Exploring the Lipid-Modulating, Haematological and Antioxidant Potential of *Vernonia Amygdalina* and *Celosia Argentea* in Potassium Bromate-Induced Toxicity in Rats

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ABSTRACT

Background: Potassium bromate ($KBrO_3$) is a widely used food preservative known for its potential toxicological effects, including oxidative stress and alterations in haematological parameters. **Objectives:** This study aimed to investigate the lipid-modulating, haematological, and antioxidant potential of Vernonia amygdalina (bitter leaf) and Celosia argentea (shoko) in mitigating potassium bromate-induced toxicity in Wistar rats. **Materials and Methods:** Male and female Wistar rats (6-7 weeks old) were randomly assigned to four groups: Control (Group A), Potassium Bromate (Group B), Potassium Bromate + Vernonia amygdalina (Group C), and Potassium Bromate + Celosia argentea (Group D). The rats were administered their respective treatments for 60 consecutive days. Lipid profiles, oxidative stress markers, and haematological parameters were assessed. **Results:** Potassium bromate significantly increased total cholesterol, HDL, and white blood cell count while decreasing LDL and altering haematological parameters. The administration of Vernonia amygdalina and Celosia argentea extracts demonstrated varying degrees of reversal in these effects. Vernonia amygdalina led to significant improvements in cholesterol and HDL levels but did not significantly alter triglycerides or LDL. Celosia argentea also reversed some lipid profile changes but showed differential impacts on oxidative stress markers. Both extracts had significant effects on white blood cell count and differential counts. **Conclusion:** The study highlights the potential of Vernonia amygdalina and Celosia argentea as effective mitigators of potassium bromate-induced toxicity. The plant extracts exhibited varying degrees of protective effects, particularly in lipid modulation, oxidative stress reduction, and haematological parameter normalization. These findings support the use of these natural remedies as adjuncts in managing oxidative stress and lipid disorders induced by toxic substances. To completely understand the mechanisms behind these effects and investigate their possible uses in toxicological and therapeutic interventions, more research is necessary.

Keywords: Potassium bromate, *Vernonia amygdalina*, *Celosia argentea*, lipid profile, oxidative stress, haematology, Wistar rats

INTRODUCTION

Potassium bromate ($KBrO_3$) is a potent oxidizing agent extensively utilized in the food industry, particularly as a dough conditioner in bread production due to its ability to strengthen dough and improve its baking quality [1]. However, its use has been controversial owing to its carcinogenic potential and its tendency to induce oxidative stress in biological systems. Potassium bromate has been classified as a Group 2B carcinogen by [1], meaning it is possibly carcinogenic to humans based on sufficient evidence from animal models but limited evidence in humans [1].

Oxidative stress, which occurs when there is an overproduction of reactive oxygen species (ROS) combined with insufficient antioxidant defenses, plays a major role in the development of various diseases, such as cancer, cardiovascular conditions, and metabolic syndromes [2]. Potassium bromate metabolism generates

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ROS, leading to lipid peroxidation, protein oxidation, and DNA damage [3]. These oxidative effects disrupt cellular homeostasis and contribute to lipid dysregulation, *haematological* abnormalities, and compromised antioxidant defense systems. Lipid metabolism disturbances induced by oxidative stress are commonly manifested as altered serum lipid profiles.

Exposure to potassium bromate has been linked to elevated levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides, while high-density lipoprotein cholesterol (HDL-C) levels are often reduced [4]. This dyslipidemia exacerbates the possibility of atherosclerosis and other cardiovascular diseases. Similarly, oxidative stress impacts *haematological* parameters, leading to anaemia, reduced red blood cell count, lower haemoglobin concentration, and altered haematocrit levels [5]. These changes signifies systemic oxidative damage and impaired blood cell production.

To counteract the toxic effects of potassium bromate, there is a growing interest in natural antioxidants that can mitigate oxidative damage and restore physiological balance. *Vernonia amygdalina* (bitter leaf) and *Celosia argentea* (cock's comb) are two such plants renowned for their antioxidant properties. *Vernonia amygdalina*, commonly used in traditional medicine, is rich in bioactive compounds such like flavonoids, saponins, and alkaloids, that have been demonstrated to possess significant antioxidant and anti-inflammatory effects [6];[7]. These compounds contribute regarding its capcity to scavenge free radicals, reduce oxidative stress, and modulate lipid metabolism. Similarly, *Celosia argentea* is known for its high content of polyphenols and flavonoids, which confer potent antioxidant activity [8]. The plant has been reported to have a protective effect against oxidative stress and inflammation, potentially enhancing its role in managing lipid abnormalities and improving haematological profiles. The antioxidant capacity of *Celosia argentea* is ascribed to its capacity to neutralize ROS and inhibit lipid peroxidation, thereby preventing oxidative damage.

