Original Research Article

Nephron-protective Efficacy of African Locust Bean Seed against Potassium Bromate-induced Renal Damage

ABSTRACT

Background: Potassium bromate ($KBrO_3$) has been utilized extensively to sterilize water, dye hair, oxidize food, add to bread dough as a maturing agent, and condition wheat dough, thereby entering into human body. It has been claimed to cause a number of toxicities including nephrotoxicity.

Aim: This study, therefore, sought to investigate the nephron-protective efficacy of African locust bean (ALB) seed against potassium bromate-induced renal damage

Methodology: Using a soxhlet extractor with ethanol as the solvent, ALB was extracted. Twenty-four mature male Wistar rats were randomly divided into groups A, B, C, and D after being acclimated in the lab. Oral distilled water was administered to Group A. Although groups C and D likewise received 100 and 200 mg/kg body weight of ALB, respectively, the animals in groups B, C, and D received 100 mg/kg body weight of potassium bromate. Rats received daily doses of freshly produced potassium bromate and ALB extract by oral gavage. Blood and kidney sample were taken after the prescribed 28-day course of medication. Standard techniques were used to assess renal biomarkers.

Results: When compared to the control group, potassium bromate treatment led to significant ($P<0.05$) increases in the serum levels of creatinine, urea, uric acid, sodium (Na^+), potassium (K^+), chloride (Cl^-), and bicarbonate (HCO_3^-). Renal levels of tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) were likewise elevated by $KBrO_3$ poisoning in comparison to the control group. However, combined administration of $KBrO_3$ and ALB seed extract resulted in significant dose-dependent reductions in the levels of all kidney biomarkers examined, with 200 mg/kg being the most effective dose.

Conclusion: This study revealed that potassium bromate indeed induced nephrotoxicity by unhinging renal biomarkers investigated in this study. It was further observed that seed extract of African locust bean (ALB) alleviated these adverse effects on the kidney by resisting the perturbations, thereby exhibiting nephron-protective effect. The biochemical composition of ALB has conferred it with this ability.

Keywords: African locust bean; potassium bromate; nephron-protective efficacy; renal damage

1. INTRODUCTION

The usage of medicinal plants as a source of medication and to enhance human health dates back thousands of years. A number of plants contain bioactive components including phenolic and polyphenolic chemicals that control different immune pathways. Herbs that are high in flavonoids and phenolic compounds may also be anti-inflammatory and antioxidant [1]. African locust bean (*Parkia biglobosa*) is one of these plants. It is a perennial tree that belongs to the Leguminosae genus of legumes [2]. The plant's seeds are encased in an edible pulp that is yellowish, mealy, and sweet-tasting [3]. It is common knowledge that this plant contains a significant number of phenolic chemicals [4]. Epigallocatechin, epicatechin 3-O-gallate, and epigallocatechin 3-O-gallate were all present in the plant's bark [5]. Heart and saponin glycosides are present in leaf extract [6]. Protein and lactose are abundant in the fruit's pulp and seeds [5]. Phytate, tannin, oxyalate, and hydrogen cyanide are a few antinutritional components found in seeds [2]. The extract of African locust bean (ALB) is antibacterial [4], antidiabetic [7], antifungal [8], anti-inflammatory [9], anti-diarrheal [10], anti-hypertensive [11], hypoglycemia [12], hypolipidemic [13], and hepatoprotective [14] in addition to having many beneficial effects. A recent study by Ezirim et al. [15] shown that ALB seed can alleviate testicular toxicity caused by potassium bromate.

To improve the quality of meals, certain compounds known as food additives are added during processing [16]. Food additives can generally be divided into two categories: those that are purposefully added to food and those that contaminate food in minute quantities as a result of handling and storage procedures [17]. A maximum limit has also been established for each additive by the Codex Alimentarus [18] Commission in consideration of any potential harmful consequences [17]. Potassium bromate ($KBrO_3$) is a white, crystalline salt that has been used for many years in the baking and confectionery industries to improve the flavor of goods [16]. It is classified as a flour treatment agent by FAO/WHO [19]. Since IARC categorized potassium bromate as a Category 2B carcinogen, its official ban on use has been contested [20]. According to toxicological research, potassium bromate is hazardous to organs and has the capacity to rupture cell plasma membranes as an oxidizing agent and cause cells to release their internal contents into the extracellular environment [21,22]. In experimental animals and humans, potassium bromate was found to cause kidney toxicity [23]. It has also been linked to DNA damage and lipid peroxidation [24]. Additionally, it has been suggested that potassium bromate may cause cancer [25,26]. Following the injection of potassium bromate to the membrane lining the abdominal cavity of laboratory animals, an increase in the incidence of both malignant and benign tumors was seen [27]. Additionally, giving animals potassium bromate caused a substantial rise in malignancies of the thyroid, kidneys, and other organs [28]. Therefore, the purpose of this study was to determine whether extract of ALB seed can prevent kidney damage from potassium bromate.

