



Attenuation of KCN-induced Neurotoxicity by Solvent Fractions of *Antiaris africana* Leaf

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Authors' contributions

This work was carried out in collaboration between all authors. Authors RA and OBI designed and conducted the study under the supervision of authors ACA, TMO and AAA. Authors OOC and KCK were involved in data analysis and development of the manuscript. Author OBI wrote the protocol and author RA wrote the first draft of the manuscript. Authors OBI and RA managed the literature searches. All authors were involved in proofreading and approving the manuscript.

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ABSTRACT

Antiaris africana belongs to the family Moraceae, it is commonly called "False Iroko" tree and one of the medicinal plants used in treatment of mental and nervous disorders in Nigeria. We have previously established the neuroprotective properties of crude extract of *A. africana*. The present study was thus designed to investigate the neuroprotective effect of different solvent fractions of *A. africana* against cyanide neurotoxicity in vitro. Cyanide induced a significant ($P < 0.01$) inhibition of NADH succinate dehydrogenase, a key enzyme in mitochondria function as well as significant increase in oxidative stress as observed in the high level of malondialdehyde (MDA), protein carbonyl (PC) and activity of monoamine oxidase (MAO) and decreased concentration of reduced glutathione (GSH) as compared to the control. Co-administration with different solvent fractions of

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A. africana (hexane fraction [HFA], dichloromethane fraction [DFA] and methanolic fraction [MFA]) significantly ameliorated the toxic effect of KCN as compared to the induced, untreated group ($P < 0.05$). The results in this study showed that HFA (79.04% reversal of NSD inhibitory activity of KCN), DFA (63.68% and 72.6% activity against KCN induced LPO and PC respectively). However, MFA showed the best activity against GSH depletion caused by KCN (12.21%) and inhibition of MAO activity induced by KCN (94.63%). In conclusion, all the fractions possess neuroprotective activities at varying degrees against mitochondria damage by KCN. This result further substantiated the ethnomedicinal usage of *A. africana* and can provide novel compounds in the treatment of mitochondria-related neurodegenerative diseases.

Keywords: *Antiaris africana*; potassium cyanide; neuroprotective; oxidative stress; mitochondria; phytochemistry.

1. INTRODUCTION

Oxygen is required for energy metabolism, survival and normal functions of most eukaryotic organisms [1]. It is also partially reduced into superoxide, a basic free radical that can be converted eventually into other forms of reactive oxygen species (ROS), such as superoxide anion radical (O_2^-), hydroxyl radicals ($\cdot OH$), and the non-radical hydrogen peroxide (H_2O_2) along the respiratory chain [2]. Reactive oxygen species (ROS) are balanced with antioxidant systems to keep their level constant in living organisms [3]. However, breaking the balance by over production of reactive oxygen species and/or reduction of antioxidants can be deleterious, and is termed oxidative stress [4]. Under these conditions, excessive free radicals can destroy cell membrane via oxidation of the lipid and protein component of the membrane, and intracellularly modifying signal and structural proteins causing loss of function, and oxidizing RNA/DNA to interrupt transcription process [5].

Mitochondrial electron transport chain is an important source of ROS generation in the form of superoxide anion radical (O_2^-) [6] and has been described as key regulators of cell survival and death [7,8]. Decline in the activity of the organelle can further increase the production of O_2^- , causing oxidative stress. Thus, defect in mitochondria integrity has a deleterious effect on cellular functions in the brain and neurons [9]. Mitochondria thus control the neuronal cell fate via mediation of apoptotic and necrotic cell death. Mitochondrial metabolism decline and mitochondrial oxidative stress have been directly implicated in ageing, arising as a risk factor for the sporadic forms of the neurodegenerative diseases [10]. Cyanide salts such potassium cyanide and sodium cyanide are odorless when dry. They are a potent inhibitor of cellular respiration and works to inhibit ATP production

by blocking the electron transport chain in mitochondria [11].

Cyanide exerts its primary toxicological effects by binding to the metallic cofactor in metalloenzymes, thereby impairing enzyme and cell function. Cytochrome c oxidase (an enzyme in the mitochondrial respiratory chain) is the most significant target of cyanide exposure since its inhibition prevents tissues from using oxygen. The result is a reduction in oxygen sufficient to cause tissue damage (histiotoxic hypoxia) throughout the body. In addition to binding to cytochrome c oxidase, cyanide inhibits catalase, peroxidase, hydroxycobalamin, phosphatase, tyrosinase, ascorbic acid oxidase, xanthine oxidase, and succinic dehydrogenase activities, which may also contribute to the signs of its toxicity [12]. These properties of KCN has made it a good chemical to model neurotoxicity.

