**TITLE PAGE**

**HYPOLIPIDEMIC AND ANTIOXIDANT CAPACITY OF METHANOL LEAF EXTRACT OF KIGELIA AFRICANA IN ALLOXAN-INDUCED DIABETIC RATS**

**BY**

**MATTHEW VICTORIA OJOACHEONE**

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**SUPERVISOR**

**DR. UHUO, EMMANUEL.N.**

**JULY 2018**

**CERTIFICATION PAGE**

I, MATTHEW VICTORIA OJOACHEONE an undergraduate of the department of chemical sciences with registration number U14/NAS/BCH/022, hereby certify that the work embodied in this project is original and has not been submitted in part or full in any other degree programme of this university or any other university.

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Dr. Uhuo Emmanuel N. Date

Project Supervisor

**------------------------------ ------------------**

Mr. Ayuk Eugene Date

Head of Department

------------------------------------------ -----------------

Prof. Chidi Ughegbu Date

Dean of Natural and Applied Science

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External Supervisor Date

**DEDICATION**

I dedicate this work to the pillar of my life the almighty God who has always being my source of inspiration and knowledge, my beloved parents Mr. and Mrs. Joel Haruna Matthew and my wonderful siblings Victor and Wisdom Matthew - who stood by me against all odds, encouraging me with their prayers and also finance.

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My prayer is that God will reward those that contributed immensely for me towards this project directly or indirectly.

**ABSTRACT**

Diabetes mellitus is a metabolic disorder resulting from the presence of excess sugar in the blood as a result of defect of insulin secretion, insulin action or both. Insulin deficiency in turn leads to chronic hyperglycaemia with disturbances of carbohydrate fat and protein metabolism. Globally it has been estimated that the incidence of diabetes and project for year 2030, as given by international diabetes federation is 350million**.** This work is aimed at evaluating the antioxidant potential and hypolipidemic properties of the plant. Methanol leaf extract of *Kigelia africana* used for the study. Alloxan diabetes was induced into 20 rats and the rats weighed 125g. They were grouped into four groups: group 1 Normal control group, group 2 diabetes not treated, group 3 diabetes treated with 0.6 g of modern drugs (glibenclamide), group 4 diabetes treated with 500 mg/kg body weight of the extract of *K.africana* orally for 14days. At the 14th day, rats were bled and blood samples obtained were used for parameter analysis. From the result, glucose level increased as the body weight of the rats in all test groups decreases when compared with normal control (group 1). Oral administration of *K.africana* causes an increase although not significant (P˂0.05) of MDA in the test group treated with leaf extract of *K.africana* (group 4) compared with other test groups. The result also showed a significant increase (P˂0.05) in Catalase (CAT) activity in diabetic rat treated with glibenclamide (group 3) and rats treated with leaf extract (group 4) when compared with normal groups (group 1&2). A significant increase (P˂0.05) was observed in the cholesterol level of diabetic rats treated with *K.africana* when compared with group1and 2. High density lipoprotein increased significantly (P˂0.05) in the test group (group 4) when compared with other test groups. Low density lipoprotein decreased significantly (P˂0.05) in the test group treated with *K.africana* leaf extract (group 4) compared with normal control (group 1). Therefore, from the results gotten, it can be said that Kigelia *africana* has an hypolipidemic and antioxidant Capacity in diabetic conditions.

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**CHAPTER ONE**

**INTRODUCTION**

**1.1 Background of study**

Diabetes mellitus is a metabolic disorder resulting from a defect of insulin secretion, which is insulin action or both. Insulin deficiency in turn leads to chronic hyperglycaemia with disturbances of carbohydrate fat and protein metabolism (Kumar *et al*., 2011).

Globally the estimated incidence of diabetes and project for year 2030, as given by international diabetes federation is 350million (Ananda *et al*., 2012). Currently available pharmotherapies for the treatment of diabetes mellitus include oral hypoglycaemic agent and insulin. However these current drugs do not restore normal glucose homeostasis and they are free from side effects (Bandawane *et al.,* 2011).

In view of the adverse effect associated with the synthetic drugs and as plants are safer, cheaper, and as much effective. Conventional and anti-diabetic plants can be explored (Kumar *et al.,* 2010). Over 400 traditional plants have been reported for the treatment of diabetes (Ramachandran *et al*., 2011).

Furthermore after world Health Organisation recommended investigation of hypoglycaemic agents from medicinal plants has become more important (Kumar *et al*., 2010). Also diabetes has been treated orally with several medicinal plants or their extract based on folklore medicine since ancient times.

*Kigelia africana* (Lam) Benth (Family: Bignoniaceae) is widely distributed in south central and West Africa. It is known as the cucumber or sausage tree because of its huge fruits (average 0.6cm in length and 44kg in weight) which hang from fibrous stalks. It is also known as balm Khene in Hindi and it is distributed all over India but found in abundance in West Bengal. It is found mostly in water areas and spreads abundantly across wet savannah and riverine areas (Sofowaora *et al*., 1980).

Experimentally, the plant has shown antibacterial, antifungal, antineoplastic, analgesic, anti-inflammatory and antioxidant properties (Saini *et al*., 2009). The roots, the wood and leaves have been found to contain kigelinone, vernolic acids, kigelin, iridoids, luteolin and 6-hydroxyluteolin (Picerno *et al*., 2005). Crude extract of herbs and species and other materials rich in phenolic are of increasing interest in the food industry because they retard oxidative degradation of lipids and thereby improving the quality and nutritional value of food (Frankel, 1995).

The baked fruits of *Kigelia africana* are used for fermentation of beer. It also has internal application including treatment of dysentery, ringworm, tapeworm, malaria, diabetes, pneumonia, haemorrhage and tooth care (Gills, 1992).

In West Africa, the roots and unripe fruit are used as vermifuge and as treatment for haemorrhoids and rheumatism. The bark is traditionally used as remedy for syphilis and gonorrhoea. The fruits and bark ground and boiled in water are taken orally or used as an enema in treating children’s stomach ailment usually tapeworm (Walt *et al*., 1962)

**1.2 Statement of the problem**

As impressive improvement has occurred in global health status in the past century which has become a cause for celebration. Therefore, public health professionals can feel proud of their contribution to these achievements even as they appreciate the complexity of the underlying driving force, many of which lie outside traditional public health work. But this satisfaction must be tempered by emerging concerns (Sen and Bonita, 2000) against the recent evidence suggesting that based current trends many low income countries are unlikely to achieve desired health target by 2015 due to devastating disease and overwhelming failing health system (Travis *et al*., 2004).

The literature review survey revealed that there is no experimental evidence of antidiabetic and hypolipidemic effect of the plant. Therefore the present work was undertaken to explore the antidiabetic and hypolipidemic potential of *Kigelia africana* methanol leaf extract of the plant in alloxan induced diabetic rats.