Despite the promising therapeutic potentials of *Vernonia amygdalina* and *Celosia argentea*, there remains a need for comprehensive studies to evaluate their efficacy in mitigating potassium bromate-induced toxicity. This research aims to explore the lipid-modulating, *haematological*, and antioxidant potential of these plants in a potassium bromate-induced toxicity model using rats. By assessing their protective effects, this study seeks to provide valuable insights into their role as natural therapeutic agents in combating oxidative stress and improving health outcomes related to lipid dysregulation and haematological disturbances.

MATERIALS AND METHODS

Test substance and preparation of $KBrO_3$, and $NaNO_2$ stock solution:

Potassium bromate (KBrO3, CAS No. 7758-01-2, product code 17000), with a purity of 99.5%, white colour, and powder form, was purchased from MOLYCHEM Co., Mumbai, India. According to Patnaik [9], the oral LD50 of potassium bromate in rats is approximately 157 mg/kg body weight, indicating a relatively low acute toxicity. This information was used to determine the suitable dosage for the current study.

Collection, identification and preparation of plant extract

Fresh leaves of *Vernonia amygdalina* (Bitter Leaf) and *Celosia argentea* (Lagos Spinach) were procured from a local market in Effurun, Delta State. The plants' taxonomic identities were verified by the Department of Environmental Management and Toxicology at the College of Sciences, Federal University of Petroleum Resources, Effurun, Delta State, Nigeria. The phytochemical components of the leaf powders were determined following standard techniques as delineated by [10];[11];[12]. For this study, the leaf extracts of *Vernonia amygdalina* and *Celosia argentea* were used. The fresh leaves were dried in the laboratory at around 30 ± 2°C until crisp, a process that took about two weeks. After drying, the leaves were coarsely pounded with a pestle and mortar, then finely pulverized using a Viking Exclusive Joncod machine (Model: YLH2M2-4). A total of 25 grams of the powdered leaves from each plant was extracted with 250 mL of water over 48 hours. The extract was filtered using sterile Whatman paper No. 1, and the filtrate was dried into a solid form using a freeze dryer. The dried extract was then reconstituted in distilled water to achieve the desired concentrations for the study. Previous research indicated that the oral LD50 of *Vernonia amygdalina* and *Celosia argentea*

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extracts in rats is approximately 2,500 mg/kg and 5,000 mg/kg body weight, respectively, suggesting a low level of acute toxicity [13]; [14].

Collection and Acclimatization of experimental rats

Male rats, aged 6-7 weeks and weighing between 125g and 150g, were sourced from the Anatomy Department of the University of Benin, Nigeria. The rats were acclimatized for two weeks until they reached 8-9 weeks of age, at which point their weights were recorded. The animals were housed separately by gender in wooden cages with wire mesh covers. They were provided with standard rodent chow (Bendel Livestock Feeds Limited, Ewu, Edo State, Nigeria) and had access to distilled water ad libitum. Following the acclimatization period, the rats were randomly allocated randomly to four groups, labelled A-D, and subjected to the treatment protocols outlined below.

Group A – Control (C)

Group B - Potassium bromate (PB)

Group C - Potassium bromate + *Vernonia amygdalina* leaf (PB+BTL)

Group D - Potassium bromate + *Celosia argentea* leaf (PB+SHK)

Potassium bromate was mixed with distilled water at a concentration of 90 mg per kg of body weight. The mixture was shaken for five minutes to evenly distribute the particles before being given to the rats. *Vernonia amygdalina* and *Celosia argentea* were prepared by steeping them in hot water, with concentrations of 150 mg/kg and 100 mg/kg body weight, respectively. The rats were kept in standard lab conditions and were given free access to drinking water and regular rodent food. Each rat received the specified treatment every other day for 60 days. After this period, the surviving rats were subjected to overnight fasting and then sacrificed under light anesthesia. Blood samples were collected for further analysis. Blood was drawn from a large vein using a sterile syringe and placed into tubes containing EDTA and plain tubes for testing. The blood in the plain tubes was allowed to clot and then spun in a centrifuge to separate the serum. The serum was stored at -80°C until it was ready for analysis.

Laboratory Analysis

Haematological analysis was performed using a Sysmex KX-21N automated machine (Sysmex Corporation, Kobe, Japan) according to the manufacturer's guidelines. The blood sample was mixed and then placed in contact with the machine's sample probe. When the machine emitted two beeps and displayed 'ANALYZING' on the screen, the sample was removed. The machine then automatically analyzed the sample, and the results were displayed on the screen and printed out.

Serum biochemical markers were measured to assess different health indicators. For lipid profile, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides were analyzed. Hormonal levels such as testosterone, estrogen, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) were measured for hormonal profiling. Hydrogen peroxide was measured to assess reactive oxygen species. Markers of oxidative stress, including malondialdehyde (MDA), superoxide dismutase (SOD), catalyse (CAT), glutathione peroxidase (GPx), glutathione (GSH), total antioxidant capacity (TAC), vitamin C, and protein levels, were also evaluated. These biomarkers were determined using standard ready-to-use kits, following the manufacturer's instructions. The absorbance of the tests was measured using a spectrophotometer (OPTIMA, SP-300, Japan).

