and 12/12 light and dark cycle. They were fed with animal pellets (Ladokun Feeds Ltd. Ibadan) and allowed free access to pure drinkable water.

Drugs

L-arginine (LA), Ascorbic Acid (AA) and potassium bromate (PB) were obtained from Sigma-Aldich company, UK.

Experimental procedure

Rats were assigned to five groups (n = 6 per group) and treated as follows: Group A (control) was treated with distilled water. Rats in group B were given $KBrO_3$ (200 mg/kg bw) only. After administering $KBrO_3$, groups C, D, and F were treated with ascorbic acid (500 mg/kg bw), L-arginine (500 mg/kg bw), and combined regimen of ascorbic acid (500 mg/kg bw) and L-arginine (500mg/kg bw) respectively. The drugs were administered by means of an intragastric cannula daily for 28 days. Rats were made to fast overnight and then euthanized on the 29th day. Blood samples collected from retro-orbital sinus were centrifuged at 3000 rpm for 10 minutes. Liver and kidney were harvested for histological study. Serum samples obtained were used for biochemical assays.

Biochemical analysis

Serum creatinine, urea, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were analyzed using an automatic analyzer, TBA 120 FR (Toshiba Medical Systems, Co., Ltd. Japan). Seru m glutathione peroxidase (GPx) was determined by t he method previously described by Rotruck *et al*. (1973). Superoxide dismutase (SOD) was analyzed by the method of Kakkar et al. (1984). Serum catalase (CAT) was also determined by the method previously described (Sinha, 1972).

Histological analysis

Liver and kidney tissues were prepared for histological examination by the method described by Krause (2001). Sections (5 µm thick) were cut with microtome and stained with H/E. The stained sections were observed under a photomicroscope (Model N-400ME (CEL-TECH Diagnostics, Hamburg, Germany), and photomicrographs were taken and interpreted by a pathologist.

Statistical analysis

Data obtained were analyzed and presented as mean ± standard error of mean (SEM). Differences between groups were analyzed by one way Analysis of Variance (ANOVA) followed by Student's t-test, and $p < 0.05$ was considered significant. GraphPad Prism version 6.1 for Windows (GraphPad software, San Diego California, USA) was used for the analysis.

RESULTS

Potassium bromate significantly raised serum levels of creatinine, urea, ALT, and AST compared to distilled water-treated control. AST was raised from 41.23 ± 3.73 to 58.52 ± 4.90 U/L, while ALT was raised from 32.60 ± 3.81 to 44.64 ± 4.15 U/L. On the other hand, potassium bromate significantly reduced the levels of SOD, CAT, and GPx. Administration of ascorbic acid in $KBrO_3$-treated rats caused slight reduction in the serum levels of urea, creatinine, AST, and ALT. Non-significant increase in the serum levels of SOD, CAT, and GPx was also observed in rats treated with ascorbic acid. L-arginine similarly caused non-significant changes in all these parameters except AST. Treatment with combined regimen of L-arginine and ascorbic acid resulted in significant reduction in the serum levels of creatinine (Figure 1), AST and ALT (Table 1), and significant increase in the serum levels of SOD, CAT and GPx (Table 2) compared to the control. SOD was increased from 1.61 ± 0.11 to 3.71 ± 0.33 units/ml, CAT was raised from 13.52 ± 2.50 to 21.80 ± 2.01 units/ml, and GPx was increased from 2.60 ± 1.30 to 4.46 ± 0.51 units/ml. No significant alteration was observed in urea level (Figure 2).