**1.3. Aim of the study**

The research is aimed at investigating the hypolipidemic and antioxidant capacity of methanol leaf extract of *Kigelia africana* in alloxan induced diabetic rats.

**1.4 Objective of the study**

Specifically the study sort to:

1. Determine the effects of *Kigelia africana* methanol leaf extract on antioxidant enzyme.
2. Determine the effects of *Kigelia africana* methanol leaf extract on lipid profile of diabetic rats.
3. Determine the effects of *Kigelia africana* methanol leaf extract on oxidative parameters of alloxan-induced diabetic rats.

**CHAPTER TWO**

**LITERATURE REVIEW**

**2.1 Scientific classification**

Kingdom: Plantae

(Unranked): Angiosperms

(Unranked): Eudicots

(Unranked): Asterids

Order: Lamiales

Family: Bignoniaceae

Tribe: Coleceae

Binomial name: *Kigelia africana* (Lam.) Benth

Igbo name: Ogbeala

****

**Figure 1: Leaf of *Kigelia africana*** (Eliud, 2018)

**2.2 General information**

*K. africana* (Lam) Benth. K.pinnata belongs to the family of Bignoniaceae. Its common names include sausage tree (Eng); worsboom (Afr); um vunguta, umfongothi (Zulu); modukguhulu (North sotho); muvevha (Venda) (coats-palgrave, 1988) pandoro (west Nigeria) (Aiyelola *et al.,* 2006) Saucissonnier; Faux baobab (Fr) mvungunya, mwegea, mwicha, mranaa (sw) (Grace *et al.,*2002). It is a tree growing up to 20 m tall or more. The bark is grey and smooth at first, peeling on older trees. It can be thick as 6 mm on a 15 cm branch. The wood is pale brown or yellowish, undifferentiated and not prone to cracking. (Roodot, 1992) the tree is evergreen where rainfall occurs throughout the year, but deciduous where there is a long dry season. The leaves are opposite or in whorls of three, 30-50 cm long, pinnate, with six to ten oval leaflets up to 20 cm long and 6 cm broad; its terminal leaflet can be either present or absent. The flowers (and later the fruit) hang down from branches on long flexible stems (2-6 m long).

Flowers are produced in panicles; they are bell shaped (similar to those of the Africa tulip tree but darker and more waxy), orange to reddish or purplish green and about 10 cm wide

Individual flowers do not hang down but horizontally (Joffe, 2003) some birds are attracted to these flowers and the strong stem of each flowers make idea footholds their scent us most notable at night indicating their reliance on pollination by bats, which visits them for pollen and nectar. (Hoyo, 1997). Flowers are bisexual, very large; pedicel up to 11 (-13.5) cm long up curved at tip; calyx shortly tubular to campanulate, 2-4.5 cm long, suddenly widening and incurving upwards, limp 2-lipped, with the super or lip 2-lobed , the lower one 3- lobed and recurved (Grace *et al.,* 2002). The fruit is a woody berry from 30-100 cm long and up to 18 cm broad; weighs between 5-10 kg hangs down on a long rope- like peduncles (Joffe, 2003).

The fruit is indehiscent, with woody wall and heavily marked with lenticels at the surface. It is grey-brown and many seeded when matured seeds are obovoids, ca. 10 mm × 7 mm with leathery testa, embedded in a fibrous pulp (Grace *et al.,* 2002). The fruit is eaten by several species of mammals, including baboon, pigs, savannah Elephants, Giraffes, Hippopotami, monkeys and porcupines. The seeds are dispersed in their dung. The seeds are also eaten by brown parrots and brown- headed parrots and the foliage by elephants and greater kudu (Mukherjee, 2002).

**2.2.1 Ecology**

The tree is found on riverbanks, along streams and on floodplains, also in open woodland, from Kwazulu- Natal to Tanzania. The plant is widely distributed in the South, Central and West Africa (Burkil, 1985). K.africana grows along water courses, in riverine fringes, alluvial and open woodland, high rainfall savannah, and shrub land and in rain forest. It occurs on loamy red clay soils, sometimes rocky, damp or peaty, from sea levels up to zoom altitude (Grace *et al*, 2002).

**2.2.2 Traditional Uses**

The Kigelia plants have medicinal properties not only because of its perceived characteristics such as bitterness astringent taste or smell but also because of forces that it seems to emit in connection with its location, orientation and association with other plants. It has long a long history of use by rural and African countries particularly for medicinal properties. Several parts of the plant are employed for medicinal purposes by certain aboringal people (Burkil, 1985). In Malawi during famine the seeds are roasted to eat. Baked fruits are ferment beer and boiled ones yield a red dye. Most commonly traditional healers used it to treat a wide range of skin ailments like fungal infections boils, psoriasis and eczema. It also has internal application including the treatment in dysentery, ringworm, tape-worm, post- partum haemorrhage, malaria, diabetes, pneumonia and toothache (Gill, 1992). The Tonga women of Zambezi valley regularly apply cosmetic preparation of Kigelia africana fruits to their face to ensure a blemish free complexion (Pooley, 1993) in the folk medicine; the fruit of the plant are used as dressing for ulcer purgative and to increase the flow of milk in lactating women. (Oliver-Bever, 1986). Roots are said to yield a bright yellow dye. The shona people tend to use the bark and roots as powder or infusion for application to ulcer, drunk or applied in the treatment of pneumonia, as a gargle for toothache and the leaves n a compound applied for backache. (Masiri and Gundidza, 1996). In West Africa, the root and fruits is used as a vermifuge and as treatment for haemorrhoids and rheumatism (Irvine, 1961). The bark is traditionally used as an enema in treating children’s stomach ailments-usually worms. Unripe fruit is used in central Africa as a dressing for wounds, haemorrhoids and rheumatism. Venereal diseases are commonly treated with the tree extracts usually in palm wine as oral medication (Walt, 1996).

**2.3 Chemical Constituents of *Kigelia Africana* Leaf**

The hexane extract of the leaf of *Kigelia africana* has been reported to be rich in hydrocarbons and some volatile compounds. In a study that qualitatively and quantitatively analyzed the hexane extract for various chemical compositions, it was revealed to contain twelve compounds with the major ones identified as n-hentriacontane,1-tricosene,11-(2,2- dimethylpropylheneicosane,2,6,10trimethyldodecane,pentafluoroheptadecylester,2ethylhexyloctadecyl sulfurous acid ester, heneicosane and hexyloctylsulfurous acid ester (Khan *et al*., 1999;Govindachari *et al.,* 1971 and Joshi *et al*., 1982) Others are 4,4-dimethylundecane, methyl-12-methyltetradecanoate, 1- iodohexadecane and 1-iododecane.Hentria contane have been reported to have a possible anti-tumour activity while methyl-12- methyltetradecanoate has also been reported for its inhibition capacity on the development of coneal angiogenesis, which is responsible for blindness and other infections (Atolani *et al.,* 2010)Flavonoids and iridoids and a 7-O-glucoside (Moideen *et al*., 1994 and Houghton *et al*., 1994)have also been found in the leaves.

