UNIVERSITY OF ILORIN

ONE HUNDRED AND FORTY-SIXTH (146TH)
INAUGURAL LECTURE

"DREADABLE UNPAIRED SPECIES: BIOCHEMICAL APPROACH AS PANACEA"

BY

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All other Academic Colleagues,
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My lords spiritual and temporal,
Distinguished students of Biochemistry,
Gentlemen of the Print and Electronic Media,
Distinguished Invited Guests,
Great Unilorites,
Ladies and Gentlemen.

Preamble

It is with a heart of gratitude and praise to the almighty God who not only has kept me but has given me the privilege to deliver the 146th Inaugural Lecture of the University of Ilorin, the 'Better by Far' University today. It is funny that I have to be giving an inaugural lecture 14 years after I became a Professor of Biochemistry and at the

age of 60 years. Institutional and domestic challenges beyond my control are causative agents.

My being in the academics was because my late father of the blessed memory, a primary school teacher, had always wanted one of his children to be a teacher with the highest qualification in the teaching profession. He provided the enabling motivation and encouragement, in spite of all odds, for me to be the best in all my classes. I too keyed into the idea more so that only few women were into teaching profession at that time. Today, I give praises to God that my father's dream has been realized years after his demise and resting at the bosom of his creator. Providence gave me an academic career at this University by bestowing me as a 'biblical helper' to Professor Oluwafemi Olaiya BALOGUN who was appointed a lecturer into the Department of Biochemistry, University of Ilorin in 1979 and I had to follow him to Ilorin to continue to fulfill the biblical injunctions to 'ordained helpers'. In 1980, I was employed as an assistant lecturer to teach Biochemistry in the Department of Physiology and Biochemistry, Faculty of Health Sciences, University of Ilorin. At that time, the two expatriates that were teaching Biochemistry resigned their appointments when the first Nigerian became the Dean of the Faculty. It was a great task for me being the only lecturer to teach both the 200 and 300 Level Medical Biochemistry courses. Our colleagues in the Department of Biochemistry of Faculty of Science were not willing to join me. Two years later more academic staff were recruited and I remained there for 26years before we were re-located to the Department of Biochemistry, Faculty of Science in 2006. Mr. Vice-Chancellor Sir, I can humbly say that I was the first female Professor in the Faculty of Health Sciences of this

university and today the first female Professor to have the unique honour and privilege to give 146th Inaugural lecture in the newly created Faculty of Life Sciences titled: "DREADABLE UNPAIRED SPECIES: BIOCHEMICAL APPROACH AS PANACEA".

Introduction

Earlier inaugural lecturers from the Department of Biochemistry of this University had enlightened us on what Biochemistry is all about. Professor S. O. Malomo, the Supervisor of my Doctor of Philosophy degree programme had given some tips in our overlapped areas of specialization and research, Antimalarial chemotherapy and Biochemical Toxicology, while delivering 127th inaugural lecture titled "The Invisible behind and beyond the Visible". I intend not to bore you by repeating some of the facts contained in that lecture.

I had a brief research sojourn in nutritional biochemistry before providential research orientation led me to an academic career fulfillment as a result of collaborative research focus on antimalarial drugs; their mechanisms of action and toxicology and phytomedicine. Our research efforts in the latter are at the verge of launching this University into global recognition.

In the course of my research I discovered that our God's admonition (according to my Bible) that it is not good for a man to dwell alone, is also true of Oxygen. Oxygen which is the most important and beneficial to all living things may not be beneficial in certain states and in fact may be so injurious to cells and tissues of which living organisms are made of. This Mr. Vice-Chancellor Sir, is the focus of this lecture

In the course of this lecture we will be taking a brief voyage through the archive of existing knowledge on Reactive Oxygen Species (ROS) which contain unpaired electrons, the consequences of their being silent killers and my contributions through research into the ameliorative effects of natural products.

What exactly are Reactive Oxygen Species (ROS)? They are chemically reactive molecules containing oxygen, chemical species with unpaired electrons. The oxygen we breathe in is molecular oxygen (O_2). These ROS are activated oxygen which include free radicals such as superoxide anion radicals (O^{2-}), perhydroxyl radical (HO_2^-), hyroxy radicals (OH^-), free radical nitric oxide ($NO^{\bullet}$) and non-free radicals such as hydrogen peroxide (H_2O_2), and singlet oxygen ($^1O_2$) (Halliwell 1995). They are very reactive species because electrons like to pair up to form stable two electron bonds (Linus Pauling,1954). There are exogenous and endogenous reactive oxygen species.

Exogenous Reactive Oxygen Species: These can be produced from pollutants, tobacco smoke, drugs, xenobiotics or radiation. In the presence of ionizing radiation water which as a major component of the body loses an electron and becomes highly reactive. In the process water is converted to hydroxyl radical ($^{\bullet}OH$), hydrogen peroxide (H_2O_2), super oxide radical (O_2^-) and ultimately Oxygen (O_2). The ($^{\bullet}OH$) hydroxyl radical removes electrons from any molecule in its path turning the molecule into Hydrogen peroxide (H_2O_2) which is even more damaging to DNA than hydroxyl radical.

Endogenous Reactive Oxygen Species: These are produced intracellularly through multiple mechanisms and depending on the cell and tissue type. The major source is

NADPH oxidase complexes in cell membranes, mitochondria, peroxisomes and endoplasmic reticulum. In aerobic organisms like humans, O_2 is converted to water at the end of the respiratory chain in the mitochondria. Mitochondria are the power plants in our cells that provide the energy needed to maintain normal body function and metabolism.

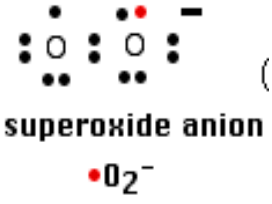
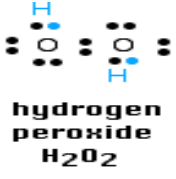
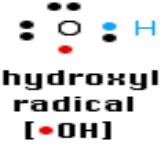
In the mitochondria during oxidative phosphorylation (the process whereby ATP is produced in the mitochondria) the last destination for an electron along the chain is an 0_2 molecule. Under normal condition the O_2 is reduced to produce water (H_2O) but under other conditions, oxygen is partially reduced to form superoxide which is a radical. The production of superoxide in the mitochondria is a continuous process. Like I said earlier normally the 0_2 forms water but 1-2 % of the electrons travelling down the respiratory chain never make it to the end rather they form superoxide. Other endogenous sources include respiratory burst by leucocytes (white blood cells) while attacking microorganisms or other pathogens invading our bodies. It is important to note that most other environmental pollutants to which we are exposed do not contribute significantly to the total load of free radicals and ROS. It may interest you to know that for a person weighing 150lbs the production of superoxide is about 4lbs/yr which is a substantial amount.

The superoxide is converted to other reactive oxygen species. In the presence of Iron or copper, hydroxyl radicals may be formed which are highly reactive and cause severe damage to cells and tissues (Frei, 1994).

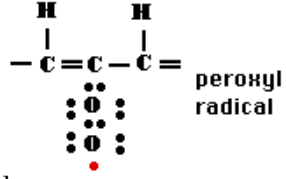
Ladies and gentlemen we are constantly exposed to ROS generated from exogenous and endogenous sources.

ROS also form in plant cells as a consequence of myriad of stimuli ranging from abiotic and biotic stress production of hormonal regulators as well as cell processes such as polar growth and programmed cell death. These ROS are generated at a number of cellular sites including mitochondria, chloroplasts, peroxisomes and at the extracellular side of the plasma membrane. ROS trigger signal transduction events such as nitrogen activated protein kinase cascades eliciting specific cellular responses. The influence of these molecules on cellular processes is mediated by both the perpetuation of the production and the amelioration by scavenging enzymes such as superoxide dismutase (SOD), Ascorbate, peroxidase and catalase.