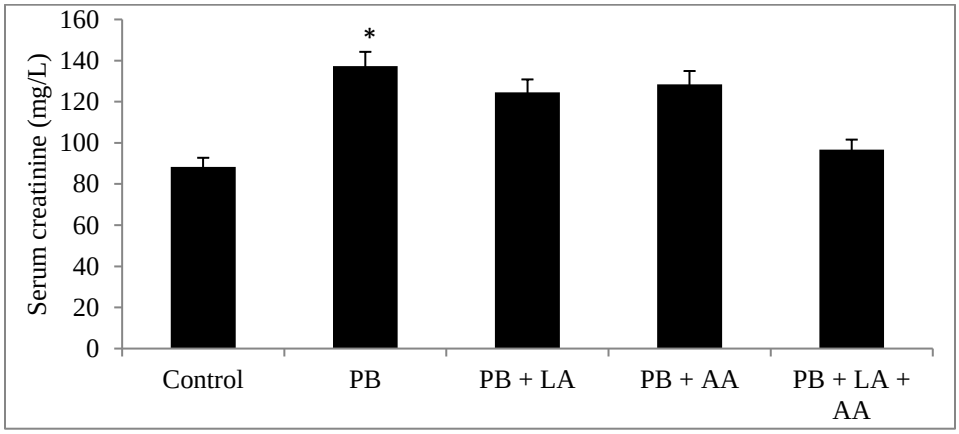

Figure 1. Effects of L-arginine and ascorbic acid on serum creatinine in $KBrO_3$-treated rats. PB = potassium bromate, LA = L-arginine, AA = ascorbic acid. Values represent mean ± SEM (n = 6); *p < 0.05 compared with normal control, **p < 0.05 compared with potassium bromate control

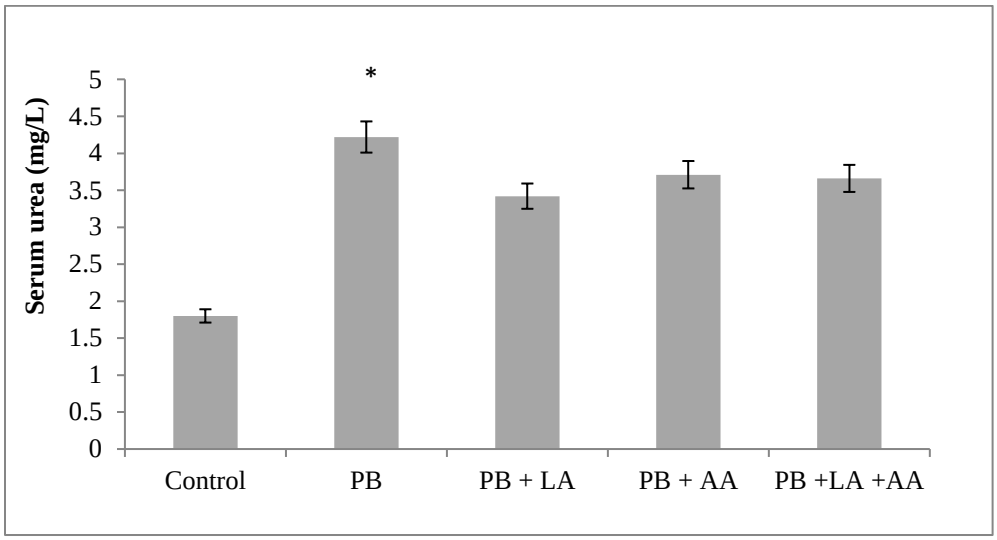

Figure 2. Effects of L-arginine and ascorbic acid on serum urea in $KBrO_3$-treated rats. PB = potassium bromate, LA = L-arginine, AA = ascorbic acid. Values represent mean ± SEM (n = 6); *p < 0.05 compared with normal control, **p < 0.05 compared with potassium bromate control

Table 1. Effects of L-arginine and ascorbic acid on AST and ALT in potassium bromate- treated rats

Group	AST (U/L)	ALT (U/L)
Control	41.23 ± 3.73	32.60 ± 3.81
PB	58.52 ± 4.90*	44.64 ± 4.15*
PB + LA	48.86 ± 3.50**	39.51 ± 3.14
PB + AA	51.25 ± 4.66	40.30 ± 4.32
PB + LA + AA	44.66 ± 3,40**	32.10 ± 3.22**

PB = potassium bromate, LA = L-arginine, AA = ascorbic acid. Values represent mean ± SEM (n = 6); *p < 0.05 compared with normal control, **p < 0.05 compared with potassium bromate control

Table 2. Effects of L-arginine and ascorbic acid on SOD, CAT, and GPx in potassium bromate- treated rats