Medicinal plants have been identified and used throughout human history [12]. The easy accessibility and lower toxicity of medicinal plants have resuscitated the importance of medicinal plants in the treatment of chronic diseases such as neurodegenerative diseases. *Antiaris africana* is a large attractive deciduous timber tree, which grows up to 120 ft (30-40 m) high [13]. They are found in the drier forest of tropical Africa, Oceania and South East Asian. They are referred to by many common names such as 'Oro' by the Yoruba speaking part of Nigeria, 'Ojianwu' by the Igbo speaking people and 'Farin loko' by the Hausa speaking people of Nigeria [14,15]. The plant is utilized traditionally in ethno-medicine for epilepsy, lumbago, skin irritant, purgative, nervous disorders [16]. *Antiaris africana* is rich in antioxidant, anti-inflammatory, antimicrobial and anticancer phytochemicals [13-16]. The leaves and root are also used to treat mental illnesses. Previously, we reported the neuroprotective properties of the crude

extract of *A. africana* [17] this experiment is designed to investigate if the different solvent fraction of *A. africana* and also if the mechanism of protection involves mitochondria preservation.

2. MATERIALS AND METHODS

Chemicals: reduced nicotinamide adenine dinucleotide (NADH), potassium cyanide (KCN), dinitrophenyl hydrazine (DNPH), benzylamine hydrochloride (BAHC), trichloroacetic acid (TCA), thiobarbituric acid (TBA), succinate, sucrose, ethylene diamine tetra acetic acid (EDTA), dichlorophenol indophenol (DPI) were purchased from Sigma Chemical Corporation, St. Louis, MO, USA.

2.1 Plant Collection, Preparation of Extract and Partition

Leaves of *A. africana* were collected from Forestry Research Institute of Nigeria, Ibadan, Oyo State, Nigeria and identified at the Botany Department, University of Ibadan, Oyo State, where a voucher specimen number 070613M was deposited. They were air dried, and pulverized. Exactly 1 kg of the pulverized sample was macerated in 5 L of 80% methanol for 72 h and then filtered. A portion of the crude extract (50 g) was partitioned with n-hexane, dichloromethane and methane. Each fractions collected was concentrated in a rotary evaporator to obtain 2.09 g of n-hexane fraction (HFA), 1.89 of dichloromethane fraction (DFA) and 1.45 of methanolic fraction (MFA), which were used for analysis. They were stored in an amber bottle and stored at -4°C until use.

2.2 Animal Handling and Care

Male Wistar rats (200 ± 30) g, bred and housed in the primate colony of the animal house of the Department of Animal Production and Health, Federal University of Technology, Akure, were used for the study. They were maintained in laboratory conditions under natural light, dark cycle and fed with standard rat chow and water *ad libitum*. Animals were handled and used in accordance with the international guide for the care and use of laboratory animals.

2.3 Tissue Preparation

Male Wistar rats (200 ± 30) g were sacrificed and the brain rapidly excised before carefully rinsed and weighed. The cerebellum and cerebral cortex regions were carefully separated from the brain, rinsed (0.25 M sucrose). Each was

weighed and homogenized (0.1 M phosphate buffer saline, pH 7.4) in a manual glass–Teflon homogeniser on ice to obtain a 10% w/v homogenate. Which was used for biochemical assays.

2.4 Experimental Design

The neuroprotective activity of various solvents fraction of *A. africana* under an *in vitro* condition were carried out by incubating cerebellum and cerebral cortex preparation with varying concentration of each solvent fraction of *A. africana* (50-1000 µg/ml) in the presence of 1 mM potassium cyanide (KCN) [18] in a solution containing potassium phosphate buffer (0.1 M and pH 7.4) and sucrose EDTA (0.25 M) for 2 h, this will be referred to as the reaction mixture (RM). The untreated group contains all the RM except the fractions and the control contains an equal volume of the vehicle used in dissolving KCN and fractions.