Table 1: List of ROS

ROS	Description	Electronic spectrum
$^{\bullet}O_2^-$ Superoxide anion	One electron reduction state of O_2, formed in many autooxidation reactions and by the transport chain rather unreactive but can release Fe^{2+} from iron-sulfur proteins and ferritin.Undergoes dismutation to form H_2O_2 spontaneously or by enzymatic catalase and is a precursor for metal catalyzed $^{\bullet}CH$ formation.	
H_2O_2 Hydrogen peroxide	2 electron reduction state, formed by dismutation of $^{\bullet}O_2^-$ or by direct reduction of O_2. It is lipid soluble i.e able to diffuse across membranes.	
$^{\bullet}OH$ Hydroxyl radical	Three-electron reduction state formed by Fenton reaction and decomposition of peroxynitrite. Extremely reactive will attack most cellular components.	

ROOH, Organic	Formed by radical reactions with cellular hydro peroxide components such as lipids and nucleobases.
RO• alkoxy and ROO• peroxy radical	O_2 centered organic radicals. Lipid forms participate in lipid peroxidation reaction. Produced in the presence of O_2 by radical addition to double bonds or hydrogen abstraction.
HOCL hypochlorus acid	Formed for H_2O_2 by myeloperoxide, lipid soluble and highly reactive. Will readily oxidize protein constituents including thiol groups, amino groups and methionine.
ONOO Peroxynitrite	Formed in a rapid reaction between $^{\bullet}O_2^-$ and NO• Lipid soluble and similar in reactivity to hyprochlorous acid. Protonation forms peroxynitrous acid which can undergo hemolytic cleavage to form hyroxy radical and nitrogen dioxide.



Source: Sies, (1985)

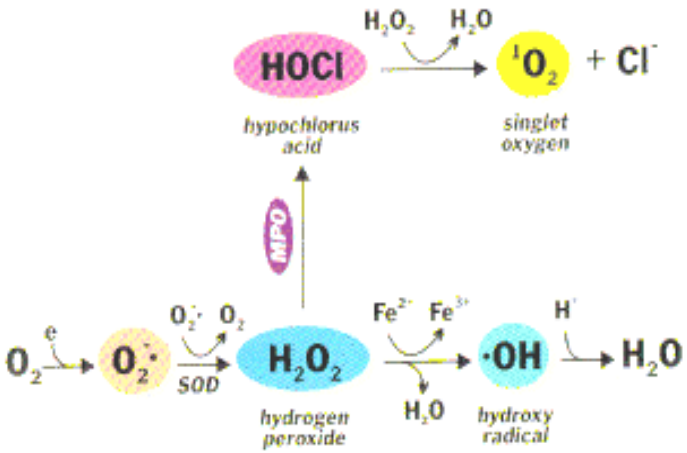


Figure 1: Formation of Reactive Oxygen Species
Source: Moslem, (1994).

Formation of superoxide anion radical leads to a cascade of other ROS. Superoxide dismutates to hydrogen peroxide (H_2O_2) and oxygen. This reaction is spontaneous and fast, but the SOD-catalyzed reaction is four orders of magnitude faster. Clearly, O_2- is more toxic than H_2O_2 and its rapid removal is important. H_2O_2 is reduced by three general mechanisms. 1) It is the substrate for two enzymes, catalase and glutathione (GSH) peroxidase, that catalyze the conversion of H_2O_2 to $H_2O + O_2$; this presumably is a detoxification mechanism. 2) H_2O_2 is converted by myeloperoxidase (MPO) in neutrophils to hypochlorous acid (HOC1). This appears to be a mechanism for a physiological toxic agent, since HOCl is a strong oxidant that acts as a bactericidal agent in phagocytic cells. Reaction of HOCl with H_2O_2 yields singlet oxygen (O_2) and water.

3) H_2O_2 is converted in a spontaneous reaction catalyzed by Fe^{2+} (Fenton reaction) to the highly reactive hydroxyl radical (•OH). The hydroxyl radical reacts instantaneously with any biological molecule (RH) from which it can abstract a hydrogen atom. The resulting free radical (R•) is more stable and hence longer-lived than the hydroxyl radical.

Oxidative Stress: According to Merriam-Webster dictionary, oxidative stress is a physiological stress in the body that is caused by the cumulative damage done by free radicals inadequately neutralized by antioxidants. It can also be said to be an imbalance between the production of free radicals and the ability of the body to counteract or detoxify their harmful effects through neutralization by antioxidants. Antioxidants are molecules present in cells that prevent the above reactions by donating an electron to the free radicals without becoming destabilized themselves.

Disorders Caused by Oxidative Stress

ROS create oxidative stress which results in numerous diseases and disorders. Such as cancer (Sies, 1997), neurodegenerative disease (Wang *et al*, 2006), onset of stroke (Gey *et al* 1993), Parkinson's disease (Bolton *et al* 2000), alcohol induced liver disease (Artel, 2003) and ageing (Frei, 1994).

ROS can cause oxidative damage to various biological molecules; for example, hydroxyl radical can damage cell membranes and lipoproteins (they carry cholesterol and fat in the blood stream) by a process called lipid peroxidation. Lipid peroxidation once started spreads and affects a great number of lipid molecules. This plays an important role in atherosclerosis. Atherosclerosis and

the resulting complications of heart attack, stroke and hypertension make it one of the killer diseases in the world today. ROS may also be implicated in cardiovascular diseases due to its role in inflammatory responses. Proteins may also be damaged by ROS leading to loss of structural changes and loss of enzyme activities (Yoshikawa and Naito, 2002).

ROS related oxidation of DNA occurs at a high rate leading to mutations although there are DNA repair enzymes that can remove DNA lesions produced yet they accumulate with age and eventually may contribute to cancer.

It may be involved in hearing impairment via Cochlear damage induced by elevated sound levels.

Aging: Oxidative damage initiated by reactive oxygen species is a major contributor to the functional decline that is characteristic of aging (Muller *et al,* 2007). Memory capabilities decline with age as evident in human degenerative diseases such as Alzheimer's disease. It is also a contributor to senescence. Complications of oxidative damage may lead to cognitive dysfunction.

Role in Carcinogenesis: ROS at low levels facilitate cancer cell survival time since cell cycle progression driven by growth factors and receptor tyrosine kinases require ROS for activation.

Diabetes: Both types of diabetes display increased levels of reactive oxygen species. The onset of diabetes has been associated with oxidative stress either due to damage of proteins by ROS or the contribution of ROS byproducts to insulin resistance.

Figure 2: Disorders caused by oxidative stress
Source: *www.oxidativestressresource.org*

List of Disorders Caused by Oxidative Stress

Alzheimer's disease
Angina
Anxiety
Arrhythmia
Asthma
Atherosclerosis
Benign Prostatic hyperplasia (BPH)
Carpal Tunnel Syndrome
Bipolar disorder
Cancer
Cardiovascular diseases
Cataracts
Celiacs disease
Childhood neurodevelopmental disorders
Chronic fatigue syndrome
COPD
Congestive heart failure
Crohn's disease
Sleep Apnea
Systemic lupus Erythmetosus (SLE)
Depression
Dermatitis
Diabetes
Erectile dysfunction
Fibromyalgia
GERD
Glaucoma
Hypercholesterolemia
Hypertension
Hyperthyrodism
Influenza
Kidney stones
Hyme disease
Muscular degeneration
Multiple schlerosis
Parkinson's disease
Psoriasis
Rheumatoid Arthritis
Thrombosis
Tinnitus

Advantages of ROS:

It is important to know that not all reactive oxygen species are harmful to the body. Some of them are useful. For example,

(1) **Pathogen response**: When a plant recognizes an attacking pathogen, one of the first induced reaction is to rapidly produce superoxide or hydrogen peroxide to strengthen the cell wall. This prevents the spread of the pathogen to other parts of the plant. In mammals, ROS is also induced as an

antimicrobial defence, this it does by damaging the microbial DNA.

(2) Platelets involved in wound healing or repair and blood homeostasis release ROS to recruit additional platelets to site of injury. They also provide a link to adaptive immune system via the recruitment of leucocytes.

(3) Killing of Cancer Cells: A high level of ROS can suppress tumor growth through the sustained activation of cell cycle inhibitor and induction of cell death. As a matter of fact most chemotherapeutic and radio therapeutic agents kill cancer cells by augmenting ROS stress.

