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Seasonal variation in the protective property of Ficus exasperata leaf extract against potassium bromate-induced toxicity

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ABSTRACT

Background: Potassium bromate ($KBrO_3$) is illicitly used by food producers, especially bakers, in the preparation of bread and pastries, posing health risks to consumers. Identifying protective agents against $KBrO_3$-induced toxicity is therefore critical.
Objectives: This study aimed to evaluate the protective effects of *Ficus exasperata* leaf extracts
against $KBrO_3$-induced toxicity in rats and to investigate the influence of seasonal variation on the efficacy of the extracts.
Methods: Leaf extracts of *Ficus exasperata* were prepared from leaves harvested in January (FEJAN) and July (FEJUL). Twenty-four rats were randomly assigned to four groups (n = 6 per group) and orally treated for 21 days as follows: Group 1 (control) received 1% dimethyl sulfoxide (DMSO); Group 2 received $KBrO_3$ (25 mg/kg body weight); Group 3 received $KBrO_3$ plus FEJAN (50 mg/kg body weight); and Group 4 received $KBrO_3$ plus FEJUL (50 mg/kg body weight). After treatment, animals were euthanized for collection of blood samples for biochemical and hematological analyses. Histopathological evaluations of liver and kidney tissues were also performed. Data were analyzed using one-way ANOVA followed by Tukey's post hoc test, with significance set at $p < 0.05$.
Results: Co-treatment with FEJAN and FEJUL significantly increased packed cell volume (PCV), red blood cell (RBC), white blood cell (WBC), and platelet (PLT) counts compared to the $KBrO_3$-only group ($p < 0.05$). Conversely, serum levels of urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and malondialdehyde (MDA) were significantly reduced in the extract-treated groups ($p < 0.05$). Histological examination revealed that FEJAN and FEJUL ameliorated $KBrO_3$-induced hepatic and renal tissue damage. Notably, FEJUL demonstrated greater protective efficacy than FEJAN.
Conclusion: *Ficus exasperata* leaf extracts confer significant protection against $KBrO_3$-induced toxicity in rats. The extract from leaves harvested during July (FEJUL) exhibited superior protective effects compared to those harvested in January (FEJAN).

INTRODUCTION

Potassium bromate ($KBrO_3$) is widely used in baking industry. Its deleterious effects on human health are widely reported. For over 60 years, it has been used to condition dough, but in the early 1990s, it was reported that it can cause cancer and kidney disease. Other serious toxic effects of potassium bromate include cough, abdominal pain, nausea, and diarrhea among others. For this reason, the use of potassium bromate in food processing was banned by many countries[1]. Despite regulatory bans, potassium bromate continues to be widely used by food industries in several countries. This underscores the urgent need to identify effective remedies to mitigate the toxic effects associated with potassium bromate exposure. Notably, many secondary metabolites produced by medicinal plants possess significant biological activity, making them promising candidates for therapeutic intervention.

They are produced in small quantities and accumulate in plants during primary metabolic processes. Unlike the primary metabolites, secondary metabolites do not have direct effect on the growth and development of plants. Rather, they play important role in defense and adaptation of plants to their environment[2]. Several secondary metabolites have been reported to possess significant therapeutic value and are widely used in the prevention and treatment of various diseases. These compounds exhibit a broad spectrum of biological activities, including anti-inflammatory, antioxidant, anthelmintic, antimicrobial, antiplasmodial, and anticancer effects. When used either as isolated compounds or as complex mixtures, secondary metabolites often serve as effective and safe medicines, sometimes outperforming synthetic drugs. Their efficacy is frequently enhanced through potentiation and synergistic interactions among the different compounds present in such preparations[3]. Climate has been shown to have significant effect on the rate of production of the secondary metabolites that are responsible for therapeutic effects of medicinal plants. Efficacy of preparations from medicinal plants usually varies according to the proportion of their active components during different seasons of the year [4]. This variation is due to the effects of environmental factors like rainfall, temperature, and sunlight which influence plant growth and metabolic process[5].

Ficus exasperata is a medicinal plant widely used for the treatment of anemia in Nigeria and other African countries. The plant was also reported to have anti-inflammatory and antioxidant effects[6, 7]. These pharmacological properties are essential for preventing and/or alleviating health conditions associated with inflammation and oxidative stress. Understanding the seasonal variation in the therapeutic efficacy of medicinal plants is crucial to maximizing their benefits. In this study, we evaluated the protective effect of *Ficus exasperata* leaf extract against potassium bromate-induced toxicity in rats, with a focus on possible differences in efficacy between leaves harvested during the rainy and dry seasons.

