KWARA STATE UNIVERSITY, MALETE, NIGERIA

The Green University for Community Development and Entrepreneurship

The Nineth (9th) Inaugural Lecture

Title

Man Versus Diseases: The Green Remedy

By

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Great students of Kwara State University (Greatest KWASITES)

Distinguished students of Biochemistry (Greatest METABOLITES),

Members of my family; nuclear and extended,

Gentlemen of the print and electronic media,

Esteemed invited guests,

Friends and relations,

Distinguished ladies and gentlemen

1.0 PREAMBLE

Mr Vice Chancellor Sir, for me, it is evidence of grace and a mark of great honour to deliver the 9th Inaugural lecture of Kwara State University to this very distinguished audience here today. I am highly delighted that I have this unique opportunity to share my research experiences and findings over the years with the town and gown. An occasion such as this is what every academic looks forward to, and for me, it is a dream come true. For this I give all glory and praise to God **who makes all things beautiful in His own time (Ecclesiastes 3: 11)**. It is indeed a great joy for me that I have this rare privilege of presenting the first Inaugural lecture from the Faculty of Pure and Applied Sciences of our great University, the very first from KWASU Biochemistry and the first to be presented by a sitting Dean of Faculty in our University - I sincerely thank God for this uncommon privilege.

Mr Vice Chancellor sir, Biochemistry was one of the foundation programmes of Kwara State University in 2009, although it admitted its first set of students a year later. At inception, KWASU Biochemistry was a unit, domiciled in the Department of Biosciences and Biotechnology which as at that time also housed Microbiology, Zoology and Plant and Environmental Biology units. This status was maintained until 2017 when the Department of Biochemistry was carved out of Biosciences and Biotechnology to become a full-fledged Department and was thereafter domiciled in the School of Basic Medical Sciences alongside Public Health and Medical Laboratory Science Departments. In that same year, the nomenclature of the Department was changed to Medical Biochemistry and Pharmacology. With the advent of the present KWASU management under the leadership of our dynamic Vice Chancellor, Professor Muhammed Mustapha Akanbi SAN and following the change from Collegiate to Faculty system, Biochemistry became one of the Departments in the Faculty of Pure and Applied Sciences. The Biochemistry programme is fully accredited by the National Universities Commission and has produced six (6) sets of graduates. Four of the graduates of the programme are presently employed as members of the academic staff in the Department.

1.1 Background to the Lecture

Biochemistry: The Chemistry of Life Processes

Early in the 19th Century, scientists combined Biology, Chemistry and Physiology to investigate the chemistry of living systems. It is from this that Biochemistry emerged as a distinct subject. As at that time, Biochemistry was named "Physiological Chemistry". This feat has been historically credited to Anselm Payen, a French chemist who in 1833 discovered the first enzyme, diastase, now referred to as amylase (Fessner, 2000). Biochemistry can therefore truly be said to be a modern hybrid science from two traditional sciences, Biology/Physiology and Chemistry. The name Biochemistry, by which it is now known, was introduced in 1903 by Carl Neuberg, a German Chemist, who is also referred

to as the Father of Biochemistry. Biochemistry focuses on the molecular basis of life's vital processes and as such it relies on the techniques of analytical, organic and physical chemistry as well as those of physiology. Biochemistry, primarily seeks to explain how:

1. the structures of biomolecules (proteins, lipids, carbohydrates, nucleic acids, vitamins, enzymes, hormones etc.) relate to their functions;
2. biochemical processes operate within the cells at the molecular level and
3. cells communicate with each other.

Therefore, Biochemistry can be described as a science that provides explanations for life processes at the molecular level. The subject of study in biochemistry is the chemical processes in living organisms, the discovery and understanding of the complex components of life and the elucidation of pathways of biochemical processes. A biochemist, therefore, from this background can be described as a person involved in studying the chemistry of living systems. He takes delight in understanding the structures and functions of cellular components and seeks to know the pathways of metabolism of these cellular components and flow of chemical energy through their metabolism. He finds answers to how biological molecules give rise to the processes that occur within living cells and focuses attention on the biochemical processes involved in the control of information flow through biochemical signalling, and how they relate to the functioning of whole organisms. Indeed, Biochemistry is a subject of science that is of enormous fascination and utility and that which in no small measure affects every area of human life. Through Biochemistry, we understand the detailed reactions that give rise to the synthesis and degradation of components of life and how these chemical reactions are regulated to keep us fit for our daily activities.