Group	SOD (units/ml)	CAT (units/ml)	GPx (units/ml)
Control	4.04 ± 0.12	25.41 ± 4.55	5.62 ± 1.08
PB	1.61 ± 0.11*	13.52 ± 2.50*	2.60 ± 1.30*
PB + LA	2.14 ± 0.13	18.22 ± 2.10	3.15 ± 1.08
PB + AA	2.07 ± 0.20	18.30 ± 2.21	2.32 ± 1.02
PB + LA + AA	3.71 ± 0.33**	21.80 ± 2.01**	4.46 ± 0.51**

PB = potassium bromate, LA = L-arginine, AA = ascorbic acid. Values represent mean ± SEM (n = 6); *p < 0.05 compared with normal control, **p < 0.05 compared with potassium bromate control

Histological examination showed noticeable distortions in the architecture of renal and hepatic tissues of rats treated with $KBrO_3$ compared to the control. Hemorrhage and dilation of blood vessels were seen in tissues of $KBrO_3$-treated rats. These distortions were ameliorated and were not clearly noticed in renal and hepatic tissues of rats treated with combined ascorbic acid and L-arginine. The histology of both renal and hepatic tissues in this group appeared almost normal compared with the control (Figure 3).

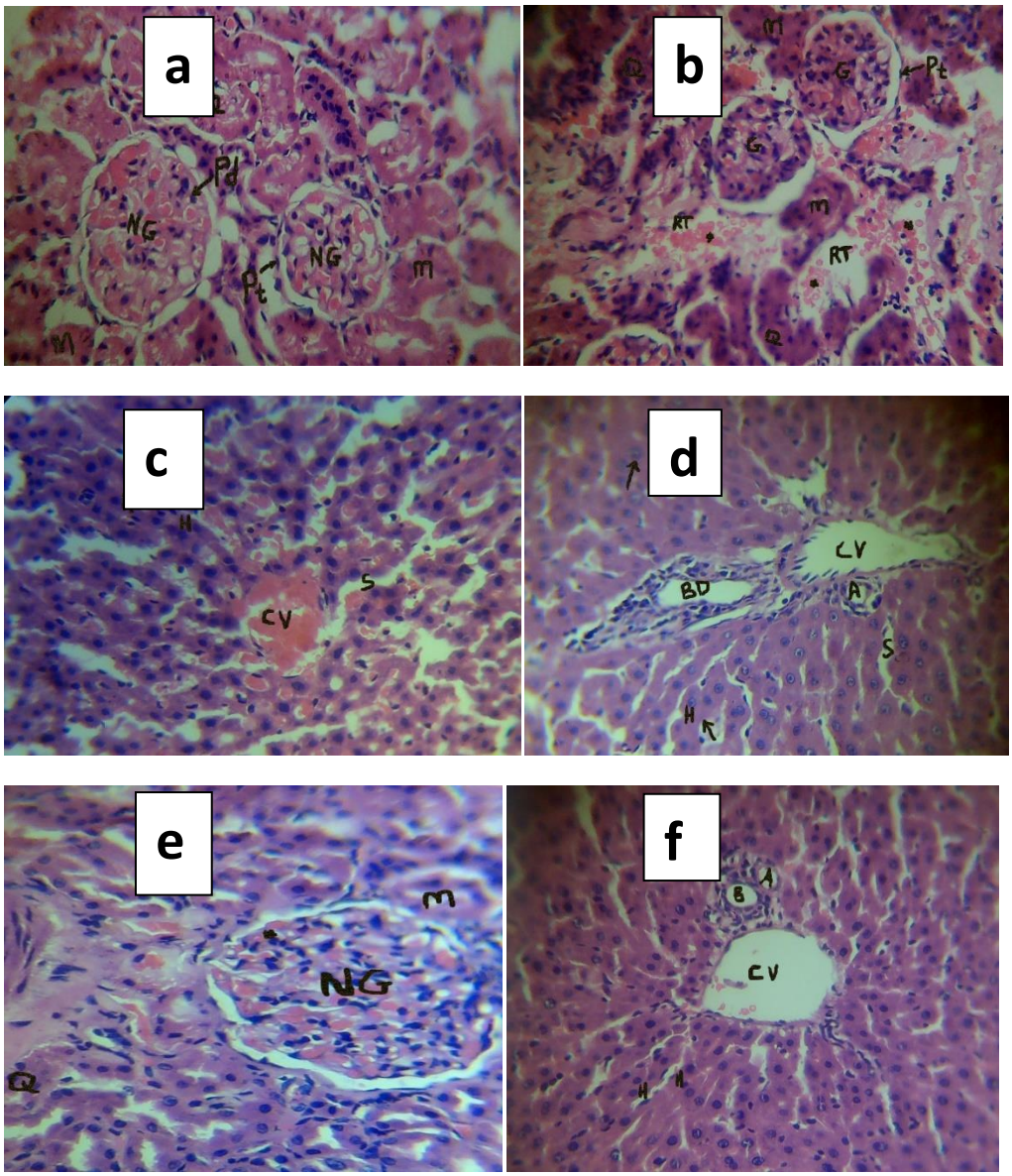

Figure 3. Effects of combined L-arginine and ascorbic acid on the liver and kidney of potassium bromate-treated rats. a = kidney section of rats in the distilled water-treated control group showing normal architecture of renal glomerulus (NG) with normal proximal tubules (m) and distal renal tubule (Q); b = kidney section of rats in the potassium bromate-treated control group showing some distorted glomerular cells (G) closely packed together, normal parietal cell (Pt), shrunk proximal (m) and distal (Q) tubules, some ruptured renal tubules (RT) with leakage of red blood cells into the surrounding renal tissues (*); c = liver section of rats in the distilled water-treated control group showing preserved liver architecture with closely packed hepatocytes (H), central vein (CV), and sinusoid (S) which appear normal and free of inflammatory cells; d = liver section of rats in the potassium bromate-treated control group showing hepatocytes (H) with distorted architecture. The tissue appears edematous and the sinusoids (s) are more prominent. Central vein (CV) and bile duct (BD) appear more pronounced and distorted. There are inflammatory cells seen around portal arterial membrane (A); e = kidney section of rats treated with combined L-arginine and ascorbic acid showing near normal glomerulus (NG), proximal (m) and distal (Q) tubules; f = liver section of rats treated with combined L-arginine and ascorbic acid showing tissue with normal architecture. Central vein, hepatocytes (H), bile duct (B) and portal artery (A) all appear normal (x 200 magnification).

