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Original Research Article

Impact of *Corchorus olitorius* Leaf Extract on Potassium Bromate-Induced Haematological Parameters Derangement in Rats

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ABSTRACT

Blood is one of the human tissues in which potassium bromate ($KBrO_3$) is hazardous. This investigation aims to assess the impact of *Corchorus olitorius* (*C. olitorius*) on $KBrO_3$-induced haematological parameters derangement. *C. olitorius* leaves were extracted with a soxhlet extractor and a solvent of 95% ethanol. Groups A, B, C, and D were created from twenty-four mature male Wistar rats acclimated for seven days. Group A was given distilled water orally. In addition to the 100 mg/kg b.w of $KBrO_3$ given to groups B, C, and D of animals, 100 and 200 mg/kg body weight of *C. olitorius* were also administered to groups C and D respectively. After the 28-day treatment period, blood samples were collected for examination. Animals intoxicated with $KBrO_3$ demonstrated substantial ($P<0.05$) decrease in most blood parameters compared to the animals in the control group (haemoglobin level, red blood cell count, packed cell volume, total white cell count, neutrophil count, lymphocyte count, monocyte count and platelet count). The disordered haematological parameters were, however, dose-dependently corrected in the potassium bromate-intoxicated rats treated with *C. olitorius*. $KBrO_3$ caused a significant decrease in haemoglobin level, red blood cell count, packed cell volume, total white blood cell count, neutrophil count, lymphocyte count, monocyte count and platelet count as well as elevated erythrocyte sedimentation rate (ESR), but *C. olitorius* treatment reversed these effects. Therefore, more studies are needed to further validate these findings.

Keywords: *Corchorus olitorius*, Haemoglobin level, Platelet, Potassium bromate, White blood cell

Introduction

Potassium bromate ($KBrO_3$) is a white crystal granule that is colourless, odourless, and tasteless.[1] It is added to beer, cheese, bread, and fish paste as a conditioner, and flour as a maturing agent, while having no medicinal use.[2] Furthermore, $KBrO_3$ is utilized in cold-waving hair treatments.[3]

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Potassium bromate has a density of 3.27 (g/cm^3) and a vapour density of 5.8 (air=1), which can cause a fire when it comes into contact with flammable materials. It cannot coexist with reducing agents, aluminium, organic materials, finely powdered metals, and other substances.[4] It releases deadly bromine fumes when heated. It is completely soluble in water and should mostly take on an ionic form at the pH of drinking water.[5] The potassium bromate issue originally surfaced during the ozonation of drinking water, which results in bromate as the main waste. Six rats exposed to $KBrO_3$-containing water developed kidney cancer, according to research carried out to validate the safety of ozone-infused water. Numerous nations, health organizations, and agencies began outlawing the use of $KBrO_3$ as a result of these results. Potassium bromate was prohibited in some nations like the United Kingdom in 1990 and Canada in 1994. Belgium, Greece, Norway, Denmark, Spain, Portugal, Japan, and Switzerland are more nations where $KBrO_3$ has been taken from the list of approved food additives.[2] In 1993, WHO also prohibited the use of $KBrO_3$.[5] The National Agency for Food and Drug Administration and Control (NAFDAC) in Nigeria undertook consultations with the Association of Master Bakers across the nation in 2002 regarding the risks associated with using $KBrO_3$ in bread and the necessity of ceasing usage of it. Many bakers continue to use the prohibited drug