Defense Mechanism against damage caused by ROS:

Mammalian cells possess elaborate defense mechanisms to detoxify radicals. The key metabolic steps are the dismutation of superoxide to hydrogen peroxide by SOD and the conversion of H_2O_2 to $2H_2O$ by glutathione peroxidase or to O_2 and H_2O by catalase. Since the reaction catalyzed by glutathione peroxidase requires GSH as substrate and depends in part on the ratio of GSSG:GSH, the concentrations of these reactants and their ratio, which is a reflection of the redox state of the cell, are important to ROS detoxification. Similarly, redox-active metals, such as iron, catalyze formation of some ROS. This is minimized by keeping the concentrations of these metal ions very low by binding them to storage and transport proteins (*e.g.*, ferritin, transferrin, lactoferrin), thereby minimizing •OH formation. Finally, radical-scavenging antioxidants (*e.g.*, vitamin E) interrupt the chain reactions by capturing the radical; the vitamin E radical is relatively stable, and it can be enzymatically converted back to its non-radical form.

Radical scavengers thus terminate the chain reaction of radical damage (Ahmed *et al*, 1998).

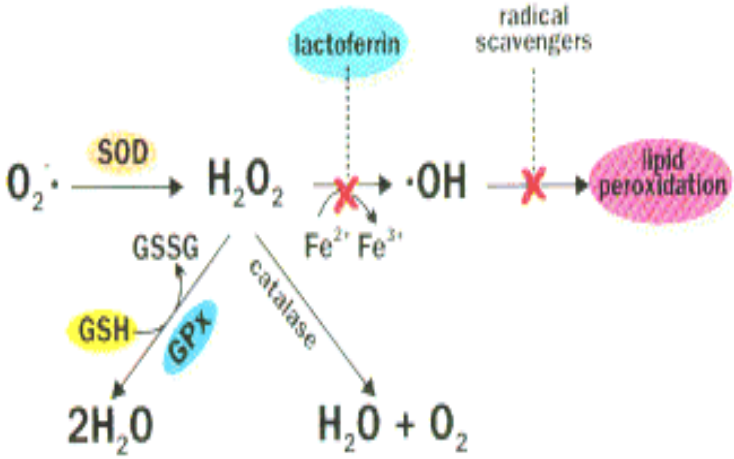


Figure 3: Defense Mechanism against damage by ROS. Source: Moslen,(1994)

Antioxidants: Antioxidants are molecules present in cells. They protect us because they can scavenge ROS before they cause damage to the various biological molecules or prevent oxidative stress from spreading for example by intercepting the radical chain reaction of lipid peroxidation. The antioxidant systems in the human body are extensive and consist of multiple layers which protect at different sites and against different types of ROS. There are enzymic and non-enzymic antioxidants.

Non-enzymic antioxidants: Some molecules playing antioxidant roles are important in blood and the fluids in the extracellular spaces where antioxidant enzymes are abscent or present in small quantities. There are:

(i) lipid soluble antioxidants located in cellular membranes and lipoproteins.

(ii) Water soluble antioxidants in blood and fluids within and around cells ȁ - tocopherol (most active form of vitamin E is the most abundant in man), β-carotene (a vitamin A precursor), carotenoid such as ȁ-carotene, lycopene (the red colour in tomatoes) lutein and zeaxanthine. Carotenoids are weaker antioxidants compared to vitamin E.

(iii) Vitamin C (ascorbic acid) is a water-soluble vitamin and has been shown to be a major antioxidant in human plasma as well as in and across cell membranes (May, 1999). It reduces ȁ-tocopherol as well as peroxides and ROS such as superoxide (Buettner, 1993). The vitamin serves mainly to prevent lipid hydroperoxide formation in plasma lipoproteins, e.g. LDL, by reducing ȁ-tocopherol radicals formed upon reaction with lipid peroxyl radicals (Sies *et al., 1992).* This is in turn an important function in the prevention of atherosclerotic plaque formation (Chopra and Thurnham 1999). Ascorbate also protects lipids in cell membranes by this mechanism. Intracellularly, in the aqueous phase, ascorbate and GSH act in concert to protect the cell from oxidative damage (Meister, 1995).

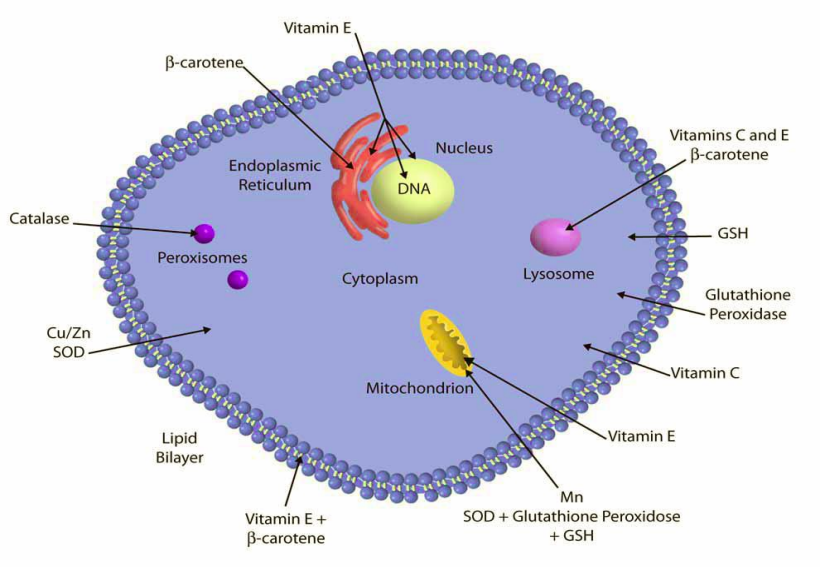


Figure 4: Antioxidant system in cells
Source: Caballero, (2006)

Antioxidant Enzymes: They are part of the antioxidant defence system inside cells e.g. superoxide dismutase (SOD) which scavenges superoxide and convert it to less reactive species. Others are catalase, glutathione peroxidase etc. Their presence show the importance of oxidative damage as a real threat to cellular and organismal survival.

Superoxide dismutase (SOD): Superoxide dismutase (EC 1.15.1.1) belongs to an important enzyme family in living cells for maintaining normal physiological conditions and for coping with stress (Olawale *et al.*, 2008). Superoxide dismutase is a prime antioxidant enzyme found in two forms. One complexed with zinc and copper, is localized

in the cytosol, while the other bound with manganese, is found in the mitochondrial matrix. There is another one that is extracellular which makes use of copper and zinc. These metalloenzymes catalyse the inactivation of destructive reactive oxygen species superoxide anion by converting it to hydrogen peroxide which is then transformed to water and oxygen by the enzyme catalase (Davies *et al*, 1997).

Glutathione peroxidase (GPx): Glutathione peroxidase (EC. 1. 11. 1. 9) is an important part of the antioxidant defense system. They are present in almost every cell of animals, but the tissue distribution of the isoforms show high variation (Miklos *et al.,* 2003). There are at least four different GPx(1 – 4), all of them containing selenocystein (Ursini *et al.,* 1995). GPx1 and GPx4 (or phospholipid hydroperoxide GPx) are both cytosolic enzymes abundant in most tissues. All glutathione peroxidases catalyze the reduction of H_2O_2 using glutathione as substrate. They can also reduce other peroxides (e.g., lipid peroxides in cell membranes) to alcohols (De Haan, 1998, Mates 1999). The catalytic mechanism proposed for reduction of hydroperoxides by GPx involves oxidation of the active site selenolate (Se) to selenenic acid (SeOH). Upon addition of one molecule of GSH, the selenenic acid is transformed to a selenenysulfide adduct with glutathione (Se-SG), which can be regenerated to the active selenolate and glutathione disulfide (GSSG by addition of a second molecule of GSH. Thus, in the reaction, two molecules of GSH are oxidized to GSSG that subsequently can be reduced by Glutathione reductase(GR), the major mammalian GSSG-reducing enzyme (Epp *et al.,* 1983). Some data has indicated that GPx should be of high antioxidant importance under physiological conditions (Jones *et. al.,* 1981). While others

place the enzymes as $2GSH + H_2O_2 \longrightarrow G\text{-}S\text{-}S\text{-}G + 2H_2O$ important only at events of oxidative stress (Kelner and Bagnell, 1990) Cellular GPx is present in all tissues and its activity is influenced by diseases.