Mr. Vice Chancellor sir, for me, becoming a Biochemist was not an outcome of a deliberate choice, but may rather be described as a fulfilment of divine purpose. Indeed, **"A man's heart deviseth his way; but the Lord directeth his steps" (Proverb 16:19).** My academic pursuit would have been truncated sometimes in 1982. That was the year that I was promoted to form 4 and it was that same year that school fees for us who were living in the dormitory of Government Secondary School, Ipee, was increased to N49.50. It was only the determination of my mother and her love to keep me in school that saw to my transfer to Oyun Baptist High School, Ijagbo, where I had to continue my secondary school education as a day student because of the huge financial burden of continuing at G.S.S. Ipee. After my "A" level programme at School of Basic Studies, Kwara State College of Technology (now Kwara State Polytechnic), Ilorin, I applied to study Medicine and Surgery at Ahmadu Bello University, Zaria but was offered admission to study Microbiology. Angered by the fact that I was not admitted into the medical programme (even though I met the required IJMB score),

I chose to reject the admission offer but to instead wait and re-apply in the following year. It was late Mr. Enock Kolawole, who then was a technologist in Biochemistry Department, Ahmadu Bello University, Zaria that persuaded me to accept the offer. He also suggested that I apply for a change of course of study from Microbiology to Biochemistry. I was afraid of taking to his advice because it was well reported then that graduating with a good grade from the Department of Biochemistry, Ahmadu Bello University, Zaria was like experiencing a torrential rain at the peak of a dry season. I was however encouraged when he said to me, "Omo iya agba, I know that you will excel as a Biochemist, if you make up your mind to do it". This was how my journey through the world of Biochemistry began. Biochemistry Department at Ahmadu Bello University, Zaria as at then had a tradition of assigning only professors and senior academics to teach 200 level General Biochemistry Courses. Thus, in my first year in the University, I was taught and mentored by great Biochemists in the likes of Professors Godwin Haruna Ogbadu, C. O. Ikediobi, Danladi A. Ameh, late Professor Jonathan Nok Andrew and late Dr. J. A. Elegbede. It was through the mentorship of these erudite scholars that I was eventually motivated to develop interest in Biochemistry.

Since inception, when Biochemistry was first seen as an offshoot of Biology and Chemistry, Biochemistry has progressively advanced and gone through series of metamorphosis. This to a great extent has been aided by the developments in the areas of bioinformatics, proteomics and genomics. Further advances in techniques for biochemistry research have made the discipline to be more desirable such that it has now become a toast for virtually everyone in the life sciences. Although, physical scientists ruled the twentieth century, what may not be denied is that this twenty first century will be ruled by life scientists. The developments that Biochemistry has undergone over the years have today led to the emergence of various distinct subject areas such as Biochemical Pharmacology, Bioenergetics, Biotechnology, Enzymology, Forensic Biochemistry, Nutritional Biochemistry, Membrane Biochemistry, Proteomics, Plant Biochemistry, Phytopharmacology, Xenobiotics, Phytomedicine, Pharmaceutical Biochemistry, Toxicology, etc. Over the past twenty years of my academic research, my studies have been focused on **Phytopharmacology, Toxicology** and **Functional foods**. This inaugural lecture therefore will address issues about the contributions of Biochemistry and specifically Plant Biochemistry to the investigation and treatment of diseases.