despite NAFDAC raising awareness of the risks associated with using $KBrO_3$ as a flour enhancer.[4] In Nigeria, no technology is currently available to identify food products containing $KBrO_3$ or the potentially harmful effects it may have on human health. However, numerous studies conducted in various nations of the world have demonstrated that $KBrO_3$, whether eaten in food or water, is harmful to health. Its nephrotoxicity has been demonstrated in both experimental animals and humans.[7] Additionally, it leads to thyroid follicular cell tumours, peritoneal mesotheliomas, and renal cell tumours.[8] Renal failure, methaemoglobinaemia, and kidney cancer have all been linked to potassium bromate's kidney-damaging oxidative stress.[9,10] The development of blood cells is known as haemopoiesis and occurs in the bone marrow throughout life. Haematopoietic stem cells are the origin of all cellular blood components.[11] In order to keep the peripheral circulation's steady state levels, an adult in good health produces 10^{11}–10^{12} new blood cells every day.[12,13] Haemolysis is typically used to remove defective red blood cells (RBCs) from circulation.[14] After a banked blood transfusion, haemolysis might also happen. Particularly, mounting data support the idea that prolonging the time between blood donation and transfusion reduces RBC recovery, which in turn heightens post-transfusional haemolysis.[15,16] Red blood cells (erythrocytes) are lysed, releasing their cytoplasmic content into the plasma.[17] Both *in vivo* and *in vitro* haemolysis are possible. Haemolysins, toxin-producing bacteria or fungi that are pathogenic, are one source of haemolysis. Another factor is intense exercise.[18] Haemolysins break down the RBC's membrane, causing lysis and ultimately the cell's termination.[19] In non-industrialized countries, medicinal plants are more affordable than the majority of expensive pharmaceutical goods used to cure illnesses, and this trend is rapidly accelerating.[20] Despite advancements in traditional medicine, herbs have been adopted into healthcare systems throughout several countries. When used properly and in the right amount, natural products are thought to be less dangerous than synthetic ones, which frequently have adverse effects.[20] Mallow leaves from the *Corchorus olitorius* (Malvaceae) plant are frequently used as a leafy vegetable. Various ailments, including tumours, chest pain, gonorrhoea, enteritis, fever, dysentery, and others, were reportedly treated with the leaves in traditional medicine.[21] 'Ewedu' is the common name for a green leafy vegetable (*C. olitorius*) in southwestern Nigeria. Although *C. olitorius* is also known as bush okra or jute mallow in English, the Igbo people of southeast Nigeria refer to it as "Ahihara." The *C. olitorius* plant can also be found in Egypt, Sudan, Malaysia, South America, the Caribbean, and Nigeria.[22]

A significant number of mucilaginous polysaccharides, ascorbic acid, carotene, calcium, potassium, phosphate, iron, and other nutrients form the composition of the plant.[23] The toxicological effect and makeup of the phytochemicals have both been studied.[23] Because of its demulcent, diuretic, purgative, bitter tonic, laxative, refrigerant, carminative, and lactagogue properties, *C. olitorius* is used in medicine.[24] Positive results have been seen when utilising the leaf extract to treat chronic cystitis and dysuria. It has a strong antibacterial effect that has been documented, consistent with its historical use to treat gonorrhoea, fever, and dysentery.[23,24] According to Airaodion et al. [25], the leaves effectively attenuate oxidative stress in Wistar rats induced by ethanol administration. Furthermore, its hypolipidemic and hypoglycemic effects have been noted.[26] A recent investigation revealed the hematopoietic properties of *C. olitorius* leaves.[22] However, there are few studies documenting the benefit of ethanolic extracts of *C. olitorius on* haematological parameters in potassium Bromate-intoxicated Wistar rats. As a result, this study used Wistar rats to conduct an experimental investigation into the impact of $KBrO_3$ on haematological indices and the probable protective effects of *C. olitorius* ethanolic leaf extract.

Materials and methods

Plant collection and identification

Fresh *C. olitorius* (jute) plants were obtained from the Institute of Agricultural Research and Training in Ibadan, Nigeria in May 2021. They were identified and authenticated with the voucher number IART106752**.** The spoilt ones were discarded after carefully detaching the leaves from the stem. They were thoroughly cleansed to remove the impurities while submerged in water. They were air-dried in the laboratory at room temperature for 14 days and then processed through an electric blender to form a powder.

