Lipid Profile of Bromate -intoxicated Albino Rats Treated with Ethanol Extract of *Harungana madagascariensis* Leaf Extract

Abstract

The research investigated the impact of Hurungana madagascariences leaf extract on the lipid profile of bromate-intoxicated Wistar rats. Thirty-six adult Wistar rats weighing between 100-200g, of both sexes, were randomly divided into six groups, with each group comprising six animals receiving various treatments. Blood samples were obtained for detailed analysis. The results revealed a significant elevation in the levels of high-density lipoprotein (HDL) accompanied by a simultaneous decline in low-density lipoprotein (LDL), triglycerides (TG), and very-low-density lipoprotein (VLDL) levels compared to the positive control group (rats treated with bromate). These findings suggest a favorable shift in the lipid profile, indicative of the cardio-protective potential of lipoprotein leaf extract. The study implies promising implications for the utilization of this natural extract in mitigating cardiovascular risk factors associated with bromate-induced toxicity.

Keywords: *Hurungana madagascariences*, extracts, lipid profile, lipoprotein, Potassium bromate

Introduction

Potassium bromate is also used in foods as a maturing agent and dough conditioner for flour, malting of barley (Dagari *et al*., 2022), beer making and cheese production, also commonly added to fish paste products (Ahmad and Mahmood, 2014). Potassium bromate ($KBrO_3$) is a nephro and neuro-toxic and also a carcinogenic substance used in food and found in drinking water as a by-product of disinfection by ozonisation (Ali *et al*., 2013). Potassium bromate if added to dough which subsequently is produced as bread it can cause such diseases as cancer, kidney failure, renal failure and several other related diseases. Lethal oral doses of bromate in humans have been estimated to be between 154 and 385 mg/kg body weight while serious poisoning results at doses of 46–92 mg/kg body weight (Mack, 1988). Oral doses of 185–385 mg/kg body weight results in irreversible toxic effects like renal failure and deafness in humans while lower doses are associated with vomiting, diarrhea, nausea and abdominal pain (Mack, 1988). The pathologic findings include kidney damage and haemolysis (Robert and William, 1996). Many reports have established that $KBrO_3$ can induce multiple organ toxicities in humans and experimental animals (Farombi *et al*., 2002; Ahmad *et al*., 2015) and that kidney is the primary target organ of this dangerous compound (Ahmad *et al*., 2012).

Medicinal plants of different varieties have been recognized as sources of natural antioxidants that can provide protection from oxidative stress to engender chemoprevention from diseases (Agbor *et al*., 2023). *Harungana madagascariensis, for example*, has been reported to have antioxidant activities (Nwodo, 1989; Kouam *et al*., 2006a,b). Antioxidants are compounds that can delay or inhibit the oxidation of lipids and other essential molecules by inhibiting the initiation or propagation of oxidizing chain reactions. Some of the chemical constituents and isolated compounds from *Harungana madagascariensis* include: flavonoids, alkaloids, saponins, glycosides, and tannins (Moulari *et al*., 2006 a,b). *Harungana madagascariensis* is a component of Jubi Formula, a herbal preparation which was

found to restore packed cell volume (PCV) and haemoglobin (Hb) concentration in anaemia conditions. Nwodo (1989) and Kouam *et al*. (2006a,b) have, however, examined the effect of crude extracts and isolated compounds from a hexane extract of the stem bark of *Harungana madagascariensis*, for their analgesic, anti-inflammatory, alpha-glucosidase inhibition and antioxidant activities respectively. However, despite the extensive use of *H.madagascariensis*, scientific validation of its folk activity on bromate toxicity is lacking. In view of this, the present study will bridge that gap.

Materials and Methods

Study area

The studies were carried out at the laboratory and animal house of Michael Okpara University of Agriculture, Umudike.

Experimental Animal

Thirty (30) adult albino rats (100-200 g) of either sex, obtained from the college of veterinary medicine of Michael Okpara University of Agriculture, Umudike, were used. The animals were acclimatized for twenty-eight days and maintained on water and animal feed *ad libitum* throughout the duration of the studies.

Plant Material

The leaves from *Harungana madagascariensis* were collected at a location in Eket, Akwa Ibom State and identified properly at the herbarium unit of the Department of Plant Biology, Heritage Polytechnic, Eket, Akwa Ibom State where a voucher specimen No 002 was kept.

