INAUGURAL LECTURE SERIES 18

LADOKE AKINTOLA
UNIVERSITY OF TECHNOLOGY
OGBOMOSO, NIGERIA

MEDICAL BIOCHEMISTRY:

The Bed Rock and Molecular Basis of Medicine

PROF. AYOADE ABDULFATAI ADESOKAN

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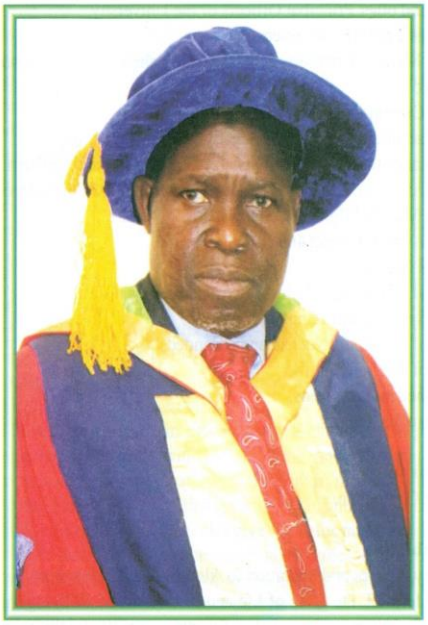

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Your Royal Highnesses,
Members of Academic, Administrative and Technical staff,
My Lords Spiritual and Temporal,
Members of my family, Nuclear and Extended,
Members of the Lions family,
Distinguished invited guests,
Gentlemen of the Press,
Friends,
Great Ladokites,
Ladies and Gentlemen.

1.0 Preamble

I give glory, praises and adoration to Almighty Allah, the most Beneficent, the most Merciful, the giver of life and the creator of all living things, the Fountain of wisdom and knowledge, for sparing my life till this moment and enabling me to deliver the 18th Inaugural Lecture of Ladoke Akintola University of Technology, Ogbomoso. This is the First Inaugural lecture from the Department of Biochemistry, the second from the Faculty of Basic Medical Sciences and the third from the College of Health Sciences of this University.

Today, I feel highly honoured and privileged to be allowed to deliver the 18th Inaugural Lecture of Ladoke Akintola University of Technology, titled **"Medical Biochemistry, the Bedrock and Molecular Basis of Medicine."**

2.0 Introduction

Medical Biochemistry precisely relates biochemical events at the cellular level to physiological processes in the mammalian tissues, as well as abnormal biochemical processes in human disease. Information from biochemical investigations of prokaryotes and eukaryotes as it relates to causation of human diseases are not left out either.

The history of biochemistry (Ton van Helvoort, 2000) can be said to have started with the ancient Greeks, who were interested in the composition and processes of life, although biochemistry as a specific scientific discipline has its beginning around the early 19th Century, precisely in 1833, when Anselme Payen (Hunter,2002), discovered the first enzyme, diastase, now called amylase. Justus von Liebig in 1842 termed the new discipline Animal Chemistry or Organic Chemistry in its applications to physiology and pathology. In 1877, however, Felix Hoppe-Seyler used the term ('Biochemie' in German) in the forward to the 1st issue of Physiological Chemistry. The actual coinage "Biochemistry" was credited to the German Chemist Carl Neuberg in 1903(Singh *et al*., 2004).

The subject of study in biochemistry is the chemical processes in living organisms that deals with the structures and functions of cellular components such as proteins, carbohydrates, lipids, nucleic acids and other biomolecules, their metabolic pathways and flow of chemical energy through metabolism; how biological molecules give rise to the processes that occur in living cells; it also focuses on the biochemical processes involved in the control of information flow through biochemical signaling, and how they relate to the functioning of the whole organism.

The field of molecular biochemistry started with the discovery of DNA structure by Watson and Crick in 1953, but became revolutionized with the introduction of Polymerase Chain Reaction (PCR), creating waves from every field of medicine. This has helped to establish better therapy for various diseases through introduction of gene therapy (Singh *et al*., 2004).

The Science of Biochemistry has enjoyed development so much so that today, there are various distinct areas that have been established (Akanji, 2002). Some of these distinct areas are Medical (Clinical) Biochemistry and Biochemical Toxicology.

2.1 Medical Biochemistry as a Career

Mr. Vice Chancellor sir, distinguished ladies and gentlemen, my foray into the field of Medical Biochemistry dated back to my pre-clinical years at the College of Medicine, University of Lagos, precisely in 1976, when I came out with distinction in Medical Biochemistry at the First Professional MBBS examination. The University offered Scholarship to those who had distinction in Medical biochemistry, provided they agree to spend one extra year to complete

B.Sc degree in Biochemistry and thereafter continue with the MBBS program. I was in a dilemma, whether to accept or reject the offer. It was my senior brother, a retired Permanent Secretary in Oyo State, Chief Olaniyi Adesokan, who offered me a wise counsel that I should accept the offer. I still hesitated, telling him that my classmates would graduate as doctors before me, but he insisted, then I had no choice than to accept the offer. I finished the B.Sc degree in 1977 and came out with **First Class** honours, under the supervision of Prof. A. Aboderin, who remain my mentor and role model in Biochemistry. I was immediately employed as Part-Time Lecturer by the College of Medicine, in the Department of Biochemistry from 1977 to 1981, when I completed the Internship. Thereafter, the College wanted to retain me but the NYSC authority refused, and that aborted my plan to commence M.Sc degree in Biochemistry.

After the completion of NYSC in 1982, I was offered employment as a Senior House Officer by the University of Ilorin Teaching Hospital for residency program in Internal Medicine, with the aim of becoming a Metabolic Physician. That was not to be, as I was among the officers of the Nigerian Medical Association (NMA) and Association of Resident Doctors (ARD), who were dismissed during the doctors' crises of 1985. I was appointed as Associate Lecturer in the Department of Physiology and Biochemistry, from 1983-1985, where I joined Mrs. E.A Balogun, now Prof. Mrs E. A. Balogun and Mr. Pade James.

It was in 1999 when I was seeking admission for my son to read medicine that I went to the Faculty of Medicine, University of Ilorin where I met Prof. Matthew Akinyemi Araoye, the Dean of the Faculty then, who ordered me to write an application for the position of Lecturer II in Medical Biochemistry, which he pursued till I was offered a Temporary employment as Lecturer II in the Department of Physiology and Biochemistry in September, 2000. I wasted no time and quickly enrolled for M.Sc in 2001 and completed in 2003, enrolled for Ph.D program in 2004 which I completed in 2007, under the supervision of Prof. Musbau Adewumi Akanji, former Vice Chancellor, Al-Hikmah University, Ilorin, and Federal University of Technology, Minna, to whom I am eternally grateful.

3.0 Medical Biochemistry in health and disease

Medical Biochemistry is a discipline that gives a firm grounding in modern biochemistry, with particular reference to the ways in which it relates to medicine and health issues, and explains biochemical mechanisms in human diseases. It has long been recognized that manifestation of disease conditions is virtually preceded by changes/derangement of one or more biochemical processes in the tissue or even cells.

Human metabolism is a key component of the basic science knowledge that underlies the practice of medicine and allied health professions. It is

fundamental to understanding how the body adapts to physiologic stress, how defects in metabolism result in disease, and why data from the clinical chemistry laboratory are useful to diagnose disease and monitor efficacy of treatment.

Over more than three decades that I have been teaching medical biochemistry to medical students, I have found students increasingly overwhelmed with details that tend to obscure rather than elucidate principles of human metabolism. So what I have tried to do is provide students of medicine and other health professions with simple and concise resource that will help them understand and appreciate the functions, constituent reactions and regulatory aspects of the core pathways that constitute human metabolism; and which are responsible for maintaining homeostasis and well being in humans. I tried to accomplish this by emphasizing function, regulation and disease processes, while minimizing discussion of reaction mechanisms and details of enzyme structure.

Intermediary metabolism is the name given to the sequence of biochemical reactions that degrade, synthesize, or interconvert small molecules inside living cells. Knowledge of the core metabolic pathways and their interrelations is critical to understanding both normal function and the metabolic basis of most human diseases. Furthermore, knowledge of key biochemical reactions of core metabolic pathways in humans is essential for understanding of the molecular basis of drug action, drug interactions, and many genetic diseases that are caused by the absence or deficiency of the activity of a particular protein or enzyme. Normal biochemical processes are the basis for remaining healthy.

