Original Research Article

Hepatoprotective Potency of Ethanolic Extract of *Garcinia kola* (Heckel) Seed against Acute Ethanol-Induced Oxidative Stress in Wistar Rats

ABSTRACT

Aim: Hepatoprotective Potency of Ethanolic Extract of *Garcinia kola* (Heckel) Seed against Acute Ethanol-Induced Oxidative Stress in Wistar Rats

Materials and Methods: *G. kola* seeds were purchased from a local market in Ibadan, Nigeria. The seeds were chopped to smaller pieces after the outer coats were removed. They were air-dried and finally ground to fine powder using a blender. 500 g of the powder was transferred to an 80% ethanol solution in a 1 litre round-bottomed flask, and kept airtight for 72 hours. It was filtered and the filtrate was concentrated by means of a rotary evaporator at 40 ^{o}C. The resulting residue was further air-dried. The percentage yield was 14.72% of the dried sample. 20 adult Wistar rats with body weight between 150 and 180 g were used for this study. They were acclimatized for 7 days during which they were fed *ad libitum* with standard feed and drinking water. They were randomly divided into 4 groups of 5 rats each. Animals in groups 1 and 2 were administered normal saline solution while those in groups 3 and 4 were administered *G. kola* extract for twenty-eight days. The animals were administered the extract and saline solution at a dose of 4 mL per 100 g body weight 12 hourly via oral route. At the end of the treatment, they were fasted overnight and animals in groups 2 and 4 were exposed to a single dose of 70% ethanol at 12 mL/kg body weight to induce oxidative stress. After 12 hours of ethanol administration, the animals were anaesthetized using diethyl ether and were sacrificed. Biochemical parameters were determined using standard methods.

Results: Ethanol-induced oxidative stress significantly increased the activities of AST, ALT, LDH, LPO, CAT, SOD and GPx but decreased GSH. These effects were regulated by *G. kola* administration.

Conclusion: Results from this present study have shown that *G. kola* possesses hepatoprotective potency against ethanol-induced oxidative stress.

Keywords: *G. kola* seed, hepatoprotective potency, ethanol-induced oxidative stress

1. INTRODUCTION

Garcinia kola (Heckel) is forest tree indigenous to sub-Saharan Africa and has been referred to as a 'wonder plant' because almost every part of it has been found to be of medicinal importance [1]. It occurs naturally from Sierra Lone to Southern Nigeria and on into Zaire and Angola, but is further distributed by man and is often found cultivated around villages. *G. kola* belongs to a family of tropical plants known as Guttifera [2]. It is an evergreen tree grown in the tropical rainforest of West Africa [3,4]. It grows to a

height of about 30metres high, and the fruit, which is in the size of an orange, is smooth and reddish yellow with peach-like skin and yellow pulp and contains three or four seeds covered with brown seed coat [5]. The seed is an edible nut [4]. It is generally known and called Bitter Kola in Nigeria, and commonly called “Namiji goro” in Hausa, “Orogbo” in Yoruba and “Aku-ilu” in Igbo [6].

Fig. 1: *Garcinia kola* Seeds

The seed is a masticatory used in traditional medicine, cultural and social ceremonies. Extractive of the plant have been traditionally used for ailments such as laryngitis, liver diseases and cough [7]. The seeds are used to prevent or relieve colic, cure head or chest colds and relieve cough [8]. The seed also has anti-inflammatory, antimicrobial, antidiabetic and antiviral [9] as well as antiulcer properties [10].

Phytochemical and biochemical studies of *G. kola* showed the presence of sterols, terpenoids, flavonoids, glycosides, pseudotannins, saponin, proteins and starch [11,12]. Maduniyi [13] reported that some workers isolated kolanone, a poly-isoprenyl-benzophenone compound from the fruit pulp. *G. kola* is a reasonable source of ascorbic acid, some micro-elements including nitrogen, potassium, phosphorus, magnesium and calcium, a trace amount of chromium [14]. Another medicinal constituent of *G. kola* is hydroxycitric acid (HCA) [15]. Xanthones, xanthone derivatives, and polyisoprenylated benzophenones have also been isolated from *G. kola* [16,17].

G. kola also contains toxic substances such as tannins, phytic and hydrocyanic acids at a low concentration. Other constituents include ash and crude protein, crude fiber, crude lipid, water–soluble oxalate, terpenoids and fat [5].