Data Analysis

All statistical analyses were carried out using SPSS and Microsoft Excel software. The data are presented as mean ± standard error (SE). To compare the differences between the groups, a one-way ANOVA was used. Specific differences between groups were identified using Duncan's Multiple Range Test. A p-value of less than 0.05 was considered statistically significant.

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RESULTS

The results of the lipid profile for Wistar rats treated with potassium bromate, along with other abatement treatments, are presented in Table 1. The findings showed that administering potassium bromate led to an increase in TC(121.16±36.52mg/dL), total triglycerides (135.45±0.00mg/dL), and high-density lipoprotein (HDL) (81.72±1.35mg/dL), while low-density lipoprotein (LDL) decreased (66.53±35.17mg/dL) compared to the control group. When potassium bromate was given together with aqueous extracts of bitter leaf and *Celosia argentea*, there was a reversal in the levels of TC and HDL. However, there was no significant change (P<0.05) in total triglycerides and LDL compared to the rats that received only potassium bromate.

Table 1. Lipid profileof wistar rats given potassium bromated food preservatives and possible abatements

	Experimental setup				**P-Value**
	CTR	**PB**	**PB+BTL**	**PB+SHK**	
TC(mg/dL)	106.67±13.04	121.16±36.52	78.55±6.09	93.04±2.61	P<0.05
Triglyceride (mg/dL)	125.93±5.82	135.45±0.00	136.77±5.56	132.01±1.32	P>0.05
HDL (mg/dL)	57.34±1.13	81.72±1.35	53.50±0.23	57.34±3.61	P<0.05
LDL (mg/dL)	74.52±13.08	66.53±35.17	52.41±7.42	62.11±0.74	P>0.05

NB: HDL = high density lipoprotein LDL= Low density lipoprotein

The serum oxidative stress parameters and levels of reactive oxidative species in Wistar rats treated with potassium bromate and potential abatement treatments are presented in Table 2. The results showed that potassium bromate caused a slight, non-significant decrease in catalase (CAT) (0.19±0.00) and glutathione peroxidase (GPx) (1.05±0.05). In contrast, there was a significant increase in glutathione (GSH) (208.57±8.57), vitamin C (67.52±1.46), protein (3.40±0.11), total antioxidant capacity (159.12±5.03), and hydrogen peroxide (159.12±5.03) compared to the control group. The levels of superoxide dismutase (SOD) and malondialdehyde (MDA) in the blood were similar to those in the control rats.

When potassium bromate was administered along with bitter leaf extract, there was a slight, non-significant increase in SOD (0.49±0.00) and GPx (1.08±0.00), but a significant decrease in CAT (0.16±0.08), GSH (190.48±15.24), vitamin C (61.13±20.26), protein (3.49±0.02), total antioxidant capacity (64.31±0.79), and hydrogen peroxide (85.36±13.87) compared to the group that only received potassium bromate. Rats treated with potassium bromate and *Celosia argentea* showed a slight, non-significant decrease in SOD (0.45±0.05), CAT (0.12±0.11), GPx (1.06±0.00), vitamin C (49.45±4.93), protein (3.47±0.09), and total antioxidant capacity (96.70±18.08), while GSH (96.70±18.08) and hydrogen peroxide (175.34±97.11) levels increased.

Table 2. Serum oxidative stressand Reactive oxidative species of wistar rats given potassium bromate food preservatives and possible abatements

	Experimental setup				**P-Value**
	CTR	**PB**	**PB+BTL**	**PB+SHK**	
SOD (U/g)	0.48±0.00	0.48±0.00	0.49±0.00	0.45±0.05	P>0.05
Catalase (U/g)	0.22±0.01	0.19±0.00	0.16±0.08	0.12±0.11	P<0.05
GPx (U/g)	1.10±0.03	1.05±0.05	1.08±0.00	1.06±0.00	P>0.05
MDA (mol/g)	0.08±0.00	0.08±0.00	0.08±0.00	0.08±0.00	P>0.05
Red. GSH (µg/mL)	165.71±50.95	208.57±8.57	190.48±15.24	214.29±94.29	P<0.05
Vitamin C (µg/mL)	44.53±7.66	67.52±1.46	61.13±20.26	49.45±4.93	P<0.05
Protein (g/dL)	3.40±0.11	3.59±0.18	3.49±0.02	3.47±0.09	P>0.05
TAC (µg/mL)	94.65±9.75	159.12±5.03	64.31±0.79	96.70±18.08	P<0.05
H_2O_2 (µg/mL)	46.63±13.10	173.70±13.58	85.36±13.87	175.34±97.11	P<0.05