Glutathione reductase (GR): Glutathione reductase (EC 1.6.4.2) is a ubiquitous enzyme required for the conversion of oxidized glutathione (GSSG) to reduce glutathione (GSH) concomitantly oxidizing reduced nicotinamide adenine dinucleotide phosphate (NADPH) in a reaction essential for the stability and integrity of red cells (Warsy and El-Hazmy, 1999). It is found in all tissues and works in concert with glutathione peroxidase to recycle glutathione. GR inhibition disturbs cellular prooxidant-antioxidant balance and may contribute to the genesis of many diseases.

Catalase: Catalases (EC 1.11.1.6) are the class of enzymes which catalyze the decomposition of hydrogen peroxide to molecular oxygen and water. Although the predominant subcellular localization in mammalian cells is in peroxisomes, catalase is also found in the blood, bone marrow, mucous membrane, kidney and liver. Catalase also has functions in detoxifying other substrates, e.g., phenols and alcohols, via coupled reduction of hydrogen peroxide. One antioxidative role of catalase is to lower the risk of hydroxyl radical formation from H_2O_2 via the Fenton reaction catalyzed by Cu or Fe ions (Fridovich, 1999, Halliwell, 1999). $H_2O_2 \rightarrow H_2O_2 + O_2$.

In vitro Models for Assessing Antioxidant Activities

1. **Superoxide anion scavenging assay:** O^{2-} is generated as a by-product in aerobic organisms from a number of physiological reactions and redox

reactions in cells. It reacts with hydrogen peroxide to produce hydroxyl radical (OH^-) (Wang et al, 2008).

2. **Hydrogen peroxide scavenging assay:** H_2O_2 is not a free radical but is nonetheless highly important because of its ability to penetrate biological membranes. It plays a radical forming role as an intermediate in the production of more reactive ROS molecules including hypochlorous acid (HOCL) in the formation of $^{\bullet}OH$ via oxidation of transition metals (Jonas and Elias, 2001).
3. **Reducing power assay:** The ability of compounds to reduce ferric ion (Fe^{3+}) is used to determine in vitro antioxidant activity. Reducing power is associated with antioxidant activity. Compounds that possess reducing power are usually electron donors and can reduce the intermedia of lipid peroxidation processes thus acting as primary and secondary antioxidants (Chanda and Dave, 2009).
4. **1,1 diphenyl-2-picryl-hydrazyl or 2,2-diphenyl-1-picryl hydrazyl (DPPH) radical scavenging assay**: is a stable free radical used to assess the radical scavenging activity of antioxidant compounds. It takes part in an electron transfer reaction from an electron donor to DPPH which is both fast and sensitive (Braca *et al*, 2001).

   The in vitro models can be completed with invivo antioxidant assays to monitor antioxidant activities.

Phytochemicals

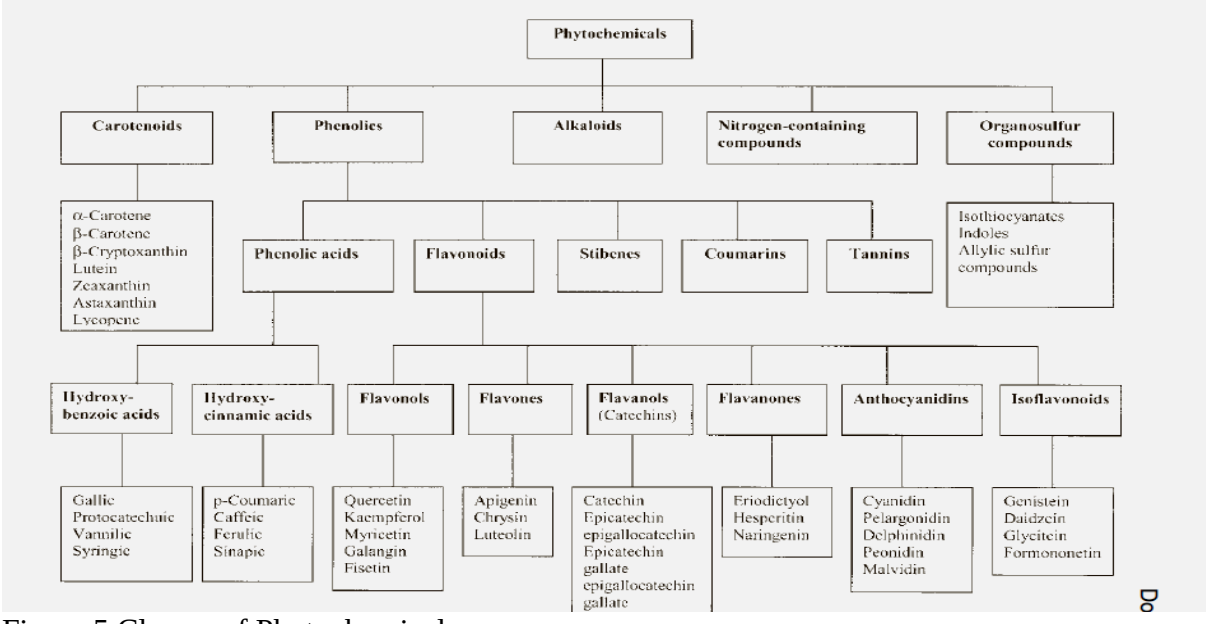


Figure 5 Classes of Phytochemicals
Source: Liu, (2004).

They are non-nutritive plant chemicals. Some possess protective or disease preventive properties while others exhibit toxic effects. Plants produce these chemicals to protect themselves but recent researches demonstrate that they can also protect humans against diseases. There are more than 1000 known phytochemicals. Some of the well-known phytochemicals are lycopene in tomatoes, isoflavones in soy and flavonoids in fruits. Each of them works differently. Probable actions are:

1. Antioxidant activity: Most phytochemicals have antioxidant activity and protect our cells against oxidative damage and reduce the risk of developing certain types of cancer e.g. carotenoids (Carrots, fruits), flavonoids, polyphenols (tea, grape).
2. Hormonal action: Isoflavones found in soy imitate human estrogen and help to reduce menopausal symptoms and osteoporosis.
3. Stimulation of Enzymes: Indoles which are found in cabbages stimulate enzymes that make the estrogen less effective and could reduce the risk of breast cancer.
4. Interference with DNA replication: Saponins interfere with the replication of cell DNA thereby preventing the replication of cancer cells.
5. Antibacterial effect: e.g. Allicin has antibacterial properties.
6. Physical Action: Some phytochemicals bind physically to cell walls thereby preventing the adhesion of pathogens to cell walls.

Common examples are:

Tannins: Tannins are astringent, bitter tasting plant polyphenols that bind and precipitate proteins. They play a role in plant defense by contributing to the toughness of the

plant. Oak bark has traditionally been the primary source of tannery tannin though inorganic tanning agents are also in use today. Tannins may be employed medicinally as antidiarrheal, antitumor and anti-haemorrhoidal compounds (Vatterm *et al*., 2005); they also possess anti-inflammatory and reproductive effects (Souza *et al*., 2006). They have also been reported to have antioxidant, antimalarial and antimicrobial activities (Reddy *et al*., 2007).

Alkaloids: These are naturally occurring amines produced by plants. They are usually derivatives of amino acids and may have a bitter taste. They are formed as secondary metabolites in plants animals and fungi; while many alkaloids are poisonous, neurotoxins, traditional psychedelics and social drugs, some are used medicinally as analgesics, antimalarials (Silva *et al*., 2012), CNS stimulants or even as aphrodisiacs in the treatment of erectile dysfunction (Yakubu, 2006). Structures of some alkaloids are shown in Fig 6.