- Group I:** **Control;** contained homogenate and distilled water
- Group II:** **KCN;** contained homogenate and KCN
- Group III:** **50 µg/ml+KCN;** contained homogenate and (50 µg) solvent fraction and KCN
- Group IV:** **100 µg/ml+KCN;** contained homogenate and (100 µg) solvent fraction and KCN
- Group V:** **200 µg/ml+KCN;** contained homogenate and (200 µg) solvent fraction and KCN
- Group VI:** **400 µg/ml+KCN;** contained homogenate and (400 µg) solvent fraction and KCN
- Group VII:** **600 µg/ml+KCN;** contained homogenate and (600 µg) solvent fraction and KCN
- Group VIII:** **800 µg/ml+KCN;** contained homogenate and (800 µg) solvent fraction and KCN
- Group IX:** **1000 µg/ml+KCN;** contained homogenate and (1000 µg) solvent fraction and KCN

2.5 Biological Oxidation

This activity was carried out based on the ability to reduce p-iodonitro tetrazolium violet, as described by Pennington et al. [19]. Mitochondrial suspensions were prepared by differential centrifugation as described previously [20]. Briefly, the homogenate was centrifuged for

10 min at 10,000 g at 4°C. The residue was rinsed and resuspended in the buffer medium, before centrifugation to obtain mitochondria fractions. This was suspended in sucrose buffer (0.32 M, pH 7.4) to obtain 10-15 mg/ml protein concentration. Oxidation was induced by adding 1 mM KCN in the presence or absence of different solvents fraction of *A. africana* to the mitochondria suspension and incubated in a solution containing phosphate buffer (50 mM), sodium succinate (0.01 M) and p-iodonitro tetrazolium (INT) (2.5 µg/ml) at room temperature for 10 minutes. After incubation, TCA (10%) and ethyl acetate/ethanol/TCA (5:5:1, v: v: w) was added. Absorbance was read at 490 nm and the results expressed as nmol of INT/ mg protein.

2.6 Estimation of Reduced Glutathione (GSH) Level

Reduced GSH content was determined as previously reported [21]. Distilled water and TCA (1 %) were added to the RM, and the mixture was centrifuged at 3500 g for 5 min. Elman's reagent was added to the clear supernatant and absorbance was read 412 nm. The concentration of GSH was determined from the standard curve.

2.7 Lipid Peroxidation Inhibitory Activity

The lipid peroxidation inhibitory activity was evaluated by measuring the formation of TBA reactive substances (TBARS) according to the method of Okhawa et al. [22]. To the RM, Tris-KCl buffer (0.15 M), TCA (30%) and TBA (0.75%) were added. The mixture was incubated for 30 min in a control water bath at 85°C. This was then cooled on ice and centrifuged at 3000 g for 3 minutes. The absorbance of the clear supernatant was read at 532 nm. The malonaldehyde (MDA) level was calculated according to the method of Adam-Vizi and Seregi [23]. Lipid peroxidation in unit/mg protein was computed with a molar extinction coefficient of $1.56 \times 10^5 \text{ M}^{-1} \text{ cm}^{-1}$.

2.8 Determination of Protein Carbonyl Contents

Protein carbonyl levels in the samples were quantified according to the method described by Floor and Wetzel [24]. It is based on the reaction of DNPH with protein carbonyl contents to produce the corresponding hydrazone. The RM was allowed to react with 10 mM DNPH in 2 M

HCl for 1 h at room temperature and precipitated with 20% TCA. The pellet was washed thrice with acetone and dissolved in 2 mM Tris-HCl buffer (pH 7.4, containing 2% SDS). The mixture was centrifuged at 1600 g for 5 min to remove any trace of insoluble material. The carbonyl content was measured spectrophotometrically at 340 nm. The results were expressed as nmol DNPH incorporated/mg protein based on the molar extinction coefficient of $2.1 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$.

2.9 Determination of Monoamine Oxidase Activity (MAO)

MAO was measured using the method developed by Holt et al. [25], and described by Chaudhary and Parvez [26]. Briefly, the RM was incubated with 0.1 M benzylamine hydrochloride (BAHC) and 0.1 M phosphate buffer at room temperature for 30 min. This was followed by the addition of 10% perchloric acid, and the mixture was centrifuged for 10 min at 1500 g. The enzyme activity was calculated as nmol BAHC hydrolysed/min/mg protein using a molar extinction coefficient of $7.6925 \text{ M}^{-1} \text{ cm}^{-1}$ at 280 nm.