Plant Extraction

The extraction was carried out using a soxhlet device using ethanol as the solvent, following the guidelines provided by Airaodion et al. [28, 27] A round-bottom flask holding 250 mL of 95% ethanol was filled with twenty-five grams (25 g) of the sample, which was then connected to a heating mantle along with a condenser and soxhlet extractor. The heating mantle heated the solvent as it went through the apparatus and caused it to evaporate at the condenser. The sample-carrying thimble was held in a reservoir that the condensate fell into. The cycle was repeated when the solvent lev+el reached the siphon and was refilled into the flask with a flat bottom. An entire eighteen hours were allotted to the task. After the procedure was completed, the ethanol was evaporated at 35 ^{o}C in a rotary evaporator, yielding 2.28 g and a 9.12% yield percentage. For additional analysis, the extract was kept cold, at 4 ^{o}C, in the refrigerator.

Experimental design

Twenty-four (24) mature male Wistar rats (*Rattus norvegicus*) weighing between 140 and 160 g were used in the experiment. They had seven (7) days to get used to the laboratory environment before the experiment. The rats had unrestricted access to rat food and water in cages made of wire mesh. They were housed in conditions with temperature control, 12-hour light and dark cycles, and regulated humidity. This study was approved by the ethics committee with approval number FNAS2411062. The protocols and criteria set forth by the committee were adhered to throughout the experiment. Throughout this study, both the Declaration of Helsinki and the guidelines of the Committee for the Control and Supervision of Experiments with Animals were adhered to. Furthermore, the National Studies Council's rules were followed when conducting animal studies.[29] The rats were divided into groups A, B, C, and D at random. As a therapy, Group A (control group) was given distilled water orally. In addition to groups B, C, and D receiving 100 mg/kg body weight of potassium bromate, animals in groups C and D also received 100 and 200 mg/kg body weight of *C. olitorius* extract. Rats were given oral doses of *C. olitorius* extract and freshly made potassium bromate solution every day for 28 days. The animals were given modest diethyl ether sedation and then murdered twenty-four hours after the previous treatment. A heart puncture was used to obtain blood.

Estimation of haematological parameters

Following the manufacturer's instruction, full blood count and red blood cell indices were done using a haematology auto-analyser.

Estimation of erythrocyte sedimentation rate (ESR

The Westergreen method, as outlined by Ogbuagu et al., [30] was utilized in the estimation of the ESR. The anticoagulated blood sample was put into a syringe containing 0.4 mL of 2.8% sodium citrate at the 2 ml mark. Following its elevation over the zero point in the calibrated Westergren tube, the mixture was suctioned upward. With the index finger, the tube's top was swiftly sealed, and it was then slowly spun until the upper level of blood was precisely at the zero mark. Following that, the clock was set to run for an hour while the temperature was also recorded. After one hour, the height of the clear fluid above the top of the red blood cell column was measured in mm/hr.

Statistical analysis

The Anderson-Darling test was utilized to assess the data's normality and check for homogeneity variances before further statistical investigation. The mean and standard deviation were used to express the normally distributed data. PRISM statistical software (Graph Pad

Software) was used to analyse significant differences between the groups using one-way ANOVA and Tukey's test for multiple comparisons. At *P<0.05*, differences were deemed statistically significant.

Results and Discussion

Effect of C. olitorius on red blood cell parameters of potassium bromate-induced rats