Excessive acute or chronic alcohol consumption poses a serious health hazard and can result into several metabolic disorders in hepatic and extra-hepatic diseases [18]. Alcohol is a commonly used hepatotoxin in experimental hepatopathy. Although the pathogenesis of alcohol-induced liver disease is not clearly defined, there is evidence that ethanol-induced liver injury is due to oxidative stress that leads to fibrosis and impaired liver functions [19]. Alcohol overuse is also characterized by central nervous system (CNS) intoxication symptoms, impaired brain activity, poor motor coordination, and behavioral changes [20]. Excessive alcohol consumption commonly causes hepatic, gastrointestinal, nervous and cardiovascular injuries leading to physiological dysfunctions [21]. Cellular disturbances resulting from excessive alcohol consumption results in increased formation of oxidative stress biomarkers such as malondialdehyde (MDA); reduction in the level of reduced glutathione and a decrease in the activities of antioxidant enzymes [22, 23]. Free radicals and reactive oxygen species (ROS) have been implicated in the oxidative damage of biomolecules and various organs of the body. Studies have shown the crucial role free radicals play in the pathogenesis of many human diseases namely, cardiovascular and pulmonary diseases, some types of cancer, immune/autoimmune diseases, inflammation, diabetes, cataracts and brain dysfunction such as Parkinson and Alzheimer [24]. However, the deleterious effect of free radicals can be corrected by antioxidants – both enzymatic and nonenzymatic. Oxidative stress is known to arise when there is an imbalance between free radical production (especially reactive oxygen species; ROS) and endogenous antioxidant defense system. This shift in balance is associated with oxidative damage to a wide range of biomolecules including lipids, proteins, and nucleic acids, which may eventually impair normal functions of various tissues and organs [25]. This study therefore focuses on the hepatoprotective potency of *G. kola* seeds against acute ethanol-induced oxidative stress in Wistar rats.

MATERIALS AND METHODS

Preparation of extract

G. kola seeds were purchased from a local market in Ibadan, Nigeria. The seeds were chopped to smaller pieces after the outer coats were removed. They were air-dried and finally ground to fine powder using a blender. 500 g of the powder was transferred to an 80% ethanol solution in a 1 litre round-bottomed flask, and kept airtight for 72 hours. It was filtered and the filtrate was concentrated by means of a rotary evaporator at 40 ^{o}C. The resulting residue was further air-dried. The percentage yield was 14.72% of the dried sample.

2.2. Experimental Design and Animal Treatment

Twenty adult male Wistar rats with body weight between 150 and 180 g were used for this study. They were acclimatized for 7 days during which they were fed *ad libitum* with standard feed and drinking water and were housed in clean cages placed in well-ventilated housing conditions (under humid tropical conditions) throughout the experiment. All the animals received humane care according to the criteria outlined in the 'Guide for the Care and Use of Laboratory Animals' prepared by the National Academy of Science and published by the National Institute of Health. They were randomly divided into four groups of five rats each. Animals in groups 1 and 2 were administered normal saline solution while those in groups 3 and 4 were administered *G. kola* extract for twenty-eight days. The animals were administered the extract and saline solution at a dose of 4 mL per 100 g body weight 12 hourly via oral route. At the end of the treatment, they were fasted overnight and animals in groups 2 and 4 were exposed to a single dose of 70% ethanol at 12 mL/kg body weight to induce oxidative stress. The dosage of ethanol used in this study has been documented to induce tissue toxicity and oxidative damage in rats [26]. After 12 hours of ethanol administration, the animals were anaesthetized using diethyl ether and were sacrificed. Liver was excised, weighed and homogenized in 50 mmol/L Tris–HCl buffer (pH 7.4) and then centrifuged at 5000 × g for 15 minutes for biochemical analysis. Supernatants were immediately kept frozen for further analysis**.**

2.3 Biochemical Analyses

2.3.1 Determination of Hepatic Marker Enzymes Activities

Alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and lactate dehydrogenase (LDH) activities were determined using Randox commercial Enzyme kits according to the method of Reitman and Frankel [27].

2.3.2 Determination of Oxidative Stress Biomarkers

Determination of Lipid Peroxidation (LPO), Reduced Glutathione (GSH), Catalase (CAT), Superoxide Dismutase (SOD) and Glutathione peroxidase (GPX) were carried out according to the methods previously described by Airaodion *et al*. [28].