It may interest you Mr Vice Chancellor sir, that I was motivated to develop interest in this area of research in my First Semester at 400 Level through the mentorship received from Dr. Hellen Kwanashie (now a professor of Pharmacology), a lecturer assigned to teach us BCHM423 (Metabolism of Drugs and Foreign Compounds). Although, Dr. Kwanashie had her first degree in Biochemistry, she later took her postgraduate degree in Pharmacology. She made her classes so

interesting and participatory and thus presents Biochemistry to me as a subject that can be understood. When I later went back to the same University for my postgraduate degree programme, I had a better opportunity to relate more closely with Dr. Kwanashie as my graduate teacher. It was this relationship that greatly influenced me in deciding to further my research in phytopharmacology. During the course of carrying out my M.Sc. research project, I benefited immensely from research publications of Prof. Musbau Akanji, FAS who then was a Biochemistry lecturer in University of Ilorin. Then, I knew nothing about Prof. M. A. Akanji FAS apart from his research publications but I was hoping that one day I will be able to relate with him one-on-one. This opportunity came in a dramatic and unexpected manner when I saw him for the first time as my external examiner for the final oral examination of my M. Sc. at Ahmadu Bello University, Zaria in 1998. To further establish the fact that the story of my success in academic will not be complete without this great Biochemist, Prof. M. A. Akanji FAS, in 2011 (13 years after my first direct contact with him), again showed up as my external examiner for the PhD oral examination, but now at Olabisi Onabanjo University, Ago-Iwoye. While he was a member of staff at University of Ilorin and again while he was the Vice Chancellor of Federal University of Technology, Minna, I made unsuccessful attempts to transfer my services to the Universities where he was working. I did all these without knowing that in 2020, this erudite scholar will eventually join the service of Kwara State University, thereby providing me the opportunity that I had sought for unsuccessfully for many years.

1.2 The Burden of Diseases

Mr Vice Chancellor sir, studies have shown that there is a close relationship between the level of our economic development and our health status and disease profile. Over the decades, there has been a transition from a cause of death pattern once dominated by infectious diseases with very high mortality (especially at young ages), to a pattern now dominated by chronic degenerative and man-made diseases with lower mortality (mostly peaking at older ages). This shift which describes what we died of or will die from is referred to as "the epidemiological transition", a term proposed by Omran in 1971 (Johan, 2022). Epidemiological transition describes the changing patterns of population distributions in relation to changing patterns of mortality, fertility, life expectancy, and leading causes of death. At any given time, different countries in the world are at different stages of epidemiologic transition. In the well-advanced countries, the major causes of death and disability which for many years were predominantly due to nutritional deficiencies and infectious diseases have now shifted to those other diseases classified as degenerative diseases such as cardiovascular diseases (CVD), cancer and diabetes (Fausto, 2020).

For most developing and middle-income countries such as Nigeria and other Sub-Saharan Africa which are in the earliest stage of development, the increased incidence of CVDs adds to the continuing burden of infectious, nutritional, and perinatal diseases, giving rise to what is now termed the "double-burden". While common infectious and parasitic diseases such as malaria and the HIV/AIDS pandemic remain largely unresolved, emerging communicable diseases such as Ebola, Corona Virus Infection Disease (COVID-19) and other non-communicable diseases relating to diet and lifestyle e.g. diabetes has also been increasing over the last few decades and impacting negatively on already over-stretched health services in these countries. This is why, Mr Vice Chancellor sir, there is dire need in Africa and particularly Nigeria, to find sustainable ways to combat these diseases. Exploring the use of plants as a readily available and effective agent to reduce the disease burden has become a very important alternative and this is why I have chosen to make my contributions in this area.