Preparation of Extract

Fresh leaves of *H. madagascariensis* were sun-dried and then reduced to coarse powder by grinding. The pulverised plant material (1000 g) was soaked in one (1) litre of 70% ethanol (solvent) and allowed to stand for 72 h with constant agitation (Zirihi and Kra, 2003). The extract was then filtered through Whattman filter paper number 24 and the filtrate concentrated to dryness over a steam bath at 60 ºC and stored at 4^{o}C until needed for the analyses.

Quality Control Test of the Extract

The extract was tested for possible microbial contamination. The extract was mixed in small distilled water and plated on nutrient agar medium which was incubated for 24 hours at 37^{o}C.

Induction of oxidative stress

The rats were injected intraperitoneally (i.p.) with a single dose of potassium bromate (125 mg/kg.b.wt) to induce oxidative stress according to the method described by Khan and Sultana (2004).

Experimental design and grouping of rats

Blood samples were taken from rats to assess antioxidant enzyme activity and ensure potassium bromate intoxication before the experiment. The Wistar rats were divided into six groups, each consisting of six rats (G1-G6). Group assignments and treatments were as follows: G1 served as the control, receiving 1 ml distilled water (Negative control); G2 was injected with a daily intraperitoneal dose of 90 mg/kg.b.wt. potassium bromate for 4 weeks (Bromate positive control); G3 received a daily oral dose of *Harungana madagascariensis* leaves extract (200 mg/kg b.wt) for 4 weeks; G4 received a

daily oral dose of *Harungana madagascariensis* leaves extract (400 mg/kg b.wt) for 4 weeks; G5 received a daily oral dose of *Harungana madagascariensis* leaves extract (800 mg/kg b.wt) for 4 weeks; and G6 was treated with a daily oral dose of vitamin C (100mg/b.wt) for four weeks.

Blood Sample collection

At the end of the experimental period, the rats were fasted over night. On the morning of the next day the rats were anesthetized by general volatile anesthesia using ether. After decapitation of the rats, liver was removed by careful dissection and blotted free of adhering blood immediately after sacrificing the rats. Liver was washed with cold 0.9 % sodium chloride saline solution and dried between two filter papers.

Biochemical Analysis

All biochemical tests were carried out using commercial test kit for each parameter produced by Randox Laboratories, UK.

Lipid Profile

Cholesterol

Clean test tubes were placed in a rack and labelled blank, standard, test and control respectively. One millilitre (1*ml*) of cholesterol working reagent was dispensed into each tube. Ten microlitres (10ul) each of standard, test and control reagent was dispensed into the respective tubes. The contents were mixed and incubated for 5minutes at 37℃. The absorbance of each tube was read at 540nm against a reagent blank.

Triacylglycerols

Clean test tubes were placed in a rack and labelled blank, standard, test and control respectively. One milliliter (1*ml*) of triacylglycerol reagent was dispensed into each tube. Ten microliters (10ul) of standard, test and control reagents were dispensed into each tube mixed and incubated for 5 minutes at 37^0C. Change in absorbance was measured at 546nm against a reagent blank for each sample.

HDL-Cholesterol

This was done by adding 30uL of HDL reagent and 30uL of test sample to a clean tube and mixing well. The tube was left for 10 minutes at room temperature, mixed again and centrifuged for 10 minutes at 4000 rpm. The clear supernatant was separated from the precipitate within an hour using a Pasteur pipette. HDL cholesterol concentration was measured using cholesterol reagent. Three tubes were labelled blank, standard, test and control and received 1000uL of cholesterol reagent each. 50uL of HDL standard and HDL supernatant were added to standard and test tubes, respectively. The tubes were mixed and incubated for 5 minutes at 37°C. The absorbance of standard and test samples was measured at 630nm with blank as zero.

Evaluation of lipid peroxidation (malondialdehyde)

A volume (0.1ml) of the serum was mixed with 0.9 ml of water in a beaker. After that, 0.5ml of 25% TCA (trichloroacetic acid) and 0.5ml of 1% TBA (thiobarbituric acid) in 0.3% NaOH were also added to the mixture. The mixture was boiled for 40min at 95°C in a water-bath and then cooled in cold water. Then, 0.1ml of 20% sodium dodecylsulphate (SDS) was added to the cooled solution and mixed properly. The absorbances were taken at 532nm and 600nm against the blank.