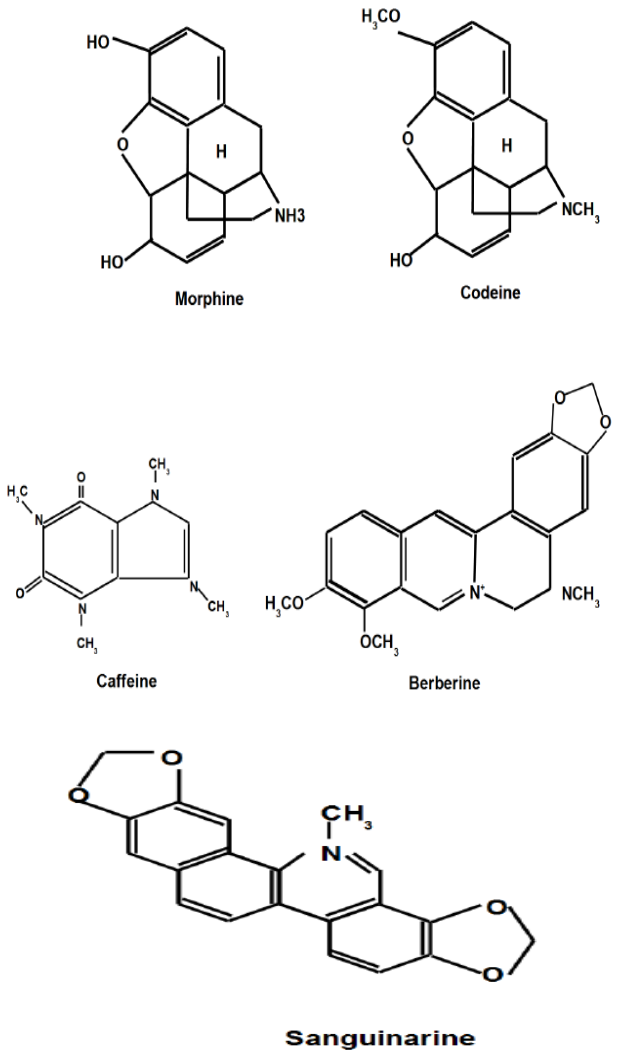
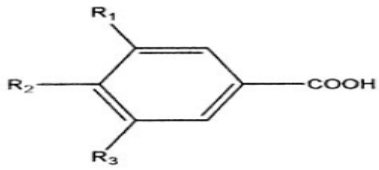


Figure 6: Basic Structures of some pharmacological important alkaloids
Source: Doughari, (2009).

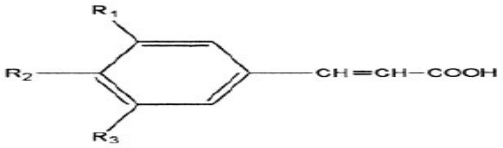
Phenolics: They are a class of chemical compounds consisting of a hydroxyl group (–OH) attached to an aromatic hydrocarbon group. Some phenols are germicidal and are used in formulating disinfectant. Others possess estrogenic or endocrine disrupting activity. They are essential for the growth and reproduction of plant and are produced as a response for defending injured plants against pathogens. They act as buffer against DNA damages. Their importance as antioxidants has reached a new height in recent years even (Aceeti, 2006). Ovenden *et al*. (2011) reported that some phenols possess antimalarial activity.

(a) Benzoic acid



Benzoic acid Derivatives	Substitutions		
	R_1	R_2	R_3
p-Hydroxybenzoic	H	OH	H
Protocatechuic	H	OH	OH
Vannilic	CH_3O	OH	H
Syringic	CH_3O	OH	CH_3O
Gallic	OH	OH	OH

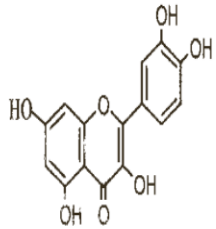
(b) Cinnamic acid



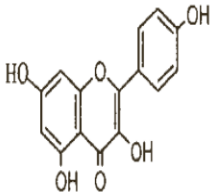
Cinnamic acid Derivatives	Substitutions		
	R_1	R_2	R_3
p-Coumaric	H	OH	H
Caffeic	OH	OH	H
Ferulic	CH_3O	OH	H
Sinapic	CH_3O	OH	CH_3O

Figure 7: Structures of common phenolic acids: (*a*) Benzoic acid and derivatives; (*b*) cinnamic acid and derivatives. Source: Liu, (2004)

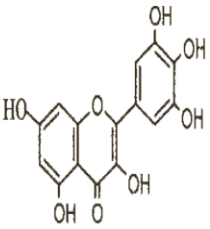
Flavonoids: They are polyphenolic compounds that are ubiquitous in nature. They are widely distributed in plants producing yellow or red/blue pigmentation in flowers to aid pollination and protection from attack by microbes and insects. They are categorized according to chemical structure into flavones,, isoflavones, catechins, anthocyanidins and chalcones. They have been reported to have antiviral, anti-allergic, anti-platelet, anti-inflammatory, anti-tumour and antioxidant activities (Yamamoto and Gaynor, 2006). The capacity of flavonoids to act as antioxidants depends upon their molecular structure. The position of the hydroxyl group and other features in the chemical structure of flavonoids is important for their antioxidant and free radical scavenging activities. Quercetin the most abundant dietary flavonol and is a potent antioxidant because it has all the right structural features for free radical scavenging activity (Stauth, 2007).



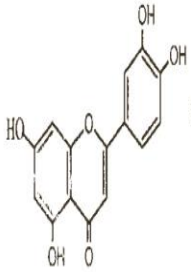
Quercetin



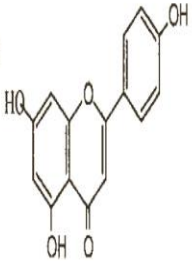
Kaempferol



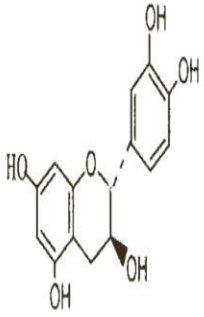
Myricetin



Luteolin



Apigenin



Catechin

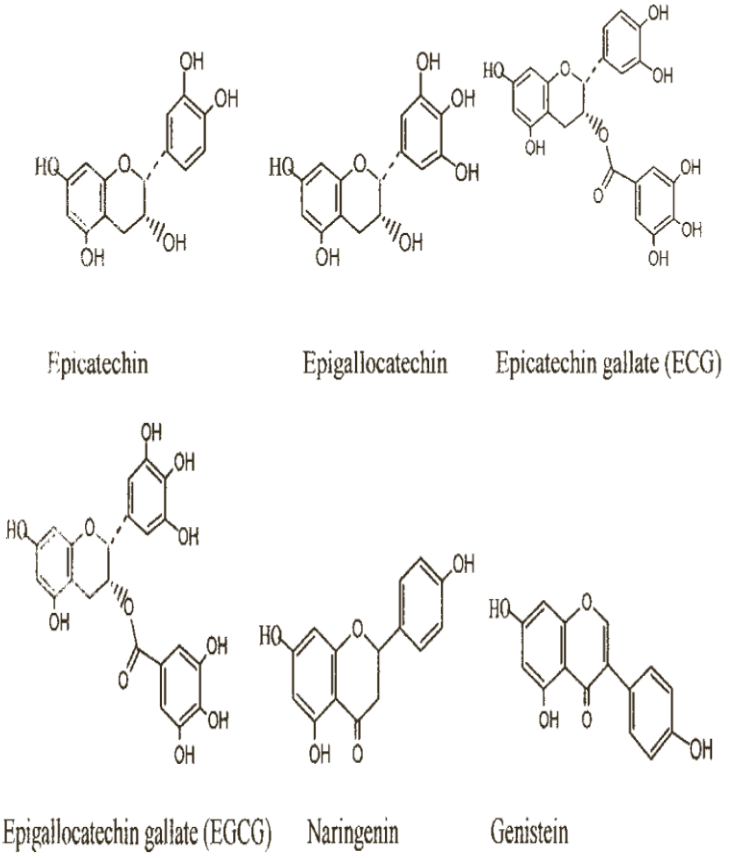


Figure 8: Chemical Structures of Common Dietary Flavonoids
Source: Liu, (2003)

Anthraquinones: These are aromatic organic compounds. They are derivatives of anthracene. They occur naturally in some plants (e.g. aloe, senna) fungi, lichens and insects where they serve as a basic skeleton for their pigments.

They have been shown to have immuno-stimulatory, anti-tumour and aphrodisiac effects. (Chov *et al*., 2012).

Saponins: These are glycosides with a distinctive foaming characteristic. They are used in toothpaste as well as in gurgles, shampoo or as foaming agents in drinks and in fire extinguishers and in photographic emulsions. They also inhibit or kill cancer cells without killing normal cells in the process. Saponins can bind cholesterol and also function as natural antibiotics for plants.