2.4 Statistical Analysis

Results are expressed as mean ± standard error of the mean (S.E.M). The levels of homogeneity among the groups were assessed using One-way analysis of variance (ANOVA) followed by Turkey's test. All analyses were done using Graph Pad Prism Software Version 5.00 and p values < 0.05 were considered statistically significant.

3. RESULTS

One major finding of this study was that ethanol indeed unhinged and perturbed the activities of hepatic marker enzymes and oxidative stress biomarkers in the animals used. These perturbations were minimized by *G. kola* seed extract administration as shown in **Tables 1 and 2**.

Table 1: Effect of *G. kola* Seeds on Hepatic Marker Enzymes of Experimental Rats after 28 Days of Administration

Hepatic Marker Enzymes	Control	70% Ethanol only	*G. kola* Extract only	*G. kola* Extract + 70% Ethanol
AST (IU/L)	98.84±4.19[a]	129.29±3.22[b]	101.05±3.32[ac]	112.18±5.03[c]
ALT (IU/L)	46.19±7.24[a]	59.26±4.03[b]	45.02±3.97[a]	49.00±4.33[a]
ALP (IU/L)	14.52±2.57[a]	23.04±3.11[b]	14.62±2.26[a]	16.77±3.29[a]
LDH (IU/L)	167.24±9.13[a]	211.32±75.32[b]	170.85±7.43[a]	189.28±3.94[c]

Values are presented as Mean±S.E.M, where n = 5. Values with different superscript along the same row are significantly different at P<0.05.

LEGEND: AST = Aspartate Amino Transferase, ALT = Alanine Amino Transferase, ALP = Alkaline Phosphatase, LDH = Lactate Dehydrogenase

Table 2: Effect of *G. kola* on Oxidative Stress Biomarkers of Experimental Rats after 28 Days of Administration

Oxidative Stress Biomarkers	Control	70% Ethanol only	*G. kola* Extract only	*G. kola* Extract + 70% Ethanol
LPO (nmol MDA/mg protein)	13.13±1.00[a]	22.30±2.78[b]	12.26±1.84[a]	14.00±2.02[a]
GSH (mg/mL)	6.85±0.14[a]	4.22 ±0.24[b]	7.04±1.02[a]	6.04±0.85[a]
CAT (Mm H_2O_2/mg protein)	11.99±1.38[a]	24.14±2.46[b]	12.23±1.09[a]	17.22±3.07[c]
SOD (U/mg protein)	10.33±1.34[a]	15.00±1.89[b]	9.83±1.99[a]	11.36±1.46[ab]
GPX (U/mg protein)	4.92±1.00[ac]	9.06 ±0..63[b]	4.64±0.55[a]	6.99±0.42[c]

Values are presented as Mean±S.E.M, where n = 5. Values with different superscript along the same row are significantly different at P<0.05.

LEGEND: LPO = lipid peroxidation, GSH = Glutathione, CAT = Catalase, SOD = Superoxide Dismutase, GPX = Glutathione Peroxidase