Activity of monoamine oxidase (BAHC hydrolysed/min/mg protein) = $(\Delta \text{abs} \times \text{vol of mixture}) / (E_{280} \text{ nm} \times \Delta \text{time})$

2.10 Statistical Analysis

Values are expressed as mean \pm SD of replicate measurements (n=3). All data were evaluated using analysis of variance (one way ANOVA) followed by Duncan's test (equal variance assumed) for post hoc multiple comparisons. The significance level was set at $P < 0.05$.

3. RESULTS

The effect *A. africana* solvents fraction on potassium cyanide-induced inhibition of mitochondrial electron transport system in rat cerebral cortex is given in Fig. 1. All concentrations of *A. africana* fractions could significantly mitigate the inhibition of mitochondrial electron transport system utilizing succinate in the rat cerebral cortex as compared to the untreated group ($P < 0.001$). The effect was dose-dependent for all fractions with maximal effect recorded at 1000 µg/ml concentration. but The HFA fraction produced the highest protective effect, 377.14% increase in activity of NSD activity as compared to KCN.

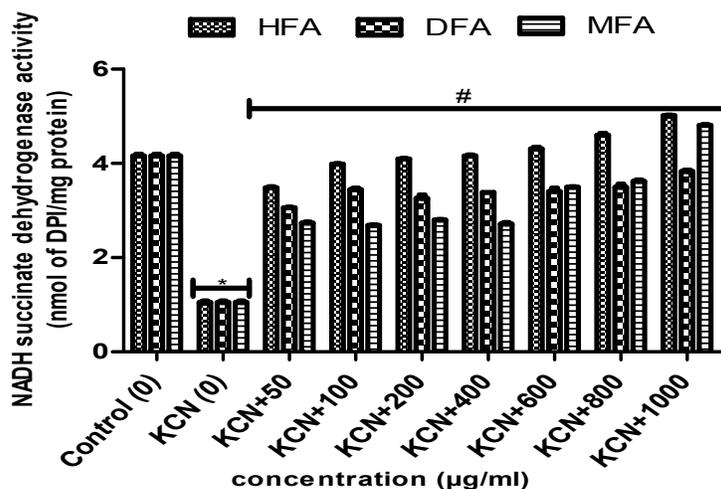


Fig. 1. Effect of *A. africana* fractions on potassium cyanide-induced inhibition of NADH succinate dehydrogenase activity in rat cerebellum and cerebral cortex
 HFA- Hexane fraction; MFA- Methanol fraction; DFA- Dichloromethane fraction; KCN-potassium cyanide
 Results are expressed as mean±S.D (% as compared to KCN, n=3). *P<0.001: Control Vs KCN, #P<0.05: KCN Vs treated

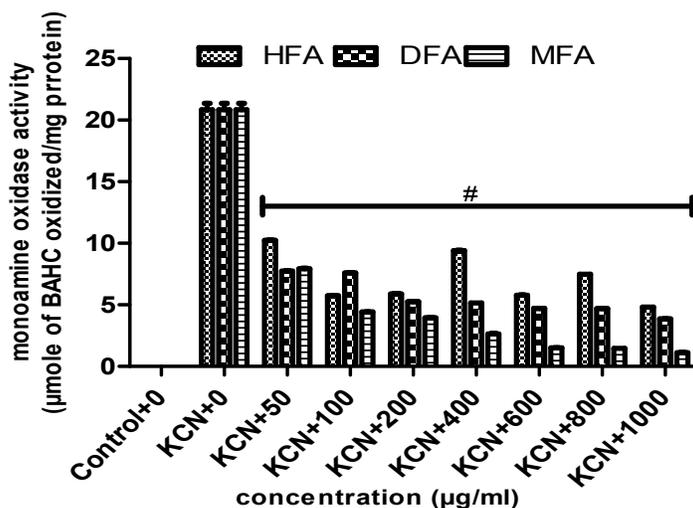


Fig. 2. Inhibition of potassium cyanide-induced increase in monoamine oxidase activity in rat cerebellum by solvent fractions of *A. africana*
 HFA- Hexane fraction; MFA- Methanol fraction; DFA- Dichloromethane fraction; KCN-potassium cyanide
 Results are expressed as mean±S.D (n=3). *P<0.001: Control Vs KCN #P<0.05: KCN Vs treated