1.3 Phytotherapy: Alternative Strategy for Sustainable Health Care

Mr Vice Chancellor sir, when God created man and gave him dominion over all the work of His hands, He also gave plants to him, both for food and as medicine. "**Then God said, 'I give you every seed-bearing plant on the face of the whole earth and every tree that has fruit with seed in it. They will be yours for food"** (Genesis 1: 29)**.** The scripture further says in Ezekiel 47:2 **"Fruit trees of all kinds will grow on both banks of the river. Their leaves will not wither, nor will their fruit fail. Every month they will bear fruit, because the water from the sanctuary flows to them. Their fruit will serve for food and their leaves for healing".** The medicinal importance of plants is further illustrated in Isaiah 38: 21 where the Lord instructed prophet Isaiah on how to get the king healed of his boil: **"Prepare a poultice of figs and apply it to the boil, and he will recover."** Plants that are used for medicinal purposes are generally referred to as **medicinal plants** or **herbs**. The World Health Organization (WHO) describes herbs or herbal preparations as **finished medicinal products that contain whole plants, parts of plants, or other plant materials, including leaves, bark, flowers, and roots, and/or their extracts as active ingredients intended for human therapeutic use or for other benefits in humans and sometimes animals** (WHO, 2018). Although, the use of plants as herbal medicines appears to be universal, however, the plants used for a particular ailment and the mode of application may vary from place to place.

The era of "modern" drugs dates back to the beginning of the nineteenth century and in 1805, the first pharmacologically-active compound, morphine was isolated from opium plant. This feat was achieved by a German pharmacist, Friedrich Sertürner (Joo, 2014). Subsequently, countless active compounds have been isolated from natural sources. For many years, these plant bioactive compounds otherwise referred to as secondary metabolites have been the source of countless

compounds and leads for drug discovery (Nature, 2020). Table 1 shows a list of some of such drugs developed from plants.

Table 1: Examples of plant-derived drugs developed on the basis of ethnobotanical information

S/N	DRUG	PHARMACOLOGICAL ACTION	LEAD COMPOUND	PLANT SOURCE	ETHNOBOTANICAL INFORMATION (ORIGIN)
1	Salicin	Anti-inflammatory, Antiagregant	Acetylsalicylic	*Salix sp (Salicaceae)*	Europe, Asia, America
2	Arteeter	Antimalarial	Artemisinin	*Artemisia annua L. (Asteraceae)*	China
3	Colchicine	Anti-gout	Colchicine	*Colchicum autumnale L. (Liliaceae)*	Europe
4	Chromoglycate	Anti-inflammatory in Asthma	Kellin	*Ammi visnaga L. (Apiaceae)*	North Africa
5	Galantamine	Colinesterase inhibitor	Galantamine	*Galanthus sp (Amaryllidaceae)*	Eastern Europe
6	Digoxin	Cardiotonic	Digoxin	*Digitalis sp (Scrophulariaceae)*	Europe
7	Etoposide	Anti-tumour	Podophylotoxin	*Podophyllum peltatum (Berberidaceae)*	North America
8	Morphine	Opioid analgesic	Morphine	*Papaver somniferum L. (Papaveraceae)*	Western Mediterranean
9	Pseudoephedrine	adrenergic agonist (Nasal decongestant)	Ephedrine	*Ephedra sinica Stapf*	China
10	Rivastigmine	Cholinesterase inhibitor	Physostigmine	*Physostigma venenosum Balf.* (Fabaceaea)	Tropical Africa
11	Vinblastine, Vincristine Vinorelbine **(Lopez, 2011)**	Ant-tumour	Vinblastine, Vincristine	*Catharanthus roseus* L. (Apocynaceae)	Madagascar

In 2018, 252 drugs were classified by the World Health Organization as basic and essential to health (Akinyemi *et al*., 2018). Interestingly, 11 % of these basic drugs that were so classified are exclusively of plant origin. Another large percentage of these drugs that are synthetic were obtained from natural precursors. A 2019 study reported that the global medicine market is worth about 1.1 trillion US dollars annually. About 35 per cent of these medicines originated directly or indirectly from natural products including: plants (25%), microorganisms (13%) and animals (about 3%) (João, 2019**)**. Between 1981 and 2014, the US Food and Drug Administration (FDA) approved 1,562 drugs. 64 (4%) were unaltered natural products, 141 (9.1%) were botanical drugs (mixture), 320 (21%) were natural product derivatives and 61 (4%) were synthetic drugs but with natural products pharmacophore. In February 2020, the Chinese State Council announced that chloroquine phosphate can be used for treating COVID-19 patients. This was after clinical evaluations in more than 10