This is what informed the definition of "Health" as adopted by the World Health Organization as "A state of complete physical, mental and social well-being and not merely the absence of disease and infirmity". This definition of 1948 has been modified in 2016 in the proposed health and health-related Sustainable Development Goals (SDGs) by 2030 Agenda with emphasis on SDG 3: Ensure healthy lives and promote well-being for all at all ages (WHO, 2016). From a strictly biochemical view point, health may be considered as a situation in which all of the many thousands of intra- and extracellular reactions that occur in the body are proceeding at rates commensurate with the organism's maximum survival in the physiologic state.

The two major concerns of physicians are the understanding and maintenance of health and the understanding and effective treatment of diseases. Medical biochemistry impacts enormously on both of these fundamental concerns of medicine. In fact, the interrelationship of biochemistry and medicine is a wide two-way street. Biochemical studies have illuminated many aspects of health and disease, conversely, the study of health and disease has opened up new areas of biochemistry. Some examples of this two-way street are illustrated in figure 1.

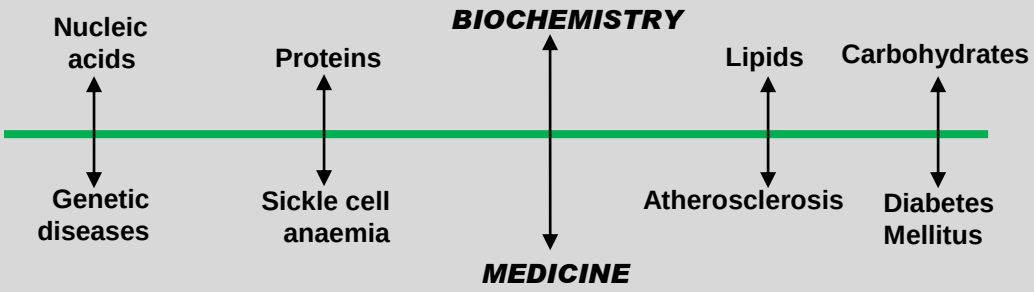

Figure 1, **(Source: Devlin, 2010)**.Examples of the two-way street connecting biochemistry and medicine. Knowledge of the biochemical molecules shown in the top part of the diagram has clarified our understanding of the diseases shown on the bottom half-and conversely, analyses of the diseases shown below have cast light on many areas of biochemistry. Note that sickle cell anemia is a genetic disease and that both atherosclerosis and diabetes mellitus have genetic components.

For instance, knowledge of protein structure and function is necessary to elucidate the single biochemical difference between normal haemoglobin and sickle cell haemoglobin. On the other hand, analysis of the sickle cell haemoglobin has contributed significantly to our understanding of the structure and function of haemoglobin and other proteins. For example, replacement of glutamic acid in position 6 of the beta chain would result in alteration of the normal haemoglobin by sickled haemoglobin, as shown in figure 2.

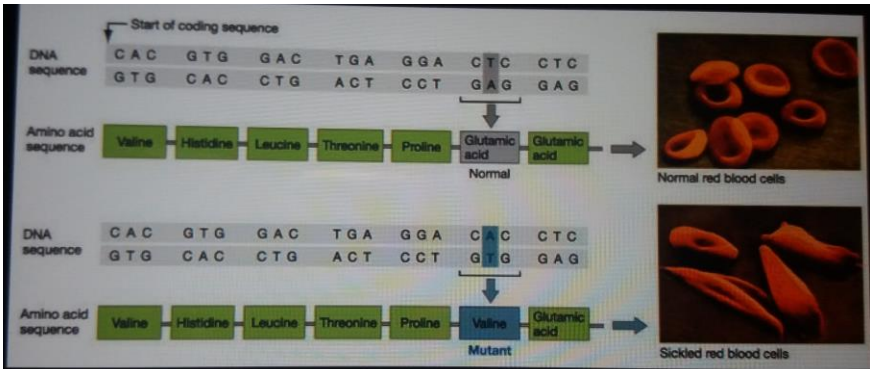

Fig.2: Normal and abnormal haemoglobin with normal and sickled Red Blood Cells.
Source: www.google.co.uk/search?q=sickle cell

Figure 2 above shows normal beta chain and normal red blood cells in the upper segment, while the lower segment shows mutation of the gene of the beta chain, changing amino acid, glutamic acid to valine with corresponding sickling of the red blood cells.

The resulting sickled cells now manifests as sickle cell disease (SCD) in homozygous children who inherited the sickle cell gene from both parents. This picture is clearly shown in figure 3:

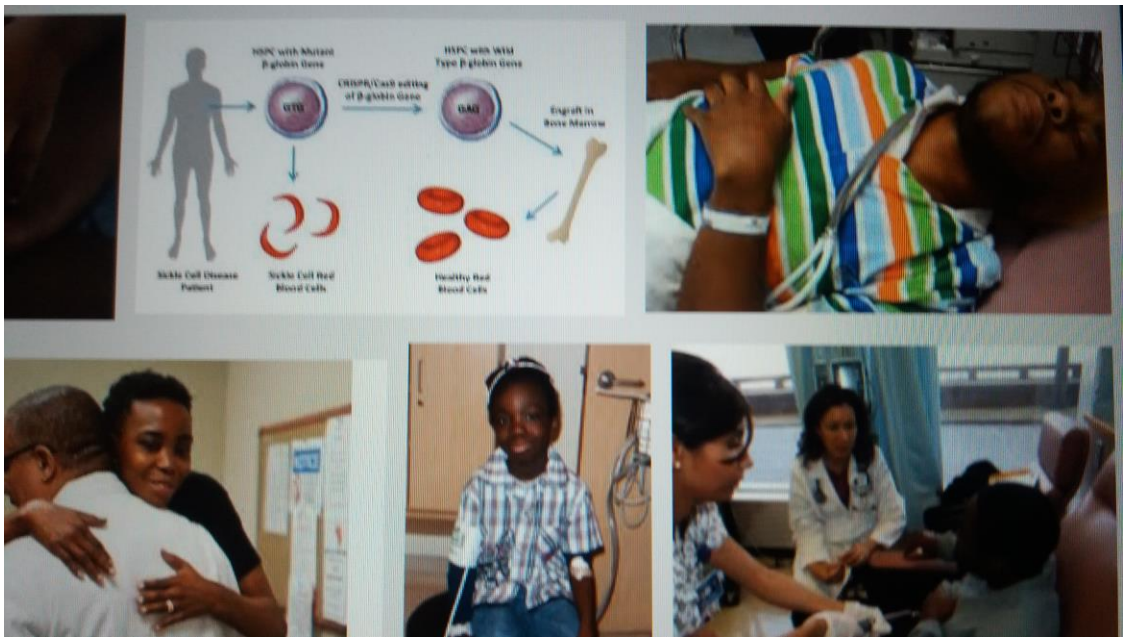

Fig. 3: Manifestation of sickle cell disease in patients afflicted.
Source: www.google.co.uk/search?q=sickle cell +disease+patient

Figure 3 shows normal and sickled red blood cells and the afflicted patients and their parents.