Fig. 2. showed the inhibitory effect of *A. africana* fractions on the activity of monoamine oxidase. KCN induced a significant increase (P<0.001) in the activity of MAO (20.84±0.528). All the fractions significantly inhibit the activity of monoamine oxidase enzyme in a concentration-dependent pattern except HFA. The highest inhibitory effect was shown at 1000 µg/ml by

HFA, MFA, and DFA with 76.82%, 81.48% and 94.63% inhibition respectively. The superior monoamine oxidase inhibitory effect of DFA over other solvent fractions is noteworthy in the present study.

KCN treatment caused moderate but significant reduction (P<0.001) in cerebellar GSH

concentration (Table 1). All the fractions of *A. africana* were effective in reversing the reduced GSH concentration due to KCN treatment as compared to the untreated group. DFA showed superior efficacy over other solvent fractions with the highest activity (12.21% reversal) against KCN effect on GSH level at 600 µg/ml compared with the highest recorded for HFA (400 µg/ml; (10.56% reversal) and MFA (800 µg/ml; (8.25% reversal).

Table 2 and Fig. 3 shows the effect of different fractions of *A. africana* on potassium cyanide-induced lipid peroxidation and protein carbonyl formation in rat cortex respectively. All the fractions of *A. africana* inhibited lipid peroxidation in the cerebral cortex in concentration dependent pattern (Table 2). MFA has the best inhibitory activity (63.68%), followed by HFA (61.97%) and DFA (61.87%). The concentration of protein carbonyl was significantly increased in KCN-

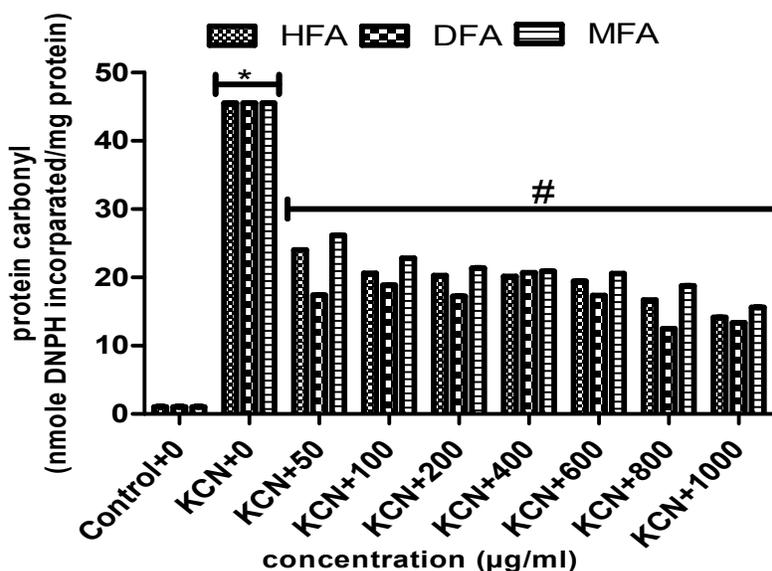


Fig. 3. Effect of different fractions of *A. africana* on potassium cyanide-induced protein carbonyl formation in cerebellum and cerebral cortex

HFA- Hexane fraction; MFA- Methanol fraction; DFA- Dichloromethane fraction; KCN-potassium cyanide
Results are expressed as mean±S.D (n=3). *P<0.001: Control Vs KCN. #P<0.05: KCN Vs treated

Table 1. Effect of *A. africana* solvent fractions on the concentration of reduced glutathione (GSH) in potassium cyanide neurotoxicity in the cerebral cortex