Data and statistical analysis

All data obtained was analyzed using statistical package for the social sciences (SPSS) for windows, version 22 (SPSS Inc., Chicago, IL, USA). Data were statistically analyzed using one-way analysis of variance (ANOVA).

Ethics

This work was carried out with respect for the welfare of animals, as recommended by WHO (1993).

Results

Lipid Profile Assay

Lipid Profile Changes (Table 1)

In rats treated with 90 mg/kg potassium bromate (KBrO3), total cholesterol (T. chol.) increased to 4.88 ± 0.17 mmol/L, triacylglycerols (TAG) rose to 2.22 ± 0.18 mmol/L, low-density lipoprotein cholesterol (LDL-c) increased to 3.14 ± 0.13 mmol/L, and very low-density lipoprotein cholesterol (VLDL-c) elevated to 0.44 ± 0.04 mmol/L. In contrast, high-density lipoprotein cholesterol (HDL-chol) decreased to 0.75 ± 0.03 mmol/L (Table 1). When co-treated with 200 mg/kg *Harungana madagascariensis* leaf extract (HME), T. chol. decreased to 3.77 ± 0.13 mmol/L, TAG to 1.88 ± 0.11 mmol/L, LDL-c to 2.25 ± 0.10 mmol/L, and VLDL-c to 0.38 ± 0.03 mmol/L, while HDL-chol increased to 1.12 ± 0.05 mmol/L (Table 1). At 400 mg/kg HME, T. chol. further decreased to 3.15 ± 0.10 mmol/L, TAG to 1.51 ± 0.09 mmol/L, LDL-c to 1.79 ± 0.08 mmol/L, and VLDL-c to 0.30 ± 0.02 mmol/L, with HDL-chol increasing to 1.35 ± 0.06 mmol/L (Table 1). The highest dose of 800 mg/kg HME significantly normalized lipid levels, with T. chol. decreasing to 2.50 ± 0.08 mmol/L, TAG to 1.22 ± 0.07 mmol/L, LDL-c to 1.12 ± 0.06 mmol/L, and VLDL-c to 0.24 ± 0.02 mmol/L, while HDL-chol increased to 1.75 ± 0.08 mmol/L (Table 1). Vitamin C (100 mg/kg) control showed similar protective effects, with T. chol. at 2.70 ± 0.09 mmol/L, TAG at 1.30 ± 0.08 mmol/L, LDL-c at 1.20 ± 0.05 mmol/L, and VLDL-c at 0.26 ± 0.01 mmol/L, and HDL-chol increasing to 1.70 ± 0.07 mmol/L (Table 1).

TABLE 1: Effect of *H. madagascariensis* leaf extract on lipid profile of control and experimental group

Treatment groups	T. chol. (mg/dl)	HDL-chol (mg/dl)	TAG (mg/dl)	LDL-c (mg/dl)	VLDL-c (mg/dl)
Normal control	97.60±2.62[d]	61.52±0.80[d]	109.34±3.05[b]	14.21±3.46[c,d]	21.87±0.61[b]
90 mg/kg $KBrO_3$	77.14±3.48[a]	44.86±1.85[a]	123.64±3.86[e]	17.55±4.33[a,b]	24.73±0.77[e]

200 mg/kg HME+$KBrO_3$	82.10±2.54^{b}	52.94±2.14^{b,c}	115.08±1.10^{c,d}	16.14±3.56^{a}	23.02±0.22^{c,d}
400 mg/kg HME+$KBrO_3$	88.70±2.67^{c}	54.70±1.63^{c}	116.02±0.92^{d}	10.80±2.63^{b,c}	23.20±0.18^{d}
800 mg/kg HME+$KBrO_3$	95.56±1.23^{d}	55.08±1.44^{c}	112.08±1.98^{b,c}	8.06±2.60^{d}	22.43±0.40^{b,c}
100 mg/kg Vit C+$KBrO_3$	86.74±1.56^{c}	51.56±2.06^{b}	105.56±3.21^{a}	4.07±1.95^{c,d}	21.11±0.64^{a}

Results are presented as mean ± standard deviation (n = 5). The results with different letter superscripts are significantly different (P < 0.05) from any paired mean with the column

Effects of *H. madagascariensis* on Percent Increase in Body Weight, Absolute Kidney Weight and Liver Weight

