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Protective and Curative Potential of Ethanol Leaf Extract of *Corchorus olitorius* against Potassium Bromate-Induced Renal Toxicity

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aim: The objective of this study was to assess the protective and curative potential of ethanol leaf extract of *Corchorus olitorius* against potassium bromate ($KBrO_3$)-induced renal toxicity.
Methodology: *Corchorus olitorius* was extracted using a soxhlet extractor and ethanol as the solvent. After becoming accustomed to the lab, 24 mature male Wistar rats were randomly assigned to groups A, B, C, and D. Group A received oral distilled water as treatment. Animals in groups B, C, and D got 100 mg/kg body weight of potassium bromate while groups C and D also received 100 and 200 mg/kg body weight of *Corchorus olitorius* respectively. Fresh potassium bromate and groups C and D extract were administered to rats every day by oral gavage. After taking the drug for the recommended 28 days, blood and kidney samples were collected. Renal biomarkers were evaluated using conventional methods.
Results: Significant ($P \leq 0.05$) increase in the serum concentrations of creatinine, urea, uric acid, sodium (Na^+), potassium (K^+), chloride (Cl^-), and bicarbonate (HCO_3^-) were observed following potassium bromate administration in comparison to the control group. $KBrO_3$ poisoning also increased the levels of the inflammatory proteins interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF- α) in the kidneys compared to the control group. Yet when $KBrO_3$ and *C. olitorius* leaf extract were administered together, levels of all kidney indicators were significantly reduced in a dosage-dependent manner, with 200 mg/kg being the most efficient dose.
Conclusion: This study found that *C. olitorius* leaf extract, particularly at the higher dose of 200 mg/kg, was successful in reducing a number of the parameters examined that had been negatively impacted by $KBrO_3$. It may be advantageous to include *C. olitorius* leaf in edible products that may contain $KBrO_3$, such as flour, bread, or cakes, as it is a well-known dietary prebiotic with established safety profiles in humans. Further research is required to determine whether *C. olitorius* leaves can reduce the toxicity of $KBrO_3$ in human organs and other animal strains, as well as perhaps treat it.

Keywords: Corchorus olitorius; potassium bromate; renal toxicity.

1. INTRODUCTION

As a frequent food ingredient and oxidising agent found in cosmetic items like permanent hair weaving solutions and textile dyes, potassium bromate ($KBrO_3$) is a significant tap water contaminant [1]. Despite being linked to the development of multiple organ damage, it is nevertheless employed in some nations, notably the United States, as flavouring for bread and cakes (both officially and illegally) [2]. It has been claimed that it is used in Nigeria to make bread [3,4]. Humans who are acutely intoxicated with $KBrO_3$ can develop renal failure, neuropathological abnormalities, and thrombocytopenia, while those who are chronically intoxicated have been shown to develop a number of renal and nonrenal malignancies [5]. According to experimental studies, $KBrO_3$ can cause oxidative stress [6], hepatotoxicity [7], nephrotoxicity [8], testicular toxicity [9], dyslipidemia [10], lower sperm quality [11], decreased male reproductive hormones [12], abnormalities in coagulation factors [13], and other negative effects.

The nephrotoxicity caused by $KBrO_3$ has been connected to reactive oxygen species (ROS), lipid peroxidation, and changes in 8-hydroxyguanosine in renal DNA [14]. The amount of oxidative stress brought about by $KBrO_3$ far surpasses the capacity of cells to ward off this stress, which has been shown to be significantly nephrotoxic in both human and animals as well as carcinogenic in test animals [15]. Hence, it is crucial for clinical practise to find ROS scavengers and antioxidants that are both safe and efficient, whether they are manufactured or naturally occurring.

A typical green leafy vegetable known as *Corchorus olitorius* L. (Tillaceae) is prized for its nutritious profile and therapeutic benefits. It is frequently referred to as jute [16]. Triterpenes, sterols, glycosides, saponins, tannins, and phenolic chemicals have been found to be present in jute leaves, in addition to mucilaginous polysaccharides and lignin. Jute leaves are frequently eaten in form of soup in Nigeria and some Middle Eastern nations [17]. The leaves are employed in herbal treatments for fevers, enteritis, dysentery, chronic cystitis, and aches and pains in addition to its culinary use [18]. Moreover, a variety of pharmacological properties, such as antioxidant [19],

cardioprotective [20], and hepatoprotective [21,22] activities, have been linked to the leaves. Moreover, it has been claimed to stop male Wistar rats from developing experimentally induced testicular toxicity [23], as well as changes to sperm quality [24] and sex hormones [25].