MATERIALS AND METHODS

Drugs and Chemicals

The following drugs and chemicals were used for the study: ethanol, potassium bromate (Medville Pharmacy, Ibadan, Nigeria), dimethyl sulfoxide (J.T. Baker, USA), 10% formalin (Merck, Germany), hematoxylin and eosin stains (Sigma-Aldrich, USA)

Collection of plant

Leaves of *Ficus exasperata* were collected from the forest near Bowen Teaching Hospital, Ogbomoso. The leaves were collected separately in January (dry season), and July (rainy season). The leaves were identified in the Department of Biology, Ladoke Akintola University of Technology, Ogbomoso, Nigeria (Identification No: LH0831).

Preparation of ethanol crude extract of *Ficus exasperata* leaves

The leaves were washed thoroughly with clean water to remove dust and debris that may contaminate the samples. The washed leaves were spread under the shade and air-dried for 7 days. The dry leaves were then pulverized by a grinding machine. The pulverized was then extracted in 80% ethanol using Soxhlet extractor. The resulting ethanol extract was concentrated at 40 ^oC in a rotary evaporator (Percentage Yield = 5.7%). Ethanolic extract of the leaves harvested in January (FEJAN) and the leaves harvested in July (FEJUL) were kept in an air-tight container and stored in a refrigerator at -20 ^oC

Experimental animals

Wistar rats weighing 160 ± 20 g were obtained from the Animal House of the College of Health Sciences, LAUTECH, Ogbomoso. The rats were kept in polypropylene cages in a well-ventilated laboratory at room temperature. Rats were fed standard commercial animal feed (Ladokun Feed Ltd, Ibadan, Nigeria). They were also allowed free access to clean water.

Ethical consideration

Ethical approval (ERCFBMS/042/2024) was obtained from Faculty of Basic Medical Science Research Ethic Committee (LAUTECH, Ogbomoso). All procedures were followed as outlined in the Guide for the Care and Use of Laboratory Animals published by the National Institute of Health [8].

Animal grouping and treatment

FEJUL and FEJAN were dissolved in 1% DMSO for the experiments. Doses of the extracts were chosen based on previous study [9]. Rats were assigned to 4 groups (n = 6) and treated orally for 21 days using oral cannula as follows:

Group I: 1% DMSO (10ml/kg, b.w)

Group II: $KBrO_3$ (25 mg/kg, b.w)

Group III: $KBrO_3$ ((25 mg/kg, b.w)/FEJAN (50 mg/kg b.w)

Group IV: $KBrO_3$ ((25 mg/kg, b.w)/FEJUL (50 mg/kg b.w)

The rats were weighed on weighing balance before and after the treatment. They were then euthanized and blood samples and organs were harvested.

Biochemical and Hematological analyzes

Blood was collected into heparinized bottles and analyzed by an automated, hematology analyzer XN-1000 (Sysmex Corporation (Japan). Serum glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT) activities were analyzed by colorimetric kits (Elabscience, USA) according to the manufacturer's instruction [10]. Serum samples were subjected to analysis of creatinine, urea, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) using an automatic analyzer, TBA-120FR (Toshiba Medical Systems, Co., Ltd., Japan). Lipid peroxidation was analyzed by measuring the formation of Malondialdehyde (MDA). MDA produced through the peroxidation of fatty acids reacts with thiobarbituric acid (TBA) to form a pink complex measured spectrophotometrically at 532nm. C-reactive protein was measured by an automated CRP analyzer (BC-7500 Shenzhen Mindray Corporation, Shenzhen, China) [11, 12].

Statistical analysis

Data obtained were expressed as mean ± standard error of mean (SEM). Data were subjected to one-way analysis of variance (ANOVA) followed by Tukey's *Post Hoc* test. A level of $P < 0.05$ was considered significant. GraphPad Prism version 5.0 for windows was used for these statistical analyses (GraphPad software, San Diego California USA)

RESULTS

Effect of *Fiscus exasperata* leaf extract on body weight

Figure 1 shows the effect of FEJAN and FEJUL extracts on body weight in rats administered potassium bromate ($KBrO_3$). There was a significant ($p < 0.05$) decrease in body weight across all groups ($KBrO_3$, $KBrO_3$/FEJAN and $KBrO_3$/FEJUL) Compared to control. However, co-administration with $KBrO_3$/FEJAN and $KBrO_3$/FEJUL significantly ($p < 0.05$) increased body weight compared to the $KBrO_3$ group. Although the values did not return to control levels, both FEJAN and FEJUL mitigated the $KBrO_3$-induced weight loss.