4. DISCUSSION

The result of this study showed that the activities of AST, ALT, ALP and LDH were not significantly different when animals treated with *G. kola* extract only where compared with those of the control group at P<0.05 (Table 1). A significant increase was however observed when the activities of AST, ALT, ALP and LDH in animals induced with 70% ethanol without pretreatment with *G. kola* extract were compared with those of the control and *G. kola* extract only groups at P<0.05 (Table 1). This might be an indication that ethanol caused liver damage to the animals [29]. Furthermore, when animals pretreated with *G. kola* extract before the induction of oxidative stress by ethanol were compared with those induced without pretreatment at p <0.05, a significant decrease was observed in the activities of AST, ALT, ALP and LDH. This could mean that pretreatment with *G. kola* seed extract resulted in increased transcription of some genes involved in glucose uptake, glycolysis and lipogenesis [30]. Glucose represses the induction of inducible operons by inhibiting the synthesis of cyclic adenosine monophosphate (cAMP) a nucleotide that is required for the initiation of transcription of a large number of inducible enzyme systems including the Lac operon. Cyclic AMP (cAMP) is required to activate an allosteric protein called catabolite activator protein (CAP) which binds to the promoter CAP site and stimulates the binding of ribonucleic acid (RNA) polymerase to the promoter for the initiation of transcription, but cAMP must be available to bind to CAP which binds to deoxyribonucleic acid (DNA) to facilitate transcription. In the presence of glucose, adenylase cyclase (AC) activity is blocked. AC is required to synthesize cAMP from adenosine triphosphate (ATP) [31, 32]. Therefore if cAMP levels are low, CAP is inactive and transcription does not occur. Thus the effect of glucose in suppressing these inducible enzymes is by lowering cyclic AMP level. The *G. kola* extract might have lowered cAMP in animals thus causing inhibition of these inducible enzymes. ALT is considered most reliable hepatocellular injury because it is solely confined to the liver, unlike AST and LDH which are also abundantly present in other body organs such as the kidneys, brain, and hearts [33]. The significant decrease observed in the activities of ALT and AST in *G. kola*-treated animals when compared to those induced without pretreatment showed that *G. kola* seed protected the liver from damage by ethanol-induced oxidative stress. Igboko, [11] has reported that *G. kola* seed have high phytochemical content while Oloyede and Afolabi [34] reported its antioxidant potential. Its hepatoprotective activities could be attributed to the presence of these phytochemicals and antioxidants. However, Chinedu et al. [35] reported that *G. kola* seed had no significant effect on the activity of AST when they studied the acute administration of aqueous extract of *Garcinia kola* on daily blood glucose level and selected biochemical indices in longevity Wistar albino rats.

Alkaline phosphatase (ALP) is involved in the hydrolysis of a wide range of phosphomonoester substrates. It is a marker enzyme for the plasma membrane and endoplasmic reticulum of tissues [36]. It is often employed to assess the integrity of the plasma membrane, since it is localized predominantly in the microvilli in the bile canaliculli, located in the plasma membrane. Since ALP hydrolyzes phosphate monoesters, its significant increase in ethanol-induced animals without pretreatment could constitute a threat to the life of the cells that are dependent on a variety of phosphate esters for their vital process as it may lead to indiscriminate hydrolysis of phosphate ester metabolite of the liver [37]. Consequently, this may adversely affect the facilitation of the transfer of metabolites across the cell membrane of ethanol-induced animals without pretreatment. This effect was rectified by pretreatment with *G. kola* seeds extract. In contrast, Chinedu et al. [35] reported that *G. kola* seed significantly increased the activity of ALP when they studied the acute administration of aqueous extract of *Garcinia kola* on daily blood glucose level and selected biochemical indices in longevity Wistar albino rats.

The significant elevation observed in the activities of markers such as ALT, AST, ALP and LDH in the liver tissue of animals induced with ethanol but without pretreatment with *G. kola* seeds when compared with the control animals and those pretreated with *G. kola* seeds before ethanol induction might be due to cellular necrosis of hepatocytes, which causes increase in the permeability of the cell. Lactate dehydrogenase (LDH) is an index of cell damage including hepatotoxicity and the endothelial disruption in blood vessel. The significant increase observed in the activity of LDH might be suggestive of the beginning of cytolysis, which is a possible indication of membrane damage including the endothelial membranes of blood vessels. This disruption of endothelial membrane, directly or indirectly, as reported earlier, includes the generation of reactive oxygen species in endothelial cells [38]. Free radicals attack unsaturated fatty acids in the membranes resulting in membrane lipid peroxidation which decreases membrane fluidity, leakage of enzyme and loss of receptor activity as well as damage membrane proteins leading to cell inactivation [28, 39]. As lipid peroxidation progressively increase, antioxidant defense system decrease equivalently resulting in oxidative stress [40]. This suggests that the administration of ethanol might have weakened the liver membrane of the rats with subsequent penetration and elevation of the hepatic biomarker enzymes.

A significant difference was observed in the activity of AST when the control animals were compared with animals pretreated with *G. kola* seeds extract before ethanol administration. This corresponds to the findings of Airaodion *et al*. [39] who studied the ameliorative efficacy of phytochemical content of *Corchorus olitorius* seeds against acute ethanol-induced oxidative stress in Wistar rats but contradicts those of Ogbuagu *et al.* [41] and Airaodion *et al.* [42] who reported a nonsignificant difference in the activity of AST when animals were pretreated with *Vernonia amygdalina* and *Talinum triangulare* leaves respectively.

