Chemotherapeutic Propensity of Africa Locust Bean
(Parkia biglobosa) Seed on Lipid Profile against
Potassium Bromate-induced Cardiotoxicity

C. N. Ugwu a, C. E. Iwuoha b, N. M. Chika-Igwenyi c, C. A. Onyeaghala d, S. F. Orji c, C. Igwenyi c, C. L. Uche e, O. I. N. Onyekachi f, g, M. U. Nwobodo c, I. O. Abali h and A. I. Airaodion i*

 a Department of Internal Medicine, Ebonyi State University, Abakaliki, Nigeria.
 b Department of Community Medicine, Abia State University, Uturu, Nigeria.
 c Department of Internal Medicine, Alex Ekwueme Federal University Teaching Hospital, Abakaliki, Ebonyi State, Nigeria.
 d Department of Internal Medicine, University of Port-Harcourt Teaching Hospital, Rivers State, Nigeria.
 e Department of Haematology, Abia State University, Uturu, Nigeria.
 f Department of Medical Microbiology, Ebonyi State University, Abakaliki, Nigeria.
 g Department of Medical Microbiology, Alex Ekwueme Federal University Teaching Hospital, Abakaliki, Ebonyi State, Nigeria.
 h Department of Surgery, Abia State University, Uturu, Nigeria.
 i Department of Biochemistry, Federal University of Technology, Owerri, Imo State, Nigeria.

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

ABSTRACT

Background: Cardiovascular disease cases are on the increase despite many standard medical practices. Some disorders have been successfully treated by medicinal plants.
Aim: The current study was designed to assess the chemotherapeutic propensity of Parkia biglobosa against potassium bromate-induced cardiotoxicity.
Methodology: Using a soxhlet extractor with ethanol as the solvent, P. biglobosa was extracted.

Twenty-four mature male Wistar rats were randomly divided into groups A, B, C, and D after being...
Keywords: African locust bean; cardiotoxicity; lipid profile; potassium bromate.

1. INTRODUCTION

African locust bean (Parkia biglobosa) is a member of the Fabaceae family, which includes the peas. The Hausa call it "Dorawa", Ibo call it "Ogili," while the Yoruba call it "iru," [1]. The fermented seeds of the African locust bean are used to season traditional soups throughout Nigeria and the west coast of Africa. The yellow pulp, which contains 60% sugar, is a food that provides a lot of energy [2]. The trees are frequently cultivated as shade trees. Traditional uses for Parkia species include food and medicine. The bark is used to treat bronchitis, pneumonia, skin infections, gores, ulcers, bilharziasis, malaria, diarrhea, and hypertension in addition to healing wounds. In the Gambia, a lotion for itchy eyes is made from the leaves and roots. Infusion of P. biglobosa stembark is also applied to the mouth to treat toothaches and as a hot bath for fever. Lemon and the pulped bark are applied topically to wounds and ulcers. Pod and root fibers are used to make sponges and musical instrument strings [2]. In northern Nigeria, the traditional Hausa structures are painted with the powdered pods. It has been determined that Parkia plants provide a source of tannin, saponins, gum, fuel, and wood. Attempts have also been made to determine the protein and mineral content of seeds from different Parkia species [3].

For many years, especially in the last stages of baking, potassium bromate (KBrO3) has been used as food additives and to improve bread dough [4,5]. It also develops as a byproduct when bromide is used to ozonize water. In animal studies, the biotransformation of KBrO3 generates free radicals that cause oxidative damage to essential macromolecules and promote carcinogenesis and nephrotoxicity [6]. Some countries, including the United Kingdom, Canada, and Nigeria, have outlawed the industrial use of KBrO3 in manufacturing and food processing businesses since 1990, 1994, and 1993, respectively [5]. However, in certain nations, compliance has not been thoroughly and efficiently monitored, which has had a negative impact on consumers [7,8].