Concentration(µg/ml)	GSH concentration (µmoles of GSH/ mg protein)		
	HFA	DFA	MFA
Control	3.44±0.08	3.44±0.08	3.44±0.08
KCN	3.03±0.08*	3.03±0.08*	3.03±0.08*
50	3.19±0.00(5.28%) [#]	3.25±0.01(7.26%) [#]	3.16±0.00(4.29%) [#]
100	3.11±0.00(2.64%) [#]	3.08±0.00(1.65%) [#]	3.19±0.00(5.28%) [#]
200	3.07±0.02(1.32%) [#]	3.17±0.00(4.62%) [#]	2.99±0.02(-1.32%) [#]
400	3.35±0.02(10.56%) [#]	3.05±0.00(0.66%) [#]	3.11±0.02(2.64%) [#]
600	3.31±0.01(9.24%) [#]	3.40±0.03(12.21%) [#]	3.07±0.01(1.32%) [#]
800	3.10±0.00(2.31%) [#]	3.02±0.01(-0.33%) [#]	3.28±0.01(8.25%) [#]
1000	3.16±0.00(4.28%) [#]	3.22±0.01(6.27%) [#]	3.13±0.01(3.33%) [#]

HFA- Hexane fraction; MFA- Methanol fraction; DFA- Dichloromethane fraction; KCN-potassium cyanide
Results are expressed as mean±S.D. (n=3). *P<0.05: Control Vs KCN. #P<0.05: KCN Vs treated

Table 2. Effect of *A. africana* solvent fractions on KCN-induced lipid peroxidation in the cerebral cortex

Concentration($\mu\text{g/ml}$)	$\mu\text{moles MDA /mg protein}$		
	HFA	DFA	MFA
Control	0.54 \pm 0.01	0.54 \pm 0.01	0.54 \pm 0.01
KCN	9.94 \pm 0.09*	9.94 \pm 0.09*	9.94 \pm 0.09*
50	7.09 \pm 0.10(28.67%) [#]	8.88 \pm 0.04(10.66%) [#]	8.84 \pm 0.11(11.07%) [#]
100	7.03 \pm 0.06(29.28%) [#]	7.57 \pm 0.04(23.84%) [#]	6.81 \pm 0.13(31.49%) [#]
200	5.01 \pm 0.13(49.60%) [#]	5.92 \pm 0.01(40.44%) [#]	6.77 \pm 0.06(31.89%) [#]
400	4.98 \pm 0.07(49.89%) [#]	4.86 \pm 0.06(51.10%) [#]	5.97 \pm 0.06(39.94%) [#]
600	3.86 \pm 0.03(61.17%) [#]	4.96 \pm 0.14(50.10%) [#]	4.77 \pm 0.01(52.01%) [#]
800	3.82 \pm 0.07(61.57%) [#]	4.77 \pm 0.06(52.01%) [#]	3.64 \pm 0.09(63.38%) [#]
1000	3.78 \pm 0.04(61.97%) [#]	3.79 \pm 0.05(61.87%) [#]	3.61 \pm 0.03(63.68%) [#]

HFA- Hexane fraction; MFA- Methanol fraction; DFA- Dichloromethane fraction; KCN-potassium cyanide
Results are expressed as mean \pm S.D. (n=3). *P<0.001: Control Vs KCN. [#]P<0.05: KCN Vs treated

induced, untreated group as compared to the control (P<0.001). However, *A. africana* fractions were able to mitigate the effect of potassium cyanide in the cerebral cortex in non-concentration dependent pattern. DFA exhibited the maximum protection against protein carbonylation at 1000 $\mu\text{g/ml}$ (70.69%), followed by HFA, (68.95%) and MFA (65.68%).

4. DISCUSSION

The application of herbal remedy in the treatment of various diseases is growing at a faster rate globally, the low toxicity and easy accessibility are one of the major contributors to this global acceptance. We previously reported the neuroprotective activities of the crude extract of *A. africana* [17]. Mitochondria damage is one of the pathologies involved in neurological disorders [27]. Potassium cyanide (KCN) toxicity is due to the release of cyanide, a hazardous chemical that is poisonous to the brain, leading to loss of muscular dysfunction as observed in neurological disorders, such as in epilepsy and Parkinson diseases [28]. Central to this toxicity is the inhibition of cytochrome oxidase in the mitochondria leading to a cascade of events that destroy the mitochondria [29]. NADH succinate dehydrogenase (NSD) is an enzyme that catalyzes the oxidation of succinate to fumarate. It is present in the inner mitochondria membrane and is a key marker of mitochondria damage [30]. One of the key mechanism of neurotoxin is the inhibition of NSD, resulting in neuronal death [31,32].