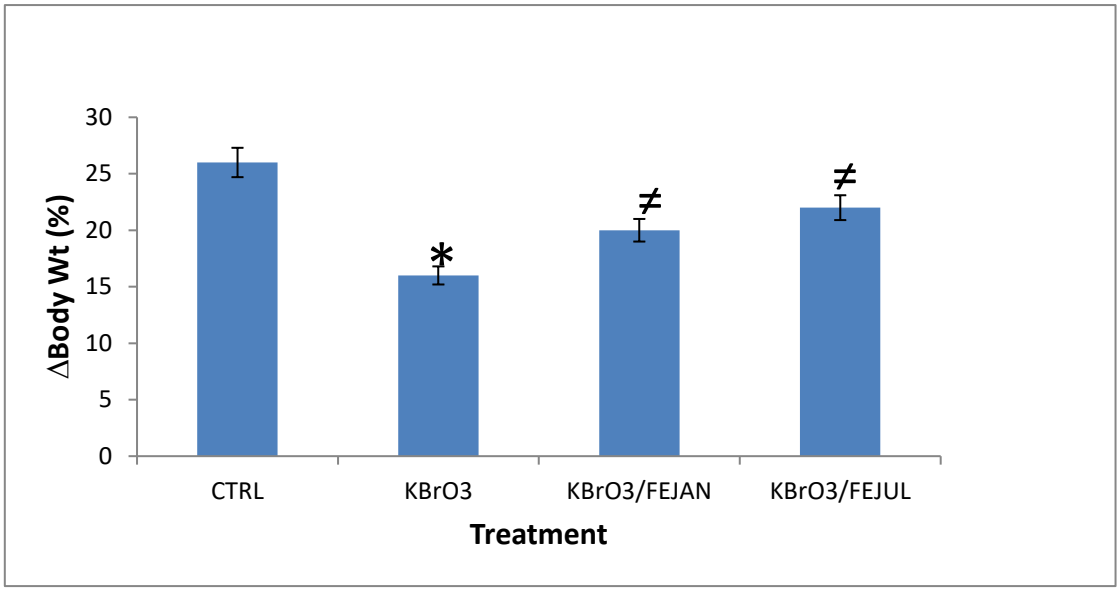

Figure 1: Effect of *Fiscus exasperata* leaf extract on change in body weight in potassium bromate-treated rats. Each bar represents Mean ± S.E.M, (n = 6), *p<0.05 compared to control. #p<0.05 compared to KBrO3-treated rats; KBrO3 = potassium bromated. FEJAN = extract of *Ficus exasperata* harvested in January; FEJUL = extract of *Ficus exasperata* harvested in July

Effects of *Ficus exasperata* extracts on hematology

Administration of $KBrO_3$ significantly reduced packed cell volume (PCV) from 31.93 ± 6.60 to 18.60 ± 4.22 %. Treatment with combined $KBrO_3$ and FEJUL significantly ($p<0.05$) raised PCV to 37.15 ± 4.40 %. When FEJAN was co-administered with $KBrO_3$, PCV was also significantly increased to 32.35 ± 6.15 %. Likewise, hemoglobin (Hb), red blood cell (RBC), and white blood cell (WBC) counts were significantly reduced by $KBrO_3$, but treatment with FEJUL and FEJAN increased the levels of hemoglobin, red blood cell and white blood cell compared to the $KBrO_3$-treated group. Administration of $KBrO_3$ decreased platelet count (PLT) significantly compared to the control. In the group treated with a combination of $KBrO_3$ and FEJUL, platelet count was raised from 82.21 ± 16.73 to 105.55 ± 10.82 while in FEJAN-treated rats, platelet count increased to 113 ± 12.20. Mean corpuscular volume (MCV) was significantly lower in $KBrO_3$-treated rats compared to control. Treatment with FEJUL and FEJAN caused a significant increase in MCV. Mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) compared to control. However, treatment with FEJUL and FEJAN caused a significant reduction in MCH and MCHC. Neutrophil count was increased while lymphocyte and monocyte counts were reduced in $KBrO_3$-treated compared with control. Both FEJUL and FEJAN significantly reduced neutrophil count (N) and raised lymphocyte (L) and monocyte (M) counts. The results are shown in Table 1