Small molecules that are hydrophobic or amphiphilic can be widely referred to as lipids. Some lipids can form vesicles, liposomes, or membranes in an aqueous environment due to their amphiphilic nature [9]. The group of naturally occurring organic chemicals known as lipids is wide and diverse, but they are linked by their solubility in nonpolar organic solvents (such as ether, chloroform, acetone, and benzene) and their general insolubility in water [10]. Fats, waxes, sterols, fat-soluble vitamins (including vitamins A, D, E, and K), monoglycerides, diglycerides, triglycerides, phospholipids, and other naturally occurring molecules make up this group of compounds [11]. Although the word "lipid" is occasionally used interchangeably with "fats," fats really belong to a subset of lipids called "triglycerides" [12]. Lipids also include sterol-containing metabolites like cholesterol as well as other fatty acid and their derivatives (such
2.2 Collection and Extraction of *Parkia biglobosa*

A botanist identified the *P. biglobosa* (African locust bean) seeds after they were purchased from a local market in Ibadan, Nigeria. After being sun-dried, they were ground into powder using a mechanical blender (Moulinex). Using a soxhlet apparatus and ethanol as the solvent, the extraction was completed in accordance with the steps described by Airaodion et al. [20,21]. About 25 g of the sample powder and a round bottom flask with a capacity of 250 mL of ethanol were added to the soxhlet extractor and condenser on a heating mantle. The solvent was heated by the heating mantle and began to evaporate as it passed through the apparatus to the condenser. The condensate dropped into a reservoir that housed the sample-containing thimble. When the solvent level reached the siphon and was poured back into the flask with a flat bottom, the cycle was resumed. The operation was given a total of 18 hours. With a yield of 2.55 g and a percentage yield of 10.20 percent, the ethanol was evaporated in a rotary evaporator at 35°C at the end of the process. Until it was needed, the extract was kept in the refrigerator.

2.3 Animal Treatment

Twenty-four (24) mature male Wistar rats (*Rattus norvegicus*) weighing between 140 and 160 g were used in the experiment. They were acclimated in a laboratory setting for seven (7) days prior to the trial. The rats were housed in wire-mesh cages with free access to commercial rat food and water. The animals were kept in standard temperature and humidity conditions with 12-hour cycles of light and dark. This inquiry was carried out in accordance with the Declaration of Helsinki and the guidelines established by the Committee for the Purpose of Control and Supervision of Experiments on Animals. Additionally, NIH policy was followed when doing animal experiments [22]. At random, they were put into groups A, B, C, and D. Group A received oral distilled water as the control while groups B, C, and D received 100 mg/kg body weight of potassium bromate. Animals in groups C and D further received 100 and 200 mg/kg body weight of *P. biglobosa*, respectively. Fresh potassium bromate and *P. biglobosa* were administered to rats every day by oral gavage. The animals had 28 days of successive treatments before being killed. The animals were sacrificed while being gently sedated with diethyl ether twenty-four hours following the last treatment. Through a heart puncture, blood was taken. The animals' hearts were also taken from them.

2.4 Preparation of Organ Homogenate

The organs (heart) were swiftly removed from the animals after being hastily dissected. Then, using a Teflon homogenizer, 10% of each organ homogenate was produced in 6.7mM potassium phosphate buffer (pH 7.4). To create a clear supernatant that could be stored in the freezer for additional analysis, the homogenate was centrifuged at 10,000 rpm for 10 minutes at 40°C.

2.5 Determination of Lipids

Lipids were extracted and determined according to previously described methods [23,24].

2.6 Statistical Analysis

Graph Pad Prism was used to conduct a variance analysis on the data. The findings were
shown as Mean Standard deviation (SD). For the purpose of comparing the means, one-way analysis of variance (ANOVA) was used, then Tukey’s post hoc analysis. At \( P \leq 0.05 \), differences between means were deemed significant.

3. RESULTS

When compared to the untreated group, the plasma levels of total cholesterol, triglycerides, LDL, VLDL, and the CHD risk ratio were significantly higher in the study's animals treated with KBrO\(_3\), while HDL and the HDL/LDL ratio were significantly lower (Table 1). According to Table 2, compared to the control group, administration of KBrO\(_3\) significantly decreased cardiac levels of total cholesterol, HDL, and HDL/LDL ratio, while increasing levels of triglycerides, LDL, and VLDL, as well as the CHD risk ratio. *P. biglobosa* ameliorated these perturbations in a dose-dependent manner.

4. DISCUSSION

Lipid profile is a key indicator of a number of pathological diseases [25]. A change in lipid profile is a sign of pathological abnormalities associated with a heart illness in clinical settings. Atherosclerosis was brought on by the sedimentation of artery wall plaques, which was characterized by an increase in LDL and a decrease in HDL levels [16]. Numerous studies have shown that elevated levels of HDL are linked to lower incidences of cardiovascular illnesses while elevated levels of LDL are linked to higher risk of atherosclerosis [26–28].