Another example is the pioneering work of Archibald Garrod (1908), a Physician in England in the early 20th Century, who studied patients with a number of relatively rare disorders (Alkaptonuria, Cystinuria and Pentosuria) and Albinism. He established that these conditions were genetically determined and designated them as inborn errors of metabolism. His insight provided a major foundation for the development of the field of human biochemical genetics. For example, albinism, or 'afin'as the name given to it in Yoruba language, arises from the deficiency of an enzyme called **tyrosinase**, in the pathway of melanin synthesis, the pigment that darkens our skin, is shown in figure 4:

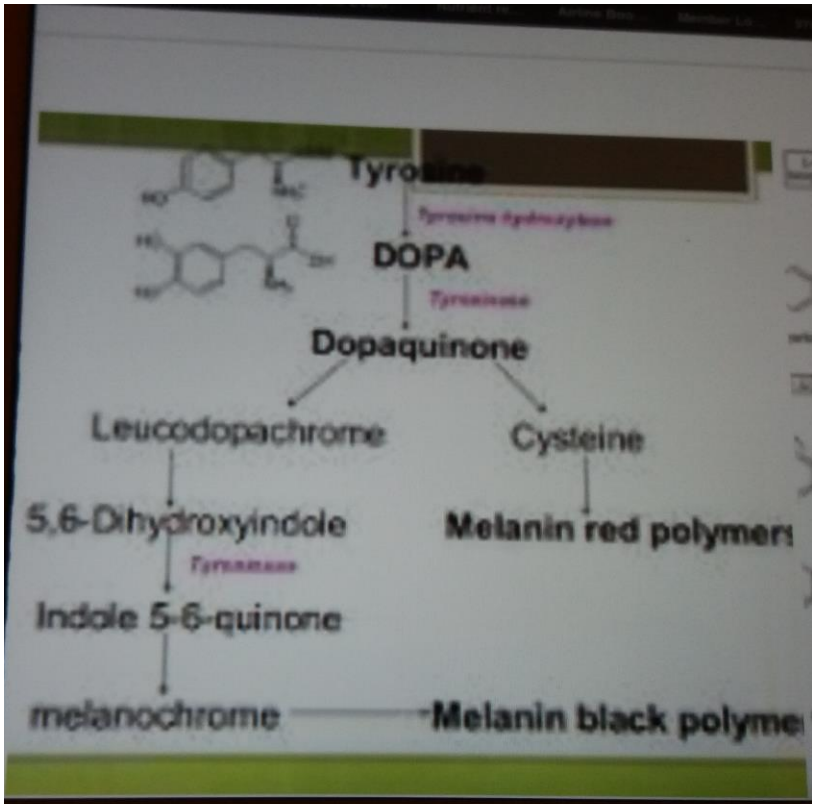

Fig. 4: Melanin synthetic pathways showing site of enzyme *tyrosinase* deficiency
Source: www.google.co.uk/search?q=melamin+synthesis

The result of the enzyme tyrosinase deficiency gives rise to a variety of oculocutaneous albinos with varying effects on impaired vision, depigmentation of the skin and hair, as shown in figure 5:

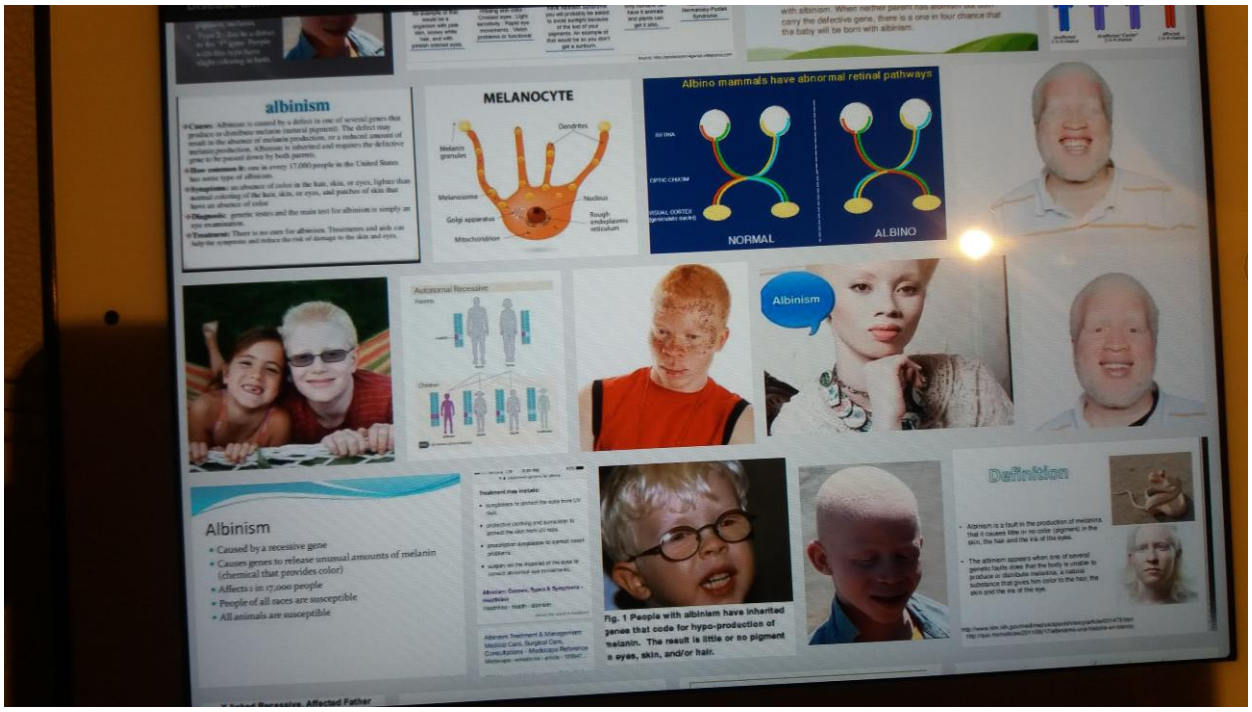

Fig. 5: Shows manifestations of varying degrees of oculocutaneous albinos
Source: www.google.co.uk/search?q= albinism

Figure 5 shows how autosomal recessive gene of albino is manifested in homozygous children who inherited from heterozygous parents and manifest various degrees of oculocutaneous albinism. From the picture albinos affect all races.

Mr. Vice Chancellor sir, Biochemical Research has impacted on Nutrition and Preventive Medicine. One major prerequisite for the maintenance of health is optimal dietary intake of a number of nutrients; the chief of which are vitamins, certain amino acids and some fatty acids (termed essential), various minerals and water. Much of the subject matter of both biochemistry and nutrition is concerned with the study of these chemicals termed nutrients, showing close relationship between the two sciences. These nutrients must also be taken in appropriate proportions, as excess may be associated with health problems. This is why, Prof. M.A. Akanji in his Inaugural Lecture in 2002 titled it "Eat and die by Little," however, we need the nutrients to stay healthy, so another Professor of Biochemistry, Prof. H.O.B Oloyede titled his own in 2005 "For the love of Nutrients," both of them from the University of Ilorin.

More emphasis is now being laid on Preventive Medicine, which is a systematic attempt to maintain health and forestall disease. Most and perhaps, all diseases have biochemical bases, as most, if not all diseases are manifestations of abnormalities of molecules, chemical reactions or biochemical processes.

4.0 Balanced diet as a panacea to healthy living

Mr. Vice Chancellor sir, distinguished ladies and gentlemen, we need varieties of food in correct proportions if we must remain in good health. A healthy diet is one that helps to maintain or improve overall health, provides the body with essential nutrition: adequate essential amino acids and fatty acids, vitamins and minerals that is termed Reference Nutrient Intakes (RNIs), is an estimate of the amount that should meet the needs of most people; while adequate calories is termed Estimated Adequate Requirement (EAR). Apart from breast milk as a food for babies, no single food contains all the essential nutrients the body needs to stay healthy. For this reason, our diets should contain a variety of different foods, to help us get the wide range of nutrients that our body needs. The British Nutrition Foundation (BNF) recommends a balanced diet as shown in figure 6 below:

Fig. 6: Varieties of foods in a balanced diet
Source: *BNF*, (2016).

The BNF Eat well guide include 8 groups of food items: Fruits and vegetables; potatoes, bread, rice and other carbohydrates; beans, fish, eggs, meat and other proteins; foods and drinks high in fat, salt and sugars; dairy and alternatives; oils and spreads such as butter, margarine and jam, etc (BNF, 2016).

How much food does one need to have a healthy diet? A healthy diet should provide us with the right amount of energy (calories) from foods and drinks to maintain energy balance. Consuming more calories than we need over a period of time will cause weight gain or obesity, if the Body Mass Index (BMI) is greater than 25. Normal range of BMI is 20 – 25, beyond 25 is overweight, while beyond 27.8 in males and 27.3 in females is obesity (Geissler *et al*,. 2014). BMI = weight in Kg/Height^2 (in m^2). Energy requirement at rest (when not sleeping) is called Basal Metabolic Rate (BMR).