$KBrO_3$ is widely included in at-home cold wave hair products as a neutralizer and bread-improving addition. This has led to several cases of unintentional child poisoning. It is forbidden in several nations due to its possible negative consequences.[31] The current investigation found that *C. olitorius* medication reduced the groups' $KBrO_3$-induced haematological alterations (table 1). The current study's reduced RBC counts could be a result of $KBrO_3$'s detrimental effects on bone marrow and haematological tissues. Additionally, oxidative stress is a crucial factor in the RBC membrane's disintegration and subsequent loss of deformability. According to earlier research, $KBrO_3$ causes oxidative stress in a few different human organs.[9, 10] Additionally, oxidative stress facilitates macrophages' elimination of faulty red blood cells from circulation.[32] These results are supported by a study that found that $KBrO_3$ therapy dramatically decreased the levels of Hb, PCV, and MCV while also lowering the counts of WBC and RBC.[33] The present study's outcomes are in line with those of a previous investigation, [34] which discovered that rats administered a 100 mg/kg body weight dose of $KBrO_3$ therapy saw noteworthy reductions in RBC and Hb. The reduction in blood erythrocyte parameters observed in this study may indicate that $KBrO_3$ reduced the kidneys' ability to release erythropoietin, the humoral regulator of RBC synthesis, blood oxygen transport capacity, and tissue oxygen uptake. Since haemoglobin (Hb) and red blood cells are necessary for the transportation of respiratory gases, the reduction in levels of RBC indices seen in this investigation may have also affected respiratory gas transportation in the treated animals.[35,36] The results demonstrate that concurrent treatment of $KBrO_3$ and *C. olitorius* ethanolic leaf extract corrected alterations in haematological parameters caused by $KBrO_3$ toxicity.

Effect of C. olitorius on white blood cell parameters and platelet of potassium bromate-induced rats

Leukocyte and platelet counts in the study's animal groups treated with $KBrO_3$ alone were observed to be considerably lower than those in the control group (table 2). Consuming compounds like bromate has also been linked to lower leucocyte counts.[37] The drop in leucocyte count is consistent with the study, [38] who reported a 30-month-old child's leucocyte count dropping from 15,500/mm^3 to 9,600/mm^3 over the course of 8 weeks following the consumption of a half glass of a neutralizer with potassium bromate as a constituent. The oxidative stress caused by potassium bromate in these cells may have resulted in DNA strand breakage, which could account for observed declines in the leucocyte and platelet counts.[39, 40] In addition, bone marrow suppression and selective megakaryocyte depression may have occurred.[39] However, it's also plausible that $KBrO_3$ damages platelets directly.[40] Thus, the reductions in RBCs, WBCs, and platelets might point to a particular systemic harmful consequence of $KBrO_3$. This result corresponds to an earlier report, [38] but it's in contrast with another investigation, [41] which showed a rise, in WBC when mice were exposed to $KBrO_3$. The study hypothesized that $KBrO_3$'s impact in causing a rise in WBC may be connected to inflammatory conditions[41]. The number of platelets (PLT) in the rats in the $KBrO_3$-administered groups significantly decreased when compared to the controls (table 2). PLT are crucial for blood clotting and help stop blood loss. The fact that the study's platelet counts significantly decreased could mean that $KBrO_3$ hindered platelet-activating factor's (PAF) activity and reduced blood clotting potentials. It might also be a sign that it might increase the production of thrombopoietin.[42] Therefore, potassium bromate may negatively impact platelet count. Akinola et al. reported similar outcomes.[43] The decrease in PLT may have been the consequence of DNA strands breaking within the cells as a result of KBrO3-induced oxidative stress.[44] $KBrO_3$ probably hampered the body's normal process of phagocytosing and getting rid of harmful bacteria, viruses, and other invaders because the animals in the $KBrO_3$ exposure group had significantly lower neutrophil counts than the animals in the control group (table 2). [45, 46] Nevertheless, the haematological parameters improved in rats treated with both $KBrO_3$ and *C. olitorius* extract. These results are in line with a previous investigation by Chipman et al. [44] This data could suggest that the tissue damage brought on by $KBrO_3$ activated the rats' immunity.[47, 48] *C. olitorius* leaf extract at similar dosages reduced the liver damage induced by $KBrO_3$, according to a recent study. The bioactive components of *C. olitorius* leaves, including saponins, flavonoids, and steroid glucosides, may be the cause of the rise in WBC indices and platelet counts.[49] It has been reported that the animals' capacity to function well under extremely stressful circumstances is correlated with their large proportion of WBC, particularly lymphocytes [50]. This is in line with the results of the study which described how *C. olitorius* leaf ethanolic extract affected Wistar rat haematological parameters.[22] The fact that the WBC and lymphocyte percentage counts increased shows that the bioactive components of the extracts induced stress responses. The presence of glycosides in this plant may be the cause of its impact on the overall WBC count. Glycosides are essential for controlling the inflammatory processes of many clinical disorders linked to bacterial infections, malaria, and hepatic ailments because they include anti-inflammatory chemicals.[51] This could also mean that *C. olitorius* leaves stimulated the immune system by controlling several cytokines.[25]