KCN causes a significant decrease in NSD activities [33]. In the present study, all the fractions of *A. africana*, at varying concentrations, reversed the inhibitory effect of

KCN on NSD. The results showed that HFA was more protective than other solvent fractions. Phytoconstituents reported in the hexane fraction of *A. africana* include terpenoids and steroids, which have been reported to possess anticancer, cardioprotective and neural functions [34-37]. The bioactivities could be linked to the high lipophilicity of the phytoconstituents which enhance their ability to cross the blood brain barrier [38-40].

Also, another key mechanism of cyanide neurotoxicity is inhibition of antioxidant enzymes, leading to an increased generation of oxidative products, such as lipid peroxides and protein carbonyl [41]. Glutathione (GSH), a tripeptide, is a major antioxidant in the brain [42] and it plays an important role in protecting neuronal cells against damaging effects of toxicants that generates oxidative stress. The mechanism of antioxidant activities involves the donation of electrons to peroxide and its product to form water. Cyanide was reported to cause a moderate decrease in cerebellar GSH concentration [43]. One of the antioxidant activities of phytochemicals involves preventing the depletion of GSH by toxicants, thus inhibiting their oxidative damage [44]. Previous work on *A. Africana*, showed that *A. africana* possesses antioxidant activities [35] in the current studies, all the fractions of *A. africana* were effective in preventing the cyanide-induced depletion of GSH and increasing the GSH concentration significantly as compared to the untreated group. In this regard, DFA proved to be more effective against KCN than other solvents fraction. Dichloromethane fractions of various plant extracts have been reported to possess antitumor, antioxidant and cytotoxic activities [45,46]. Flavonoid aglycone is abundant in

dichloromethane fraction of plants, a potent bioactive phytochemical that has been isolated from *A. africana* [47] one of the important phytochemicals in a large amount in dichloromethane fractions is the flavonoid aglycone, a very bioactive flavonoid [47].

In addition to the inhibition of mitochondria enzyme as a result of cyanide neurotoxicity, KCN can also deplete the concentration of neurochemicals such as dopamine and serotonin. KCN has been reported to inhibit aromatic hydroxylase [47] dopamine β hydroxylase [48] synthesis of norepinephrine [49] and decrease the synthesis of serotonin [50]. Increasing activity of monoamine oxidase (MAO) can further deplete neurochemical concentration by catalysing the oxidation of neurochemicals [51]. In our results, KCN caused a significant increase in the activity of MAO as compared to the control. All the solvents fraction significantly ameliorated the neurotoxic effect of KCN. Phytochemicals have been reported to possess MAO inhibitory activities [47]. The MAO inhibitory effect of *A. africana* can be can be applicable in the treatment of neurochemical related diseases such as Parkinson's disease, a dopaminergic disorder [52].

Membrane lipids in the brain contain high levels of polyunsaturated fatty acids and are therefore particularly sensitive to oxidation. Lipid peroxidation (LPO) and protein carbonyl (PC) are important biomarkers of oxidative stress which have been implicated in the aetiology of various neurological disorders. In light of this background, the toxic effects of KCN on mitochondria, the elevation of lipid peroxidation and protein carbonyl products by cyanide is not surprising as mitochondria damage leads to the high generation of free radicals triggering oxidation of lipids and protein [53-55]. In the present study, fractions of *A. africana* inhibited LPO in the cerebral cortex in a concentration-dependent pattern. One of the important properties of flavonoids and terpenoids is their high antioxidant and free radical scavenging activities. It is these properties that make them a major source of drug for the treatment of oxidative stress related diseases [44]. The superior membrane peroxidation inhibitory activity of MFA when compared with HFA and DFA might be due to the abundance of phenolic compounds [56]. Some of the abundant phenolic compounds in *A. africana* includes rutin and quercetin [35]. These compounds are among the most active antioxidant phytochemicals in plants

reported to be effective in the treatment and management of various neurological disorders [57-58]. The ability of phenolic compounds to cross the blood brain barrier also enhances their efficacy in the treatment of diseases [59].

5. CONCLUSION

The present study demonstrated the mitigation of potassium-cyanide induced mitochondrial damage to the cerebral cortex region of rat brain by various solvents fraction of *A. africana* possibly via antioxidant mechanisms and protecting mitochondria damage. The neuroprotective effects of *A. africana* in this study suggest that the plant may be a promising candidate for the treatment or management of neuronal damage.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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