Obesity causes glucose intolerance, insulin resistance, hypertension and dyslipidaemia. If intake is, however less than expenditure, there is weight loss, wasting or marasmus develops and kwashiorkor, if there is protein calorie malnutrition. Women need about 2,000 calories/day and men 2,500 calories/day. The extra calories we do not need is stored as fat. This will lead to a chain of diseases such as diabetes mellitus, atherosclerosis, hypertension and other cardiovascular diseases. It is pertinent to mention here that **cholesterol** is finally officially removed from Naughty List of *nutrient of concern* by the US government, as scientists have established that our body requires 950 mg of cholesterol per day and only 15% of it is derived from the diet as opposed to the previous belief that our body requires 300 mg of cholesterol per day (FDA, 2015).

4.1 Homeostasis in cellular metabolism

Homeostasis refers to an organism's tendency or drive to maintain the normalcy of its internal environment, including maintaining the concentration of nutrients and metabolites within relatively strict limits. A good example is glucose homeostasis. In the face of widely varying physiological conditions, such as fasting or exercise, both of which tend to lower the blood glucose or following the consumption of carbohydrate diet that raises the blood glucose concentration, the human body activates hormonal mechanisms that operate to maintain blood glucose within narrow limits 80 – 100 mg/dl or 4.4 – 5.5 mmol/L. Hypoglycaemia (low blood glucose) stimulates the release of gluconeogenic hormones such as glucagon and glucocorticoids, which promote the breakdown of liver glycogen and the synthesis of glucose in the liver (gluconeogenesis), followed by the release of glucose into the blood. On the other hand, hyperglycaemia (elevated blood glucose) stimulates the release of insulin, which promotes the uptake of glucose and its utilization, storage as glycogen, and conversion to fat.

Metabolic pathways are interconnected, some are irreversible or consist of some irreversible steps, while majority are localized to specific compartments called organelles within the cell. Figure 3 below shows various compartments within the cell and various metabolic pathways that occur within them. Those with asterisk indicate a pathway, part of which occurs in more than one compartment.

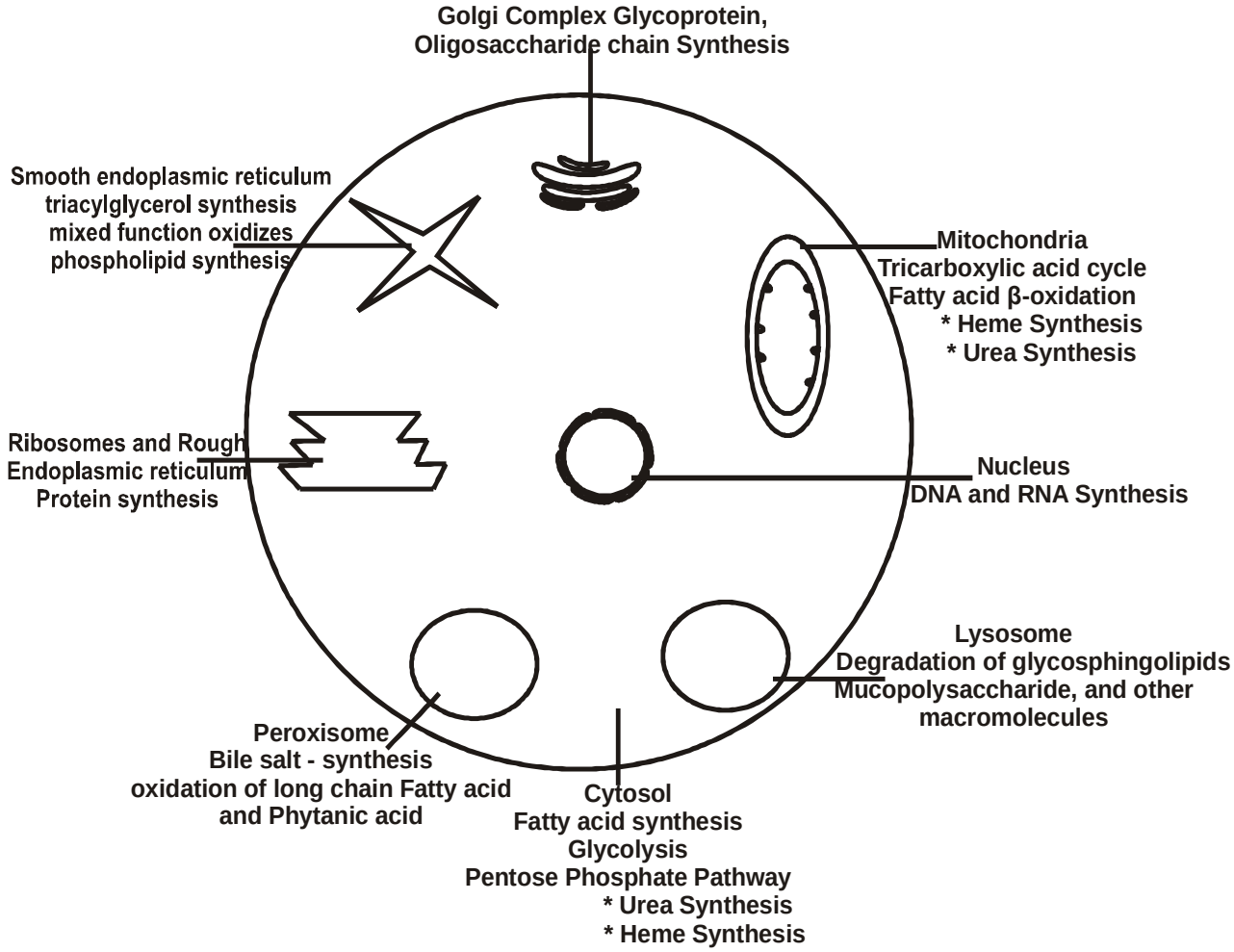

Fig. 7: Shows intracellular organelles with their peculiar metabolic pathways (Source: Bruce *et al*., 2009).

5.0 Biochemical Toxicology

Biochemical Toxicology involves the study of the adverse effects of chemical substances on living organisms and the practice of diagnosing and treating exposures to toxins and toxicants. It overlaps with biology, chemistry, pharmacology, medicine and nursing (Hodgson, 2010).

We should, therefore, avoid food additives often used to add flavour, texture, colour, appearance and consistency to food preparation and as preservatives. Examples of food additives include aspertane, benzoate, monosodium glutamate, nitrates, sulphate and tartrazine. Are they safe for consumption? One may ask, but once approved by Food and Drug Administration (FDA), they are

considered fit for human consumption, however they may not be entirely safe. Some food and colour additives have been linked to allergic reactions, asthma, cancer and birth defects. They are called foreign compounds or xenobiotics because they are alien to our body, and may be converted to toxic agents by the liver. They should therefore be avoided as much as possible.

Humans are daily bombarded with varieties of foreign compounds, therefore understanding how xenobiotics are handled at the cellular level is important in learning how to cope with the chemical onslaught. Knowledge of the metabolism of xenobiotics is basic to a rational understanding of Toxicology, Pharmacology, Therapeutics and Pharmacy, management of cancer and drug addiction. It is convenient to consider metabolism of xenobiotics in two phases.

In phase 1, the major reaction involved is hydroxylation, catalysed by members of a class of enzymes referred to as monooxygenases or cytochrome P_{450}. Hydroxylation may terminate the action of a drug, though this is not always the case. In addition to hydroxylation, these enzymes catalyse a wide range of reactions including those involving deamination, dehalogenation, desulfuration, epoxidation, peroxygenation and reduction.