Effect of C. olitorius on erythrocyte sedimentation rate (ESR) of $KBrO_3$*-induced rats*

In this investigation, we found that $KBrO_3$ raised the erythrocyte sedimentation rate (ESR) relative to the untreated animals (figure 1). According to another study, factors that could cause a rise in ESR include inflammation, pregnancy, anaemia, autoimmune diseases (including lupus and rheumatoid arthritis), infections, some kidney conditions, and some malignancies (such as lymphoma and multiple myeloma).[52] This supported the recently observed negative impact of $KBrO_3$ on the kidney and liver parameters. [8,53] Additionally, this corroborated the decreased haematological indices seen in this study. The maximum effect was observed at 200 mg/kg of *C. olitorius* extracts, which decreased the effect of $KBrO_3$ on ESR.

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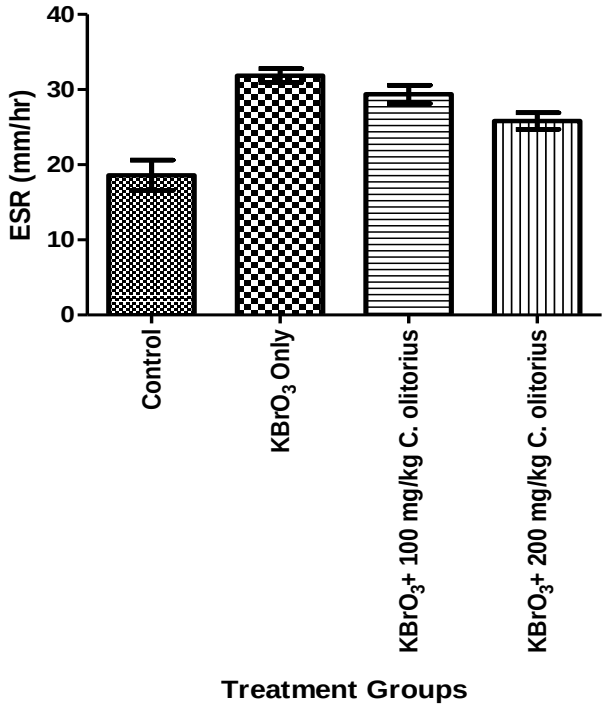

Figure 1: Effect of *C. olitorius* on Erythrocyte Sedimentation Rate (ESR) of Potassium Bromate-induced Rats

Table 1: Effect of *C. olitorius* on Red Blood Cell Parameters of Potassium Bromate-induced Rats

Parameters	Control	100 mg/kg $KBrO_3$ only	100 mg/kg $KBrO_3$ + 100 mg/kg *C. olitorius*	100 mg/kg $KBrO_3$ + 200 mg/kg *C. olitorius*	p-value
Hb (g/dL)	17.26±2.84	13.25±1.25	13.72±1.22	14.46±1.30	0.04
PCV (%)	39.73±2.58	27.93±1.44	29.37±3.42	36.36±1.49	0.03
RBC ($x10^{12}$/L)	5.12±0.83	3.47±0.22	4.51±0.44	4.86±0.88	0.01
MCV (FL)	75.10±7.23	80.49±4.53	79.25±4.94	77.83±4.92	2.36
MCH (pg)	28.85±3.84	29.54±4.24	28.83±2.62	27.15±2.48	1.52
MCHC (g/dL)	3.84±0.96	3.67±0.28	4.04±1.21	3.74±0.35	3.01