DISCUSSION

Despite the ban placed on its use by many countries around the world, potassium bromate is widely used by baking industry. Since bread is consumed regularly by almost everyone, the risk of acute and long-term effects of potassium bromate is high among a large population of consumers. Chronic effects of $KBrO_3$ include cancer, liver damage, and kidney injury (Shanmugavel *et al*., 2020). There is need to search for remedies against the toxic effects of $KBrO_3$ apart from prohibiting its use. Since $KBrO_3$ is an oxidizing agent, antioxidants may be useful in mitigating its toxic effects. In this study, potassium bromate was used to induce renal and hepatic damage in rats. $KBrO_3$ is an oxidizing agent that increases hydrogen peroxide levels, lipid peroxidation, and protein oxidation, thereby inducing oxidative stress. It has also been shown to alter the cellular antioxidant defense system by decreasing the activities of catalase, glutathione peroxidase, glucose 6-phosphate dehydrogenase (Ahmad *et al*., 2014). Reduced glutathione (GSH) is an antioxidant which protects many organs, including liver and kidney, against oxidative stress. $KBrO_3$ has been reported to decrease the tissue content of this important molecule (Parsons and Chipman, 2000). In another study, 200 mg/kg body weight of $KBrO_3$ decreased GSH in both renal and hepatic tissues in rodents, and plasma creatinine level was significantly raised (Altoom et al., 2018). Previous studies have also demonstrated that $KBrO_3$ is hepatotoxic (Ambali *et al*., 2011; Oyewo *et al*., 2013). The oxidizing effect of $KBrO_3$ is likely responsible for the renal and hepatic damage in rats observed in this study. Tissue damage following administration of potassium bromate is also evidenced from the increase in the levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT). These biochemical parameters are indicators of tissue injury, especially hepatic damage (Satpal and Punia, 2010). After administration of potassium bromate, serum levels of creatinine significantly ($P<0.05$) increased. This is an indication of renal damage, though there was no significant alteration in the serum level of urea (Levey *et al*, 1988; Bartholomae *et al*., 2022). In addition, antioxidant defense system was compromised as indicated by the significant reduction in the levels of superoxide dismutase, catalase and gluthathione peroxidase. The alterations induced by $KBrO_3$ in the levels of these parameters were significantly attenuated when the rats were treated with combined ascorbic acid and L-arginine. Several experimental studies have shown that administration of L-arginine improves cardiovascular, pulmonary, immune and digestive functions, and protects against the early stages of carcinogenesis. It is beneficial in the treatment of hepatic injury (Saad, 2012), hepatic cirrhosis, fatty liver degeneration (Amin, *et al.,* 2018) and diabetic nephropathy (Huang *et al.,* 2010, Hu *et al.,* 2012). Studies have also shown that exogenous L-arginine is able to protect the kidney against toxic injury. (Cherla and Jaimes, 2004, Shaki *et al*., 2021). The present study has demonstrated that administration of exogenous L-arginine in combination with ascorbic acid is beneficial in potassium bromate-induced organ damage in rats. Our results agree with those of previous studies which reported that doses of ascorbic acid or L-arginine between 500 and 1000 mg/kg body weight restored induced alterations in biochemical indices of kidney function in rodents, and that histological aberrations induced in renal tissues were also ameliorated (Kandhare *et al*., 2015; Shaki *et al*., 2021). The probable mechanism of action of L-arginine is its antioxidative effect elicited by direct chemical interaction with superoxide anion (Liang *et al*., 2018, Li *et al*., 2022). In line with this, L-arginine in combination with ascorbic acid, which is also an antioxidant, significantly increased the levels of superoxide dismutase, catalase and gluthathione peroxidase thus ameliorating the oxidative effects of potassium bromate in rats. When administered separately, L-arginine and ascorbic acid did not cause significant alterations in most of the parameters analyzed. However, administration of the two drugs combined significantly attenuated $KBrO_3$-induced changes in these parameters, suggesting a synergy between them. The appearance of kidney and liver tissues in various experimental groups during histological examination is consistent with the results obtained for biochemical analysis. Liver and kidney sections of rats treated with $KBrO_3$ showed prominent distortions of structural architecture. These distortions were virtually absent in tissue sections of rats treated with combined L-arginine and ascorbic acid after pretreatment with $KBrO_3$.

CONCLUSION

From the findings in this study, we conclude that L-arginine and ascorbic acid work synergistically to protect Wistar rats against $KBrO_3$-induced renal and hepatic toxicity.

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REFERENCES

Abu-Serie, M.M., El-Gamal, B.A., Mohamed, A., El-Kersh, M.A., El-Saadan, M.A. (2015). Investigation into the antioxidant role of arginine in the treatment and the protection for intralipid-induced non-alcoholic steatohepatitis. Lipid in Health and Dis. 14:128 doi: 10.1186/s12944-015-0124-0.

Ahmad, M.K., Amani, S., Mahmood, R. (2014). Potassium bromate causes cell lysis and induces oxidative stress in human erythrocytes. Environ Toxicol. 29(2):138-145 doi:10.1002/tox.20780.

Airaodion, A., Ewa, O., Ogbuagu, E., Ogbuagu, U., Agunbiade, A., and Oloruntoba, A. (2019). Evaluation of Potassium Bromate in Bread in Ibadan Metropolis: Fifteen Years after Ban in Nigeria. Asian Food Science Journal. 7(4):1-7 https://doi.org/10.9734/afsj/2019/v7i429976

Altoom, N.G., Ajarem, J., Allam, A.A., Maodaa, S.N., Abdel-Maksoud, M.A. (2018). Deleterious effects of potassium bromate administration on renal and hepatic tissues of Swiss mice. Saudi Journal of Biological Sciences 25(2):278-284. https://doi.org/10.1016/j.sjbs.2017.01.060.