According to reports in the literature, $KBrO_3$ was administered intraperitoneally or subcutaneously to cause nephrotoxicity. Yet, oral consumption of $KBrO_3$ exposes people to it. We only found two studies that employed oral administration of $KBrO_3$ to cause nephrotoxicity in rats, male Wistar rats were used in one study at a single dose of 100 mg/kg [26], and male Sprague Dawley rats were used in the other study at twice-weekly doses of 20 mg/kg over a period of four weeks [27]. Furthermore, as far as we know, no attempts have been made to employ *Corchorus olitorius* leaf extract as a viable remedy for $KBrO_3$-induced nephrotoxicity. Consequently, the current investigation used a variety of established and new biochemical markers to examine the nephrotoxic effects of oral doses of $KBrO_3$ in rats and the possible ameliorative effects of concurrent therapy with *Corchorus olitorius* leaf extract.

2. MATERIALS AND METHODS

2.1 Extraction of Plant Materials

Fresh *Corchorus olitorius* (jute) plants were gathered at the Institute of Agricultural Research and Training, Moor Plantation, Ibadan, Nigeria. The leaves were carefully separated from the stem and the damaged ones were thrown away. They were thoroughly cleansed to get rid of impurities under running water. They were allowed to air dry for 14 days at room temperature in an open laboratory setting before being ground into powder with an electric blender. According to the directions given by Airaodion et al. [28,29], the extraction was carried out using a soxhlet device with 98% ethanol as the solvent. The ethanol was evaporated on a rotary evaporator at 35 ^{o}C, producing 2.28 g or a 9.12% yield. The extract was kept in the fridge at 4 ^{o}C until it was required.

2.2 Experimental Design

Twenty-four (24) mature male Wistar rats (*Rattus norvegicus*) weighing between 140 and 160 g participated in the experiment. Prior to the trial, they got seven (7) days to adjust to the lab setting. The rats were housed in wire-mesh cages with free access to rat food and water. The animals were kept in environments with consistent temperatures, humidity levels, and 12-hour cycles of light and darkness. During the course of this inquiry, the Declaration of Helsinki and the guidelines established by the Commission for the Regulation and Supervision of Experiments on Animals were both abided by. Moreover, animal experimentation was done in accordance with NRC policy [30]. At random, they were split up into groups A, B, C, and D. Group A, which acted as the control group, received oral distilled water. Animals in groups C and D also received *C. olitorius* at dosages of 100 and 200 mg/kg body weight, respectively, in addition to the potassium bromate administered at a dose of 100 mg/kg body weight to groups B, C, and D. For 28 days, fresh potassium bromate solution and *C. olitorius* extract were given orally to rats. The animals were killed after twenty-four hours have passed since the last treatment, after which they were given gentle diethyl ether sedation. A hole was made in the heart to extract blood.

2.3 Renal Homogenates Preparation

The procedure outlined by Abali et al. [8] was followed in the preparation of the renal homogenate. After the animals were sacrificed, the kidneys were taken out, split in half, and kept in an ice-cold container to make the renal homogenates. The cortex and medulla were carefully divided with a sharp scalpel, and each was then homogenised separately in a glass Teflon homogenizer in a solution of 2 mM Tris-HCl and 50 mM mannitol buffer at pH 7.0 to make a homogenate that was 10% (w/v). After being diluted to 5% with Tris-mannitol buffer, these homogenates were subjected to high speed homogenization (20,000 rpm) in an Ultra Turrex Kunkel homogenizer. We examined the levels of interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-α) in the renal homogenate.