Values are presented as Mean±S.D, where n = 6.
Legend: PCV = Packed Cell Volume; Hb = Haemoglobin; RBC = Red Blood Cell; MCV = Mean Corpuscular Volume; MCH = Mean Corpuscular Haemoglobin; MCHC = Mean Corpuscular Haemoglobin Concentration

Table 2: Effect of *C. olitorius* on White Blood Cell Parameters and Platelet of Potassium Bromate-induced Rats

Parameters	Control	100 mg/kg $KBrO_3$ only	100 mg/kg $KBrO_3$ + 100 mg/kg *C. olitorius*	100 mg/kg $KBrO_3$ + 200 mg/kg *C. olitorius*	P Value
WBC ($x10^9$/L)	9.12±1.05	7.03±1.37	8.00±0.73	8.83±1.23	0.02
	241.26±11.34	218.25±17.34	232.32±9.36	237.72±11.75	

Platelet (x10^9/L)					0.00
Neutrophils (μL)	5.84±1.35	2.46±0.11	4.11±0.36	5.28±0.43	0.00
Lymphocytes (x10^9/L)	4.17±1.12	2.68±0.26	2.94±0.36	3.53±0.86	0.01
Monocytes (x10^9/L)	0.80±0.07	0.34±0.00	0.52±0.00	0.65±0.00	0.03

Values are presented as Mean±S.D, where n = 6.
Legend: WBC = White Blood Cell

According to reports, *C. olitorius* leaves have significant minerals such Ca, Mg, K, Na, Mn, Fe, and Zn concentrations.[23,54] The body needs calcium, a particularly significant mineral, to develop bones and neurological function.[54] Sodium is a crucial mineral that aids in controlling body fluids and preserving the electric potential that exists in body tissue. An essential element known as zinc has been linked to numerous enzymes, particularly those involved in the formation of ribonucleic acid.[55] Iron is fundamentally necessary for the production of blood and is crucial for the central nervous system's proper operation.[56] Iron also makes it easier for lipids, proteins, and carbohydrates to be oxidized. Magnesium is crucial for the metabolism of calcium in the bones and preventing cardiovascular disorders. Additionally, it helps control the release of insulin and blood pressure.[57] The body needs copper for the synthesis of enzymes and the movement of biological electrons.[55] Therefore, the extract would have superior nutritional value due to its high mineral concentration.

The presence of phytochemicals such as flavonoids, tannins, and alkaloids may also contribute to the hemopoietic stimulating actions of *C. olitorius* leaf extracts.[23,54] Flavonoids have been shown to have a range of beneficial impacts on human health and to shield erythrocytes from oxidative damage since they are anti-oxidants and can scavenge free radicals.[58] Additionally, they have demonstrated antioxidant activity and effective scavenging of superoxide and anions.[59] Alkaloids are known to inhibit the enzyme phosphodiesterase of adenosine monophosphate (cAMP), leading to a buildup of cAMP levels. Consequently, this raises the phosphorylation and synthesis of proteins, which may raise erythropoiesis.[60] This means that the alkaloids and flavonoids in the extract may function as antioxidants to shield red blood cells from harm brought on by free radicals or extremely reactive oxygen species.[61] The phytochemical composition of plants supports their anti-anemic activities in conventional medicine.[62]

Conclusion

Potassium bromate caused a significant decrease in haemoglobin level, red blood cell count, packed cell volume, total white blood cell count, neutrophil count, lymphocyte count, monocyte count and platelet count, as well as elevated ESR, but *C. olitorius* treatment mitigated these effects. Therefore, further studies are required to validate these findings.

Conflict of Interests

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article are original and that any liability for claims relating to the content of this article will be borne by them.

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