**2.4 MEDICINAL PROPERTIES OF *KIGELIA AFRICANA***

**2.4.1 Anti-diabetic and antioxidant activity**

Like many other African food (Atawodi, 2011) and medicinal plants (Atawodi *et al*., 2009;Gupta *et al*., 2012; Gidado *et al.,* 2009 and Okine *et al*., 2004), the use of *Kigelia africana* to manage diabetes is traditionally practiced and reported(Otimenyi *et al*., 2013 and Saini *et al*., 2009). The anti-diabetic activity and the antioxidant effect were studied (Nyarko *et al*., 2005). Also, in a polyherbal preparation, ADD-199, *Kigelia africana* is in combination with three other plants: Maytenus senegalenses, Annona senegalensis and Lannea welwitchii. The anti diabetic and antioxidant effects were investigated in streptozotocin-induced diabetic C3H mice and results were compared with two allopathic hypoglycaemic drugs, glibenclamide and metformin. Plasma glucose, insulin and lipids a well as liver glycogen and lipid peroxidation were measured following treatment for eight weeks.

The results indicated that plasma insulin levels normal controls at termination were about 76μmol/L compared to trace levels in untreated diabetic mice. Like glibenclamide, ADD-199 increased insulin levels in diabetic mice up to 70% of levels in untreated non-diabetic mice whilst metformin had no effect. Also, basal plasma glucose levels in diabetic controls (18.8mM) were reduced to 14.0mM by 100mg/kg ADD-199 in < 2 week s compared to 4 to 6 weeks for glibenclamide and metformin, respectively. This hypoglycaemic effect of ADD-199 was associated with the alkaloid content of the extract. Treatment with ADD-199 or the hypoglycaemic agents reversed the observed elevation in plasma lipids but increased hepatic glycogen, Triacylglycerol and cholesterol levels. Treatment also increased hepatic glucose uptake by isolated diaphragms and attenuated hepatic lipid peroxidation. These anti-hyperglycaemic and antioxidant actions of ADD-199 were comparable to those of the maximum daily therapeutic doses of glibenclamide (0.25mg/kg) and metformin at 50mg/kg. Olaleye and Rocha,(Olaleye *et al*., 2007) carried out an ex-vivo assessment of the antioxidant property of *Kigelia africana* extracts in rat liver homogenate. Administration of different pro-oxidants: 10 μM iron (II) sulphate, (FeSO4), 5μM sodium nitroprusside (SNP), and 2mM 3-nitropropionic acid led to increased formation of Thiobarbituric acid reactive substances (TBARS), which indicates lipid peroxidation in the liver. Administration of *Kigelia africana* statistically (p<0.05) reduced the production of TBARS in a concentration-dependent manner in all the prooxidant-induced oxidative stress, suggesting that the use of the plant in the treatment of various diseases, especially liver diseases could be due to its ability to act as an antioxidant (Olaleye *et al*., 2007).Saini and co-workers (Saini *et al*., 2009) attributed the antioxidant potential of *Kigelia africana* to caffeic acid derivatives and other compounds unique to the plant.

**2.4.2 Anti-Inflammatory and Analgesic Activities**

The use of the bark, stem, twigs, leaves and fruits of *Kigelia africana* to relieve rheumatism, toothache and headache has been documented (Houghton, 2002). Picerno and co-workers (Picerno *et al*., 2005) reported that the anti-inflammatory property of *Kigelia africana* fruit polar extract was due to the constituent verminoside. The compound is known to cause significant anti-inflammatory effects inhibiting both iNOS expression and NO release in the LPS-induced J774.A1 macrophage cell line. The ethanolic extract of the stem bark has been evaluated for analgesic property using acetic acid induced mouse writhing and hot plate reaction time; and anti-inflammatory property using the carrageenan-induced paw oedema. The extract showed a dose dependent significant reduction of the number of writhes with 500mg/kg body weight dose giving the highest reduction. In the carrageenan-induced paw oedema, a dose dependent significant inhibition was observed (p<0.001) between the second and the fifth hour, confirming that the ethanolic stem bark extract has significant analgesic and anti-inflammatory properties. Inhibition of the synthesis of prostaglandins and other inflammatory mediators has been suggested to be responsible for the analgesic and anti-inflammatory properties (Owolabi *et al*., 2007).

**2.4.3 Anti-Ulcer Effect of *Kigelia africana***

The use of *Kigelia africana* fruit, bark and root to treat ulcer has been reported (Saini *et al*., 2009). Owolabi and Nworgu (Owolabi *et al*., 2009) investigated the anti-ulcer activity of the ethanol extract of *Kigelia africana* stem bark in Wistar albino rats. In both preventive and curative models of ulcer respectively induced by absolute ethanol and indometacin, the extract caused marked inhibition of ulceration, suggesting a dose-dependent gastro-protective effect by the plant in the two models of ulcer (Owolabi *et al*., 2009)

**2.4.4 Anticancer Activity**

There are many reports in literature suggesting the use of *Kigelia africana* to either prevent or to treat cancer (Olatunji *et al.,* 2009; Hussain *et al.,* 2007 and Jackson *et al.,* 2000). In a study to determine the effect of *Kigelia africana* seed oil on cell proliferation in culture, human colon adenocarcinoma (Caco-2) and human embryonic kidney (HEK-293) cells were maintained and treated with various concentrations (0, 20, 40, 80, 100 and 120mg/l) of *Kigelia africana* seed oil. The trypan blue dye exclusion method was used to determine cell growth 48 hours after oil treatment. The seed oil suppressed both Caco-2 and HEK-293 cell growth in a dose dependent manner. The seed oil did not cause increase cell death as the number dead cells remained unchanged under control and oil-treated conditions. The oil significantly suppressed Caco-2 cell growth compared to HEK-293 cell growth at all oil concentrations. The suppression of Caco-2 and HEK-293 cell proliferation by *Kigelia africana* seed oil suggest a potential antiproliferative effect of the oil on the two cell lines (Chivand *et al*., 2012).

Methanolic extract of the root of *Kigelia africana* contains the constituent lapachol (Hussain *et* *al*., 2007) which is reported to be effective in the treatment of solar keratosis, skin cancer and Kaposi sarcoma, an HIV-related skin ailment (Jackson *et al*., 2000). Serial dilutions of standardized aqueous, ethanol and dichloromethane extracts of the stem bark and fruits of *Kigelia africana* were tested for their growth inhibitory effects against four melanoma cell lines and a renal cell carcinoma line (Caki-2) using two different assays (3-(4,5- Dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide, MTT and Sulforhodamine B, SRB assays). Lapachol, a possible constituent of these extracts, together with known therapeutic anti-neoplastic agents evaluated this way, showed significant inhibitory activity of the dichloromethane extract of the stem bark and lapachol in a dose-dependent and time dependent manner. Chemosensitivity of the elanoma cell lines to the stem bark was greater than that seen for the renal adenocarcinoma line, but in marked contrast sensitivity to lapachol was similar amongst the five cell lines, suggesting that lapachol is the active ingredient that exhibit anti-cancer property (Houghton *et al*., 1994).