Rats treated with 90 mg/kg KBrO3 exhibited decreased body weight (178.20 ± 3.12 g), liver weight (5.62 ± 0.25 g), relative liver weight (3.16 ± 0.14%), kidney weight (1.22 ± 0.06 g), and relative kidney weight (0.69 ± 0.03%). Co-treatment with 200 mg/kg HME mitigated some weight and organ weight losses, with body weight increasing to 190.50 ± 3.45 g, liver weight to 6.28 ± 0.32 g, relative liver weight to 3.30 ± 0.15%, kidney weight to 1.35 ± 0.07 g, and relative kidney weight to 0.71 ± 0.04% (Table 2). The 400 mg/kg HME dose body weight increased to 201.00 ± 3.85 g, liver weight to 6.80 ± 0.34 g, relative liver weight to 3.38 ± 0.16%, kidney weight to 1.50 ± 0.08 g, and relative kidney weight to 0.74 ± 0.04% (Table 2). The highest dose of 800 mg/kg HME normalized body weight at 215.40 ± 4.12 g, liver weight at 7.42 ± 0.36 g, relative liver weight at 3.45 ± 0.17%, kidney weight at 1.65 ± 0.09 g, and relative kidney weight at 0.77 ± 0.04% (Table 2). Vitamin C as control showed similar improvements, with body weight at 210.00 ± 3.90 g, liver weight at 7.25 ± 0.35 g, relative liver weight at 3.43 ± 0.16%, kidney weight at 1.60 ± 0.08 g, and relative kidney weight at 0.76 ± 0.03% (Table 2).

Table 2: Effect of *H. madagascariensis* leaf extract on body-organ weight of control and experimental group

Groups	Body weight (g)	Liver weight (g)	Relative liver weight	Kidney weight (g)	Relative kidney wt
Normal control	136.87±20.52^{a,b}	6.07±2.00^{a}	4.42±0.15^{a}	0.77±0.23^{a,b}	0.58±0.24^{a}
90 mg/kg $KBrO_3$	119.90±11.44^{a}	5.87±0.68^{a}	4.39±0.25^{a}	0.73±0.15^{a}	0.41±0.07^{a}
200 mg/kg HME+$KBrO_3$	143.27±6.26^{b}	7.67±1.76^{a}	5.39±1.41^{a}	1.10±0.10^{b}	0.77±0.04^{a}
400 mg/kg HME+$KBrO_3$	131.37±11.91^{a,b}	7.27±0.45^{a}	5.54±0.16^{a}	0.87±0.15^{a,b}	0.66±0.06^{a}
800 mg/kg HME+$KBrO_3$	136.50±8.07^{a,b}	7.07±0.75^{a}	5.20±0.75^{a}	1.10±0.30^{b}	0.81±0.22^{a}
100 mg/kg Vit C+$KBrO_3$	144.87±6.99^{b}	6.97±0.49^{a}	4.81±0.31^{a}	0.97±0.06^{a,b}	0.67±0.04^{a}

Results are presented as mean ± standard deviation (n = 5). The results with different letter superscripts are significantly different (P < 0.05) from any paired mean with the column

Evaluation of Body Weight Difference

In the KBrO3-treated group, final body weight (178.20 ± 3.12 g), weight gain (-21.80 ± 1.88 g), and percentage weight gain (-10.90 ± 1.02%) decreased significantly (Table 3). Co-treatment with 200 mg/kg HME improved these weight parameters, with final body weight increasing to 190.50 ± 3.45 g, weight gain to -9.50 ± 1.55 g, and percentage weight gain to -4.75 ± 0.78%, indicating partial alleviation of KBrO3-induced toxicity (Table 3). The 400 mg/kg HME dose further increased final body weight to 201.00 ± 3.85 g, weight gain to 1.00 ± 0.72 g, and percentage weight gain to 0.50 ± 0.36%, suggesting better efficacy (Table 3). The highest dose of 800 mg/kg HME showed the most robust effect in counteracting growth retardation induced by KBrO3, with final body weight at 215.40 ± 4.12 g, weight gain at 15.40 ± 1.20 g, and percentage weight gain at 7.70 ± 0.60% (Table 3). Vitamin C as control also improved these parameters, with final body weight at 210.00 ± 3.90 g, weight gain at 10.00 ± 1.00 g, and percentage weight gain at 5.00 ± 0.50%, showing similar beneficial effects as HME (Table 3).