Glycosides: Glycosides are certain molecules in which a carbohydrate residue is bound to some other moieties that are non-carbohydrate residue. Many plant glycosides are used as medications. In animals including humans poisons are often bound to sugar molecules in order to remove them from the body.

Triterpenes: Terpenes are a large and varied class of hydrocarbons produced by a variety of plants, especially conifers. They are the major components of resin and turpentine produced from resin. Many of them possess ideal active ingredients that make them useful as natural agricultural pesticides. It has been reported that they possess anti-allergy, anti-inflammatory, anti-tumour and antimalarial activities (Gherraf *et al*., 2010; Da Silva *et al*., 2013).

Steroids: Phytosterols (plant sterols) are a group of steroid alcohol phytochemicals naturally occurring in plants. They are very important in growth and development, cell division and resistance to damage as a food ingredient or additive phytosterols. They have cholesterol lowering properties (lowering cholesterol absorption in intestines) (Ostlund *et al*., 2003). This may help to control body total cholesterol levels.

Phlobatannins: They are referred to as condensed phlobaphene forming tannins. Condensed tannins from *Lithocarpus glaber* have been reported to have a potent free radical scavenging activity (Zhang and Lin, 2008).

Mr. Vice-Chancellor Sir, the life threatening consequences of the Reactive Oxygen Species (ROS) and the devastating effects of malaria scourge on the productivity and livability of human beings remain evergreen challenges to scientists for affordable solutions. Passion for the redemption from the scourge of the disease and the University's provision of conducive academic environment and encouraging research grant support motivated me to venture into contributing my quota.

Contributions to Knowledge

1. Our recent study had elucidated the antidiabetic and toxicological effects of aqueous extracts of root of *Jatropha curcas* and *Jatropha gossypiifolia* separately and as a mixture on alloxan induced diabetic rats. The results of this work revealed that they both contain flavonoids, tannins, saponins and Phlobatannins (only on *J. curcas*). All the extracts administered (250 and 450 kg b.w.t) reduced significantly blood glucose and increased liver glycogen. It improved body weight gain, hematological indices, reduced total cholesterol, TAG, LDL-cholesterol but increased HDL-cholesterol. Evaluation of the aqueous extract for safety revealed significant ($p< 0.05$) reduction in the serum and tissues of the marker enzymes of the kidney and liver function tests. Histopathology of the organ studied revealed that only 250mg/kg b.w.t

is safe for consumption as higher doses exhibited varying degree of pathological changes showing injury to the tissues studied (Aladodo R.A. Ph.D 2013).

2. We have chronicled the biochemical and histological changes associated with treatment of malaria and diabetics mellitus in mice with methanolic extracts of *Mormodiaca charantia* (Bitter melon). Phytochemicals of the extracts showed the presence of phenolics, steroids, flavonoids, and a trace of alkaloids. There was a decrease in parasiteamia and glucose concentration in mice compared to control when treated separately. The treated group also had lower values of total peroxidative and oxidative stress indices compared to groups treated with both standard drugs. Histological observations showed no visual changes in the pancreas of the co-infected group treated with the plant extract (Balogun *et al,* 2012).
3. In another study on aflatoxin B_1 poisoning and protein energy malnutrition –induced oxidative damage in some rat tissues (Liver, Brain, Kidneys, Lung, heart and Spleen), we have established that the co-existence pathological conditions significantly ($p<0.05$) decreased glutathione, glutathione transferase and superoxide dismutase activities while they significantly increased activities of peroxidases in all the organs. Catalase was increased only in the liver. There was DNA damage in all the organs. The results of this study suggest that subchronic exposure of protein malnourished animals to AFB1 would result in oxidative stress with genomic DNA fragmentation

in the tissues of weanling rats. This result was presented at SOT 2014 (Rotimi *et al*, 2014)

4. Aqueous extract of *Morinda morindoides* leaf, a well known medicinal plant in some African countries, was administered to rats to determine the enzymic and non-enzymic antioxidant status. Results showed that the extract is rich in phenolic and flavonoid compounds, caused reduction in plasma concentration of MDA in a dose-dependent manner, erythrocyte GPX and GSH.RD activities and liver activities of SOD and catalase compared with the controls, which showed its antioxidant properties. It also exhibited scavenging effects against H_2O_2, nitric oxide, ABTS and DPPH radical (Akinloye, D.I, Sunmonu, T.O, Omotainse, S.O and Balogun, E.A 2014).
5. Of interest to orthodox and non-orthodox medicine and pharmacy is our finding that the methanolic extract of *Landophia olvariansis* leaf when compared with chloroquine did not exert detrimental effect on the tissue as compared with chloroquine phosphate. The extract contained polyphenolic compounds and antioxidant constituents which may be flavonoids, the presence of which may be linked with anti-inflammatory and analegesic activities of the extract (Ilesanmi, F.F, Balogun, E.A and Ilesanmi O.S, 2011).
6. Our study on biochemical effects of methanolic extracts of Morinda morindoides and Morinda lucidaidia on lipid profile and some marker enzymes in rats showed they did not cause any tissue damage at the doses utilized.They both contained high content of saponins and

cardenolides. The most widely used saponins are the ginenosides of ginseng which help immune system, enhance survival against stress and prolong human life. The plant extracts also possess *in vitro* and *in vivo* antimalarial activities (Balogun and Akinloye, 2012).

7. The assessment of *Terminalia suparba* (bark, leave and root) based diet to improve the ovulation of Clarias showed high fecundity count in broodstocks treated with the root extract. This was attributed to its high content of phenol, tannins, saponins, flavonoids and saponin which were much more than those of the bark and the leaves, and also its high content of antioxidants. Saponins also have effect on animal reproduction (Ikenweiwe B., Balogun E.A. et al, 2012).
8. We have also been able to show the effects of aqueous extract of *Nauclea latifolia* stem on lipid profile and liver and kidney function indices. The results showed significant increase in LDL – cholesterol and TAG concentrations, and serum concentrations of marker enzymes, indicating hepatoxic and nephrotoxic potentials of the stem at the dosage used. However, it had no effect on lipid peroxidation and contained glycoalkaloids and saponin as major components. (Arise, R.O, Akintola, A.A, Olarinoye, J.B and Balogun, E.A 2012)
9. During malaria, a primary event that occurs is increased production of ROS as part of the host defense by activated macrophages in order to tackle the parasites (Wozencraft *et al*., 1984). Oxidative stress can be caused by the parasite which consumes

most of the host cell hemoglobin and reproduce in the erythrocytes. Also the degradation of hemoglobin leads to the formation of haematin which is a pro-oxidant and catalyses the production of ROS which causes oxidative stress. Becker *et al*. (2004) reported an elaborate defense system by the host immune response against malaria parasite which includes phagocytosis, as well as enzymatic and non enzymatic antioxidants such as catalase CAT, superoxide dismutase SOD, and glutathione peroxidase GPx which counteracts, detoxifies and regulates overall ROS levels resulting from the infection so as to maintain physiological homeostasis.

We have been able to show from our research that;

(i) (Hexane, ethyl acetate and methanolic extract of *Clerodendrum violaceum* leaf contain appreciable quantities of alkaloids, flavonoids and phenolics.

(ii) They exhibited dose-dependent antimalarial activities in both *in vivo* suppressive and curative tests

(iii) The extracts possess some free radical scavenging and metal ion reducing activities, especially the methanolic extract which compared favorably with the reference antioxidant, butylated hydroxyl toluene (BHT). It induced the synthesis of SOD and CAT in the liver and blood of mice which were reduced by infection and reduced the activities of GPx and GR in the liver and blood which were increased by infection towards normal control values. It was therefore concluded that the leaf extract

exerted antioxidant effect against ROS produced *in vivo* during Plasmodium species infection; the antioxidant species present in the extract might have complemented the endogenous antioxidant system.
(Zailani, A.H. 2014).