Alcohol metabolism results in oxidative and nitrosative stress via elevation of $NADH/NAD^+$ redox ratios, induction of nitric oxide synthase (NOS) and NADPH/xanthine oxidase [29]. Lipid peroxidation, a primary mechanism of cell membrane destruction and cell damage is a common feature of both acute and chronic alcohol consumption [39]. The presence of a high concentration of oxidizable fatty acids and iron in liver significantly contributes to ROS production. A rise in lipid peroxidation level is only identified if there is oxidative damage due to the increase in free radical generation. Generally under normal conditions, the animals tend to maintain a balance between generation and neutralization of ROS in the tissues. But, when the organisms are subjected to xenobiotic stress, the rate of production of ROS including O_2^-, H_2O_2, OH^-, ROO^{--}, exceeds their scavenging capacities. All the organisms have their own cellular antioxidant defense system composed of both enzymatic and non-enzymatic components. Enzymatic antioxidant pathway consists of SOD, CAT and GPX. Superoxide anion O_2^- is dismutated by SOD to H_2O_2, which is reduced to water and molecular oxygen by CAT or is neutralized by GPX, which catalyzes the reduction of H_2O_2 to water and organic peroxide to alcohols using GSH as a source of reducing equivalent. Glutathione reductase (GR) regenerates GSH from oxidized glutathione (GSSG), which is a scavenger of ROS as well as a substrate for other enzymes. Glutathione S-transferase (GST) conjugates xenobiotics with GSH for exclusion.

The effect of *G. kola* seeds on oxidative stress biomarkers is presented in table 2. It was observed that acute ethanol exposure significantly elevated the malondialdehyde (MDA) levels in the liver indicating enhanced peroxidation and breakdown of the antioxidant defense mechanisms. Decomposition products of lipid hydroperoxide such as malanoldehyde and 4-hydroxynonenal, can cause chaotic cross-linkage with proteins and nucleic acids, which plays an important role in the process of carcinogenesis. In this investigation, hepatic lipid peroxidation (LPO) activities showed significant increase due to ethanol intoxication. Furthermore, extensive damage to tissues in a free radical mediated LPO results in membrane damage and subsequently decreases the membrane fluid content. *G. kola* pretreatment significantly reversed these alterations causing a significant decrease in MDA levels, suggesting its protective effects against ethanolic-induced oxidative damage. This is consistent with the study of Oyenihi *et al*. [38] who reported the hepato- and neuro-protective effects of watermelon juice on acute ethanol-induced oxidative stress in rats. It is also in agreement with the report of Airaodion *et al*. [28] who study

the hepatoprotective effect of *Parkia biglobosa* on acute ethanol-induced oxidative stress in Wistar rats.

Glutathione (GSH) is a tripeptide (L-α-glutamylcysteinol glycine) which is highly abundant in all cell compartments and it is the major soluble antioxidant. Glutathione directly quenches ROS such as lipid peroxides, and also plays a major role in xenobiotic metabolism [28, 29]. Glutathione detoxifies hydrogen peroxide and lipid peroxide by donating electron to hydrogen peroxide to reduce it to water and oxygen protecting macromolecules such as lipids from oxidation. In this study, the decrease in the reduced glutathione level in animals treated with ethanol only is connected with ethanol-induced oxidative stress and direct conjugation of GSH with acetaldehyde and other reactive intermediates of alcohol oxidation. This result is in agreement with the finding of Pinto *et al*. [42] who reported that acute ethanol treatment caused reduction in the glutathione levels in different tissues. It also corresponds to the findings of Airaodion *et al*. [39] who recorded a significant decrease in the concentration of GSH following ethanol administration in Wistar rats. The significant increase in the glutathione levels in the liver of *G. kola*-treated rats prior to ethanol-administration may be due to the direct ROS—scavenging effect of *G. kola* or an increase in GSH synthesis. The antioxidant potential of *G. kola* reported by Oloyede and Afolabi [34] might also be responsible in this potency.