NB: SOD = Superoxide dismutase; GPx = glutathione peroxidises; MDA = Malondialdehyde Red. GSH = glutathione; TAC = total antioxidant capacity

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The effect of potassium bromates and possible abatements on white blood cells and their differentials is shown in Table 3. The results revealed that potassium bromate caused an increase in the white blood cell count ($6.10\pm1.60\times10^3$/µL), percentage of mid-sized cells (7.85±0.45%), and percentage of granulocytes (2.60±0.40%), along with a decrease in the percentage of lymphocytes (89.55±0.85%) compared to the control group. In the group of rats given potassium bromate along with bitter leaf extract, the white blood cell count increased further. However, the percentage of lymphocytes (92.50±0.05%), mid-sized cells (4.70±0.20%), and granulocytes (1.80±0.15%) showed a reversal in trend compared to the rats treated only with potassium bromate. In the group treated with potassium bromate and *Celosia argentea* extract, there was a reversal in the trends for white blood cell count ($4.65\pm1.00\times10^3$/µL), percentage of lymphocytes (92.75±0.60%), mid-sized cells (1.65±0.00%), and granulocytes (1.65±0.00%).

Table 3. white blood cell and differentials of wistar rats given potassium bromate food preservatives and possible abatements

	Experimental setup				p-Value
	CTR	PB	PB+BTL	PB+SHK	
White blood cell ($\times10^3$/µL)	4.60±1.10	6.10±1.60	6.60±0.75	4.65±1.00	P>0.05
Lymphocyte (%)	94.10±1.25	89.55±0.85	92.50±0.05	92.75±0.60	P>0.05
Mid-Sized cells (%)	3.90±1.20	7.85±0.45	4.70±0.20	5.60±1.60	P<0.05
Granulocyte (%)	2.00±0.05	2.60±0.40	1.80±0.15	1.65±0.00	P>0.05
Lymphocyte ($\times10^3$/µL)	5.50±0.95	4.30±1.50	6.10±0.70	4.30±0.90	P<0.05
Mid-Sized cells ($\times10^3$/µL)	0.20±0.10	0.50±0.10	0.40±0.05	0.25±0.10	P<0.05
Granulocyte ($\times10^3$/µL)	0.10±0.05	0.10±0.00	0.10±0.00	0.10±0.00	P>0.05

The effect of potassium bromates and possible abatements on red blood cells and their measurements is shown in Table 4. The results indicated that potassium bromate caused a slight, non-significant decrease in red blood cell count ($7.74\pm0.10\times10^6$/µL), haematocrit (37.95±2.35%), and mean corpuscular haemoglobin concentration (MCHC) (32.90±1.40g/dL), while mean corpuscular haemoglobin (MCH) increased (25.65±1.95pg) compared to the control group. When potassium bromate was administered along with bitter leaf extract, there was a slight, non-significant increase in red blood cell count ($7.99\pm0.19\times10^6$/µL), mean corpuscular volume (MCV) (39.90±3.30fL), and MCH (19.05±1.60pg) compared to the group that received only potassium bromate. A different trend was observed in rats treated with potassium bromate and *Celosia argentea* extract, where there was a decrease in red blood cell count ($7.87\pm0.07\times10^6$/µL), MCV (49.40±1.45fL), and MCH (17.80±0.25pg) compared to those treated only with potassium bromate.

Table 4. Red blood cell and indicesof wistar rats given potassium bromated food preservatives and possible abatements

	Experimental setup				P-Value
	CTR	PB	PB+BTL	PB+SHK	
Red blood cell ($\times10^6$/µL)	7.82±0.11	7.74±0.29	7.99±0.19	7.87±0.07	P>0.05
Haemoglobin (g/dL)	13.10±0.60	13.10±1.20	13.95±1.10	13.20±0.85	P>0.05
Haematocrit (%)	38.00±1.30	37.95±2.35	39.90±3.30	38.90±1.60	P>0.05
MCV (fL)	48.60±0.95	49.05±1.15	50.15±3.00	49.40±1.45	P>0.05
MCH (pg)	19.30±3.00	25.65±1.95	19.05±1.60	17.80±0.25	P<0.05
MCHC (g/dL)	33.10±0.00	32.90±1.40	31.40±1.20	31.90±0.60	P>0.05
RDW-SD (%)	32.00±2.15	32.05±2.15	33.10±2.15	34.15±1.10	P>0.05
RDW-CV (fL)	15.40±0.75	15.30±0.70	15.50±0.10	16.20±0.10	P>0.05

NB: MCV= Mean corpuscular volume; MCH = Mean corpuscular Haemoglobin; MCHC = Mean corpuscular Haemoglobin concentration; RDW-CV = Red blood distribution width coefficient of variation; RDW-SD = Red blood distribution width standard deviation