2. MATERIALS AND METHODS

2.1 Collection and Extraction of ALB

The seeds of ALB were acquired at a local market in Ibadan, Nigeria, and were identified by a botanist. They were processed into powder using a mechanical blender after being sun-dried. The extraction was finished using a soxhlet device and ethanol as the solvent in accordance with the procedures outlined by Airaodion et al. [29,30]. The ethanol was evaporated in a rotary evaporator at 35 ^{o}C with a yield of 2.55 g and a percentage yield of 10.20 percent. The extract was kept in the fridge until it was required.

2.2 Animal Treatment

The experiment involved twenty-four (24) mature male Wistar rats (*Rattus norvegicus*) weighing between 140 and 160 g. Prior to the study, they were acclimated in a lab setting for seven (7) days. The rats were kept in cages made of wire mesh, and they had unrestricted access to commercial rat food and water. The animals

were housed at regular temperatures and humidity levels with 12-hour light and dark cycles. The Declaration of Helsinki and the regulations set by the Committee for the Purpose of Control and Supervision of Experiments on Animals were followed in conducting this investigation. Additionally, while using animals in research, NIH guideline was followed [31]. They were divided into groups A, B, C, and D at random. As usual, Group A received oral distilled water. The animals in groups B, C, and D received 100 mg/kg body weight of potassium bromate whereas groups C and D also received 100 and 200 mg/kg body weight of ALB, respectively. Rats were given daily oral gavages of ALB and fresh potassium bromate. Twenty-four hours after the last dose, the animals were slaughtered while being softly sedated with diethyl ether. Blood was drawn by puncturing the heart.

2.3 Renal Homogenates Preparation

The kidneys were removed from the animal after the sacrifice, cut in half, and maintained in an ice-cold container to prepare the renal homogenates. The cortex and medulla were carefully cut apart using a sharp scalpel, and each was homogenized separately in a glass Teflon homogenizer in a solution of 2 mM Tris-HCl and 50 mM mannitol buffer at pH 7.0 to create 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. The renal homogenate was tested for interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) concentrations.

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, whereas 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. Using kits from Teco Diagnostics in Anaheim, California, the serum concentrations of the ions sodium (Na^+), potassium (K^+), chloride (Cl^-), and bicarbonate (HCO_3^-) were all measured by spectrophotometric analysis. Rat ELISA kits with monoclonal antibodies specific for rat TNF-α and IL-6 were used, according to Mohamed and Saddek [32].

2.5 Statistical Analysis

Every piece of data is presented as mean $\pm$ standard deviation. To examine the data by comparing the outcomes of the treatment groups to the control group, analysis of variance was utilized in conjunction with a Post-Hoc test (Tukey's comparison test) using Graph Pad Prism software. All deviations with $p \leq 0.05$ were deemed significant.

3. RESULTS

When compared to the control group, potassium bromate treatment led to significant ($P \leq 0.05$) increases in the serum levels of creatinine, urea, uric acid (table 1), sodium (Na^+), potassium (K^+), chloride (Cl^-), and bicarbonate (HCO_3^-) (table 2). Renal levels of tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) were likewise elevated by $KBrO_3$ poisoning in comparison to the control group (table 3). However, combined administration of $KBrO_3$ and ALB seed extract resulted in significant dose-dependent reductions in the levels of all kidney biomarkers examined, with 200 mg/kg being the most effective dose.

Table 1: Effect of ALB Seed 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 ALB	1.21±0.00	28.28±1.34	6.05±1.05
100 mg/kg $KBrO_3$ + 200 mg/kg ALB	1.03±0.01	23.94±2.92	5.25±0.28
p-value	0.05	0.00	0.02

Results are presented as mean±SEM with n = 6.

Table 2: Effect of ALB Seed 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 ALB	164.04±8.29	5.34±0.83	111.18±9.33	31.58±5.13
100 mg/kg $KBrO_3$ + 200 mg/kg ALB	143.78±9.54	4.73±0.26	102.94±7.16	28.67±5.83
p-value	0.04	0.01	0.01	0.05

Results are presented as mean±SD with n = 6.

Table 3: Effect of ALB Seed 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 ALB	4.84±0.36	7.53±0.72
100 mg/kg $KBrO_3$ + 200 mg/kg ALB	3.92±0.78	6.36±1.01
p-value	0.01	0.03

Results are presented as mean±SD with n = 6.

4. DISCUSSION

Plants have long been utilized as folk medicine to treat a variety of illnesses. Even today, medical professionals and village doctors in many nations use unprocessed plant extracts to treat human illnesses [33,34]. To assess the effectiveness of various plants against chemically induced toxicity, experimental work has been done on them [35,36].

It may be possible to identify renal impairment brought on by $KBrO_3$ poisoning by measuring serum levels of urea, creatinine, and uric acid, which were previously utilized as early indicators of renal failure [37,38]. The significant increase in blood urea, creatinine, and uric acid in the $KBrO_3$-treated rats suggests the onset of renal failure and a reduced glomerular filtration rate. Acute renal failure was the outcome of accidental potassium bromate poisoning, according to Adeleke and Asani [39].