Ambali, S. F., Ayo, J. O., Esievo, K. A.and Ojo, S.A. (2011). Hemotoxicity induced by chronic chlorpyrifos exposure in Wistar rats: Mitigating effect of vitamin C. Vet Med Int. 2011:945439. https://doi.org/10.4061/2011/945439

Amin, D.M., Abaza, M.T., Sarhaan, W.M., Ahmed, A.I., and Moustafa, A.A. (2018). The ameliorative effect of L-arginin and omega-3 fatty acid against sodium valproate induced hepatotoxicity. J Toxicol Environ Health Sci. 10(4): 20-33. https://doi.org/10.5897/JTEHS2018.0411

Bartholomae, Eric., Knurick, Jessica., and Johnston, C.S. (2022). Serum creatinine as an indicator of lean body mass in vegetarians and omnivores. Front Nutr. 9: 996541. https://doi.org/10.3389/fnut.2022.996541

Cherla, G. and Jaimes, E.A. (2004). Role of L-arginine in the pathogenesis and treatment of renal disease. J Nutr. 10: 107-112. https://doi.org/10.1093/jn/134.10.2801S

El Ati-Hellal, M., Doggui, R., Krifa, Y., and El Ati, J. (2018). Potassium bromate as a food additive: A case study of Tunisian breads. Environ Sci Pollut Res Int. 25(3):2702-2706. https://doi.org/10.1007/s11356-017-0712-9

Hu, Y.M., Yeh, C. L. Pai, M. H., Li, C. C., Liu, J. J. and Yeh, S. L. (2012). Effects of arginine supplementation on exogenous advanced glycation end product-induced renal inflammatory mediator expression in rats. J Exp Clin Med. 53: 1126 – 1132. https://doi.org/10.1016/j.jecm.2011.11.004

Huang, K.H., Pai, M.H., Wu, C.H., Liu, J.J. and Yeh, S.L. (2010) Supplemental dietary arginine reduces renal RAGE expression and oxidative damage in rats with streptozotocin-induced type 2 diabetes. ESpen Eur E J Clin Nutr Metab. 3: 118- 124. https://doi.org/10.1016/j.eclnm.2010.02.001

Kakkar, P,, Das, B., and Viswanathan, P.N. (1984). A modified spectrophotometric assay of superoxide dismutase. Indian J Biochem Biophys. 21(2): 130-132

Kandhare, A.D., Patil, M.V., Bodhankar, S.L. (2015). L-Arginine attenuates the ethylene glycol induced urolithiasis in ininephrectomized hypertensive rats: role of KIM-1, NGAL, and NOs. Ren Fail. 37(4):709-21. doi: 10.3109/0886022X.2015.1011967.

Krause, W.J. (2001). The Art of Examining and Interpreting Histological Preparations. A Student Handbook. The Parthenon Publishing Group, New York, London, p. 176

Kurokawa, Y., Maekawa, A., Takahashi, M., and Hayashi, Y. (1990). Toxicity and carcinogenicity of potassium bromate--a new renal carcinogen. Environ Health Perspect. 87:309-35 https://doi.org/10.1289/ehp.9087309

Levey, A.S., Perrone, R.D., and Madias, N.E. (1988). Serum creatinine and renal function. Annu Rev Med. 39:465-90

Li, Z., Wang, L., Ren, Y., Huang, Y., Liu, W., Lv, Z., Qian, L., Yu, Y., and Xiong Y. (2022). Arginase: shedding light on the mechanisms and opportunities in cardiovascular diseases. Cell Death Discov. 8:413

Liang, M., Wang, Z., Li H, Cai, L., Pan, J., He, H., Wu, Q., Tang, Y., Ma, J., and Yang, L. (2018). L-arginine induces antioxidant response to prevent oxidative stress via stimulation of glutathione synthesis and activation of Nrf2 pathway. Food Chem Toxicol. 115:315-328 https://doi.org/ 10.1016/j.fct.2018.03.029

Magomya, A.M., Yebpella, G.G., Udiba, U.U., Amos, H.S., and Latayo, M.S. (2013). Potassium Bromate and Heavy Metal Content of Selected Bread Samples Produced in Zaria, Nigeria, Inter. J. of Sc. Tech. 2(2): 232-237

Mode, M.A., Dandare, S.U., and Umar, R.A. (2023). Ban on the Use of Potassium Bromate in Nigeria: A Review on Bread Bakers' Compliance with Regulations. J. Appl. Sci. Environ. Manage. 27 (3): 401-419. https://doi.org/10.4314/jasem.v27i3.3