**2.4.5 Anti-Diarrhoeal Activity**

One important local use of *Kigelia africana* is the use of the leaf for treating diarrhea (Akah, 2011). An administration of a dose of 100 or 200 mg/kg of aqueous leaf extract to experimental animals caused anti-diarrhea activity. It also reduced the reduced fecal output in castor oil – induced diarrhea in animals and remarkably decreased the propulsive movement of the gastro-intestinal contents (Otimenyin *et al*., 2012). On the isolated guinea pig ileum, the extract did not appreciably affect acetylcholine and histamine induced contractions. In an anti-diarrhoeal activity studied using castor oil to induce diarrhea in rats (in vivo) and using isolated jejunum, 500 and 1000mg/kg ethanol root extract (in vitro) significantly reduced the frequency of diarrheal stool and the spontaneous propulsive movement of isolated jejunum (Otimenyin *et al*., 2012). *Kigelia africana* root extract also produced reversible inhibition of acetylcholine induced mobility of isolated rabbit jejunum. The observed Spasmolytic effects of the extract may explain its continual use in the management of chronic abdominal pains associated with diarrhea (Otimenyin *et al*., 2012).

**2.4.6 Diuretic Activity**

The diuretic activity of *Kigelia africana* aqueous bark extract was investigated by the determination of urine volume, electrolyte concentration and diuretic potency in male albino rats. Different concentrations of the extract, 250 and 500mg/kg were orally administered to hydrated rats and their urine output was immediately measured after 5 hours of treatment. Fusemide (10mg/kg) was used as reference drug while normal saline (0.9%) was used as control. The result showed that the bark extract exhibited dose dependent diuretic property. The onset of diuretic action was within 1 hour and lasted up to 5 hours, with 500mg/kg displaying a potency of 0.8 and 250mg/kg, respectively. The extract also caused a marked increase in Na+, K+ and Cl- labels (Sharma *et al.,* 2010). The result suggests that the aqueous extract possess significant diuretic activity, justifying its use in folk medicine for kidney and urinary disorders.

### 2.5 Antioxidant

An antioxidant is a molecule stable enough to donate an electron to a rampaging free radical and neutralize it, thus reducing its capacity to damage. These antioxidants delay or inhibit cellular damage mainly through their free radical scavenging property. (Halliweli, 1995) these low-molecular-weight antioxidants can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged. Some of such antioxidants, including glutathione, ubiquinol, and uric acid, are produced during normal metabolism in the body. (Shi, 1999). Other lighter antioxidants are found in the diet. Although there is several enzymes system within the body that scavenges free radicals, the principle micronutrient (vitamins) antioxidants are vitamin E (α-tocopherol), vitamin C (ascorbic acid), and B-carotene. (Levine *et al*., 1991). The body cannot manufacture these micronutrients, so they must be supplied in the diet.

**Table 1: Classification of antioxidant**

|  |  |
| --- | --- |
| ANTIOXIDANT | ROLES |
| **ENZYMES** |  |
| Superoxide dismutase (SOD)  Mitochondrial cytoplasmic  Extracellular | Catalyses O2 to H2 O2 |
| Catalase | catalyses H2O2 to H2O |
| Glutathione perioxidase  (GSH.PX) | Removes H2O2 and lipid peroxides |
| **VITAMINS** |  |
| Alpha tocopherol | Breaks lipid peroxidation, lipid peroxide and O2 and OH scavengers |
| Beta carotene | Scavenges OH, O2 and peroxyl radicals  Prevents oxidation of vitamin A  Binds to transition metals |
| Ascorbic acid | Directly Scavenges O2, OH and H2O2  Neutralizes oxidants from stimulated neutrophils  Contribute to regeneration of vitamin E. |

Source: (Levine *et al*., 1991).

### 2.5.1 Antioxidant defences system

Antioxidants act as radical scavenger, hydrogen donor, electron donor, peroxide decomposer, singlet oxygen quencher, enzyme inhibitor, synergist, and metal-chelating agents. Both enzymatic and non enzymatic antioxidants exist in the intracellular and extracellular environment to detoxify ROS (Frie *et al*., 1988).

**2.5.2 Mechanisms of action of antioxidants**

Two principle mechanisms of action have been proposed for antioxidants. (Rice-Evans *et al.,* 2001), the first is a chain- breaking mechanism by which the primary antioxidant donates an electron to the free radical present in the systems. The second mechanism involves removal of ROS reactive nitrogen species initiators (secondary antioxidants) by quenching chain-initiating catalyst (Krinsky, 1992).

### 2.5.3 Levels of antioxidant actions

The antioxidants acting in the defense systems act at different levels such as preventive, radical scavenging, repair and de novo, and the fourth line of defense, i.e., the adaptation.

**The first line of defense** is the preventive antioxidants, which suppress the formation of free radicals. Although the precise mechanism and site of radical formation in vivo are not well elucidated yet, the metal-induced decompositions of hydroperoxides and hydrogen peroxide must be one of the important sources. To suppress such reactions, some antioxidants reduce hydroperoxides and hydrogen peroxide before hand to alcohols and water, respectively, without generation of free radicals and some proteins sequester metal ions. Glutathione peroxidase, glutathione-s-transferase, phospholipids hydroperoxides glutathione peroxidase (PHGPX), and peroxidase are known to decompose lipid hydroperoxides to corresponding alcohols. Glutathione peroxidase and catalase reduce hydrogen peroxide to water.

**The second line of defense** is the antioxidants that scavenge the active radicals to suppress chain initiation and/or break the chain propagation reactions. Various endogenous radical-scavenging antioxidants are known: some are hydrophilic and others are lipophilic. Vitamin C, uric acid, bilirubin, albumin, and thiols are hydrophilic, radical-scavenging antioxidants, while vitamin E and ubiquinol are lipophilic radical-scavenging antioxidants. Vitamin E is accepted as the most potent radical-scavenging lipophilic antioxidant.

**The third line of defense** is the repair and de novo antioxidants. The proteolytic enzymes, proteinases, proteases, and peptidases, present in the cytosol and in the mitochondria of mammalian cells, recognize, degrade, and remove oxidatively modified proteins and prevent the accumulation of oxidized proteins.

The DNA repair systems also play an important role in the total defense system against oxidative damage. Various kinds of enzymes such as glycosylases and nucleases, which repair the damaged DNA, are known.

**The forth line of defense**: There is another important function called adaptation where the signal for the production and reactions of free radicals induces formation and transport of the appropriate antioxidant to the right site (Niki, 1993).