10. Our further study on the efficacy of herbal products as anti-malarial therapy continually suggests that ethanolic extract of *Clerodendrum v* leaves is of potential antimalaria activity when administered to mice. It also improved heamatological parameters such as higher Hb, PCV, RBC, WBC and platelets counts respectively. The activity might have been due to the presence of alkaloids and phenols which was high in the extract. Toxicological studies showed non toxicity of the extract in the liver and kidney tissues of rats (Balogun, E.A, Adebayo, J.O, Zailani, A.H, Kolawole, O.M and Ademowo, O.G 2009).
11. Mr. Vice-Chancellor Sir, of heart-warming and credit to this University is our collaborative research on Cocos nuciferia as a follow up on work done by Adebayo,J.O. and Kretti, A.U(2012) was carried out in our search for novel antimalarials involved researchers from other departments in the Faculties of Life, Physical Sciences and Basic Medical Sciences, University of Ilorin and supported by a central Based Senate Research Grant of the University of Ilorin. Results of this work, of which I was the Chief Researcher, was presented at the 2012 Nigerian Universities Research Development Fair (NURESDEF), which was held at the University of Technology Minna on 8 – 12

October, 2012 came first in the Individual Award in Life Sciences and Medicine Research Category. The other members of the team are Prof S.O Malamo (Biochemistry), Dr. J.O Adebayo (Biochemistry), Prof A.O Soladoye (Physiology), Dr O.M Kolawole (Microbiology), Dr O.S Oguntoye (Chemistry), Dr O.B Akinola (Anatomy), Dr A.S Babatunde (Hematology) and Dr L.A Olatunji (Physiology). The results of the study suggest that West African tall ethyl acetate fraction (the only active extract fraction) possesses antimalaria activity. The extract contained alkaloids, tannins and flavonoids and was active against *Plasmodium falciparum* W2 strain maintained in continuous culture. It was also active *in vivo* against *Plasmodium berghei* NK65 causing more than 50% reduction in parasitaemia and may not adversely affect normal liver function nor predispose subjects to cardiovascular diseases but may impair normal kidney function at higher doses. Right now we are trying to isolate the active principles as to the real one that is potent against malaria parasite.

Mr. Vice-Chancellor Sir, my research focus now and for almost two decades has been majorly on studying the toxicity of several antimalaria drugs including the very numerous herbs and their phytochemicals features that are now used locally not only for the therapy of malaria, but also for other diseases. This University that is 'Better by far' is now at the verge of gaining world recognition in this field of human endeavour.

12. The continuous spread in the bid to develop novel agents to treat bacterial infections led Obaleye, J.A, Akinremi, C.A, Balogun, E.A and Adebayo, J.O (2007) to synthesize and characterized some ion complexes of Ciprofloxacin a normal antibiotics, it was discovered that the complexes showed comparable antimicrobial activity with the free ligand. Toxicological studies of the complexes in rat showed that they were non toxic.

In another study some metal complexes of norfloxacin and ofloxacin (also antibiotics) were synthesized and characterized. They showed antimicrobial characteristics. Toxicological studies compared favourably with the parent drug. (Obaleye, J.A., Akinremi, C. Balogun, E.A., Adebayo, J.O. and Omotowa, 2009).

13. The application of inorganic chemistry to medicine is a rapidly developing field and novel therapeutic and diagnostic metal complexes are now having an impact on medical practice. Advances in coordination chemistry are crucial for improving the design of compounds.

As part of the team for the step B project awarded to Prof Obaleye in 2007, we were able to synthesize, characterize and analyze the structure of some metal complexes of known antimalarial drugs such as quinine, mefloquine, trimethoprim, dapsone, sulphadizine, and sulphadimedine. Out of the metal complexes, $[(MefH^{+})_2\ (FeSO_4)_2]^2$, [Zn (QUIN) $Cl(SO_4)]^2$, $MefH^{+}\ [CuCl_2]^2 4H_2O$. and Fe(QUIN)Cl $H_2O)SO_4.3H_2O$ exhibited higher antimalarial activities than their ligands when screened against *Plasmodium berghei*. All the complexes were more active against *E.coli*, *S.A Aureues* and *P. phaseolicola* than their ligands (J.A.

Obaleye, M.R. Caura, A.C Tella, E.A. Balogun and O. Awotunde 2007).

14. Another aspect of the work " metal based anti-parasitic drugs synthesis, analysis, and biological potency was presented at the 40th International coordination chemistry conference held at Valencia, Spain in Sept 2012.The entire collaborators are J. Obaleye, A. Tella, E. Balogun, O. Awotunde, J. Adebayo, P. Omojasola, G. Obiyenwa, N. Simon, W. Osunniran, M. Bamigboye and C. Akinremi.
15. Abstract of part of the work has also been accepted to be presented in July 2014 at the 41st congress of ICCC in Singapore. The title is 'Some mixed Antimalarial-antibiotic complexes: preparation spectroscopic investigation and their biological efficacy'
16. CO- supervision in heavy metal toxicology

- In a bid to study the association between inorganic arsenic exposure and cardiovascular diseases, rats were exposed to sodium arsenite and sodium arsenate in their drinking water. Paraoxoanase activity towards paroxon and phenylacetate in plasma lipoproteins, liver and brain microsomal fractions showed decreased PON activity which may be an incipient biochemical event in the cardiovascular event of arsenic. Modulation of PON activity may be mediated through change in membrane fluidity brought about by changes in the concentration of cholesterol in the microsomes. PON inhibits the accumulation of lipid peroxides in LDL but protects HDL from oxidation and preserves its integrity (Oda *et al.*, 2002). Arsenite

induced a dose dependent inhibition of paraoxonase while arsenate induced a dose dependent inhibition of ARtase (arylesterase) Ademuyiwa, Afolabi *et al*, 2013.

- Hypocholesterolemia characterized the effect of arsenite at all doses but arsenate- induced hypercholesterolemia at the higher doses. FFA was increased by both Arsenate and caused hypertryglyceridemia. The two forms of inorganic arsenic up or down regulate different pathway in the lipid metabolism at low or high doses. . The high burdens of CVD in developing countries are attributable to the increasing incidence of atherosclerotic diseases perhaps due to urbanization and higher risk factor levels such as obesity, diabetes, dyslipidemia and hypertension. The burdens afflict both men and women causing stroke and heart attack.

17. Effect of cadmium on lipid metabolism: It up or down regulated different pathways at low or high doses. e.g. it inhibited both hepatic and brain HMG CoA reductase by 49% and 61% respectively, exhibited hypocholesterolemia and hypotriglyceridemia but plasma free fatty acid was increased, renal and brain cholesterol and TAG were also decreased(. A.D Wusu, O. Ademuyiwa, *et al*., 2013).

In order to explain the mechanism underlying the increased risk of cardiovascular diseases as a result of inorganic mercury exposure, Paraoxonase, an enzyme located in the HDL and known to protect CAD was investigated in male and female rats

exposed to mercury (0.5, 1.0 and 1.5mg/kg for 12 weeks. Also, Arylesterase in plasma, lipoprotein and brain microsomal fraction were determined. For the hepatic microsomal fraction, PONase enzyme was inhibited in males, but only at the highest dosage in females. Brain microsomal cholesterol was increased in males but decreased in females. It also activated AREase.

Recommendations

Antioxidants based drugs/ formulations for the prevention and treatment of complex diseases like atherosclerosis, stroke, diabetes, Alzheimers disease and cancer have appeared during the last 3 decades. This has attracted a great deal of research interest in natural antioxidants. Subsequently, a worldwide trend towards the use of natural phytochemicals present in berry crops, tea, herbs, oilseeds, beans, fruits and vegetables has increased.
The majority of the active antioxidant compounds are flavonoids, isoflavones, flavones, anthocyanins, coumarins, lignans, catechins and isocatechins apart from the vitamins C, E, β carotene and α- tocopherols which are also found in plant products.

1. In the course of my research on sourcing for antimalarials from plant extracts, I discovered that some of these phytochemicals that are responsible for the activities against malaria parasites are also responsible for their antioxidant activities. I believe that more efforts should be diverted to these areas of research.
2. While the University of Ilorin's passionate commitment to 'raising the bar' of excellence in scholarship and community service; being 'better by

far' in the indices for reputability; and striving to encourage qualitative research by making the 'scratching – of – the surface' research a past issue, I wish to humbly recommend for POSITIVE CONSIDERATION the release of special Research Intervention Fund for the production, quality control, patenting and marketing of natural/herbal anti-malarial drugs from the avalanche of research outputs by the multi-displinary team involved in the exercise in the University. One billion naira (N1bn) will suffice as take-off intervention fund in this regard.