hospitals across several provinces in China showed this antimalarial drug to be able to alleviate the symptoms for most COVID-19 patients and expedites virus seroconversion (Weng, 2020). Another clinical study in France also showed promising results of chloroquine and hydroxychloroquine in reducing the SARS CoV-2 viral load in COVID-19 patients (Gautret *et al*., 2020). A 3D homology model of the sequence was therefore used to screen against a medicinal plant library with 32,297 potential antiviral phytochemicals and traditional Chinese medicinal compounds. This study, led to the identification of 9 specific plant molecules (Table 2) that may be used to develop drugs against COVID-19. Chloroquine and hydroxychloroquine are synthetic analogue of quinine, originally extracted from the bark of cinchona trees. Diammonium glycyrrhizinate, an extract of *Glycyrrhiza glabra* (liquorice*)* root was also shown in a study to have potential for the treatment of COVID-19 (Nature, 2020). All these studies point to the efficacy of medicinal plants against many debilitating diseases.

This is the reason many decision-makers, governments, international agencies, and pharmaceutical companies in many countries are committing themselves to the development of natural products as medicinal agents. Mr Vice Chancellor sir, in Nigeria today, there are no truly effective drug treatments for many diseases. Coupled with this, is the fact that drug resistance to existing chemotherapeutic regimens for fungal and bacterial infections and for malaria is increasing. Unfortunately, however, what we have failed to explore is how we can maximize the use of natural products in overcoming these health challenges.

Table 2. Potential phytochemicals for COVID-19 drug development

Phytochemical name	**Plant source**
5,7,3′b,4′-Tetrahydroxy-2'-(3,3-dimethylallyl) isoflavone	Mojave indigo bush *(Psorothamnus arborescens)*
Myricitrin	Wax myrtle (*Myrica cerifera*)
Methyl rosmarinate	Marubio oscuro (*Hyptis atrorubens Poit*
3,5,7,3′,4′,5′-hexahydroxy flavanone-3-O-beta-D-glucopyranoside	Common bean (*Phaseolus vulgaris*)
(2S)-Eriodictyol 7-O-(6″-O-galloyl)-beta-D-glucopyranoside	Indian gooseberry (*Phyllanthus emblica*)
Calceolarioside B	Chinese flowering ash (*Fraxinus sieboldiana*)
Myricetin 3-O-beta-D-glucopyranoside	Tea tree (*Camellia sinensis*)
Licoleafol	Chinese liquorice (*Glycyrrhiza uralensis*)
Amaranthin	Edible amaranth (*Amaranthus tricolor*)

Source: Qamar *et al* (2020)

Our response as a nation to the COVID-19 pandemic challenge clearly illustrates this fact. Nigeria, like many other nations of the world currently depends solely on vaccines developed by other nations to fight the global pandemic. No doubt, we would have done better if we had encouraged researches into natural products. The use of herbal remedies has been widely embraced in many developed countries with Complementary and Alternative Medicines (CAMs) now becoming mainstream in the UK and the rest of Europe, and also in North America and Australia (Braun *et al*., 2010; Anquez-Traxler, 2011). In some high-income countries where the health system structure is typically well-developed, Traditional Medicine (TM) is used as complementary therapy. In Singapore and the Republic of Korea for example, 76% and 86% of the respective populations still commonly use Traditional Medicine. As at 2017, 98 member states of the World Health Organization have incorporated Traditional and Complementary Medicine (T&CM) in their national health systems, 109 had launched national laws or regulations on T&CM and 124 had implemented regulations on herbal medicines (Fattahi *et al*., 2017).