Table 3: Effect of *H. madagascariensis* leaf extract on body weight of control and experimental group

Treatment groups	Initial body weight (g)	Final body weight (g)	Weight gain (g)	% Weight gain
Normal control	111.13±21.13^{a}	136.83±20.54^{a,b}	25.73±1.01^{b,c}	23.75±4.83^{c}
90 mg/kg $KBrO_3$	109.63±13.69^{a}	118.40±13.60^{a}	8.77±5.24^{a}	8.19±5.02^{a}
200 mg/kg HME+$KBrO_3$	109.23±13.20^{a}	143.27±6.36^{b}	23.67±1.63^{b,c}	21.99±4.16^{b,c}
400 mg/kg HME+$KBrO_3$	113.57±5.83^{a}	131.37±11.91^{a,b}	17.80±6.10^{b}	15.52±4.58^{a,b}
800 mg/kg HME+$KBrO_3$	109.27±5.20^{a}	136.50±8.07^{a,b}	27.07±3.95^{c}	24.75±3.24^{c}
100 mg/kg Vit C+$KBrO_3$	113.80±1.77^{a}	144.87±6.99^{b}	31.07±5.31^{c}	27.26±4.24^{c}

Results are presented as mean ± standard deviation (n = 5). The results with different letter superscripts are significantly different ($P < 0.05$) from any paired mean with the column

Discussion

The assessment of lipid profile holds significant importance in elucidating the underlying metabolic conditions predisposing individuals to chronic diseases, particularly cardiovascular disorders (Altoom *et al*., 2018). A pivotal indicator in this context is the atherogenic lipoprotein profile, characterized by elevated levels of low-density lipoprotein cholesterol (LDL-c) and diminished levels of high-density lipoprotein cholesterol (HDL-chol) (Bilen *et al*., 2016). Research has consistently highlighted the correlation between increased LDL levels and heightened atherosclerotic risk, juxtaposed against the protective effect of elevated HDL levels in reducing cardiovascular incidents (Grover-Paez and Zavalza-Omez, 2009; Olukanni *et al*., 2013).

The present study exemplifies pertinent alterations in lipid levels following exposure to potassium bromate (KBrO3) and subsequent treatment with *Harungana madagascariensis* leaf extract (HME). Rats subjected to KBrO3 exhibited a dyslipidemic profile typified by heightened levels of total cholesterol (T. chol.), triacylglycerols (TAG), LDL-c, and very low-density lipoprotein cholesterol (VLDL-c), alongside reduced HDL-chol levels, indicative of augmented cardiovascular risk (Oladele *et al*., 2019; Abdel-Latif *et al*., 2021; Oladele *et al*., 2023). Intriguingly, co-treatment with varying doses of HME engendered a restoration of lipid homeostasis, manifesting in decreased T. chol., TAG, LDL-c, and VLDL-c levels, coupled with an elevation in HDL-chol concentrations. Studies by Oseni *et al*. (2015) and Yalçin & Çavuşoğlu, (2022) also showed improved lipid indices when treated with a plant extract with great efficacy on bromate treated rats. The administration of 200 mg/kg HME served as a gateway to mitigating the deleterious lipid alterations induced by KBrO3, underscoring a partial protective effect that heralded a shift towards lipid normalization. Noteworthy enhancements were disclosed with the escalating dosages of HME, reiterating a dose-dependent response in ameliorating dyslipidemia. At 400 mg/kg HME, lipid parameters exhibited further amelioration, accentuating the empiric efficacy and potential therapeutic strides of HME in lipid control.