**2.6 Lipid Peroxidation**

Lipid peroxidation refers to the oxidative deterioration of lipid. It is the process in which free radicals ‘steal’ electrons from the lipids in cell membranes resulting in cell damage. Lipid peroxidation proceeds by free radical chain reaction*.* Polyunsaturated fatty acids are most often being affected because of the presence of multiple double bonds in between which lie methylene bridges (-CH2-) that possess reactive hydrogen. When the radical removes hydrogen atom, it leaves behind an unpaired electron in the lipid (Niki, 2009). This in turn leads to chain reaction.

The lipid radicals formed lead to cell damage. Three mechanisms are able to induce lipid peroxidation: autoxidation (by free radicals reaction), photoxidation and enzyme action. Autoxidation is a radical-chain process involving three stages: initiation, propagation and termination.

**2.6.1 Stages of lipid peroxidation**

The general process of lipid peroxidation consists of three stages: Initiation, propagation and termination.

**Initiation** occurs when oxygen is partly reduced by Fe2+ to species able to abstract a hydrogen atom from a methylene carbon .The resulting alkyl radical reacts with oxygen to form a peroxy radical (LOO .), which itself can liberate LOOH *via* hydrogen abstraction from a neighbouring alkyl bonds.

In **propagation**, fatty acid radicals react with molecular oxygen forming a peroxyl-fatty acid radical. This radical is also an unstable species that reacts with another free radical acid, producing a different fatty radical and a lipid peroxide or acyclic peroxide if it had reacted with itself. The cycle continues as the new fatty acid radical react in the same way.

**Termination** occurs when new radicals reacts and produce a non-radical species. Antioxidant

Vitamin E and antioxidant enzymes play a major role in the termination process (Marnett, 2002).

**2.6.2 Malondialdehyde (MDA)**

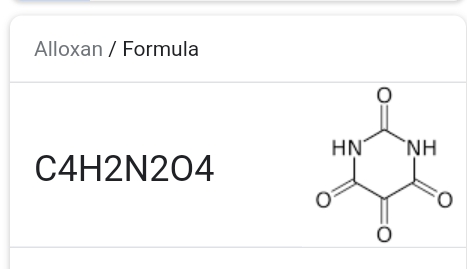
Malondialdehyde (MDA) is a late–stage lipid oxidation by-product that can be formed none enzymatically as a by-product of cycloxygenase activity (Slatter *et al.,* 2002). MDA is a highly toxic product formed in part by lipid oxidation-derived free radicals. Many studies have shown that its concentration is considerably high in diabetes mellitus correlating with poor glycemic control (Slatter *et al.,* 2002, Hoff *et al.,* 2003). MDA is a volatile molecule that reacts, via Schiff base formation, with free amine groups of proteins, lipids and DNA. It is estimated that up to 80% of MDA is protein-bound (Slatter *et al.,* 2002). In addition, accumulation of MDA affects membrane organization by increasing phosphotidyl serine (PS) externalization. Accumulation of MDA and MDA adducts were correlated with many disease state, such as hepatitis C, Down syndrome (Muchova *et al*., 2001), cancer (Marneth *et al*., 2002), liver injury (Tuma, 2002), neurodegenerative disease and diabetes mellitus (Slatter *et* *al.*, 2002).

**2.7 Alloxan and its mechanism of action**

Alloxan and streptozotocin are the most prominent diabetogenic chemicals in diabetes research. Both are cytotoxic glucose analogues. Although their cytotoxicity is achieved via different pathways, their mechanisms of beta cell selective action are identical (Lenzen, 2007). In 1938 Wohler and Liebig synthesized a pyrmidine derivative, which they later called alloxan (Lenzen *et al.,* 1996). In 1943, interest in alloxan increased when Dunn and Mc letchie reported that it could induce diabetes in animals as a result of the specific necrosis of the pancreatic beta cells (Peschke *et al.,* 2000). The resulting insulinopenia causes a state of experimental diabetes mellitus called alloxan diabetes. The reduction product of alloxan, dialuric acid, has been shown to be diabetogenic in animals and to cause ultrastructural changes identical to those observed in response to alloxan (Jorns *et al.*, 1997). It was reported that streptozotocin is diabetogenic and could cause diabetes by specific necrosis of the pancreatic beta cell. Research has provided a unifying explanation for selective toxicity of these most prominent diabetogenic agents.

**2.7.1 Mechanism of Action**

Alloxan has two distinct pathological effects: it selectively inhibits glucose-induced insulin secretion through specific inhibition of glucokinase, the glucose sensor of the beta cell, and causes a state of insulin-dependent diabetes through its ability to induce ROS formation, resulting in the selective necrosis of beta cells (Lenzen, 2008). Due to its chemical properties, in particular the greater stability (Table 2), streptozotocin is the agent of choice for reproducible induction of a diabetic metabolic state in experimental animals (Lenzen *et al.,* 1996). Alloxan on the other hand, as a model compound of ROS-mediated beta cell toxicity, is the agent with the greater impact upon the understanding of ROS mediated mechanisms of beta cell death in type 1 and type 2 diabetes mellitus.

**C4H2N2O4**

**Figure 2: chemical structure of Alloxan.**

**Source from: The Merck Index, 2018. (**[**https://en.m.wikipedia.org/wiki/Alloxan**](https://en.m.wikipedia.org/wiki/Alloxan)**)**

**CHAPTER THREE**

**MATERIALS AND METHODS**

**3.1 Chemicals and Reagents**

All the reagents used were of analytical grade, only few of the reagents grades were further used without further purification.

All reagents used for the analysis were obtained from Godfrey Okoye university biochemistry laboratories.

**3.1.1 Reagents**

Methanol (CH3OH), Alloxan (C4H2N2O4), Distilled water (H2O), Phosphate buffer (H2KO4P), Xanthine Oxidase, hydrogen peroxides (H2O2), lipid profile Kit, Normal saline (NaH2O).

**3.1.2 Equipments**

Glucometer, water bath, centrifuge, spectrophotometer, electronic weighing balance, electronic blender, oven, stirrer, beaker, measuring cylinder.

**3.2 Collection of leaves**

Fresh leaves of Kigelia africana was obtained from Omege, Ekwetekwe, Umuzeroko, Ebonyi state. Nigeria and was authenticated by Department of Plant Environmental Sciences, University Of Nigeria, Nsukka.

**3.3 Preparation of Plant Extracts**

Fresh leaves of Kigelia africana was shade-dried for 3 days and milled to powder with an electric blender and kept air tigh.t container. A total of 500.82 g of the dried and powered leaves were soaked with 500 ml of methanol in a beaker. The contents were vigorously shaken for some minutes and allowed to stand for 72hours. The mixtures were filtered using a clean cheese cloth and re-filtered using filter paper. The filtrate was evaporated to dryness using rotary evaporator of 270C.