Table 1. Effect of *P. biglobosa* on the plasma lipid profile of potassium bromate-induced cardiac toxicity

| Lipid Profile | Control | KBrO\(_3\) Only | KBrO\(_3\) + 100 mg/kg *P. biglobosa* | KBrO\(_3\) + 200 mg/kg *P. biglobosa* | p-value |
|---------------|---------|----------------|-----------------------------------|-----------------------------------|---------|
| TC (mg/dL)    | 148.32±8.25 | 232.42±12.35 | 204.82±6.81                          | 166.27±4.25                          | 0.00    |
| TG (mg/dL)    | 96.46±6.22  | 171.37±8.26  | 144.44±8.16                          | 127.65±4.38                          | 0.01    |
| HDL-C (mg/dL) | 49.46±3.26  | 32.28±5.36   | 38.35±2.56                           | 44.44±3.67                           | 0.02    |
| LDL-C (mg/dL) | 47.24±1.48  | 74.26±3.17   | 62.39±2.40                           | 55.03±3.25                           | 0.02    |
| VLDL-C (mg/dL)| 19.24±1.92  | 34.27±2.64   | 28.88±2.78                           | 25.56±2.64                           | 0.01    |
| HDL:LDL ratio | 1.06±0.09   | 0.41±0.04    | 0.64±0.06                            | 0.80±0.07                            | 0.00    |
| CHD risk ratio| 2.96±0.18   | 7.23±0.12    | 5.34±0.23                            | 3.71±0.19                            | 0.00    |

Values are presented as Mean±SD, where \( n = 6 \).

Legend: TC = Total Cholesterol, TG = Triglyceride, HDL-C = High Density Lipoprotein Cholesterol, LDL-C = Low Density Lipoprotein Cholesterol, VLDL-C = Very Low Density Lipoprotein Cholesterol, CHD = Coronary Heart Disease

Table 2. Effect of *P. biglobosa* on the Heart Lipid Profile of Potassium Bromate-induced Cardiac Toxicity

| Lipid Profile | Control | KBrO\(_3\) Only | KBrO\(_3\) + 100 mg/kg *P. biglobosa* | KBrO\(_3\) + 200 mg/kg *P. biglobosa* | p-value |
|---------------|---------|----------------|-----------------------------------|-----------------------------------|---------|
| TC (mg/dL)    | 116.46±3.38 | 81.20±7.82  | 88.63±5.26                          | 108.22±6.87                          | 0.01    |
| TG (mg/dL)    | 136.28±3.01 | 159.77±9.32 | 161.26±4.25                          | 140.00±6.78                          | 0.01    |
| HDL-C (mg/dL) | 58.29±2.15  | 38.31±2.94   | 46.44±2.82                           | 53.89±2.94                           | 0.00    |
| LDL-C (mg/dL) | 46.86±2.02  | 59.20±3.22   | 53.72±1.93                           | 49.00±3.01                           | 0.04    |
| VLDL-C (mg/dL)| 27.23±3.76  | 31.97±1.84   | 32.22±2.22                           | 28.08±4.11                           | 0.05    |
| HDL:LDL ratio | 1.24±0.01   | 0.67±0.06    | 0.840.03                             | 1.09±0.09                            | 0.03    |
| CHD risk ratio| 1.99±0.12   | 2.10±0.09    | 1.93±0.04                            | 2.00±0.11                            | 0.61    |

Values are presented as Mean±SD, where \( n = 6 \).

Legend: TC = Total Cholesterol, TG = Triglyceride, HDL-C = High Density Lipoprotein Cholesterol, LDL-C = Low Density Lipoprotein Cholesterol, VLDL-C = Very Low Density Lipoprotein Cholesterol, CHD risk ratio = Coronary Heart Disease Risk Ratio
Insulin is known to play a significant role in the metabolism of lipids in addition to controlling blood sugar levels [29–31]. Relative molecular ordering of the remaining phospholipids due to hypercholesterolemia has been linked to a reduction in membrane fluidity [32]. One of the main risk factors for coronary heart disease is triglyceride buildup (CHD). A number of disease disorders’ development and progression are significantly influenced by changes in lipid and lipoproteins [33].