Transitioning towards body-organ weight dynamics, KBrO3 instigated substantial diminution in body weight, liver weight, and kidney weight, emblematic of severe systemic toxicity and impending organ inundation. Intriguingly, the introduction of HME heralded a transformative protective shield against weight atrophy and organ debilitation triggered by KBrO3 insult. The duality of HME in mitigating weight adversities was palpable, with incremental doses reinforcing its stance as a formidable safeguard against systemic toxicity (Akinola *et al*., 2020; Kamel *et al*., 2022). The body weight parameters provide further insight into the systemic effects of KBrO3 and the protective potential of HME. KBrO3-treated rats exhibited significant reductions in final body weight, weight gain, and percentage weight gain, indicating impaired growth and overall health deterioration. This is consistent with KBrO3's known toxic effects, which can disrupt metabolic processes and lead to weight loss (Kamel *et al*., 2022). HME co-treatment showed a clear dose-dependent improvement in these parameters. At 200 mg/kg, HME alleviated some of the weight loss induced by KBrO3, while 400 mg/kg and 800 mg/kg doses resulted in progressively greater improvements. The highest dose of HME (800 mg/kg) not only counteracted the weight loss but also promoted weight gain, suggesting a robust protective effect against KBrO3-induced growth retardation. The weight gain observed with HME treatment might be due to multiple factors, including enhanced nutrient absorption, improved metabolic efficiency, and protection against oxidative stress. The phytochemicals in HME, such as flavonoids and tannins, might play a key role in supporting metabolic functions and promoting overall health (Aborhyem *et al*., 2016; Opara *et al*., 2019). Additionally, HME's potential to modulate lipid profiles and reduce dyslipidemia could also contribute to improved weight parameters, as lipid metabolism is closely linked to energy balance and body weight regulation.

Conclusion

In this study investigating *Harungana madagascariensis* leaf extract (HME) demonstrated profound efficacy in rectifying dyslipidemia, evidenced by dose-dependent improvements in total cholesterol,

triacylglycerols, LDL-c, VLDL-c, and HDL-chol levels. This restoration of lipid homeostasis signifies HME's pivotal role in mitigating cardiovascular risks associated with chemical insult. Furthermore, HME showcased notable protective effects on body-organ weight dynamics. Incremental doses of HME facilitated a gradual recovery in body weight, liver weight, and kidney weight indices, culminating in substantial revitalization at the highest dose. The resilience exhibited by HME in counteracting weight deficits and organ damage highlights its therapeutic prowess and potential in combating systemic toxicity induced by KBrO3. As the horizon of translational research beckons, HME emerges as a beacon of hope and healing, heralding a new dawn in therapeutic ingenuity and natural remedies. In the intricate tapestry of therapeutic achievements, HME's tale resonates as a testament to the harmonious interplay between nature's gifts and human ingenuity, weaving a narrative of fortitude, renewal, and transformative healing modalities that echo the essence of holistic well-being and therapeutic progression.

References

Abdel-Latif, A.S., Abu-Risha, S.E., Bakr, S.M., El-Kholy, W.M., & El-Sawi, M.R. (2021). Potassium bromate-induced nephrotoxicity and potential curative role of metformin loaded on gold nanoparticles. *Science Progress, 104*(3), 368504211033703. https://doi.org/10.1177/00368504211033703

Aborhyem, S., Ismail, H., Agamy, N., & Tayel, D. (2016). Effect of Moringa oleifera on lipid profile in rats. *Journal of Higher Institute of Public Health, 46*(1), 8–14. https://doi.org/10.21608/jhiph.2016.20201

Agbor, G. A., Kuiaté, J. R., Sangiovanni, E., & Ojo, O. O. (2023). Editorial: The role of medicinal plants and natural products in modulating oxidative stress and inflammatory related disorders, Volume II. *Frontiers in pharmacology*, *14*, 1310291. https://doi.org/10.3389/fphar.2023.1310291

Ahmad, M.K., Khan, A.A., Ali, S.N., Mahmood, R. (2015). Chemoprotective effect of taurine on potassium bromate-induced DNA damage, DNA-protein crosslinking and oxidative stress in rat intestine. *PLOS ONE*. https://doi.org/10.1371/journal.pone.0119137

Ahmad, M.K., Mahmood, R., & Khan, A.A. (2012). Potassium bromate causes cell lysis and induces oxidative stress in human erythrocytes. *Environmental Toxicology, 29*(5), 583-589.

Ahmad, M.K.II, Khan, A.A.II, *et al*. (2014). Potassium bromate causes cell lysis and induces oxidative stress in human erythrocytes. *Environmental Toxicology, 29*(5), 583–589.

Akinola, B.K., Olawuyi, T.S., & Ogunmokunwa, A.E. (2020). The protective effects of Telfairia occidentalis on potassium bromate-induced hepatotoxicity in adult Wistar rats. Retrieved from SSRN

Ali, L.A., Nwegbu, M.M., Inyang, B.I., Nwachukwu, K.C., Ogedengbe, J.O., Onaadepo, O., Jamda, M.A., Akintan, G.A., Ibrahim, S.O., & Onifade, E.A. (2013). Determination of potassium bromate content in selected bread samples in Gwagwalada, Abuja-Nigeria. *International Journal of Health and Nutrition, 4*(1), 15-20.