**3.4 Animal care**

Twenty Wister Albino rats were purchased from Department of Zoology and Environmental Biology university of Nigeria Nsukka. They were maintained in the Biological Science animal house Godfrey Okoye University Enugu for one week acclimatization before the commencement of the experiment.

**3.4.1 Animal grouping and preparation of Extract for Administration**

Twenty male and female albino rats with the average weight of x +125 g were assigned into four groups comprising of five rats in a group.

Group 1: Normal rats + feed and water only.

Group 2: Diabetic rats untreated + feed + water

Group 3: Diabetic rats + 0.6mg of glibenclamide

Group 4: Diabetic rats + 500mg/kg Bw of the leaf extract of *Kigelia africana* treatment was done for 14days

**3.5 Alloxan Mode of Administration**

The glucose level of each rat was measured before the administration of alloxan after 24hours fasting.

The induction was done intraperitoneally with 180mg/kg Body weight of the alloxan and diabetes was confirmed after 72hours.

**3.6 Collection of blood**

Blood samples used for the analysis was collected through ocular puncture into they EDTA sample collection bottle.

**3.6 Assessment of biochemical parameters**

**3.6.1 Glucose level**

**Principle**

Glucose is oxidized to gluconic acid and hydrogen peroxide in the presence of glucose oxidase. Hydrogen peroxide further reacts with phenol and 4-aminoantipyrine by the catalytic action of peroxide to form a red colored quinonemine dye complex. Intensity of the colour formed is directly proportional to the amount of glucose present in the sample.

Glucose + O2 +H2O glucose oxidase Gluconate + H2O2

H2O2 + 4 Aminoantipyrine + phenol Peroxidase Red Quinoneimine dye + H2O

***Reagents***

ONE TOUCH Glucometer (lifescan inc. Johnson- Johnson Company, USA) and test strips were used.

The composition of the test strips is:

Glucose oxidase (14/U)

Peroxidase (11/U)

3-methyl-2-benzothiazolinonehydrazone hydrochloride (0.06 mg)

3-dimethylaminobenzoic acid (0.12 mg) .

**Procedure**

Code key was inserted into the Glucometer code key opening and ensured that the code on the Glucometer matches the code on the test strip. A fresh new strip was inserted with the orange pad facing up until it went no further into the Glucometer opening for test strips. The blood sample (0.1 ml) was placed on test strip and result was displayed after 5 seconds in mg/dl.

**3.6.2 Determination of Malondialdehyde Concentration**

Malondialdehyde concentration was determined by the method of Wallin *et al.* (1993).

**Principle**

Under certain condition, malondialdehyde (MDA) produced from peroxidation of membrane fatty acids and food products react with chromogenic reagents, 2-thiobarbturic acid (TBA), to yield a pink colored complex with maximum absorbance at 532nm and fluorescence at 553nm.

The pink chromophore is readily extractable into organic solvents such as butanol.

MDA + 2TBA MDA: TBA adduct + H2O

**Reagent Preparation**

(a) Thiobarbituric acid was prepared by dissolving 1.0 g of the compound in 83 ml of distilled water on warming. After complete dissolution the volume was made up to 100 ml with distilled water.

(b) 25% Trichloroacetic acid (TCA): Trichloroacetic acid (12.5 g) was dissolved in distilled water and made up to 100 ml in a volumetric flask with distilled water.

(c) Normal saline: Sodium chloride (0.3 g) was dissolved in 10 ml of distilled water and make up to 100 ml with distilled water.

**Procedure**

* To 0.1 ml plasma in the test tube was added 0.45 ml of normal saline and mixed thoroughly before adding 0.5 ml of 25% trichloroacetic acid (TCA) and 0.5 ml of 1% thiobarbituric acid.
* To the blank was added the same volume of trichloroacetic acid, thiobarbituric acid and saline and 0.10 ml of distilled water instead of plasma.
* The mixture was placed in the water bath and heated at 95oC for 40 minutes. The turbidity was removed by centrifuging the mixture.
* It was allowed to cool before reading the absorbance of the clear supernatant against reagent blank at 532 nm and 600nm.
* Thiobarbituric acid reacting substances were quantified as lipid peroxidation product by referring to a standard curve of malondialdehyde (MDA) concentration equivalent generated by acid hydrolysis of 1,1,3,3–tetraethoxypropane (TEP) prepared by serial dilution of a stock solution.

**3.6.3 Assay of catalase activity**

Catalase was assayed by the method described by Aebi (1983)

**Principle**

The ultraviolet absorption of hydrogen peroxide can be easily measured at 240 nm. On the decomposition of hydrogen peroxide with catalase, the absorption decreases with time and from this decrease catalase activity can be measured.

**Reagent**

Phosphate buffer, pH 7

3.522 g KH2 PO4 and

A quantity of 7.268 g of Na2HPO42H2O was dissolved in 1000ml of water

Hydrogen peroxide solution.

A given quantity of 0.085ml of 30% of hydrogen peroxide was dissolved in 25ml of phosphate buffer

**Procedure**

Immediately following the addition of 1ml phosphate buffer and 2 ml diluted haemolysate into the blank test tube (B) and 1 ml hydrogen peroxide and 2 ml haemolysate into the sample test tube (T), the change of absorbance of test sample against blank at 240 nm was recorded every 15 seconds for 1 minute on a spectrophotometer.

**Calculation:**

Catalytic concentration (unit/L) = 0.23 × Log (A1/ A2)

0.00693

Where A1 is absorbance at time t = 0 seconds

A2 is absorbance at time t = 15 seconds 0.23 And 0.00693 are constant

**3.6.4 Determination of Total Cholesterol Concentration**

**Principle**

The cholesterol is determined after enzymatic hydrolysis and oxidation. The indicator quinoneimine is formed from hydrogen peroxide and 4-aminoantipyrine in the presence of phenol and peroxidase.

**Reagent**

Reagents used are commercial kit obtained from Randox Lab Limited, UK.

Content Concentration.

4-Aminoantipyrine 0.30 mmol/L

Phenol 6 mmol/L

Peroxidase > 0.5 u/ml

Cholesterol esterase > 0.15 u/ml

Cholesterol oxidase >0.1u/ml

Pipes buffer 80 mmol, PH 6.8

CAL Standard

**Procedure**

Three test tubes were labeled blank, standard and sample respectively. Into the blank were added 10 ml of distilled water and 10 μl of standard to the standard labeled test tubes.

Sample serum (10 μl) was added to the appropriately labeled test tube. Reagent (1000 μl) was

Added to the three sets of the tubes, mixed and incubated at 370c for 5 minutes. The absorbance of the sample (A sample) was measured against the reagent blank within 60 minutes at 500 nm.