In phase 2, the hydroxylated or other compounds produced in phase 1 are converted by specific enzymes to various polar metabolites by conjugation with glucuronic acid, sulphate, acetate, glutathione or certain amino acids, or by methylation. The overall purpose of the two phases of metabolism of xenobiotics is to increase their water solubility and thus excretion from the body. The term "detoxification" is sometimes used for many of the reactions cited above (Wilkinson. 2005). Responses to xenobiotics include pharmacologic, toxic, immunologic and carcinogenic effects, most simply referred to as cell injury. The scenario can be summarized in a schematic form:

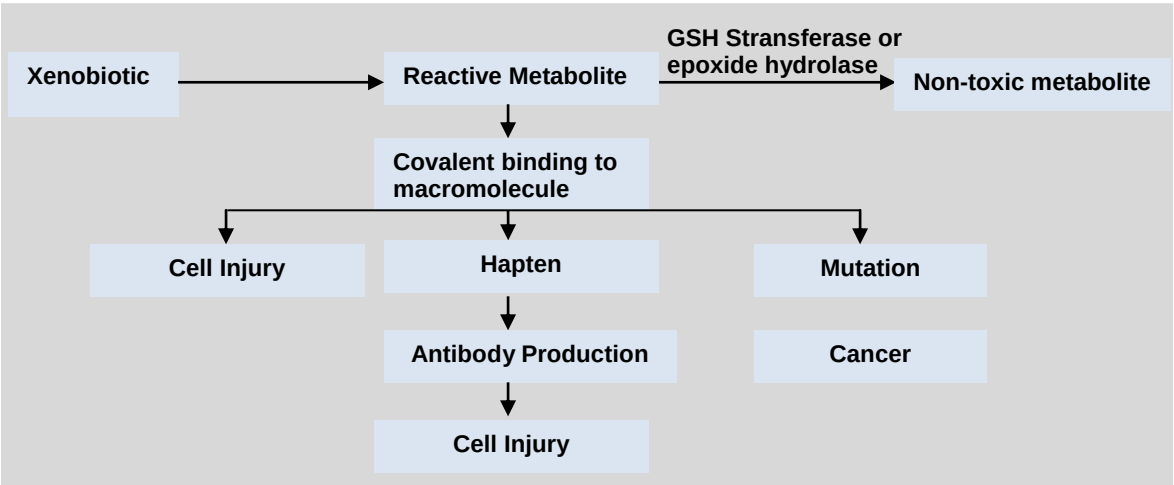

Fig. 8: Shows the possible effects of degradation of xenobiotics leading to cell injury. Source: Vasudevan *et al*., 2013

6.0 My Research Efforts

6.1 Antimalarial medicinal plants

Malaria remains the major cause of morbidity and mortality among the inhabitants of Tropical Africa, South Asia, Central and South America, the Carribean, the Middle East and Oceania. It is estimated that over 200 million cases of malaria infection occur annually while over 400,000 people die of the disease (especially children below age 5 and pregnant women), with over 90% from sub-Sahara Africa (WHO, 2016).

Prevention of mosquito bite from dusk to dawn is the first line of defence against malaria, and the use of Insecticide Treated Nets (ITN), insecticide sprays, window netting and protective clothing. Most of all these are not accessible to most people who live in rural communities. The next line of action is treatment of the disease. The causative agents are the *Plasmodium* species of *P. falciparum, P. ovale, P. malariae, P. vivax* and *P. kurnesi*, but the most severe form of malaria is caused by *P. falciparum*. This form is associated with complications such as cereberal malaria, febrile convulsion, massive haemolysis and severe anaemia. The poor rural dwellers have no access to health facilities and cannot afford the cost of effective Artemisinin-based Combination Therapy (ACT).The cheaper, accessible and easily available mode of treatment is the use of medicinal plants.

Traditional herbal medicines have been used to treat malaria for thousands of years in various parts of the world. The first antimalaria used in the tropical Andean forests of western South American countries of Colombia, Ecuador, Peru and Bolivia, was extracted from the stem bark of Cinchona plant (*Rubiaceae* species). The alkaloid quinine was extracted from the plant and is still very effective till today (Wilcox and Bodeker, 2004). Another ancient medicinal plant of millennium use in the West is *Artemisia annua*, rediscovered in China in the seventies, as an important source of the antimalaria, Artemisinin (Wilcox and Bodeker, 2004). Artemisinin Combination Therapy (ACT), was formally adopted as first line treatment of uncomplicated malaria in Nigeria in 2005 (FMOH, 2005). Neither *Cinchona* plants nor *Artemisia annua* are indigenous to sub-Sahara Africa.

Tropical rain forest plants are known to have higher concentrations of natural chemical defences and greater diversity. The list of medicinal plants used for the treatment of malaria are legion and inexhaustible (Odugbemi *et al*., 2007; Adebayo and Kretlli, 2011), but the one that caught my attention during my ethnobotanical survey is *Enantia chlorantha* (*Annonaceae*). When I inquired from the herbal seller at Baboko market in Ilorin what plant, when used alone, is very effective against malaria, the woman brought out a yellowish stem back and called it “dokita ‘gbo), meaning doctor in the bush or (‘awogba’/’awopa’), depending on the dialect of the Yoruba speaking people of the South-West and

Kwara/Kogi states. It is indeed the name “dokita ‘gbo” that fascinated me as a Medical biochemist.

Fig. 9: Stem bark of *Enantia chlorantha*

The *Enantia chlorantha* stem bark was obtained from the bark of an ornamental tree of up to 30 m high with dense foliage and spreading crown, from Ifetedo, Osun State and was identified at the Department of Botany, Obafemi Awolowo University, Ile-Ife, with voucher number Oliv. IFE No 13968 (*Annonaceae*).
The first step was to investigate its acute toxicological profile (Adesokan and Akanji, 2003; 2004); and its chronic toxicological profile (Akanji and Adesokan, 2005); (Adesokan and Akanji, 2006; 2007). The aqueous extracts were found to be essentially safe with reversal of enzyme activity changes when the extract was withdrawn for about one week. The major phytochemicals discovered in the extract included alkaloids (46.2%), saponins (26.8%), phenolics (18.8%), flavonoids (6.7%) and glycosides (1.4%). After confirming its safety, we proceeded to investigate its antimalarial bioactivity, using chloroquine sensitive NK65 strain of *Plasmodium berghei berghei* in mice. The results showed that aqueous extract of *E. chlorantha* possessed potent antimalarial activity, based on 100% parasite clearance at 400 mg/kg dose of the extract (chloroquine 98.6%); elongation of the mean survival time (MST) of 19.6 days compared to chloroquine (19.8 days) used as the standard drug (Adesokan and Akanji, 2010). The observed pharmacologic activity has been linked to significant presence of alkaloids in the extract which caused inhibition of hemozoin formation in the parasite or antioxidant inhibitory effect on Nitric Oxide (NO) production in the macrophages (Adesokan and Akanji, 2008). The specific active principles of palmatine, coloumbamine and jatrorrhizine were earlier isolated from *E. chlorantha* alkaloids (Lewis, 2001).

In a related study, we also investigated another medicinal plant that is popular in Nothern Nigeria, *Acacia nilotica*, and found it to be safe (LD_{50} was 5000mg/kg) for acute toxicity test. Aqueous extract of the root was found to have potent prophylactic, suppressive and curative activities in rodent *Plasmodium berghei berghei* in mice (Alli *et al*., 2011).

Further investigation also revealed that aqueous extract of *E. chlorantha* was effective against another parasite, *Trypanosome brucei brucei* in mice with potent trypanocidal activity (Ajadi and Adesokan, 2014).

6.2 Antibacterial activity of *E. chlorantha*

There have been several reports on the resistance to antibiotics of several strains of bacteria (Ozumba, 2003). The development of new generation of antibiotics to overcome resistance by the older ones is very expensive which makes its prices to be out of reach of majority of Africans who are poor. This has necessitated the search for medicinal plants with antibacterial activities which are easily available and affordable by majority of poor Africans.

We investigated the antibacterial potentials of aqueous extract of *E. chlorantha* against clinical isolates of *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Salmonella typhymurium* and *Pseudomonas aeruginosa*. We found that aqueous extract of *E. chlorantha* possess potent broad spectrum antibacterial activity against all the clinical isolates listed above. The zones of inhibition of *S. aureus* > *B. subtilis* > *E. coli* > *S. typhymurium* > *P. aeruginosa.* In addition, the Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) of the extract on the isolates followed the above pattern i.e. *S. aureus*< *B. subtilis* < *E. coli* < *S. typhymurium* < *P. aeruginosa* (Adesokan *et al*., 2007).

The observed antibacterial pharmacologic activity was due to the preponderance of identified alkaloids of palmatine, coloumbamine and jatrorrhizine, which intercalate with the DNA of the microorganisms, as the mechanism of their antibacterial activity.

6.3 Sperm quality improved by *E. chlorantha*

Unlike published research findings with chloroquine and quinine that possess spermatotoxic effects (Adeeko and Dada, 1998; Raji *et al*., 2003), we found low doses of aqueous extract of *E. chlorantha* to improve sperm motility, viability and count (Salman and Adesokan, 2008). This is attributable to the presence of simple sugars in the phytochemical analysis of *E. chlorantha* (Adesokan and Akanji, 2007), which were absent in chloroquine and quinine, that also caused hypoglycaemia. Pyruvate has been proven to be preferred substrate for the survival of sperm cells which is the final metabolite of simple sugars (Egbunike *et al*., 1986).