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The effect of potassium bromates and possible abatements on platelet count and its measurements is shown in Table 5. The results revealed that potassium bromate caused a significant increase in platelet count (600.00±183.00×10^3/µL) and a slight, non-significant increase in mean platelet volume (MPV) (7.15±0.35fL) and plateletcrit (PCT) (0.43±0.15%). However, there was a slight, non-significant decrease in platelet distribution width (PDW) (9.05±0.65%) and platelet-large cell ratio (P-LCR) (2.90±2.90%) compared to the control group. In rats treated with potassium bromate and bitter leaf extract, there was a significant decrease in platelet count (429.50±17.00×10^3/µL), with a slight, non-significant decrease in MPV (7.05±0.15fL) and PCT (0.30±0.34%). There was also a slight, non-significant increase in PDW (9.70±0.90%) and P-LCR (3.30±0.00%) compared to the rats that received only potassium bromate. Similarly, rats treated with potassium bromate and *Celosia argentea* extract showed a decrease in platelet count (400.00±26.50×10^3/µL), with no significant decrease in MPV (6.75±0.05fL), and a slight, non-significant increase in PDW and P-LCR compared to the potassium bromate-treated rats."

Table 5. Platelet count and differentialsof wistar rats given potassium bromatefood preservatives and possible abatements

	Experimental setup				P-Value
	CTR	PB	PB+BTL	PB+SHK	
Platelet (×10^3/µL)	518.00±120.00	600.00±183.00	429.50±17.00	400.00±26.50	P<0.05
MPV (fL)	7.00±0.25	7.15±0.35	7.05±0.15	6.75±0.05	P>0.05
PDW (%)	9.70±0.15	9.05±0.65	9.70±0.90	9.10±0.80	P>0.05
PCT (%)	0.36±0.10	0.43±0.15	0.30±0.34	0.61±0.02	P<0.05
P-LCR (%)	3.50±1.35	2.90±2.90	3.30±0.00	0.30±0.03	P<0.05

NB: MPV= Mean platelet volume; PDW = Platelet distribution width; PCT = plateletcrit; P-LCR = Platelet large cell ratio

DISCUSSIONS

A lipid profile is a crucial diagnostic tool used to analyze the level of different types of lipids in the blood, providing important insights into an individual's cardiovascular health and risk for cardiovascular disease. The primary components measured in a lipid profile include total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides. Total Cholesterol (TC) represents the overall level of cholesterol in the blood. It includes both HDL and LDL cholesterol, along with other lipid fractions [14]. HDL Cholesterol, often referred to as "good" cholesterol, helps remove excess cholesterol from the bloodstream and transports it to the liver for excretion [15]. LDL Cholesterol, or "bad" cholesterol, is responsible for transferring cholesterol from the liver to the cells [16]. Triglycerides are another type of lipid found in the bloodstream. They store excess energy from the diet and are released into the bloodstream between meals [17]. Regular monitoring of these lipid parameters helps in assessing an individual's risk for cardiac diseases and aids in managing illment such as hyperlipidemia. Lifestyle changes, including diet and exercise, as well as medications, can be prescribed based on the results to help manage lipid levels and reduce cardiovascular risk [18].

The administration of potassium bromates led to significant changes in the lipid profile of Wistar rats, marked by increase in total cholesterol, triglycerides, and HDL levels, alongside a reduction in LDL levels compared to the control group. This pattern of lipid dysregulation is likely tied to potassium bromate's oxidative stress-inducing properties, which are known to disturb lipid metabolism—a known risk factor for cardiovascular diseases [3]; [4]. Interestingly, the concurrent administration of potassium bromates with aqueous extracts of *Vernonia amygdalina* and *Celosia argentea* reversed the increases in TCand HDL levels, although the alterations in triglycerides and LDL were not statistically significant. This implies that both plant extracts possess lipid-modulating properties, which align with their recognized antioxidant and hypolipidemic effects [6]; [7].

The elevation in HDL observed after potassium bromate administration might represent a compensatory response to oxidative stress, given HDL’s role in reverse cholesterol transport and antioxidative functions [2].

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The pronounced increase in TCand triglycerides, alongside elevated HDL, points to an imbalance in lipid metabolism induced by oxidative damage. The antioxidant-rich profiles of *Vernonia amygdalina* and *Celosia argentea* likely contributed to their efficacy in mitigating these effects, as evidenced by their ability to enhance lipid metabolism and reduce oxidative stress [7]; [8]. These findings align with existing research that links potassium bromate to lipid dysregulation and oxidative stress, and they underscore the potential of natural antioxidants to reverse lipid abnormalities induced by such stress. Our study contributes to the growing body of evidence by highlighting the specific impact of *Vernonia amygdalina* and *Celosia argentea* on lipid metabolism, offering valuable insights into their potential therapeutic use in countering the adverse effects of food preservatives [4].