According to the findings of this study, plasma levels of total cholesterol, triglycerides, LDL, VLDL, and CHD risk ratio were significantly elevated in animals treated with KBrO3 compared to the untreated group, while HDL and HDL/LDL ratio were significantly decreased (table 1). This caused an increase in atherogenic index, which is a reliable indicator of the development of atherosclerotic disorders in KBrO3-treated animals. The induced dyslipidemia was lessened in rats treated with 100 and 200 mg/kg of P. biglobosa seed extract with KBrO3 exposure. This may be an indication that P. biglobosa has the ability to stop coronary heart disease (CHD) from getting worse. Its significant phytochemical content and antioxidant capabilities, which were documented by Ajaiyeoba [34], may have contributed to this potential. Despite the availability of well-known CHD drugs, herbal therapies are being utilized more and more successfully to treat this condition and better control its complications [35,36]. Additionally, it has been asserted that medicinal plants and herbal formulations are less toxic and have less adverse effects than synthetic treatments, which is why more people are turning to herbal cures rather than synthetic ones [37–41]. The World Health Organization (WHO)'s interest in hypolipidemic drugs of plant origin employed in the conventional treatment of cardiovascular illnesses may have been influenced by increased results of therapeutic effectiveness of herbal medications [42].

CHD has been linked to hypertriglyceridaemia [35,43]. This was found to be caused by increased endogenous production of triglyceride-enriched hepatic VLDL cholesterol and decreased triglyceride uptake in peripheral tissues, as well as increased absorption and formation of triglycerides in the form of chylomicrons as a result of exogenous consumption of a diet high in fat [44]. The P. biglobosa’s impact seen in this study would indicate that the seed has the ability to lessen absorption and chyomicron production of triglycerides. CHD has also been linked to hypercholesterolemia [45]. This was linked to the increased absorption of dietary cholesterol from the small intestine as a result of eating a high-fat diet [44].

In contrast, when compared to rats exposed to KBrO3 but left untreated in the current investigation, the concentrations of serum triglycerides, VLDL-cholesterol, and total cholesterol were considerably lower in animals treated with different dosages of P. biglobosa. Furthermore, it is conceivable that P. biglobosa's effects on lipid levels result from its phenolic components inhibiting the synthesis of hepatic cholesterol, triglycerides, and perhaps fatty acids [44].

High blood pressure is predicted by hypertriglyceridaemia [46]. Endothelial cells in the peripheral vascular system depend on lipoproteins at this location for the transport of neutral sterols. Lecithin cholesterol acyl transferase (LCAT) maintains the concentration toward the HDL core and maintains the hydrophobic nature that facilitates the transfer, even though free cholesterol is transferred to HDL-cholesterol particles through the activity of a designated HDL-cholesterol receptor [47]. The product of cholesterol esterification is cholesterol ester (CE), which is concentrated in HDL core and can be transported to apo-B-containing lipoproteins via cholesterol ester transfer protein (CETP) in the plasma compartment in place of triglyceride. Increased CETP activity has traditionally been regarded as pro-atherogenic [45,48] since it would imply an enrichment of apo-B lipoproteins in plasma while concurrently lowering HDL cholesterol. Given that a high HDL-cholesterol/LDL-cholesterol ratio has been demonstrated to be advantageous and to be a sign of a lower risk of cardiovascular diseases, this likely explains why P. biglobosa may reduce the chance of developing heart ailments [49].

Two of the four major subgroups of plasma lipoproteins, HDL and LDL, are involved in lipid metabolism and the transfer of triglycerides, cholesterol, and cholesterol esters between tissues [50,51]. According to numerous studies, there is a negative correlation between plasma HDL cholesterol levels and the risk of cardiovascular disease, suggesting that HDL cholesterol has some protective effects against atherosclerosis [19,44]. Some of these factors seem to have anti-inflammatory and antioxidant
properties that could prevent the processes that lead to atherogenesis [52,53].

Increased blood levels of total cholesterol and/or LDL cholesterol are significant risk factors for coronary heart disease, according to epidemiological studies [54,55]. A higher tendency for atherosclerosis to develop may be implied by an increased CHD risk ratio brought on by KBrO₃. Despite having a need for cholesterol, the majority of extra-hepatic tissues have a low activity of the cholesterol biosynthetic pathway. LDL, which is internalized by receptor-mediated endocytosis, meets their need for cholesterol [44]. By removing extra cholesterol from peripheral tissues, esterifying it with lecithin: cholesterolacyltransferase, and then delivering it to the liver and steroidogenic organs for subsequent synthesis of bile acids and lipoproteins and ultimate removal from the body, HDL-cholesterol plays a key role in enhancing reverse cholesterol transport [56,57]. According to reports, HDL cholesterol plays this role and is the reason for its atheroprotective qualities [45,54]. Additionally, HDL-cholesterol controls how different lipoproteins exchange lipids and proteins [35,44].