6.4 Antipyretic activity of *E. chlorantha* and *Acacia nilotica*

Pyrexia is a clinical condition that results in rise in body temperature arising from any form of infection which could be parasitic such as malaria, bacterial or viral. Any chemical agent that lowers the temperature of an organism is said to possess antipyretic activity. Using an animal model, pyrexia was induced by subcutaneous administration of 20% (w/v) of brewer's yeast. Aqueous and ethanolic extracts of *E. chlorantha* significantly reduced the temperature within 60 minutes and was sustained throughout the duration of the experiment (Adesokan *et al*., 2008). The antipyretic activity was due to inhibition of prostaglandin synthetase or suppression of interleukin-1alpha production and inhibition of cyclooxygenase type II (Luo *et al.,* 2005). In like manner, we investigated analgesic and antipyretic activities of aqueous extract of *Acacia nilotica* root in mice and found that the extract possessed potent analgesic and antipyretic activities (Alli *et al*., 2014).

6.5 Medicinal plants and Diabetes mellitus

Diabetes mellitus is a metabolic disorder characterized by hyperglycaemia and alteration in carbohydrate, lipid and protein metabolism caused by absence or deficiency of insulin, insulin resistance or both (Blupesh *et al*., 2009). The incidence of diabetes mellitus has reached an epidemic proportion worldwide. It is estimated that 2.8% of the world's population suffer from diabetes according to World Health Organization (Wild *et al*., 2004). Cardiovascular diseases account for 80% of diabetic mortality. The increase in incidence has been associated with rapidly changing lifestyle and environmental factors (Lang *et al*., 2008; Mozaffarian *et al*., 2009).

The use of herbal medicine is widespread throughout the world, while many medicinal plants have been confirmed to possess hypoglycaemic properties. Some of them include *Allum sativum*, *Azadirachta indica* (Akinola, 2010), unripe fruit of *Carica papaya* (Oloyede, 2005).

We investigated *Aloe barbadensis* Miller (Aloe vera) (Adesokan *et al*., 2006); *Aframomium meligueta* (Adesokan *et al*., 2010); *Cocos nucifera* (Coconut water) (Adewumi and Adesokan, 2016), and found them to possess potent hypoglycaemic and hypolipidaemic properties in Alloxan induced diabetic rats.

6.6(i) Oxidative stress and adverse effects on our body

A free radical is a molecule or molecular fragment that contains one or more unpaired electrons in its outer orbital. Oxidation reactions ensure that molecular oxygen is completely reduced to water. The products of partial reduction of oxygen are highly reactive and create havoc in our body (Vasudevan *et al*., 2013). Hence they are also called Reactive Oxygen Species (ROS). The following are members of ROS as shown in figure 10.

Superoxide anion radical (O_2^{-}*)
Hydroxyl radical (OH*)
Hydroperoxyl radical (HOO*)
Hydrogen peroxide (H_2O_2)
Lipid peroxide radical (ROO*)
Singlet oxygen ($^1O_2$)
Nitric oxide (NO*)
Peroxyl nitrite (ONOO*)

Fig. 10: Members of Reactive Oxygen Species (ROS)
Source: Vasudevan *et al*., 2013.

Damage produced by free radicals or ROS is referred to as **oxidative stress**. When a free radical reacts with a normal compound, other free radicals are generated. This chain reaction leads to thousands of events called **propagation phase**. Peroxidation of poly-unsaturated fatty acids in plasma membrane leads to loss of membrane functions. Almost all biologic macromolecules are damaged by free radicals and they include lipids, proteins, polysaccharides, nucleic acids especially DNA. The malondialdehyde (MDA) produced from lipid peroxidation intercalate with DNA thereby causing cell death, mutation and carcinogenesis (Wilkinson, 2005). The figure below shows pictorial form of damage by ROS.

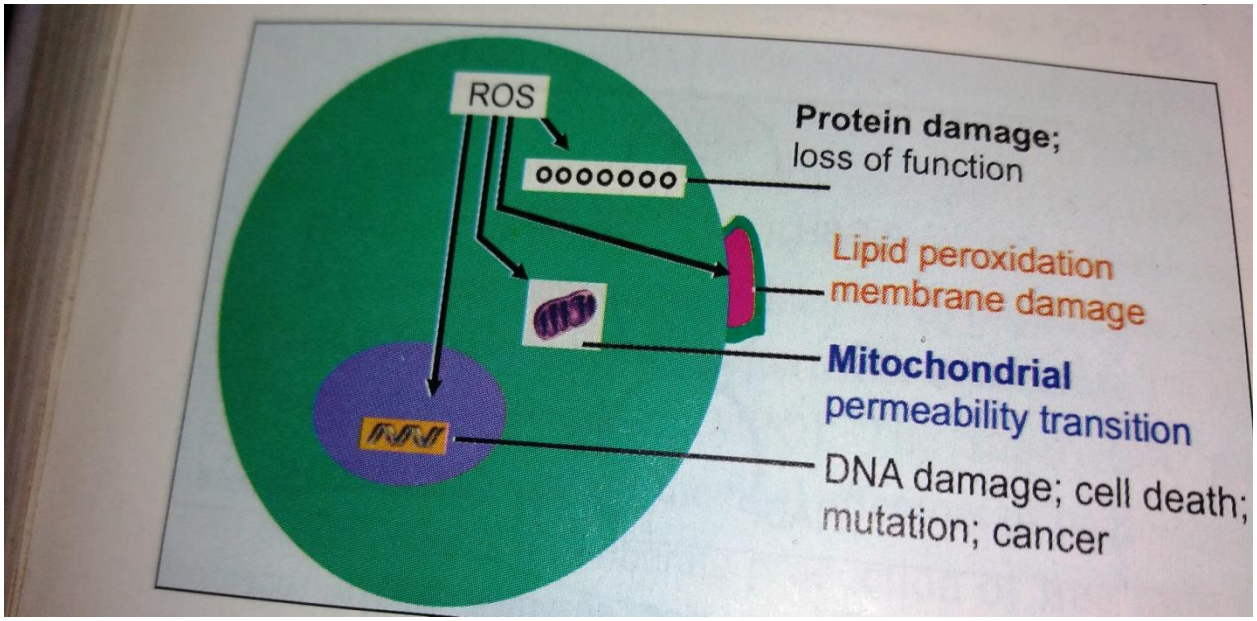

Fig. 11: Damage of various biomolecules by ROS
Source: Hodgson, 2010

6.6 (ii) Antioxidants – medicinal plants, vegetables and fruits

Antioxidants inhibit free radicals by preventing their formation, scavenging or by promoting their decomposition. With increased oxidative stress, the natural endogenous antioxidants are overwhelmed and oxidative damage to macromolecules occurs. Antioxidants can broadly be grouped into two, preventive and chain breaking antioxidants. Preventive antioxidants include glutathione, glutathione peroxidase and catalase, while chain breaking antioxidants are superoxide dismutase (SOD), uric acid, vitamin E (alpha tocopherol), caffeine, vitamin C, beta carotene and polyphenols from medicinal plants, vegetables, fruits and spices. Vitamin E is the most effective naturally occurring chain breaking antioxidant. The active components of medicinal plants, fruits and vegetables with antioxidant properties include flavonoids, flavones, isoflavones and anthocyanins (Adesokan and Akanji, 2008).

Mr. Vice Chancellor sir, distinguished ladies and gentlemen, in furthering our research efforts, Adunmo and Adesokan investigated oxidative stress in North Eastern Nigerian smokers and found out that elevated levels of products of oxidative damage such as malonaldehyde, uric acid and reduced total antioxidant status were both dependent on the number of cigarette smoked per day and the duration of smoking in years (Adunmo *et al.*, 2015 and 2016). And evaluation of some cardiovascular risk factors showed that smokers are more prone to develop cardiovascular diseases than non smokers (Adunmo *et al*., 2017). Adetutu, Oyewo and Adesokan also investigated and detected potent antioxidant polyphenols in *Vernonia amygdalina* (bitter leaf) (Adetutu *et al*., 2013). Extracts of *Moringa oleifera* was also found to modulate immunoreactivity in wistar rats (Oyewo *et al*., 2013).