Oxidative stress is a condition characterized by an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize them with antioxidants. This imbalance leads to the aggregation of ROS, which can damage cellular components such as lipids, proteins, and DNA, contributing to the progression of various diseases. Reactive Oxygen Species (ROS) are highly reactive molecules containing oxygen. They are naturally produced in the body as derivatives of normal cellular metabolism, particularly during the process of energy production in the mitochondria. While ROS is pivotal to cell signalling and homeostasis, their excessive production can overwhelm the body’s antioxidant defenses, leading to oxidative stress [19]. Antioxidants are molecules that neutralize ROS, inhibiting them from causing damage. The body’s antioxidant defense system includes enzymatic antioxidants like superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), as well as non-enzymatic antioxidants like vitamin C, vitamin E, and glutathione (GSH) [20]. When the stability between ROS production and antioxidant defenses is disrupted, oxidative stress is induced. This condition is implicated in the onset of numerous chronic diseases, including cardiac diseases, brain degenerative disorders, diabetes, and cancer. For example, oxidative stress can induce the oxidation of low-density lipoprotein (LDL) cholesterol, a key event in the initiation and progression of atherosclerosis, a major risk element for heart disease [21].

The administration of potassium bromates in Wistar rats resulted in significant alterations in oxidative stress markers. Notably, there was a non-significant decrease in the activities of enzymatic antioxidants like catalase (CAT) and glutathione peroxidase (GPx), suggesting a potential reduction in the antioxidant defense system. Conversely, there was a significant increase in non-enzymatic antioxidants, such as glutathione (GSH) and vitamin C, as well as in protein levels, total antioxidant capacity, and hydrogen peroxide (H_2O_2) levels compared to the control group. This pattern indicates that potassium bromate induces oxidative stress, evidenced by the elevated oxidative stress markers and the compensatory increase in certain antioxidant parameters. The significant rise in H_2O_2 levels aligns with the hypothesis of oxidative stress since H_2O_2 is a key reactive oxygen species (ROS) contributing to cellular damage (Halliwell & Gutteridge, 2015). Interestingly, the levels of superoxide dismutase (SOD) and malondialdehyde (MDA) remained unchanged, suggesting that the oxidative stress induced by potassium bromate does not significantly impact these parameters, or that the damage might be mitigated by other mechanisms not directly reflected in MDA levels [3].

When potassium bromate was co-administered with *Vernonia amygdalina* extract, there was a non-significant increase in SOD and GPx, while significant decreases were observed in CAT, GSH, vitamin C, protein levels, total antioxidant capacity, and H_2O_2 compared to the potassium bromate group. This suggests that *Vernonia amygdalina* may exert protective effects by enhancing certain aspects of the antioxidant defense system and reducing oxidative damage, although some parameters, such as CAT and GSH, remained significantly altered. In contrast, the combination of potassium bromates with *Celosia argentea* extract resulted in a non-significant decrease in SOD, CAT, GPx, vitamin C, protein levels, and total antioxidant capacity, alongside an increase in GSH and H_2O_2 levels. The rise in GSH suggests a potential compensatory response to oxidative stress, while the elevated H_2O_2 levels indicate ongoing oxidative damage.

These findings illustrate the oxidative damage induced by potassium bromate, characterized by impaired enzymatic antioxidant responses, as evidenced by the decrease in CAT and GPx activities, leading to reduced detoxification of ROS [20]. The increase in GSH and vitamin C reflects a compensatory mechanism aimed at counteracting oxidative stress, yet the persistent elevation in H_2O_2 levels suggests that the oxidative damage may be substantial, potentially overwhelming the antioxidant defenses. The differential effects observed with

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Vernonia amygdalina and *Celosia argentea* are likely due to their distinct phytochemical compositions and antioxidant capacities. *Vernonia amygdalina*, known for its high flavonoid and saponin content, appears to more effectively enhance antioxidant enzyme activities and reduce oxidative stress [6]. Conversely, the polyphenolic compounds in *Celosia argentea* may offer a less robust antioxidant response, as reflected by the continued increase in H_2O_2 levels.

White blood cells (WBCs), or leukocytes, are key players in the immune system, defending the body against infections and foreign invaders. Unlike red blood cells, which carry oxygen, WBCs protect the body by combating pathogens, removing dead cells, and responding to immune challenges. WBCs are categorized into five main types: neutrophils (60-70%), which are the first to respond to infections; lymphocytes (20-40%), including T cells, B cells, and NK cells that manage immune responses; monocytes (2-8%), which turn into macrophages in tissues to help with defense and repair; eosinophils (1-4%), involved in fighting parasites and allergic reactions; and basophils (less than 1%), which play a role in allergic responses and inflammation. Monitoring WBC counts is crucial in diagnosing and managing diseases, guiding treatments, and evaluating the body's immune response, especially in patients undergoing chemotherapy.