Moreira, A.S., Estato, V., Malvar, D.C, Sanches, G.S., Gomes, F., Tibirica, E., Daniel-Ribeiro, C.T., Carvalho, L.J.M. (2019). L-arginine supplementation and thromboxane synthase inhibition increases cerebral blood flow in experimental cerebral malaria. Sci Rep. 9:13621. https://doi.org/10.1038/s41598-019-49855-x

Ncheuveu, N.T., Fon, T.P., and Navti, L.K. (2023). Potassium bromate in bread, health risks to bread consumers and toxicity symptoms amongst bakers in Bamenda, North West Region of Cameroon. Heliyon 9(2):e13146 https://doi.org/10.1016/j.heliyon.2023.e13146

Oyekunle, J.A.O., Adekunle, A.S., Ogunfowokan, A.O., Olutona, G.O., and Omolere, O.B. (2014). Bromate and trace metal levels in bread loaves from outlets within Ile-Ife Metropolis, South-western Nigeria. Toxicol. Rep. 1: 224-230. https://doi.org/10.1016/j.toxrep.2014.05.007

Oyewo, O.O., Onyije, F.M., Awoniran, P.O. (2013). Hepatotoxic effect of potassium bromated on the liver of Wistar rats. J Morphol Sci. 30:107-114

Parson, J.L., Chipman, J.K. (2000). The role of glutathione in DNA damage by potassium bromated in vitro. Mutagenesis 15:311-316

Ranjbar, K., Nazem, F., Nazari, A. (2016). Effect of exercise training and L-arginine on oxidative stress and left ventricular function in the post-ischemic failing rat heart. Cardiovasc Toxicol. 16(2):122-129 doi:10.1007/s12012-015-9319-x

Rolo, A.P., Teodoro, J.S., Palmeira, C.M. (2012). Role of oxidative stress in the pathogenesis of nonalcoholic steatohepatitis. Free Radic Biol Med. 2012;52(1):59–69. doi: 10.1016/j.freeradbiomed.2011.10.003.

Rotruck, J.T., Pope, A.L., Ganther, H.E., Swanson, A.B., Hafeman, D.G., and Hoekstra, W.G. (1973). Selenium: Biochemical role as a component of glutathione peroxidase. Science 179:588-590. https://doi.org/10.1126/science.179.4073.588

Saad, E.A. (2012) Curative and protective effects of L- arginine on carbon tetrachloride-induced hepatotoxicity in mice. Biochem Biophys Res Commun. 423(1):147-51. https://doi.org/10.1016/j.bbrc.2012.05.102

Satpal, S.K. J., and Punia, J. S. (2010). Studies on biochemical changes in subacute thiodicarb toxicity in rats. Toxicol Int. 17: 30-32 https://doi.org/10.4103/0971-6580.68347

Shaki, F., Teymoori, M., Motafeghi, F.S., Hemmati, N., and Arab-Nozari, M. (2021). L-arginine ameliorated mitochondrial oxidative damage induced by sub-chronic exposure to cadmium in mice kidney. Pharm Biomed Res. 7(2): 79-86. http://pbr.mazums.ac.ir/article-1-376-en.html

Shanmugavel, V., Komala, S.K., Kurup, A.H., Kalakandan, S., Anandharaj, A., and Rawson, A. (2020). Potassium bromate: Effects on bread components, health, environment and method of analysis: A review. Food Chem. 311:125964. https://doi.org/10.1016/j.foodchem.2019.125964

Shen, J., Griffiths, P.T., Campbell, S.J., Utinger, B., Kalberer, M., Paulson, S.E. (2021). Ascorbate oxidation by iron, copper and reactive oxygen species: review, model development and derivation of key rate constants. Sci Rep. 11:7417. https://doi.org/10.1038/s41598-021-86477-8

Sinha, A.K. (1972). Colorimetric assay of catalase. Anal Biochem. 47:389- 394. https://doi.org/ 10.1016/0003-2697(72)90132-7

*Address for correspondence: Kolawole Oyetunji
Department of Pharmacology and Therapeutics,
Ladoke Akintola University of Technology,
P.M.B. 4000,
Ogbomoso, Nigeria.
Telephone: +2348039328444
E-mails: otkolawole@lautech.edu.ng

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