Table 1: Effects of *Ficus exasperata* extracts on hematology

Haematological Parameters	Groups			
	Control	$KBrO_3$	$KBrO_3$ + FEJUL	$KBrO_3$ + FEJAN
PVC (%)	31.93 ± 6.60	18.60 ± 4.22*	37.15 ± 4.40$^{\neq}$	32.35 ± 6.15$^{\neq}$
Hb (g/L)	101.64 ± 16.20	64.53 ± 10.21*	146.50 ± 12.21$^{\neq}$	105.00 ± 13.06$^{\neq}$
RBC ($x10^{12}$/L)	5.25 ± 0.64	2.80 ± 0.41*	6.30 ± 1.10$^{\neq}$	7.80 ± 0.55$^{\neq}$
WBC ($x10^{9}$/L)	15.41 ± 2.53	8.64 ± 1.33*	14.20 ± 2.51$^{\neq}$	12.72 ± 3.30$^{\neq}$
PLT ($x10^{9}$/L)	148.66 ± 8.52	82.21 ± 12.73*	105.55 ± 10.82$^{\neq}$	113.54 ± 12.20$^{\neq}$
MCV (fl)	63.64 ± 9.84	48.75 ±11.61	69.30 ± 7.52	63.44 ± 12.21
MCH (pg)	15.60 ± 2.00	25.94 ± 4.22	18.53 ± 2.71	21.50 ± 3.42
MCHC (g/L)	212.86 ± 18.62	375.37 ± 20.33*	226.72 ± 16.35	298.50 ± 18.25
Neutrophil %	9.13 ± 1.20	33.41 ± 6.24*	12.60 ± 2.44	21.71 ± 3.02
Lymphocyte %	80.62 ± 11.20	54.81 ± 8.23*	78.11 ± 9.54	61.14 ± 8.00
Monocyte %	23.62 ± 4.65	12.72 ± 2.88*	18.60 ± 3.54	14.00 ±2.45

Each value represents mean ± SEM (n = 6), *$p<0.05$ compared to control; ≠$p<0.05$ compared to $KBrO_3$ –treated rats, $KBrO_3$ = potassium bromated. . FEJAN = extract of *Ficus exasperata* harvested in January; FEJUL = extract of *Ficus exasperata* harvested in July

Effects of *Ficus exasperata* extracts on kidney function indices

Potassium bromate significantly increased serum levels of urea and creatinine compared to the control. Treatment with FEJUL and FEJAN caused significant reduction in the levels of urea and creatinine. The results are presented in Table 2

Table 2: Effects of *Ficus exasperata* extracts on kidney function indices

Group	Urea (mg/dl)	Creatinine (μmol/L)
Control	15.34 ± 2.61	28.32 ± 5.04
$KBrO_3$	46.61 ± 4.52*	49.56 ± 8.00*
$KBrO_3$ + FEJUL	26.92 ± 3.05$^{\neq}$	35.40 ± 5.63$^{\neq}$
$KBrO_3$ + FEJAN	30.76 ± 4.24$^{\neq}$	33.08 ± 3.16$^{\neq}$

Each value represents mean ± SEM (n = 6), *$p<0.05$ compared to control; ≠$p<0.05$ compared to $KBrO_3$ –treated rats, $KBrO_3$ = potassium bromated. . FEJAN = extract of *Ficus exasperata* harvested in January; FEJUL = extract of *Ficus exasperata* harvested in July

Effects of *Ficus exasperata* extracts on liver function indices

Administration of $KBrO_3$ significantly increased ($p<0.05$) the level of both AST and ALT compared with control. From 18.85 ± 4.30, AST was increased to 53.31 ± 8.53, while ALT was increased from 9.78 ± 1.43 to 16.76 ± 2.42 after the administration of $KBrO_3$. Compared with $KBrO_3$-treated roup, AST and ALT levels were significantly reduced by as shown in Table 3.