The administration of potassium bromates led to a significant increase in total white blood cell (WBC) count and a rise in the percentages of mid-sized cells and granulocytes, along with a decrease in the percentage of lymphocytes. These changes suggest an immunological response to the toxic insult caused by potassium bromate, which is known for its carcinogenic and oxidative stress-inducing properties. The increase in total WBC count typically indicates a reactive or inflammatory response, potentially due to oxidative damage or tissue irritation [22]. The observed elevation in mid-sized cells and granulocytes likely reflects an acute inflammatory response, as these cells are involved in the early stages of inflammation and immune defense [23]. The concurrent decrease in lymphocytes may suggest a shift in immune cell distribution or an adaptive response to chronic stress or inflammation. When potassium bromate was administered in conjunction with *Vernonia amygdalina*, there was a further increase in total WBC count, alongside a reversal in the trends for lymphocytes, mid-sized cells, and granulocytes. This indicates that *Vernonia amygdalina* might mitigate some of the haematological alterations induced by potassium bromate. The increased lymphocyte percentage and decreased levels of mid-sized cells and granulocytes suggest that the bitter leaf extract may exert a balancing effect on the immune system. The phytochemical components of *Vernonia amygdalina*, such as flavonoids and alkaloids, are known for their immunomodulatory and anti-inflammatory properties, which could contribute to normalizing WBC differentials and enhancing immune response [24]. The observed normalization of lymphocyte levels might indicate improved immune regulation or restoration of immune homeostasis following intervention with the extract.

In the group treated with potassium bromate and *Celosia argentea*, there was a decrease in total WBC count and a reversal in the percentages of lymphocytes, mid-sized cells, and granulocytes. These findings suggest that *Celosia argentea* might also influence the WBC alterations induced by potassium bromate, though its overall effect appears less pronounced compared to *Vernonia amygdalina*. *Celosia argentea* contains various phytochemicals known for their antioxidant and anti-inflammatory effects, which may help reduce oxidative stress and inflammatory responses. However, the observed decrease in total WBC count, along with the reversal of differential percentages, suggests a complex interaction between the extract and the immune system. This could indicate a modulating effect that requires further investigation to fully understand its implications [25]. These findings align with previous studies demonstrating that potassium bromate induces significant changes in immune parameters due to its oxidative stress-inducing properties. Research has shown that potassium bromate can lead to elevated WBC counts and alterations in immune cell differentials as part of the inflammatory response[26]. The protective effects of *Vernonia amygdalina* observed in this study are consistent with its known potential to modulate immune responses and counteract oxidative damage [24]. Conversely, the results with *Celosia argentea* provide new insights into its potential effects on WBC parameters, though further studies are needed to elucidate its mechanisms of action and therapeutic potential fully [25].

Red blood cells (RBCs) are the most common cells in the blood, responsible for transporting oxygen from the lungs to tissues and carrying carbon dioxide back to the lungs for exhalation. Haemoglobin, the main component of RBCs, binds oxygen and gives the cells their red colour. The number and function of RBCs,

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along with specific indices like Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), and Mean Corpuscular Haemoglobin Concentration (MCHC), are essential for assessing health and diagnosing conditions like anaemia. These indices help evaluate the size, haemoglobin content, and concentration in RBCs, providing insight into various blood disorders.

Administration of potassium bromate resulted in subtle changes in red blood cell (RBC) parameters. Specifically, there was a non-significant decrease in RBC count, haematocrit, and mean corpuscular haemoglobin concentration (MCHC). Conversely, mean corpuscular haemoglobin (MCH) increased. These alterations suggest that potassium bromate may impair erythropoiesis or provoke an adaptive response to oxidative stress. The decrease in RBC count and haematocrit indicates a potential reduction in overall red blood cell mass, possibly due to decreased production or increased destruction of erythrocytes [27]. The increase in MCH suggests that the individual red blood cells may be larger or contain more haemoglobin, possibly as a compensatory mechanism for the reduced number of cells [28]. This pattern reflects an attempt to maintain adequate oxygen-carrying capacity despite reduced total red blood cell mass. In contrast, rats treated with potassium bromate and *Vernonia amygdalina* exhibited a non-significant increase in RBC count, mean corpuscular volume (MCV), and MCH. The increase in RBC count and MCV suggests that *Vernonia amygdalina* may mitigate some of the adverse effects of potassium bromate on erythrocyte production and morphology. The potential mechanisms behind these effects could involve the antioxidant and hematopoietic properties of *Vernonia amygdalina*, which might enhance red blood cell production or reduce oxidative damage to erythrocytes [24]. The increase in MCH indicates that erythrocytes may be more hemoglobin-saturated, reflecting improved red blood cell health and function.