In countries such as UK, Germany, China and France, medicinal plant extracts are now used as prescription drugs (Fattahi *et al*., 2017, Ruhsam and Hollingsworth 2017). China, for example, is able to provide adequate health care coverage for its vast urban and rural population precisely because it harnesses the precious legacy of traditional medicine. Presently, India and China are the two major countries producing and exporting drugs derived from plants and many others which are synthetic analogues based on prototype compounds isolated from plants (Chatterjee, 2002, Huang, 2020). In 2019, the total value of pharmaceutical production globally was 1.2 trillion US dollars while the global herbal medicine market size was estimated to be US$ 83 billion in the same year. With average annual growth rate of 7%, it is expected to reach US$ 550 billion by 2030 (Insight Slice, 2021). It is estimated that about 350,000 plant species exist globally and only about 20% of these has been investigated. Till date, only about 5-10% of the investigated plants have been evaluated to determine their pharmacological potential (Velend *et al*., 2017).

The World Health Organization (WHO, 2019) estimated that 80 per cent of the population of developing countries rely on traditional medicine mostly plant drugs, for their primary health care needs. The reasons for this include the believe that they are natural, safe, non-narcotic, having no side effects, cost effective, preventive and curative therapies. In Nigeria, it has been reported that the first line of treatment for 60% of children with high fever resulting from malaria is the use of herbal medicines at home and over 80% of the population consult Traditional Medicine Practitioners (TMP) before using orthodox medicine. In spite of the wide home use of herbal remedy, Nigeria like many other African countries is yet unable to develop her legacy of traditional medicine and this is partly

responsible for the current health care crisis. Medicinal plants hold a better prospect for sustainable health care compared to synthetic drugs because:

1. Medicinal plants are very cheap, thus making it readily affordable;
2. Medicinal plants can be consumed without the aid of any kind of prescription, thereby making it easily accessible;
3. Medicinal plants are known to be more effective in curing certain conditions;
4. Medicinal plants are known to be all natural and with the use of these plants, supposed side effects caused by conventional medicine are avoided;
5. In the developing countries, majority of the population do not have access to conventional pharmacological treatment;
6. Treatment of chronic diseases would require covering multiple targets which in conventional drug therapy can lead to polypharmacy. Herbal medicines however are generally complex drugs with multiple potential targets and actions.

The process that leads from the plants to readily available drugs is very long, tedious (Figure 1) and requires a multidisciplinary collaborative approach involving Botanists, Biochemists, Pharmacognosists, Chemists, Pharmacologists, and Toxicologists. In routine drug development, researchers will need to first discover a drug molecule with potential therapeutic activity against a certain target. They then optimize its structure and validate its function using an *in vitro* experiment followed by animal and clinical trials.