Table 3: Effects of *Ficus exasperata* extracts on liver function indices

Group	AST (U/L)	ALT (U/L)
Control	18.85 ± 4.30	9.78 ± 1.43
$KBrO_3$	53.31 ± 8.55*	16.76 ± 2.42*
$KBrO_3$ + FEJUL	23.31 ± 2.60$^{\neq}$	8.15 ± 1.20$^{\neq}$
$KBrO_3$ + FEJAN	28.63 ± 4.74$^{\neq}$	11.90 ± 2.50$^{\neq}$

Each value represents mean ± SEM (n = 6), *$p<0.05$ compared to control; ≠$p<0.05$ compared to $KBrO_3$ –treated rats, $KBrO_3$ = potassium bromated. FEJAN = extract of *Ficus exasperata* harvested in January; FEJUL = extract of *Ficus exasperata* harvested in July

Effects of *Ficus exasperata* extracts on antioxidants

Administration of $KBrO_3$ caused significant increase in the levels of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) compared to the control. Treatment with FEJUL and FEJAN significantly reduced the levels of these antioxidants as shown in Table 4.

Table 4: Effects of *Ficus exasperata* extracts on antioxidants

Group	SOD (U/ml)	CAT (U/ml	GPx (U/L)
Control	0.47 ± 0.08	16.25 ± 3.00	46.13 ± 9.06
$KBrO_3$	1.39 ± 0.24*	61.75 ± 8.84*	102.40 ± 16.63*
$KBrO_3$ + FEJUL	0.79 ± 0.12$^{\neq}$	24.25 ± 4.17$^{\neq}$	62.66 ± 7.52$^{\neq}$
$KBrO_3$ + FEJAN	1.16 ± 0.20	38.12 ± 5.64$^{\neq}$	79.89 ± 12.46$^{\neq}$

Each value represents mean ± SEM (n = 6), *$p<0.05$ compared to control; ≠$p<0.05$ compared to $KBrO_3$ – treated rats, $KBrO_3$ = potassium bromated. FEJAN = extract of *Ficus exasperata* harvested in January; FEJUL = extract of *Ficus exasperata* harvested in July

Effects of *Ficus exasperata* extracts on markers of inflammation and lipid peroxidation

In $KBrO_3$-treated group, serum level of C-reactive protein (CRP) increased significantly from 0.41 ± 0.11 to 2.88 ± 0.62. Malondialdehyde (MDA) level also increased from 0.46 ± 0.10 to 0.78 ± 0.21. Treatment with FEJUL and FEJAN significantly reduced CRP from 2.88 ± 0.62 to 0.81 ± 0.14 and 1.33 ± 0.20 respectively. FEJUL also reduced MDA significantly but FEJAN did not cause significant decrease in MDA level. The results are presented in Table 5.

Table 5: Effects of *Ficus exasperata* extracts on markers of inflammation and lipid peroxidation

Group	CRP (ng/L)	MDA (µM)
Control	0.41 ± 0.11	0.46 ± 0.10
$KBrO_3$	2.88 ± 0.62*	0.78 ± 0.21*
$KBrO_3$ + FEJUL	0.81 ± 0.14$^{\neq}$	0.51 ± 0.20$^{\neq}$
$KBrO_3$ + FEJAN	1.33 ± 0.20$^{\neq}$	0.61 ± 0.14

Each value represents mean ± SEM (n = 6), *p<0.05 compared to control; ≠p<0.05 compared to $KBrO_3$ –treated rats, $KBrO_3$ = potassium bromated. FEJAN = extract of *Ficus exasperata* harvested in January; FEJUL = extract of *Ficus exasperata* harvested in July

Effects of *Ficus exasperata* extracts on liver injury

Liver histoarchitecture in the control showed normal hepatic cords, distinct central vein and well-preserved sinusoids. In the $KBrO_3$-treated group, there was evidence of severe hepatocellular distortion, cytoplasmic degeneration, and congested central veins, indicating hepatotoxicity. $KBrO_3$/FEJAN –treated group displayed mild improvement in hepatic structure with moderately preserved hepatocytes and reduced vascular congestion. $KBrO_3$/FEJUL-treated group showed considerable restoration of normal liver histology with clearer hepatic cords and more organized sinusoids, indicating a protective effect of FEJUL against $KBrO_3$-induced hepatic damage. The photomicrographs of the liver sections are shown in Plate 1.