**Calculations**

Concentration of cholesterol in sample= ASample × concentration of standard in mg/dL

AStandard

**3.6.5 Determination of High Density Lipoprotein (HDL) Cholesterol Concentration**

High density lipoprotein cholesterol (HDL) level was determined by the method of Albers (1978) as contained in the QCA commercial kit used.

**Principle**

LDL and very low density lipoprotein (VLDL) and chylomicrons fraction are precipitated quantitatively by the addition of phosphotungstic acid in the presence of magnesium ions after centrifugation, the cholesterol concentration in HDL fraction, which remain in the supernatant is determined.

LDL-Cholesterol = Total Cholesterol –Cholesterol in the supernatant

Cholesterol– ester +H2O Cholesterol + Fatty acid

Cholesterol +1/2 O2+ H2O Cholestene-3-one + H2O2

2H2O2 + 4–Aminoantipyrine + DCFs Quinoneimine +H2O

**Reagent**

Reagents used are commercial kit obtained from Randox Lab Limited, UK.

Content Concentration.

4-Aminoantipyrine 0.30 mmol/L

Phenol 6 mmol/L

Peroxidase > 0.5 u/ml

Cholesterol esterase > 0.15 u/ml

Cholesterol oxidase >0.1u/ml

Pipes buffer 80 mmol, PH 6.8

**Procedure**

The procedure involved two steps.

(A) Precipitation step.

The serum sample (0.3 ml) was pipette into labeled centrifuge tubes. A drop of the precipitant solution or reagent (10g/c of dextran sulphate, IM of magnesium acetate and stabilizers) was added to each of the centrifuge tubes.

The contents in the various tubes were thoroughly mixed and allowed to stand for 15 minutes at room temperature (20-250C) and then centrifuged at 2,000 rpm. The concentration of cholesterol in the supernatant was determined and absorbance was measured at 630nm.

**Calculation:**

HDL–Cholesterol concentration in sample: ASample × concentration of standard in mg/dL

AStandard

**3.6.5 Determination of Low density lipoprotein cholesterol concentration**

**Principle**

LDL and very low density lipoprotein (VLDL) are precipitated from the serum by the action of a polysaccharide in the presence of divalent cations. Then high density lipoprotein –cholesterol (HDL –Cholesterol) present in the supernatant is determined.

LDL-Cholesterol = Total Cholesterol –Cholesterol in the supernatant

**Reagent**

**Content Concentration**

Precipitation Reagent

Polyvinyl Sulphate 0.7g/L

EDTA (Na2 salt) 5.0 mM

Polyethylene glycol monomethyl ether 170.g/L

Stabilizers

**Procedure**

**1. Precipitation Reaction**

The precipitation solution (3 drops or 0.1 ml) was carefully measured into test tubes labeled accordingly. The serum (0.2 ml) was added to the labeled test tubes. The contents were thoroughly mixed and left to stand for 15 minutes at room temperature (20-250C).Then, the mixture was centrifuged at 2,000 rpm for 15 minutes and the cholesterol concentration in the supernatant was determined.

**2. Cholesterol Determination**

The concentration of serum total cholesterol was determined according to the QCACHOD –PAP method.

**Procedure:**

A quantity of 100 microlitres of sample supernatant was added to the sample test tube, 1000microlitre was added to the sample test tube and mixed and was incubated for 10 minutes.

To the standard test tube a quantity of 100microlitre of the sample was added to the test tube and 1000microlitre of the reagent was added to the standard test tube and was incubated for 10 minutes. One hundred microlitres of distilled water and one thousand microlitres of the reagent were added to the reagent blank test tube and were used to blank the spectrophotometer. The absorbance of the sample was read at an absorbance of 500nm. And calculations were done.

**Calculations:** LDL-Cholesterol (mg/dL) = Total concentration (mg/dL) – 1.5 × supernatant cholesterol

**CHAPTER FOUR**

**RESULTS**

**Table 3: Percentage yield for extraction**

**SAMPLE EXTRACT WEIGHT (g) PERCENTAGE YIELD**

**(%)**

Leaves dried and ground 500.33

Sample

Methanol extract 3.26 0.65

**Table 4: Readings of Glucose test** Normal range is 95-150mg/dl

GROUPS 0 DAYS 3 DAYS 7DAYS 14DAYS

(Mg/dl) (Mg/dl) (Mg/dl) (Mg/dl)

Normal/ 102 101 101 96

Control` 95 96 95 90

100 97 97 95

110 110 105 98

98 98 96 93

Mean (Ẍ) 101 100 99 94

Diabetes 109 193 181 106

Not treated 101 210 187 118

111 189 179 102

97 200 179 104

102 195 180 113

Mean (Ẍ) 104 197 181 109

Diabetes treated 95 185 176 129

Glibenclamide 104 204 180 156

102 190 179 130

110 211 181 143

99 197 180 140

Mean (Ẍ) 102 197 179 139

Diabetes treated 103 213 189 116

With leaf extract 110 210 187 99

96 189 180 114

105 196 177 98 104 206 189 120

Mean (Ẍ) 103 203 184 109

* 1. **Effects of Methanol leaf extract of *Kigelia africana* on Malondialdehyde (MDA) in**

**Alloxan induced-diabetes rats.**

And an increase (p˂0.05) not too significant was observed in the test group 4 treated with the plant extract compared with other groups. A significant increase was observed in diabetic rats treated with Modern drug glibenclamide compared with the normal group 1.

**Figure 3:**

**Group 1: Normal control**

**Group 2: Diabetic untreated**

**Group 3: Diabetic treated with Modern drug (Glibenclamide)**

**Group 4: Diabetic treated with *K. Africana* methanol extract**

**3.2 Effect of *Kigelia africana* on antioxidant enzyme (catalase) in alloxan-induced diabetic rats.**

A significant increase (p˂0.05) of catalase activity was observed in diabetic rats treated with glibenclamide (group 3) and diabetic rats treated with *Kigelia africana* (group4) when compared with the control group (group 1) and diabetes not treated (group 2).

‘/

**Figure 4:**

**Group 1: Normal control**

**Group 2: Diabetic untreated**

**Group 3: Diabetic treated with Modern drug (Glibenclamide)**

**Group 4: Diabetic treated with *K. Africana* methanol extract**

**3.3 Effect of *Kigelia africana* on cholesterol level in alloxan-induced diabetic rats.**

A significant increase (P˂0.05) in cholesterol level was observed in rats treated with *k. africana* (group 4) and rats treated with glibenclamide (group 3) when compared with the normal control group (group 1).

**Figure 5:**

**Group 1: Normal control**

**Group 2: Diabetic untreated**

**Group 3: Diabetic treated with Modern drug (Glibenclamide)**

**Group 4: Diabetic treated with *K. Africana* methanol extract**

**3.6 Effect of methanol leaf extract of *Kigelia africana* on High density lipoprotein (HDL) in alloxan-induced diabetic rats.**

A significant increase (P˂ 0.05) of serum HDL-Cholesterol was observed in diabetes treated with *Kigelia africana* (group 4) compared with normal control (group 1).