Conclusion

Biomedical importance and benefits of varieties of food components that are available in the Nigerian markets cannot be over emphasized, if we must live a healthy life that is devoid of diseases associated with the inadequacies of balanced food components. The list of Nigerian medicinal plants with preventive and curative use for various ailments, with minimal side effects, is indeed very long and have been scientifically proven to be efficacious.

Mr. Vice Chancellor sir, I have been able to demonstrate that *Enantia chlorantha* a.k.a "dokita 'gbo" is truly doctor in the bush because of its efficacy as an antimalarial, trypanocidal, antipyretic, broad spectrum antibacterial activity and its ability to improve sperm quality, among others. That the popular *aloe vera*, apart from so many other uses especially in the cosmetic industry, possess potent antidiabetic and hypolipidaemic activities and is very safe. That many medicinal plants and vegetables consist of polyphenols that have been shown to have potent antioxidant properties and therefore can delay the aging process, ameliorate many chronic diseases such as diabetes mellitus,

cardiovascular diseases including atherosclerosis, myocardial ischaemia and hypertension.

Recommendations

A. **The General Populace**

1. It is hereby recommended that everybody should ensure a balanced diet on the dining table, avoid overeating and sedentary lifestyle, exercise moderately, and add varieties of fruits and vegetable to daily menu, so that we can live a healthy life.
2. That some herbal medicinal plants that have been scientifically proven to be efficacious and essentially safe can be used to prevent and cure some disease conditions.

B. The Researchers

3. There should be compilation of all scientifically proven efficacious medicinal plants for different disease conditions and make them accessible for the general populace.
4. There should be greater collaboration among researchers in various areas of medicinal plant research to improve the quality of research output.
5. There is the urgent need for researchers in Basic and Clinical Sciences to collaborate and fashion out clinical trial design that will link research output from the bench to the bedside for the benefit of our patients.

C. The Government

6. The Government should develop our traditional medicine and come up with specific policy formulation that will make it acceptable and beneficial for those who desire them.
7. The Government of Nigeria, through appropriate regulatory agencies, should draw and set policies and guidelines for the use of medicinal plants by her people.
8. The National Agency for Food and Drug Administration and Control (NAFDAC) and other agencies should step up their regulatory mechanisms and evaluation to make Nigerian herbal products meet good practices and global standards.
9. Government should facilitate through appropriate policies, collaboration between modern health specialists, Basic scientists and Traditional herbal medicine practitioners.
10. Herbal remedies should be packaged and properly labeled for its efficacies and warnings on proven adverse effects.
11. Government should roll out legislation for the management and conservation, planting and commercialization of herbal remedies.

D. The University

Ladoke Akintola University of Technology, Ogbomoso, Nigeria should set up and equip Trado-medical laboratory with state-of-the-art facilities and equipment in Central Research Laboratory designated for medicinal plant research, which can also generate IGR for the University.

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References

Adebayo JO, Kreltti AU. Potential antimalarials from Nigerian plants a review. *J. Ethnopharmacol* 2011, 133 (2): 269-302.

Adeeko AO, Dada OA (1998). Chloroquine reduces the fertilizing capacity of epididymal sperm in rats. *Afr. J. Med. Sci.* 27: 63-68

Adesokan, A. A. and Akanji, M. A. (2003). Effect of administration of aqueous extract of *Enantia chlorantha* on the activities of some enzymes in the small intestine of rats. *Nigerian Journal of Biochemistry and Molecular Biology. 18, 103-105.*

Adesokan, A. A. and Akanji, M. A. (2004). Responses of selected rat kidney enzyme activities to administration of aqueous extract of *Enantia chlorantha. Nigerian Journal of Pure and Applied Sciences. 19, 1592 - 1596.*

Adesokan, A. A., Akanji, M. A., Balogun, E.A. and Aderibigbe, A. (2006). Effect of Oral Administration of *Aloe-Barbadensis-Miller* juice on Selected Biochemical Parameters of Rat Liver and Kidney. *Recent Progress in Medicinal Plants. 13,74 - 80.*

Adesokan, A. A. and Akanji, M. A. [2006]. Effect of repeated administration of aqueous stem extract of *Enantia chlorantha* on the integrity of rat liver cellular system. *Nigerian Journal of Biochemistry and Molecular Biology. 21,89 –96.*

Adesokan, A. A., Akanji, M. A. and Yakubu, M. T. [2007]. Antibacterial potentials of aqueous extract of *Enantia chlorantha* stem bark. *African Journal of Biotechnology. 6 (22) 2502 – 2505.*

Adesokan, A. A. and Akanji, M. A. [2007]. Renal enzyme changes induced by chronic administration of aqueous extract of *Enantia chlorantha* stem bark in albino rats. *Nigerian Journal of Biochemistry and Molecular Biology, 22, 19-22.*

Adesokan, A. A., Yakubu, M. T., Owoyele, B.V.O., Akanji, M. A., Soladoye, A. O. and Lawal, O. K.[2008]. Effect of administration of Aqueous and Ethanolic extracts of *Enantia chlorantha* Stem bark on brewer's yeast induced pyresis in rats. *African Journal of Biochemistry Research Vol.2 (7) 165 - 169.*

Adesokan, A. A., and Akanji, M. A.[2008].Effect of chronic administration of *Enantia chlorantha* extract on some Renal Function Parameters in Experimental rats. *The Tropical Journal of Health Sciences.* Vol 10, No 2 (July) 2009.

Adesokan, A. A., Oyewole, O. I. and Turay, B. M. S. (2009). Kidney and Liver Function Parameters in Alloxan-induced Diabetic Rats Treated with *Aloe Barbadensis* Juice Extract *Sierra Leone Journal of Biomedical Research*, Vol 1(1) pp 33-37.

Adesokan, A. A. and Akanji, M. A. (2009). Antimalarial Bioactivity of *Enantia chlorantha* Stem Bark. In the book, *Medicinal Plants: Phytochemistry, Pharmacology and Therapeutics.* Vol 1 (2010), pages 441-447.

Adesokan, A. A. and Akanji, M. A. [2009]. Haematological changes followingchronic administration of aqueous extract of *Enantia chlorantha* to albino rats. *The Tropical Journal of Health Sciences.* Vol 17 No 1(January 2010).

Adesokan, A. A., Akanji, M. A. and Adewara, G. S. (2010). Evaluation of Hypoglycaemic Efficacy of Aqueous Seed Extract of *Aframomum melegueta* in Alloxan-induced Diabetic Rats. *Sierra Leone Journal of Biomedical Research* Vol 2 [2] pp 91 – 94, December, 2010.

Adetutu Adewale, **Adesokan A. Ayoade** and Ezekiel Ayinde Alani (2013). Determination of Vitamins in five Selected West African green leafy vegetables. *Journal of American Science* 9(2s) pp 40-43.

Adewale Adetutu1, AO Ogundare2, AO Odeleye3 , Owolabi OQ1 and **AA Adesokan** (2012). Antibacterial and Toxicological Effects of Methanolic Leaf Extract of *Pyrenacantha staudtii* (ENGL.). *Canadian Journal of pure & applied sciences* Vol. 6 No.3, pp 2073 – 2077.

Adewumi T (2016). Comparison of hypoglycaemic effects of coconut water, coconut milk and the mixture on Streptozocin-induced diabetes in wistar rats. M.Sc Dissertation, Ladoke Akintola University of Technology, Ogbomoso.

Adunmo G.O., **Adesokan A.A.**, Akanji M.A., Biliaminu S.A. and Adunmo E.O.(2015). Lipid Peroxide levels, antioxidant status and protein changes in Nigerian Smokers.
International Journal of Sciences: Basic and Applied Research; 20(1): pp 69-77.

Adunmo G.O, **Adesokan A.A**. ,Biliaminu, S.A., Abdulazeez, I.M. and Adunmo E.O. (2016). Effects of Chronic Cigarette smoking on lipid profile – A Pilot Study in North-Eastern Nigeria. *Sokoto Journal of Medical Laboratory Science 1(1): 94-99.*

Adunmo G.O, **Adesokan A.A.** , Desalu O.O., Biliaminu, S.A., Abdulazeez, I.M. and Adunmo E.O. (2017).Novel Cardiovascular Risks Factors in Nigerian Cigarette Smokers. *International Journal of Applied and Basic Medical Research..* Doi !0.4103/Ijambr.140-16.