2.4 Determination of Renal Biomarkers

Using a kit from Randox Laboratories Ltd. in the UK and the diacetyl monoxime method, serum urea was quantified. The level of uric acid was determined using a kit from Linear Chemicals Barcelona in Spain using the quinoneimine dye complex, while the level of creatinine was determined using kits from Randox Laboratories Ltd. in the UK based on its reaction with

saturated picric acid to produce a yellow-red complex. Spectrophotometric analysis was used to measure the serum concentrations of the ions sodium (Na^+), potassium (K^+), chloride (Cl^-), and bicarbonate (HCO_3^-) using kits from Teco Diagnostics in Anaheim, California. Rat ELISA kits with monoclonal antibodies specific for rat TNF- α and IL-6 were used, according to Mohamed and Saddek [31].

2.5 Statistical Analysis

Each item of data is displayed together with its mean and standard deviation. In order to analyse the data by comparing the outcomes of the treatment groups to the control group, Graph Pad Prism was used along with one-way analysis of variance (ANOVA) and a Post-Hoc test (also known as a Tukey's comparison test). A 0.05 p-value was used to determine whether a variation was significant.

3. RESULTS

Significant ($P \leq 0.05$) increase in the serum concentrations of creatinine, urea, uric acid, sodium (Na^+), potassium (K^+), chloride (Cl^-), and bicarbonate (HCO_3^-) were observed following potassium bromate administration in comparison to the control group (Table 2). $KBrO_3$ poisoning also increased the levels of the inflammatory proteins interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF- α) in the kidneys compared to the control group (Table 3). Yet when $KBrO_3$ and

Table 1. Effect of *C. olitorius* leaves on serum creatinine, urea and uric acid concentrations of potassium bromate induced nephrotoxicity

Treatment group	Creatinine (mg/dL)	Urea (mg/dL)	Uric Acid (mg/dL)
Control	0.89±0.01	19.64±1.29	4.78±0.78
100 mg/kg $KBrO_3$ only	1.47±0.02	32.67±4.08	7.77±0.93
100 mg/kg $KBrO_3$ + 100 mg/kg *C. olitorius*	1.39±0.01	30.15±2.82	7.12±1.11
100 mg/kg $KBrO_3$ + 200 mg/kg *C. olitorius*	1.12±0.01	25.25±2.11	5.19±0.28
p-value	0.04	0.01	0.01

Results are presented as mean±standard deviation (SD) with n = 6.
Legend: The p-value represents the difference between control and treatment group

Table 2. Effect of *C. olitorius* leaves on plasma electrolytes concentrations of potassium bromate induced nephrotoxicity

Treatment group	Sodium (mEq/L)	Potassium (mmol/L)	Chloride (mmol/L)	Bicarbonate (mEq/L)
Control	137.34±9.28	3.96±0.82	97.78±6.24	26.93±3.26
100 mg/kg $KBrO_3$ only	178.36±11.02	6.02±1.92	123.65±9.19	33.62±2.97
100 mg/kg $KBrO_3$ + 100 mg/kg *C. olitorius*	159.26±5.26	5.82±0.27	118.26±7.82	31.62±3.27
100 mg/kg $KBrO_3$ + 200 mg/kg *C. olitorius*	140.55±9.12	4.11±0.39	111.23±8.35	27.28±2.25
p-value	0.03	0.01	0.01	0.03

Results are presented as mean±SD with n = 6.
Legend: The p-value represents the difference between control and treatment group

Table 3. Effect of *C. olitorius* leaves on Tumor Necrosis Factor–Alpha (TNF-α) and Interleukins-6 (IL-6) of Potassium Bromate induced Nephrotoxicity

Treatment group	TNF-α (pg/mL)	IL-6 (pg/mL)
Control	3.67±0.48	5.93±0.74
100 mg/kg $KBrO_3$ only	6.18±1.05	8.63±1.06
100 mg/kg $KBrO_3$ + 100 mg/kg *C. olitorius*	5.26±1.00	7.94±1.10
100 mg/kg $KBrO_3$ + 200 mg/kg *C. olitorius*	4.00±0.52	6.18±0.76
p-value	0.03	0.03

Results are presented as mean±SD with n = 6.
Legend: The p-value represents the difference between control and treatment group

C. olitorius leaf extract were administered together, levels of all kidney indicators were significantly reduced in a dosage-dependent manner when compared with those exposed to potassium bromate only, with 200 mg/kg being the most efficient dose.