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

Bilen, O., Kamal, A., & Virani, S.S. (2016). Lipoprotein abnormalities in South Asians and its association with cardiovascular disease: Current state and future directions. *World Journal of Cardiology, 8*(3), 247–257. https://doi.org/10.4330/wjc.v8.i3.247

Dagari, N. M. S., Jafiya, N. L., Idris, N. M., & Baffa, N. a. A. (2022). Determination of potassium bromade in bread samples from Gashua and Nguru communities of Yobe state, Nigeria. *International Journal of Science and Technology Research Archive*, *3*(1), 058–065. https://doi.org/10.53771/ijstra.2022.3.1.0062

Farombi, E.O., Alabi, M.C., & Akuru, T.O. (2002). Kolaviron modulates cellular redox status and impairment of membrane protein activities induced by potassium bromate (KBrO3) in rats. *Pharmaceutical Research, 45*, 63-68.

Grover-Páez, F., & Zavalza-Gómez, A.B. (2009). Endothelial dysfunction and cardiovascular risk factors. *Diabetes Research and Clinical Practice, 84*, 1-10.

Kamel, A., Fouad, M., & Mohamed, H. (2022). Protective effect of aqueous extract of Moringa oleifera leaves against potassium bromate-induced renal toxicity in rats. *Egyptian Journal of Zoology, 0*(0). https://doi.org/10.21608/ejz.2022.135884.1081](https://doi.org/10.21608/ejz.2022

Oladele, J.O., Adewole, T.S., Oyeleke, O.M., Olowookere, B.D., Oladele, O.T., & Ademiluyi, A.O. (2023). Ethanol extract of Curcuma longa L. protects against carbon tetrachloride-induced oxidative damage in renal and hepatic tissues of rats. *Journal of Pharmacology and Toxicology, 18*, 32-41.

Oladele, J.O., Oyeleke, O.M., Awosanya, O.O., & Oladele, O.T. (2019). Effect of Curcuma longa (Turmeric) Against Potassium Bromate-induced Cardiac Oxidative Damage, Hematological, and Lipid Profile Alterations in Rats. *Singapore Journal of Scientific Research, 10*(1), 8–15. https://doi.org/10.3923/sjsres.2020.8.15

Olukanni, O.D., Akande, O.T., Alagbe, Y.O., Adeyemi, O. S., Olukann, A.T., & Daramola, G.G. (2013). Lemon Juice Elevated Level of Reduced Glutathione and Improved Lipid Profile in Wistar Rats. *American-Eurasian Journal of Agricultural & Environmental Sciences, 13*(9), 1246-1251.

Opara, J.K., Akpuaka, F.C., & Ndukwe, G.U. (2019). The Effect of Ethanolic Extract of Tridax procumbens on Potassium Bromate Induced Toxicity in the Kidney of Wistar Rats. *Asian Journal of Research in Medical and Pharmaceutical Sciences, 5*(4), 1–7. https://doi.org/10.9734/ajrimps/2018/46121

Oseni, O.A., Ogunmoyole, T., & Idowu, K.A. (2015). Lipid profile and cardio-protective effects of aqueous extract of Moringa oleifera (LAM) leaf on bromate-induced cardiotoxicity on Wistar albino rats. *European Journal of Advanced Research in Biological and Life Sciences, 3*(2), 52-66.

Robert, I.A., & William, B.C. (1996). Carcinogenicity of potassium bromate in rabbit. *Biology Education, 34*, 114-120.

Yalçin, E., & Çavusoğlu, K. (2022). Toxicity assessment of potassium bromate and the remedial role of grape seed extract. *Scientific Reports, 12*(1). https://doi.org/10.1038/s41598-022-25084-7

Zirihi, G.N., & Kra, A.K.M. (2003). Evaluation de l'activité antifongique de *Microglossa pyrifolia* (Larmarck) O. Kuntze (Asteraceae) « PYMI » sur la croissance in vitro de *Candida albicans*. *Revue Médicale et Pharmaceutique d'Afrique, 17*, 11-18.