Ajadi A. A., **Adesokan A. A.**, Atata R. F., Bashir M. (2014). Effects of Aqueous Extract
From *Enantia chlorantha* on Trypanosome Infected Rats. *International Journal of Applied Research and Technology.* ISSN 2277-0585. Vol. 3, No. 5 May 2014. 81 – 87.

Akanji, M. A. and **Adesokan, A. A.** (2005). Effect of repeated administration of aqueous extract of *Enantia chloranta* stem bark on selected enzyme activitie of rat liver. *Biokemistri. 17, 1) 13 – 18.* (Publisher -Nigerian Society for Experimental Biology].

Akinola OB (2010). Antidiabetic Activity of Ethanolic Leaf Extract of Neem (*Azadirachta indica* A Juss) in Streptozocin-Induced Diabetic Wistar Rats. PhD Thesis, University of Ilorin, Ilorin, Nigeria.

Alli, L.A., **Adesokan, A.A.**, Salawu, O.A., Akanji, M.A. and Tijani, A.Y. (2011). Anti-

Plasmodial Activity of aqueous root extract of *Acacia nilotica. African Journal of Biochemistry Research,* Vol.5(7), pp 214-219.

Alli, L.A., Okochi, V.I. and **Adesookan, A.A.** (2011). Trypanocidal Activity and Haematological Effects of Aqueous Leaf Extract of *Morinda lucida* on *Trypanosomal brucei brucei* Infected Rats. *Medicinal Plants: Phytochemistry, Pharmacology andTherapeutics* Vol. 2, pp 153-160.

Alli LA, Oluwole OP, Aniah JA, **Adesokan AA** (2015). Histopathological Effects of Aqueous Extract of *Acacia nilotica* root on Rat Liver, Kidney and Lungs. *The Journal of Anatomical Sciences* 6(1):12-18.

Alli LA, **Adesokan AA**, Salawu AO (2016). Antimalarial activity of fractions of aqueous extract of Acacia nilotica root. *Journal of Intercultural Ethnopharmacology*, 5(2): 180-185. doi: 10:5455/jice.20160331064817.

Bates et al., (2012). National Diet and Nutrition Survey. London HMSO.

Blupesh CS, Jittendra G, Sonia S, Yogesh K and Mahendra G (2009). Antihyperglycaemic Activity of Root of *Berberis aristata* DC in Alloxan-Induced Diabetic Rats. *Internatnal J Green Pharm.* 3 (3): 259 – 262

British Nutrition Foundation (BNF) (2016). Available at: https://www.nutrition.org.uk/healthy living/healthy diet/eatwell.html

Bruce Alberts, Dennis Bray, Karen Hopkin, Alexander Johnson, Juliana Lewis, Martin Raff, Keith Roberts, Peter Walter. *Essential Cell Biology,* 3rd edn, Garland Science (2009).

Devlin TM, ed (2010). Texbook of Biochemistry with Clinical correlations, 7th edn, pp 1240. New York: John Wiley.

Egbunike GN,Branscheid W, Pfisterer J, Holtz W (1986). Changes in porcine sperm lactate dehydrogenase isoenzymes during sperm maturation. *A*ndrologia, 18: 108-113

Federal Ministry of Health (FMOH) (2005). National Antimalaria Treatment Policy, FMOH, National Malarial and Vector Control Division, Abuja.

Food and Drug Administration (FDA) (2015). Available at: https://www.washintonpost.com/news/wonk/wp/2015/02/10/feds-oised-to-withdraw-longstanding-warnings-about-dietary-cholesterol/?utm_term=1982832f86fa

Geissler PJ, Davies K and Roostaeian J (2014). Improving fat transfer viability: the role of ageing, body mass index and harvest site. Plastic and Reconstructive Surgery, 134 (2); 227 – 232.

Hodgson, Ernest (2010). A Texbook of Modern Toxicology. John Willie and Sons. p. 10. ISBN 0-470-46206-X.

Hunter, G. K. (2000). Vital forces: The discovery of the molecular basis of life. Academic Press.

Lang IA, Galloway TS and Scarleff A, Henley WE, Depledge M, Wallace RB and Melzer D (2008). Association of Urinary BPA Concentration with Medical Disorders and Laboratory Abnormalities in Adult. *JAMA.* 300: 1303-1310

Lewis K (2010). I search of National Substrates and inhibitors of MDR pumps. *J. Mol. Microbiol. Biotechnol.* 3: 247-254

Lukman A. Alli, Mikhail O. Nafiu, **Abdulfatai A. Adesokan**, Musbau A. Akanji, Adeniyi Y. Tijani, Oluwakanyinsola A. Salawu (2014). Antipyretic and analgesic activities of aqueous extract of *Acacia nilotica* root. *Biokemistri*, Vol. 26 (2) 55 – 62.

Lukman Adewale ALLI, **Abdulfatai Ayoade ADESOKAN,** Oluwakanyinsola Adeola SALAWU, Musbau Adewunmi AKANJI (2015). Toxicological studies of aqueous extract of *Acacia nilotica* root. *Interdiscip Toxicol*, 2015, Vol. 8(1) 48-54.

Luo C, He ML and Bohlin L (2005). Is Cox-2 a perpetrator or a protector? Selective COX-2 inhibitors remain controversial. *Acta Pharmacol* Sin. 26: 926-933

Merlin L Willcox and Gerald Bodeker (2004). Traditional herbal medicines for malaria. *BMJ,* No 13: 329 (7475) 1156.

Mozaffarian D, Kamineni A, Carnethan M, Djousse L, Mukamal K and Siscovick D (2009). Lifestyle Risk Factors and New-onset Diabetes Mellitus in Older Adults: the Cardiovascular Health Study. *Arch Internal Med.* 169: 798-807

Oloyede FO (2005). Hypoglycaemic properties and biochemical parameters of aqueous extract of unripe fruit of *Carica papaya* in rabbits. PhD Thesis. University of Ilorin, Ilorin, Nigeria p 269

Ozumba UC (2003). Antibiotic sensitivity of isolates of *Pseudomonas aeruginosa* in Enugu, Nigeria. *Afr. J. Clin.Exp. Microbiol.* 4: 48-51

Raji Y, Udoh US, Mewoyeka OO, Onoye FC, Bolarinwa AF (2003). Implication of reproductive endocrine malfunction in male antifertility efficacy of *Azadirachta indica* extract in rats. *Afr. J. Med. Sci.* 32: 159-165

Salman, T. M. and **Adesokan, A. A.** [2008]. Sperm Quality in Male Rats Treated with Aqueous Extract of *Enantia chlorantha* stem bark. *African Journal of Biotechnology. 7 (7) 865 – 867.*

Singh P, Batra HS, Naithani M (2004). History of Biochemistry. *Bull Indian Inst Hist Med Hyderabad*. Jan-Jun.

Tan Van Helvoort (2000). Anne Hessenbruch, ed. Reader's Guide to the History of Science. Fitzroy Dearburn Publishing p 81.

Tolu O Odugbemi, Odunayo R Akinsulire and Peter O Fabeku (2007). Medicinal Plants Useful for Malaria Therapy in Okeigbo, Southwestern Nigeria. *African Journal of Traditional, Complimentary and Alternative Medicine.* 4(2), 191-198.

Vasudevan DM, Sreekumari S, Kannan Vaidyanathan (2013). Textbook of Biochemistry for Medical Students, 7th edn, Japee Brothers Medical Publishers (P) Ltd. New Delhi. P 436

Wilkinson D, Sandhu JK, Breneman JW, Tucker JD and Birnboin HC (2005). MDA intercalate with DNA causing mutation and carcinogenesis. British Journal of Cancer, 72: 1234 – 1240.

World Health Organization (WHO) (2008). World Malaria Report, pp 7 – 10.

WHO (2016). World Health Organization. Available at: http://www.who.int/definition/en/print

Wild S, Roglic G, Green A, Sicree R and King H (2004). Global Prevalence of Diabetes: Estimates for 2000 and Projections for 2030. *Diabetes Care.* 27(5): 1047-1053

www.google.co.uk/search ?q=sickle cell disease+patient

www.google.co.uk/search?q=melanin+synthesis+albinism