4. DISCUSSION

In diverse animal species and strains, and at varied doses, $KBrO_3$ was found to cause renal impairments, according to several researchers [8,32,33]. Nonetheless, some researchers [34] have found scant to no indication of renal abnormalities in Fischer 334 rats. Studying the nephrotoxicity of this substance in male rats of a particular strain (Wistar rats) was our goal in this case. Also, we wanted to see if the nephrotoxicity of $KBrO_3$ may be reduced by co-treatment with a naturally occurring dietary prebiotic, *C. olitorius* leaf. All our findings showed that giving male Wistar rats oral dosages of $KBrO_3$ for 28 days at a dosage of 100 mg/kg body weight caused severe renal impairment. Many differences in the $KBrO_3$ dosages necessary to cause renal impairment were found in the literature on $KBrO_3$ nephrotoxicity. Ahmad et al. [27], for instance, employed adult male Wistar rats and discovered that a single 100 mg/kg aqueous dose of $KBrO_3$ elicited multiple nephrotoxic symptoms. Nevertheless, Khan et al. [26] discovered that $KBrO_3$ generated more severe renal impairments in male Sprague-Dawley rats when administered orally at a dose of 20 mg/kg twice weekly for 28 days than was observed in this study. It is unknown why these (and other) disparities exist, but they could be brought about by variations in strains, irregularities in the experimental setup, or other unidentified factors.

It has been reported that numerous efforts have been made to identify potential protective medications against the organ toxicity caused by $KBrO_3$, in particular nephrotoxicity. The substances examined included *Parkia biglobosa* [8], taurine [26], *Nymphaea alba* L. [33], and rutin [35]. The fact that these agents all possess potent anti-oxidant properties unites them, and it is widely known that the formation of ROS reduces enzymatic and non-enzymatic antioxidants and initiates lipid peroxidation, is a key mechanism of $KBrO_3$-induced nephrotoxicity [36,37]. These actions will ultimately result in oxidative stress. The European Medicines Agency and the Food and Drug Administration have recently evaluated and approved the use of many novel kidney, plasma, and urine nephrotoxicity biomarkers in preclinical research. To detect early acute kidney injury (AKI) in this study, we used both traditional and new biomarkers. Researchers and nephrologists are very interested in finding new and accurate biomarkers for spotting AKI symptoms and signs early. They include creatinine, urea, uric acid, electrolytes, pro-inflammatory markers such as tumour necrosis factor-alpha (TNF- α) and Interleukins-6 (IL-6). These were elevated by $KBrO_3$ in this study, supporting a previously proposed free radical-based mechanism for kidney injury [8].

When compared to the normal control, rats intoxicated with potassium bromate had raised levels of creatinine, urea, and uric acid—all crucial nephrotic indicators. Renal illness is characterised by severe liver disease with cell death that impairs the urea cycle and results in decreased glomerular filtration, retention of urea, and urea excretion [38]. Kidney impairment is indicated by a build-up of creatinine in the blood [39]. This study's findings agree with those of Akomolafe et al. [40] and Abd-Elmaksoud et al. [41]. These outcomes could be anticipated as a result of the kidney's failure to do its purification and removal of metabolites functions due to structural changes in the renal tissues following injection of $KBrO_3$, as previously documented [8,42].

However based on the results, it was clear that giving rats *Corchorus olitorius* leaf extract mitigated the impacts because these parameters were almost back to normal. The extract's potential modulatory role for its potential nephro-protective properties is thus suggested [43]. The beta-carotene, iron, calcium, and vitamin C content of *Corchorus olitorius* leaf are high. A considerable amount of Vitamin E is present in the plant, which possesses antioxidant activity. Free radicals are "sponged up" by the vitamins A, C, and E in jute leaves, which removes them before they can cause cellular sabotage [44,45]. The vegetable, *Corchorus olitorius* leaf is abundant in antioxidants, which have been associated with protection from other medical disorders as well as chronic diseases like heart disease, cancer, diabetes, and hypertension [46]. This is in line with Anup et al. [47], who claimed that *Corchorus olitorius* leaf extract has a significant oxidative damage-preventative impact on the liver and kidneys. Also, it agrees with Sule et al. [48]'s work in which they discovered that rats exposed to thioacetamide could be protected and treated by an ethanol leaf extract of *Corchorus olitorius*.