The protein elements needed to activate lipoprotein lipase, which releases fatty acids that can be oxidized by the β-oxidation pathway to produce energy, are also provided by HDL-cholesterol [50,51]. Most notably, because of its antioxidant property, HDL cholesterol can lessen the oxidation of LDL cholesterol and the atherogenic consequences of oxidized LDL cholesterol [57]. LDL is a lipoprotein that moves triglycerides and cholesterol from the liver to nearby tissues. It makes it possible for fat and cholesterol to go through the blood stream's water-blood solution [54]. Since LDL is sometimes referred to as bad cholesterol, low levels are advantageous [35].

Intriguingly, when compared to the negative control animals (induced but untreated animals), the administration of *P. biglobosa* extract in varied dosages in this investigation resulted in a significant rise in the plasma level of HDL-cholesterol at P ≤ 0.05. The term "good cholesterol" refers to HDL cholesterol [23]. When compared to the negative control group (induced but untreated animals), *P. biglobosa* administration again significantly decreased the levels of LDL-cholesterol (bad cholesterol) at P ≤ 0.05. This outcome is consistent with the research by Airaodion et al. [19] who examined how oral consumption of African locust bean affected albino rats' fasting blood sugar levels and lipid profiles. When animals treated with varied doses of *P. biglobosa* extract were compared to the negative control group, the combined effects of higher HDL-cholesterol (good cholesterol) and lower LDL-cholesterol (bad cholesterol) increased HDL-cholesterol/LDL-cholesterol ratio. Because a high HDL-cholesterol/LDL-cholesterol ratio has been demonstrated to be advantageous and is suggestive of a lower risk of CHD, this strongly supports the idea that dietary supplementation with *P. biglobosa* may reduce the chance of developing heart disorders [44].

Although a number of antioxidants showed a potential ability to reduce KBrO₃-induced toxicity, few have yet been demonstrated to work specifically at the toxicity of the heart. Since this has not been well studied, the main goal of this work was to evaluate the potential protective impact of *P. biglobosa* against KBrO₃-induced cardiotoxicity. According to a recent study by Ugwu et al. [58], 100 mg/kg body weight of KBrO₃ increased lipid peroxidation and lowered GSH, CAT, SOD, and GPx in the heart of Wistar rats as compared to control animals, inducing cardiotoxicity. Evidence also points to the creation of oxygen free radicals, which can harm cells by oxidizing lipids [59]. Increased production of free radicals may also result in the creation of protein-protein cross-links and protein oxidation, which fragment proteins and change the side chains of amino acids [60]. For example, Saad et al. [61]'s study found that KBrO₃-treated rats' cardiac homogenates had much higher levels of advanced oxidation protein product (AOPP) than the controls, indicating a higher degree of protein oxidation. Oxygen-derived free radical reactions, according to Pham-Huy et al. [62], have been linked to the etiology of numerous human diseases, including cardiovascular diseases such as atherosclerosis, ischemic heart disease, cardiac hypertrophy, hypertension, shock, and trauma. *P. biglobosa* was able to counteract these effects. There have been claims that *P. biglobosa* extract has antihypertensive properties [63]. Additionally, hepatoprotective effects of *P. biglobosa* against ethanol-induced oxidative stress have been reported [64].

Despite the fact that the activities of enzymes were not examined in this study, it is possible that KBrO₃ lowered the activity of 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA)
reductase, the rate-limiting enzyme in cholesterol synthesis [24]. This could be what caused the animals exposed to KBrO₃ to have significantly lower levels of total cholesterol in their hearts than the animals in the control group (Table 2). Since sex hormones depend on cholesterol as a precursor, a considerable decrease in the production of cholesterol could have a negative impact on that process. It is interesting to know that this impact was alleviated by *P. biglobosa* extract. The action of the extract could be attributed to its phytochemical content and antioxidant potential.

5. CONCLUSION

The results from this study showed that potassium bromate caused increase in the levels of plasma triglycerides, LDL, VLDL and reduction in the HDL/LDL ratio and this effect was found to be attenuated by intake of *P. biglobosa*. This effect will result in the reduction of cardiovascular disease risk factors; this strongly supports the idea that dietary supplementation with *P. biglobosa* may reduce the chance of developing heart disease; thus, we encourage its regular consumption.

ETHICAL APPROVAL

Animal Ethic committee approval has been taken to carry out this study.

Animal Ethic committee approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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