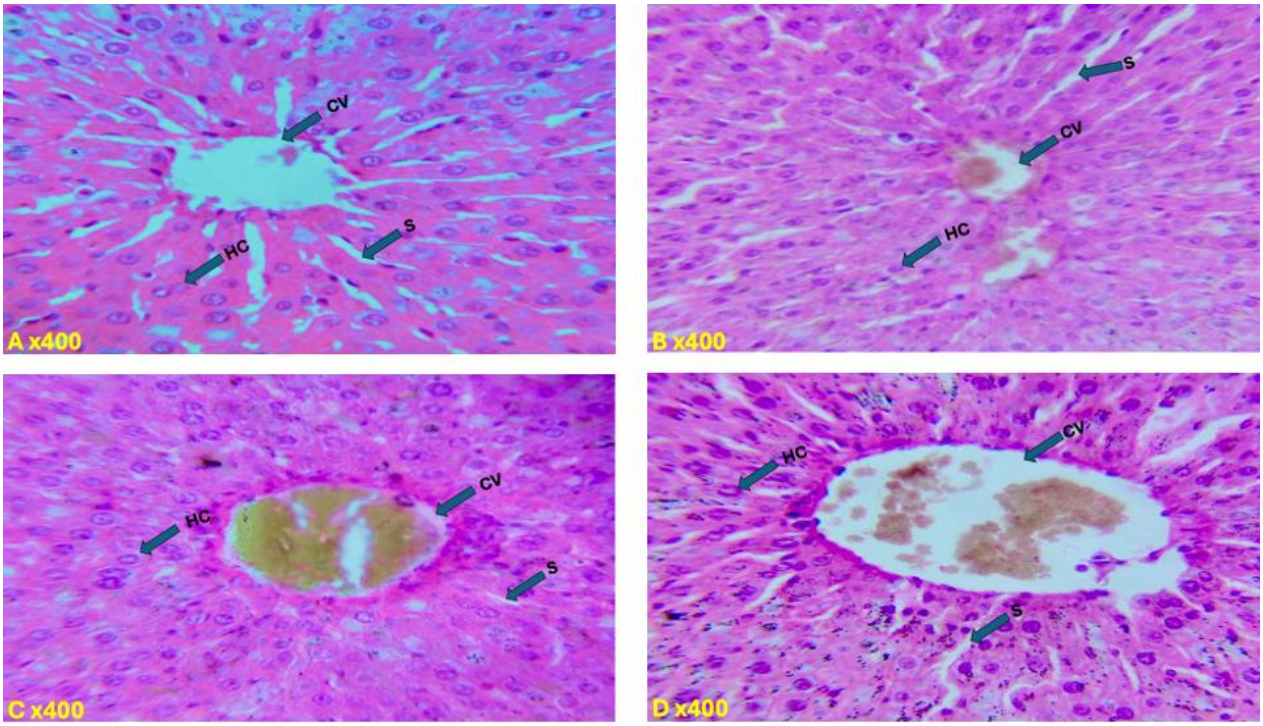

Plate 1: Photomicrographs of liver sections stained with haematoxylin and eosin

Liver histoarchitecture in group A (control) showed normal hepatic cords (HC), distinct central vein (CV), and well-preserved sinusoids (S). In group B ($KBrO_3$-treated), there was evidence of severe hepatocellular distortion, cytoplasmic degeneration, and congested central veins, indicating hepatotoxicity. Group C ($KBrO_3$/FEJAN) displayed mild improvement in hepatic structure with moderately preserved hepatocytes and reduced vascular congestion. Group D ($KBrO_3$/FEJUL) showed considerable restoration of normal liver histology with clearer hepatic cords and more organized sinusoids, indicating a protective effect of FEJUL against $KBrO_3$-induced hepatic damage. FEJAN = extract of *Ficus exasperata* harvested in January; FEJUL = extract of *Ficus exasperata* harvested in July ((Mag. ×400)

Effects of *Ficus exasperata* extracts on kidney injury

Photomicrograph of kidney sections of rats in the control group revealed normal renal corpuscle with intact glomerulus, Bowman's space, and distal tubules. $KBrO_3$-treated showed glomerular shrinkage, widened Bowman's space, and tubular distortion indicating nephrotoxicity. The group treated with $KBrO_3$/FEJAN

showed mild improvement with partial restoration of glomerular structure and reduced tubular damage, while section of the group treated with $KBrO_3$/FEJUL showed considerable restoration with improved glomerular architecture, narrowed Bowman's space, and preserved distal tubules. The photomicrographs of the kidney sections are shown in Plate 2.