3. The Medical Research Council of Nigeria should emulate the Agricultural Research Council of Nigeria to institute a well-funded competitive research grants for basic and applied researches into alternative/ unorthodox anti-malarial medication.
4. The establishment of Herbal Research Centre for the development of anti-malarial drugs in this University to consolidate its lead in solving these anti-human endeavours will be a step in the right and productive direction.
5. Outcome of the University's endeavour in solving the socio-economic problems of this country should be part of the GNS curriculum with emphasis on its contributions through research to HIV, malaria, anti-social behaviours and tendencies.
6. With high sense of responsibility, responsiveness, commitment, benefit of hind-sight and assurance of my total dedication to this University even after my retirement, I wish to heartily advise the need for synergy between the College of Health Sciences and the Department of Biochemistry, Faculty of Life

Sciences in such a way that adjunct professors/lectuerers are employed for the former from the latter and are accorded encouraging privileges and remunerations.

Mr. Vice-Chancellor Sir, permit me to limit my recommendations to 6 with each recommendation representing a decade of my sojourn on this ephemeral life.

Acknowledgements

Glory, honour and adoration to the almighty God and to my Lord and Saviour Jesus Christ, who redeemed me and the Holy Spirit, the power of God at work in my life for making today a reality in my life. I am grateful for taking me to the pinnacle of my career.

I appreciate all of you for honouring me today but I wish to mention some people for the roles they played in my career and life.

My late parents, late Pa Dcn. O Abiola and late Mummy Victoria O. Abiola for their efforts in raising me up. They encouraged me to go into academics being teachers themselves. My Uncle Capt. L.B Adedeji, and Prof and Mrs. Olusola Ojeniyi my cousin for being sources of encouragement to me in my career. I am so grateful to you all.

My coming into this University and being employed as an assistant lecturer in the department of Physiology and Biochemistry in the year 1980 was a special privilege given me by Prof. Emeritus Adeoye Adeniyi, who was the first Nigerian Dean of the then Faculty of Health Sciences at a time when he was trying to consolidate the Faculty. Sir, I am extremely grateful for this opportunity.

My supervisors for my Ph.D, Prof. Musbau Akanji, Prof (Mrs) S.O Malomo and Prof A. Odutuga (rtd). They taught me how to conduct research in Biochemistry. Words are inadequate to express my gratitude for the training you gave me and for impacting such knowledge into my life.

I am grateful to Prof. J.A Obaleye of Chemistry Department Unilorin who introduced me into inorganic and coordination chemistry and for co-opting me into his research team in the search for antimalarial drugs.

Prof. O. Ademuyiwa of the department of Biochemistry, Federal University of Agriculture Abeokuta for introducing me into the mechanics of heavy metal toxicology and for allowing me to co-supervise 3 Ph.D students in the same area. I am very grateful.

I thank God for the friends God have used to encourage me in the past 34 years of my stay at Unilorin. Prof and Dr. Mrs. Adeyemi Idowu you have been wonderful, Prof and Prof (Mrs) S.O. Olorundare, Prof and Prof. (Mrs) A.Malomo, Prof and Mrs L. Ayorinde, Prof and Mrs C.O Bewaji, Prof and Mrs G.M Babatunde, Prof and Mrs A.O Soladoye, Dr, O. Ajolore, Dr and Mrs. E. Okanla, Dr and Dr (Mrs) Adebayo, Engr and Prof. (Mrs.) Tunji Ijaiya, Mrs Bamisaye, Dr and Dr (Mrs) Lasode. May the almighty God reward you abundantly.

My academic colleagues especially those from the department of Biochemistry of this University, namely Prof and Mrs O.B Oloyede, Prof T. Oladiji, my amiable HOD, Dr M.T Yakubu, Dr and Mrs. R.O. Arise, Dr F. Sulaiyman, Dr M. Salawu, Dr M. Nafiu, Dr A.Igunnu, A. Quadri, Mrs. Muritala and Mrs. Oyegoke by extension Prof A. Adesokan and Prof T. Sumonu, Mr Adunbarin and other technical staff and the secretarial staff of the department. Thank you for giving me a conducive environment to work

in. I would like to acknowledge the staff of the department of Physiology, Faculty of Basic Medical Sciences Unilorin, Dr V. Owoyele, Dr Olayaki, Dr L. Olatunji and others for their supportive role while we were together as Department of Physiology and Biochemistry for 26 years, and also I will like to appreciate all the staff of the Department of Anatomy including Prof S.B. Agaja. I am also grateful to the staff of the Department of Biochemistry Federal University of Agriculture, Abeokuta, especially the academic staff: Prof. O. Ademuyiwa, Dr and Mrs.O. Akinloye, Dr (Mrs.) R. Ugbaja, Mrs. O. Dosunmu, Mr. B. Okunkwo, S. Babayemi and Mrs. E. Adeyi. Department of Animal Production Unilorin by family right from Prof O. Atteh, the Dean of Agriculture, Prof A Adeloye, HOD Prof. M. Belewu, , Dr S. Bolu, Dr A. Toye and everybody. The Dean and all our friends in the Faculty of Agriculture, I thank you all.

My past and present Ph.D students especially Dr (Mrs.) R Aladodo, H. Zailani, I. Akamo and O. Rotimi and my numerous Master degree students, I thank you all for allowing me to train you and inculcate the habit of being diligent in your work.

To my in- laws especially Dr Mrs.S. Alade, Prof and Mrs.I. Abimbola, Mr and Mrs. D. Fasuyi and others. I thank you.

Prof S. Oba Abdulraheem cannot be forgotten by my family. During his tenure as the Vice Chancellor of this University I became a Professor of Biochemistry and at the same time my husband became the Deputy Vice Chancellor of this great Institution, we are grateful Sir.

I wish to especially thank Prof. I. Oloyede, the immediate past V.C of our University and our dear former Registrar Mrs O.O Oyeyemi for granting me leave of

absence to enable me stay with my husband at FUNAAB when he was there as the Vice Chancellor, may the almighty God reward your family richly.

All my Pastors I thank you for your prayers and encouragements. May God's blessings and his mighty hand rest upon your families in Jesus name.

I cannot but remember late Madam Tinu Falode for the prayers she sowed into my life. Thank you ma. Her daughter is a Professor in this University. I thank her too.

I like to appreciate the special roles and support the following people have also contributed to my family; Prof Tunde Ajayi, Prof & Dr (Mrs.) K. Bamgbose, Architect & Mrs. Baiyewu, Prof & Dr (Mrs.) O.B. Kehinde, Mr & Mrs. L. Somoye, Mrs. M. Popoola, Prof & Dr (Mrs) Adewumi, Prof & Dr (Mrs.) Oluwalana, Dr F. Olubiyo, Mr & Mrs. Salaam, Engr & Engr (Mrs.)O. Banjo, Mr & Mrs. D. Ayodele, Mr O. Oloruntoba, Mr & Mrs. M. Ilesanmi, Prof (Mrs.) D. Eruvebetine, Prof T. Arowolo, Chief & Mrs. L. Osayemi, Prof & Mrs. B. Balogun, Prof & Mrs. B. Daramola, Prof & Mrs.D. Fasakin, Mr &Mrs.A. Agbaoye, Mr & Mrs.F. Imoisile, Alhaji Maxwell Ayinla,Prof. K.Okonofia Prof & Dr (Mrs.) Aletor, and Mr & Mrs. Bankole. May the Almighty God reward you greatly.

I thank Mr Tubi, I and Mrs. Adebayo, A.V. for the secretarial assistance rendered in preparing this lecture.

My wonderful children, I thank you for making parenting easy for me, for making life worth living and for being sources of joy to me. May you continue to excel in life.

Prof Oluwafemi Olaiya Balogun, my darling husband, thank you so much for your love and for teaching me how to pay attention to details in everything I do. I will forever cherish your teaching me how to be accountable.

You have been my backbone and my support in my academic career. I pray for more of God's blessings upon your life.

To God be the glory great things he has done.

I thank you all for giving me your attention.

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