Increases in blood creatinine and urea have been identified as key biomarkers of kidney disease and the degradation of the integrity of the renal tubules. These changes are damage indicators for inadequate glomerular filtration [40,41]. Increased levels of creatinine in the serum of rats treated with $KBrO_3$ supported earlier claims that $KBrO_3$ consumption results in renal injury [42,43].

Urea, which is largely made in the liver and released by the kidneys, is the main byproduct of protein catabolism [44]. It is the main method of getting harmful ammonia out of the body. The medical doctor can evaluate a patient's renal function using urea determination extremely well [37,38]. Increased urea levels are typically linked to nephritis, renal ischemia, obstruction of the urinary tract, and several extra-renal disorders. Similar to other findings [45,46], potassium bromate-induced elevation in urea concentration were seen in this investigation. Additionally, renal failure has been connected to increased urea levels, according to Akomolafe et al. [47].

Degradation of purines and pyrimidines may potentially be a contributing factor to the rise in uric acid levels. According to a study by Mohamed and Saddek [32], $KBrO_3$ increased xanthine oxidase activity, which resulted in an excess of uric acid being produced. This process may have led to the action of $KBrO_3$ in the increase of uric acid. ALB extract reduced this $KBrO_3$-induced effect on uric acid in a dose-dependent manner. The hypouricemic effects of ALB seed extract may be brought on by the presence of flavonoids, which have inhibitory effects on the enzyme activities of xanthine oxidase and xanthine dehydrogenase [48].

For animal species to survive, electrolytes are necessary [49]. A considerable increase in several electrolytes, including sodium (Na^+), potassium (K^+), chloride (Cl^-), and bicarbonate (HCO_3^-) ions, was also brought about in the current investigation by treatment with $KBrO_3$. This is a sign of significant kidney injury, which was also seen in kidney parameter pathological differences. The same outcomes were described by previous studies [50,51]. The observed increases in the serum concentrations of urea, creatinine, and uric acid were supported by the elevated levels of Na^+, K^+, HCO_3^-, and Cl^-. The kidney is in charge of controlling different electrolytes and preserving homeostasis [52]. For instance, Na^+ and K^+ are important components of extracellular and intracellular fluids, respectively. Since the kidney controls both physiological states, elevated levels of these electrolytes may suggest renal failure, especially at the glomerular and tubular levels. The transit of various non-electrolytes and the maintenance of the water equilibrium level in physiological tissue are both significantly influenced by sodium and potassium [53,54]. Additionally, as HCO_3^- and Cl^- are reabsorbed in the proximal tubule, a high level of these electrolytes may indicate tubular renal damage. This outcome is consistent with the rise in all electrolytes observed by Kanadi et al. [55] after exposure of animals to $KBrO_3$. The main anion in serum is chloride. Extracellular sodium and bicarbonate concentrations have an impact on extracellular chloride concentration [49]. However, concurrent treatment of $KBrO_3$ and ALB seed extract returned the serum levels of all

the electrolytes examined to normal, particularly in the group treated with 200 mg/kg, whose values were not substantially different from those in the normal control group. This raises the possibility of a preventive effect of ALB seed against renal damage brought on by $KBrO_3$.

Interleukin-6 (IL-6) and tumor necrosis factor (TNF-α) are two pro-inflammatory cytokines that are hypothesized to play a key role in the pathogenesis of chronic kidney diseases [56]. By activating transcription factors, which in turn cause the release of pro-inflammatory cytokines like IL-6 and TNF-α, reactive oxygen species (ROS) can trigger inflammatory processes [57]. The findings of this investigation showed that $KBrO_3$ caused an inflammatory response that was manifested by an increase in renal TNF-α and IL-6 levels, indicating nephrotoxicity. This is comparable to the increase in TNF-α and IL-6 levels found in rats exposed to potassium bromate, as reported by Mohamed and Saddek [32]. Recently, Ugwu et al. [58] found that $KBrO_3$ caused oxidative stress in the rat kidney. The large rise in renal TNF-α and IL-6 levels may be a result of the kidneys producing more ROS. The overproduction of proinflammatory cytokines TNF-α and IL-6 in renal tissue was however suppressed by ALB seed therapy and $KBrO_3$ administration, which had a protective effect against pathological kidney changes. The ability of ALB seed to attenuates nephrotoxicity caused by potassium bromate intoxication could be as a result of its rich phytochemical constituents and antioxidant potential [58].

5. CONCLUSION

This study revealed that potassium bromate indeed induced nephrotoxicity by unhinging renal biomarkers investigated in this study. It was further observed that seed extract of African locust bean (ALB) alleviated these adverse effects on the kidney by resisting the perturbations, thereby exhibiting nephron-protective effect. The biochemical composition of ALB has conferred it with this ability.

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