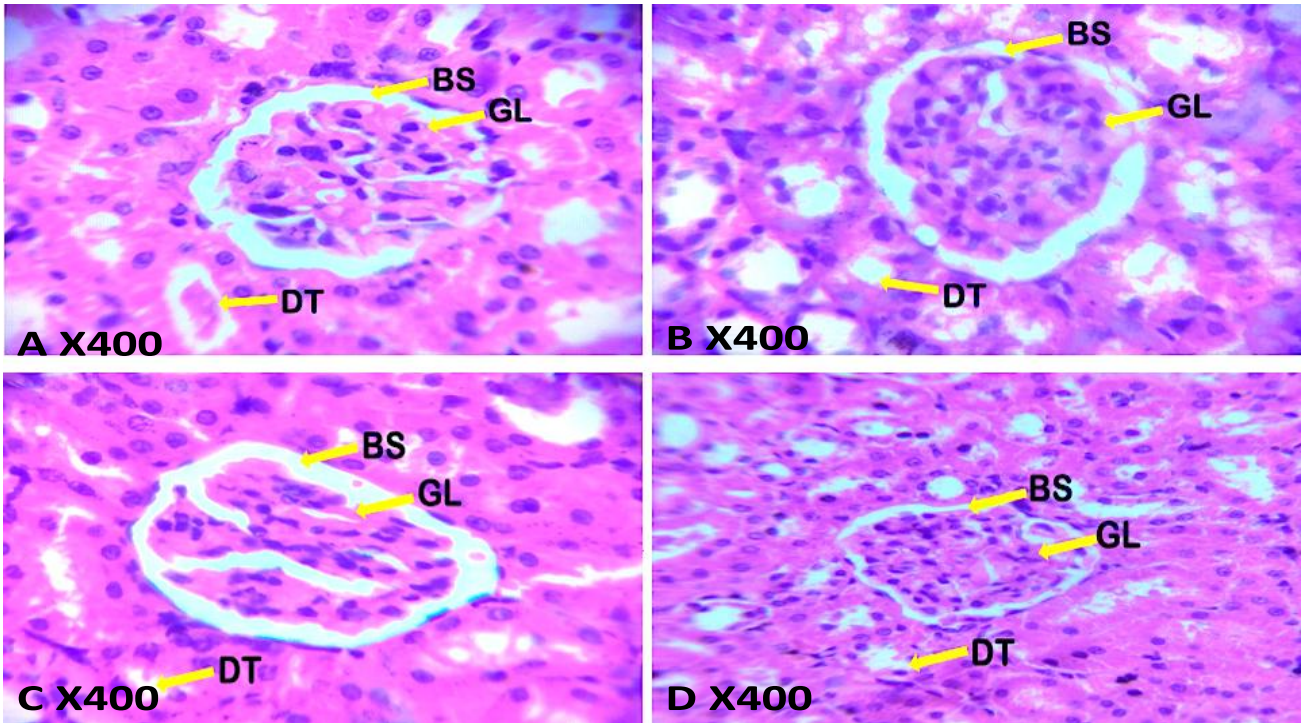

Plate 2: Photomicrographs of kidney sections stained with haematoxylin and eosin
Group A (control) revealed normal renal corpuscle with intact glomerulus (GL), Bowman's space (BS), and distal tubules (DT). Group B ($KBrO_3$-treated) showed glomerular shrinkage, widened Bowman's space, and tubular distortion indicating nephrotoxicity. Group C ($KBrO_3$/FEJAN) showed mild improvement with partial restoration of glomerular structure and reduced tubular damage. Group D ($KBrO_3$/FEJUL) showed considerable restoration with improved glomerular architecture, narrowed Bowman's space, and preserved distal tubules. FEJAN = extract of *Ficus exasperata* harvested in January; FEJUL = extract of *Ficus exasperata* harvested in July (Mag. ×400).

DISCUSSION

Administration of potassium bromate ($KBrO_3$) induced toxicity in rats, as evidenced by significant alterations in serum biochemical and hematological parameters. Notably, markers of hepatic and renal function were markedly affected, indicating the development of hepato-renal dysfunction following KBrO3 exposure.