Both managing various electrolytes and maintaining homeostasis are responsibilities of the kidney [49]. Elevated levels of these electrolytes may signify renal impairment, especially at the glomerular and tubular levels, as sodium (Na^+) and potassium (K^+) are the main constituents of extracellular and intracellular fluids, respectively [8]. The present results showed that $KBrO_3$ was related with a considerable increase in serum levels of Na^+, K^+, Cl^-, and HCO_3^- ions, in agreement with Adewale et al. [50], who reported that oral intake of $KBrO_3$ alone elevated the blood electrolytes "Na^+, Cl^-, HCO_3^- and K^+" significantly. In contrast to the animal groups that just got $KBrO_3$ alone, those animals received doses of 100 and 200 mg/kg of *Corchorus olitorius* leaf extract along with a dose-dependent reduction in serum Na^+, K^+, Cl^-, and HCO_3^- levels.

Inflammatory cytokines including IL-6 and TNF-α are produced as a result of transcription factors that ROS can activate [51]. As evidenced by the increased expression of renal TNF- α and IL-6, the current findings demonstrated that the kidneys' inflammatory reaction was heightened by $KBrO_3$. These results agree with those of Elsayed and Barakat [52], who discovered that rats given $KBrO_3$ were highly renal IL-6-depleted. TNF- α and IL-6 were significantly released in response to $KBrO_3$, which suggests that the molecule activates macrophages, according to Okoko [53]. This outcome was consistent with that of Bayomy et al. [54], who discovered that $KBrO_3$ therapy causes inflammation and the deposition of a sizable amount of collagen fibres in the tissues. They concluded that the production of pro-inflammatory and profibrotic chemicals was enhanced by ROS and oxidative stress. Our results are consistent with those of Ali et al. [55], who claimed that daily $KBrO_3$ injection for 28 days led to inflammatory cell infiltration and fibrosis in rat kidneys, which gradually increased with increasing the $KBrO_3$ dose. However, the animal population in the current study that received both $KBrO_3$ and *Corchorus olitorius* leaf extract displayed a decrease in the overproduction of TNF- α and IL-6 in renal tissue, which provided a protective effect against the degenerative alterations to the kidney. This is suggestive that the extract demonstrated that it has anti-inflammatory properties that prevented the advancement of renal inflammation in response to $KBrO_3$ administration. The primary NF-B pathway inhibition was suggested to be the main mechanism of action for *Corchorus olitorius* leaf as an anti-inflammatory [56,57]. One of the ways for reducing fibrosis is inflammatory suppression since chronic inflammation causes extracellular matrix to grow up and regeneration to fail. The findings of this study showed that *Corchorus olitorius* leaf has anti-inflammatory qualities that slowed the fibrosis process and were associated with a reduction in the production of the pro-inflammatory cytokines TNF- α and IL-6. One of the active ingredients in *Corchorus olitorius* leaves is quercetin, which has been shown to inhibit the NF-B pathway by blocking the translocation of NF-B factor p65 to the nucleus and so lowering inflammatory response [58].

5. CONCLUSION

This study found that *C. olitorius* leaf extract, particularly at the higher dose of 200 mg/kg, was successful in reducing a number of the parameters examined that had been negatively impacted by $KBrO_3$. It may be advantageous to include *C. olitorius* leaf in edible products that may contain $KBrO_3$, such as flour, bread, or cakes, as it is a well-known dietary prebiotic with established safety profiles in humans. This is especially true in countries where the use of $KBrO_3$ in food products is permitted or in nations like Nigeria where $KBrO_3$ has been banned but laws prohibiting its use are not enforced. This may be attributed to the agent's strong antioxidant properties. Further research is required to determine whether *C. olitorius* leaves can reduce the toxicity of $KBrO_3$ in human organs and other animal strains, as well as perhaps treat it.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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