**Figure 6:**

**Group 1: Normal control**

**Group 2: Diabetic untreated**

**Group 3: Diabetic treated with Modern drug (Glibenclamide)**

**Group 4: Diabetic treated with *K. Africana* methanol extract**

**3.7 Effect of *Kigelia africana* on Low density lipoprotein (LDL) in alloxan-induced diabetic rats.**

A significant increase (p˂0.05) of Low-density lipoprotein (LDL) was observed in diabetic rats treated with Modern drug (glibenclamide) when compared with other groups. A significant decreased (P˂0.05) was measured in diabetic rats treated with *Kigelia africana* (group 4).

**Figure 7**

**Group 1: Normal control**

**Group 2: Diabetic untreated**

**Group 3: Diabetic treated with Modern drug (Glibenclamide)**

**Group 4: Diabetic treated with *K. Africana* methanol extract**

**CHAPTER FIVE**

**DISCUSSION**

This study evaluated the antidiabetic and antioxidative properties of *Kigelia africana* in alloxan-induced diabetic rats. From the results obtained diabetic rats had much higher blood glucose level than that of the normal control. Changes in blood glucose levels reflect abnormalities in ß- cells structure and function. Alloxan causes glucose oxidation and reduction in insulin release by the destruction of ß- cells of the islets of langerhans (Siyem *et al.,* 2002). And Alloxan also has two distinct pathological effects: it selectively inhibits glucose-induced insulin secretion through specific inhibition of glucokinase, the glucose sensor of the beta cell, and causes a state of insulin-dependent diabetes through its ability to induce ROS formation, resulting in the selective necrosis of beta cells (Lenzen, 2008). It was considered that rats with blood glucose level of 180mg/dl and greater were considered diabetic. Administration of methanol leaf extract of *K.africana* restored glucose in the alloxan- induced diabetic rats.

A modern drug known as Glibenclamide was used as a standard drug to compare the effect of *K.africana* extract in the reference to the blood glucose level reduction. A quantity of 0.8ml of plant extract administered to the samples (rats) showed a significant effect after 14days indicating that the extract possesses ability to reduce glucose level (Hypoglycemic activities).

The comparable effect of the extract with glibenclamide may suggest similar modes of action, since the main mechanism of the action of glibenclamide is the stimulation of insulin release and the inhibition of glucagon secretion. It has been described that glibenclamide is effective in moderate diabetic state and ineffective in severe diabetic animals where pancreatic ß- cells are totally destroyed (Suba *et al*., 2004). The hypoglycemic effect of medicinal plant extracts generally depends upon the degree of ß cell destruction (Grover *et al*., 2000). Some plants have also been observed to exert hypoglycemic activity through insulin stimulatory effect (Ravi *et al*., 2004). This could be as a result of the substances the contain are glycosides, alkaloids, terpernoids, and flavonoids that are frequently implicated as having antidiabetic effects (Low and Kazkin, 2002). The alloxan-induced diabetic rats had a marked loss of body weight. Which is expected as one of the effects of diabetes is body weight loss. Free Radicals generated under hyperglycemic condition could attack major biomloecules such as proteins, DNA and lipids and which could lead to the weight loss as observed in this work. However, the diabetic rats fed orally with modern drug (glibenclamide) and *Kigelia* plant extracts had a remarkable gain in body weight compared with untreated diabetic rats.

A significant increase (P˂0.05) in MDA was discovered in diabetic untreated rats compared with normal group and an increase not too significant was noted in test group treated with *k*. *africana* extract. High concentration of MDA in diabetic untreated rats establishes oxidative stress. Many studies have shown that its concentration is considerably high in diabetes mellitus correlating with poor glycemic control (Slatter *et al.,* 2002, Hoff *et al.,* 2003).A significant decrease (P˂0.05) in MDA in the test group 4 signifies that the extract was able cause a reduction in the lipid peroxidation index in treatment group (group 4). This indicates the ability of the extracts to step down the oxidative stress by mopping up free radical that leads to lipid breakdown. The bioactive constituents of the extracts such as flavonoids, alkaloids as revealed by Phytochemistry results could be implicated in free radical scavenging properties of the extract (Uhuo *et al*., 2014). And an ex-vivo assessment of antioxidant property of *k. africana* in rat liver homogenate showed a statistical decrease (P˂0.05) in the production of TBARs in a concentration dependent manner (Olaleye et al., 2007). Saini and Co attributed this antioxidant potential of *Kigelia**africana* to the presence of caffeic acid derivatives and other compounds unique to the plant. (Saini et al., 2009).

A significant increase (P˂0.05) in catalase activity was discovered across the test group 3 and 4 compared with a significant decrease in normal control (group 1) and diabetic untreated (group 2). This shows that the extract *k. africana* administered to diabetic rats have the ability to mop up or scavenge free radicals generated under certain conditions such as oxidative stress. A significant increase (P˂0.05) was observed in cholesterol level across the test group (group 3 and group 4) although the increase was not that significant, however a significant decrease (P>0.05) of serum cholesterol was observed diabetic untreated (group 2) compared with diabetic treated with modern drugs (glibenclamide). A significant increase was observed in diabetic rats treated with modern drug (glibenclamide) compared with other groups and a decrease was observed in diabetic treated with *k. africana* extract. This explains the fact that diabetic is associated with altered lipid levels. Most commonly observed lipid abnormalities are hypercholesterolemia and hypertrigyceridemia (Shepherd, 2005 and Shikwaikar *et al*., 2006) and thus contribute to coronary artery disease (Arvind *et al*., 2002). The administration of *Kigelia africana* extracts leaf extract causes a significant decrease (P˂0.05) in the level of Serum-cholesterol and LDL (bad cholesterol) which reveals the hypolipidemic properties of the plant. A significant increase of HDL (P˂0.05) was observed in diabetic rats treated with *Kigelia africana* extract (group 4); this explains that *Kigelia africana* is a fan of” good” cholesterol.

**CONCLUSION**

Following the research carried out and the results gotten, it can be concluded that *Kigelia africana* possess anti-hyperglycemic activities which also results to an increment in the weights of diabetic rats treated with the extract.

*Kigelia africana* extract was found to exhibit antioxidant properties by reducing the concentration of malondialdehyde (MDA) therefore destroying lipid peroxidation. Antioxidant potentials of the plant extract was confirmed by the increased level of catalase activity (CAT) in the test groups.

The extract was also found to have effect in lowering the effect of lipids in diabetic rats and increased effect in HDL level which is good cholesterol. Therefore, from the results gotten, it can be said that *Kigelia africana* has a hypolipidemic and antioxidant capacity l in diabetic conditions.

**RECOMMENDATION**

It is recommended that *K.africana* can be used in the management of diabetes and lipid disease conditions if properly assessed and confirmed not to have any adverse effect.

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