On the other hand, the group treated with potassium bromate and *Celosia argentea* showed a decrease in RBC count, MCV, and MCH. This suggests that *Celosia argentea* might have a different impact on erythrocyte parameters compared to *Vernonia amygdalina*. The decrease in RBC count and MCV implies that the extract may not fully counteract the effects of potassium bromate or could even exacerbate certain aspects of erythrocyte dysfunction. The observed decrease in MCV and MCH could indicate an adverse effect on red blood cell production or maturation. Although *Celosia argentea* contains antioxidant phytochemicals, its effects on haematological parameters might be influenced by its different mechanism of action compared to *Vernonia amygdalina* [25]. These findings are consistent with existing literature highlighting potassium bromate's potential to induce oxidative stress and haematological changes, including reduced RBC count and altered MCV and MCH [26]; [27]. The protective effects of *Vernonia amygdalina* align with previous research showing its beneficial role in mitigating oxidative damage and improving haematological parameters [24]. Conversely, the results for *Celosia argentea* provide new insights into its potential impact on red blood cell parameters, suggesting a need for further research to elucidate its mechanisms and effects in different contexts [25].

Platelets, also known as thrombocytes, are small, disc-shaped cell fragments in the blood that play a critical role in haemostasis, the process of stopping bleeding at the site of an injured blood vessel. When a blood vessel is damaged, platelets quickly adhere to the injury site, aggregate with other platelets, and release chemicals that initiate the clotting process, forming a stable blood clot to prevent excessive bleeding [29]. Key platelet indices include platelet count, mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT), which provide valuable information about platelet function and potential abnormalities. The platelet count measures the number of platelets in the blood and is crucial in diagnosing conditions like thrombocytopenia (low platelet count) or thrombocytosis (high platelet count) [30]. MPV reflects the average size of platelets; an increased MPV may indicate the presence of larger, younger platelets, often seen in disorders like immune thrombocytopenic purpura (ITP) or myeloproliferative diseases [31]. PDW measures the variability in platelet size and can be used to detect abnormal platelet production or activation. A high PDW may suggest an increased number of larger or more reactive platelets, which can occur in conditions such as inflammatory disorders or cardiovascular diseases [32]. PCT, analogous to haematocrit, represents the volume percentage of platelets in the blood and can help assess the overall platelet mass, particularly in cases of extreme thrombocytopenia or thrombocytosis [33]. Understanding these indices is vital for diagnosing and managing various haematological and cardiovascular conditions, ensuring appropriate medical intervention when necessary.

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The administration of potassium bromates led to a significant increase in platelet count, suggesting a hyperplastic response of megakaryocytes or increased platelet production. This finding aligns with previous research indicating that potassium bromate can induce bone marrow hyperplasia, resulting in elevated platelet levels [26]. Despite this increase in platelet count, mean platelet volume (MPV) and plateletcrit (PCT) showed non-significant increases, indicating that while platelet count is elevated, the average platelet size and volume remain relatively stable. The non-significant decrease in platelet distribution width (PDW) and platelet-large cell ratio (P-LCR) further suggests that platelet characteristics and distribution are not significantly altered, implying that potassium bromate's effect primarily involves increased production rather than changes in platelet characteristics [27]. In contrast, rats treated with both potassium bromate and *Vernonia amygdalina* exhibited a significant decrease in platelet count compared to those treated with potassium bromate alone. This reduction indicates that *Vernonia amygdalina* may mitigate the thrombocytosis induced by potassium bromate. The lack of significant changes in MPV, PCT, and the non-significant increases in PDW and P-LCR suggest that *Vernonia amygdalina* specifically affects platelet production rather than altering platelet characteristics. This reduction in platelet count could be attributed to the anti-inflammatory and antioxidant properties of *Vernonia amygdalina*, which may counteract the hyperplastic effects of potassium bromate on the bone marrow [24].

Similarly, treatment with potassium bromate and *Celosia argentea* resulted in a decrease in platelet count. The non-significant changes in MPV, PDW, and P-LCR suggest that *Celosia argentea* also moderates the platelet count induced by potassium bromate. The reduction in platelet count may be related to the antioxidant properties of *Celosia argentea*, which could help reduce oxidative stress and the associated hyperplastic response of platelets [25]. The absence of significant changes in platelet volume and distribution indicates that the extract's primary action may be on platelet production rather than altering platelet characteristics. These findings are consistent with previous studies showing that potassium bromate induces thrombocytosis, likely due to its toxic effects on the hematopoietic system [26]. The results also support existing literature on *Vernonia amygdalina*'s therapeutic potential in managing oxidative stress and haematological changes, with protective effects against platelet dysfunction [24]. For *Celosia argentea*, the study corroborates its antioxidant and anti-inflammatory properties, suggesting its potential to counteract some of the effects of potassium bromate, although further investigation is needed to fully elucidate the mechanisms involved [25].

CONCLUSION

This study evaluated the effects of potassium bromate, a known food preservative with potential toxicological effects, on various *haematological* and biochemical parameters in Wistar rats, and assessed the ameliorative potential of *Vernonia amygdalina* (bitter leaf) and *Celosia argentea* (shoko) leaf extracts. The findings reveal significant insights into the impact of potassium bromate on lipid profiles, oxidative stress markers, and blood cell parameters, as well as the efficacy of the plant extracts in mitigating these effects.

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