Catalase (CAT) contributes to ethanol oxidation, by oxidizing a small amount of ethanol in the presence of a hydrogen peroxide (H_2O_2) generating system to form acetaldehyde [28]. In this study, a significant increase was observed in the activity of catalase in control animals and those treated with *G. kola* extract only when compared with ethanol-induced animals with *G. kola* extract pretreatment. This corresponds to the report of Airaodion *et al*. [39] who studied the ameliorative efficacy of *Corchorus olitorius* seeds on acute ethanol-induced oxidative stress in Wistar rats but contradicts the findings of Airaodion *et al*. [28] who reported a nonsignificant difference when animals were treated with *Parkia biglobosa*. The activity of catalase in animals pretreated with *G. kola* prior to ethanol induction was significantly reduced when compared with those without *G. kola* pretreatment. This might be that ethanol-induced oxidative stress generated elevated ROS in the liver which CAT tend to combat, thereby increasing its activity. *G. kola* seeds were able to reduce the ROS generation with subsequent decrease in CAT activity due to its antioxidant potential reported by Oloyede and Afolabi [34]. Increased CAT activity in this study following acute ethanol exposure suggests elevated ethanol oxidation and formation of oxidizing product-acetaldehyde. This is in agreement with the study of Airaodion *et al*. [28] and Oyenihi *et al*. [38] who reported a significantly higher CAT activity after ethanol treatment.

Superoxide dismutase (SOD) plays an important role in reducing the effect of free radicals attack, and SOD is the only enzymatic system quenching O_2- to oxygen and H_2O_2 and plays a significant role against oxidative stress [29]. These radicals have been reported to be deleterious to polyunsaturated fatty acids and proteins [28, 32]. In this study, no significant difference was observed in the activity of SOD in control animals and those treated with *G. kola* seed extract only when compared with ethanol-induced animals with *G. kola* seed extract pretreatment. This is consistent with the report of Airaodion *et al*. [29] who studied the therapeutic effect of methanolic extract of *Telfairia occidentalis* leaves against acute ethanol-induced oxidative stress in Wistar rats. However, the activity of SOD in animals pretreated with *G. kola* prior to ethanol induction was significantly reduced when compared with those without *G. kola* pretreatment. This might be that ethanol-induced oxidative stress generated elevated ROS in the liver which SOD tend to combat thereby increasing its activity. *G. kola* seed extract was able to reduce the ROS generation with subsequent decrease in SOD activity due to its antioxidant potential reported by Oloyede and Afolabi [34]. The increased activity of SOD observed in ethanol induced animals contradicts the study of Halliwell and Gutterberidge [43] who reported that SOD activity was considerably reduced during ethanol intoxication.

Glutathione peroxidase (GPx) is another enzymatic antioxidant that acts as a defense mechanism against oxidative stress [28,29]. In this study, no significant difference was observed in the activity of GPx in control animals when compared with ethanol-induced animals with *G. kola* extract pretreatment at $P<0.05$. The activity of GPx in animals pretreated with *G. kola*

prior to ethanol induction was significantly reduced when compared with those without *G. kola* pretreatment. This might be that ethanol-induced oxidative stress generated elevated ROS in the liver which GPx tend to combat thereby increasing its activity. *G. kola* was able to reduce the ROS generation with subsequent decrease in GPx activity due to its antioxidant potential reported by Oloyede and Afolabi [34]. The increased activity of GPx observed in ethanol-induced animals is in agreement with the studies of Ogbuagu *et al.* [41] and Airaodion *et al.* [42] who reported a significant difference in the activity of GPX when animals were pretreated with *Vernonia amygdalina* and *Talinum triangulare* leaves respectively but contradicts the studies of Airaodion *et al*. [38] who observed a nonsignificant difference in the activity of GPx in the study of hepatoprotective effect of *Parkia biglobosa* on acute ethanol-induced oxidative stress in Wistar rats and that of Yang *et al*. [44] who also observed a nonsignificant difference in GPx activities in rats hepatocyte exposed to varying concentrations of ethanol at an incubation time of 12 hours. The toxicity of ethanol is related to the product of its metabolic oxidation. Acetaldehyde and acetate, produced from the oxidative metabolism of alcohol are capable of forming adducts with cellular macromolecules, causing oxidative damage and affecting metabolic processes [41,42]. Catalase and glutathione peroxidase further detoxify H_2O_2 into H_2O and O_2 [28]. Thus, SOD, catalase and GPx function mutually as enzymatic antioxidative defense mechanism to counter the deleterious effect of ROS [32].

5. CONCLUSION

G. kola seed has been consumed for different purposes. Results from this present study have shown that it possesses hepatoprotective potency against ethanol-induced oxidative stress.

CONSENT

It is not applicable.

ETHICAL DISCLAIMER

Animal ethic Committee approval has been collected and preserved by the author**.**

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