Urea, a primary waste product of protein metabolism[13], is synthesized in the liver through the detoxification of ammonia and subsequently transported via the bloodstream to the kidneys for excretion. Under normal physiological conditions, healthy kidneys efficiently filter and eliminate urea from the body. An elevated serum urea concentration is therefore a recognized indicator of impaired kidney function[14]. The significant increase in serum urea observed in KBrO3-treated rats suggests renal injury and compromised kidney function, consistent with previous studies reporting potassium bromate-induced nephrotoxicity[15].

Treatment with FEJAN and FEJUL significantly reduced serum urea. In This regard, FEJUL decreased urea level more than FEJAN. Creatinine, another marker of kidney function, is formed from creatine and phosphocreatine in skeletal muscle. It is freely excreted by the kidneys. Like urea, a rise in the serum level of creatinine is an indication of kidney damage [16]. The increase in the level of creatinine after administration of potassium bromated suggests that potassium bromate induced renal toxicity. FEJAN and FEJUL were able to attenuate the toxic effects $KBrO_3$ in the kidney as indicated by a significant reduction in the serum level of creatinine following treatment with the extracts. Efficacy of medicinal plants usually varies according to the proportion of their phytoconstituents during different seasons of the year[17]. Seasonal variation in the activity of *Ficus exasperata* was also noted; FEJUL being more active

in reducing creatinine, packed cell volume, red blood cell count, white blood cell count, hemoglobin level, and platelet count were significantly lowered in rats treated with $KBrO_3$. Mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and neutrophil counts were significantly elevated following $KBrO_3$ administration, while lymphocyte and monocyte counts were reduced. These hematological changes indicate that $KBrO_3$ induced anemia in the treated rats. Treatment with FEJAN and FEJUL significantly mitigated these alterations, suggesting that *Ficus exasperata* leaf extracts possess antianemic properties. These findings are in agreement with previous studies that have demonstrated the efficacy of *Ficus exasperata* leaves in alleviating anemia in experimental animal models[18, 19]. Notably, the extract from leaves harvested in July (FEJUL) provided greater protection against KBrO3-induced hematotoxicity compared to the extract from January (FEJAN).

Administration of $KBrO_3$ caused alterations in the serum levels of AST and ALT. These are markers of liver function. The alterations suggest impairment of hepatic function [20]. FEJAN and FEJUL were able to reduce serum levels of AST and ALT. This indicates the positive effects of the extract of *Ficus exasperata* on liver function. It is widely reported that $KBrO_3$ induces oxidative stress [21]. Therefore antioxidants are expected to be helpful in protecting against $KBrO_3$ toxicity. Many medicinal plants have been reported to contain antioxidants [22]. FEJAN and FEJUL reduced the toxic effects of $KBrO_3$ by significantly reducing oxidative stress. This is evident in the reduced levels of catalase, superoxide dismutase, and glutathione peroxide after treatment with the extracts. Exposure of rats to potassium bromate ($KBrO_3$) resulted in elevated serum levels of C-reactive protein (CRP) and malondialdehyde (MDA), indicating the induction of systemic inflammation and lipid peroxidation[23, 24]. Treatment with *Ficus exasperata* leaf extracts harvested in January (FEJAN) and July (FEJUL) significantly reduced these markers, demonstrating the extracts' anti-inflammatory properties and their ability to mitigate oxidative damage. These findings are consistent with previous reports documenting the anti-inflammatory effects of *Ficus exasperata*[25].

Histopathological analyses further corroborated the biochemical and hematological results. The structural distortions in the kidney and liver tissues caused by $KBrO_3$ exposure were notably ameliorated following treatment with both FEJAN and FEJUL.

Across most evaluated parameters, FEJUL exhibited greater efficacy than FEJAN, suggesting that the concentration of bioactive compounds responsible for the observed protective effects is higher in leaves harvested during the rainy season (July) compared to the dry season (January).

CONCLUSION

Ficus exasperata leaf extracts confer significant protective effects against potassium bromate-induced hepato-renal toxicity, hematotoxicity, inflammation, and oxidative stress in rats. Moreover, seasonal variation influences the efficacy of the extract, with leaves harvested during the rainy season (July) demonstrating superior bioactivity compared to those collected in the dry season (January). These findings highlight the therapeutic potential of *Ficus exasperata* and underscore the importance of considering seasonal factors in the utilization of medicinal plants.

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Ogbomoso

Conflict of Interest

The authors declare no conflict of interest.

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