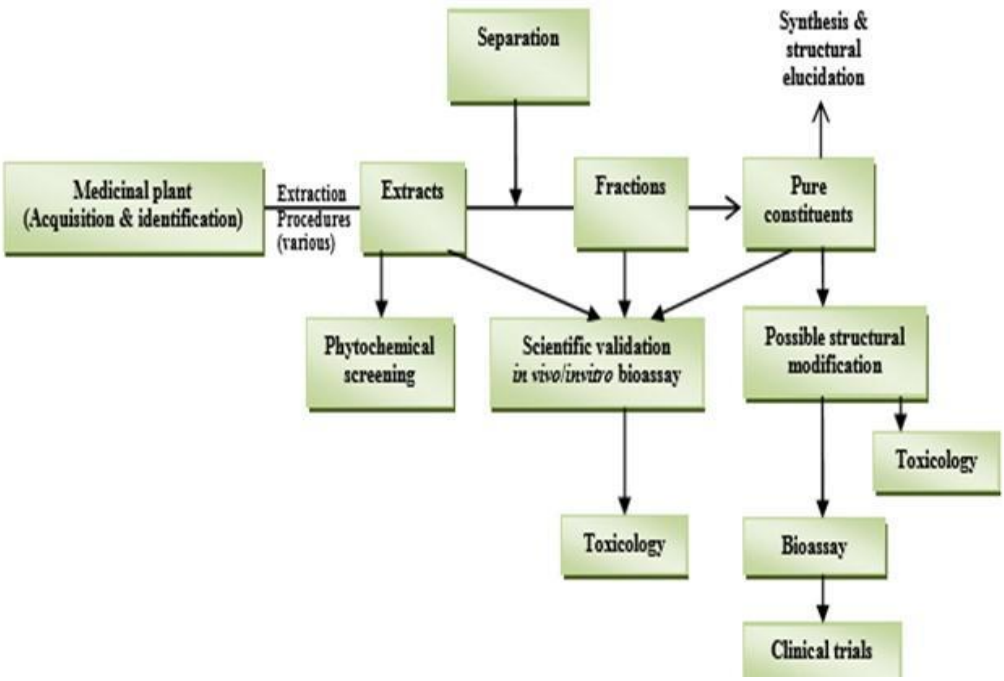


Fig. 1: Procedure for Preliminary Screening of Medicinal Plants

Mr Vice Chancellor sir, despite the advocacy for phytotherapy, one major concern that cannot be overlooked is their safety. Medicinal plant use may be associated with toxicity because many plants secrete toxic secondary metabolites as natural defence from adverse conditions or from herbivorous insects. These toxic substances are not distinguished from therapeutically active ingredients. Another predisposing factor to toxicity with herbal medicine is the dose. The popular saying of Paracelsus that "**all substances are poison; there is none which is not a poison; the right dose differentiates a poison and a remedy"** (Merlin *et al*., 2019) is an important guiding principle in phytopharmacology. Furthermore, adverse effects from the use of medicinal plants may arise from mis-identification of plants and also from the interactions between herbal medicines and synthetic drugs which may subsequently increase or decrease the pharmacological effects of either agent. The role of a phytopharmacologist in this process therefore is to develop methods and strategies that enhance the use of plants as medicine. This has been the direction of my research over the past 20 years. In doing this, Mr Vice Chancellor sir, I have focused my research on the following strategies:

1. Research validation of the claims by traditional medical practitioners on the use of some plants in the treatment and management of ailments and diseases;
2. Identification of the phytochemical constituents in medicinal plants with a view to understanding the chemical nature of the therapeutics;
3. Development of animal models of human diseases as a necessary tool for investigating mechanisms underpinning diseases and disease management;
4. Investigation and elucidation of the modes and mechanisms of actions of herbal extracts;
5. Toxicological evaluation of plant extracts at short, medium and long term and possible biochemical mitigations.

2.0 MY CONTRIBUTIONS TO PHYTOPHARMACOLOGY

2.1 Phytotherapeutic Treatment of Cardiovascular Diseases

Cardiovascular diseases (CVDs) are conditions that affect the structure or functions of the heart. It is the number one cause of death globally (Figure 2). An estimated 17.9 million people died from CVDs in 2019, representing 32% of all global deaths (Benjamin *et al*., 2019, Salim *et al*., 2021).

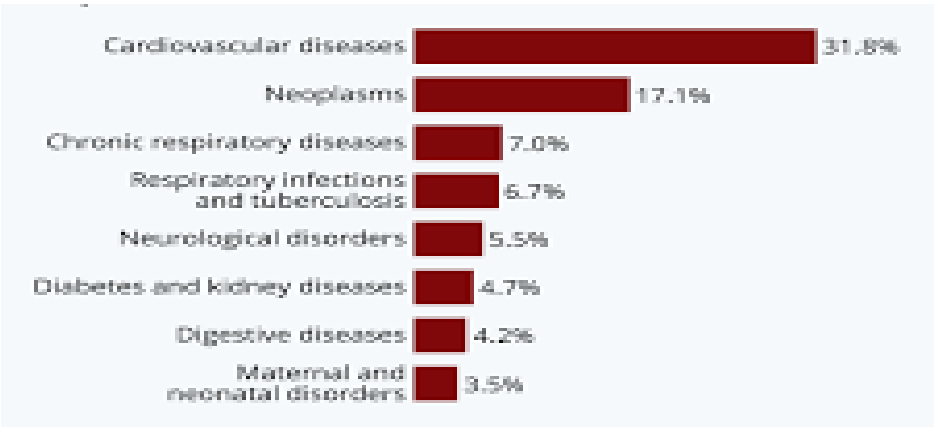


Figure 2: The global causes of death

Source: Benjamin *et al*., 2019

Individuals at risk of CVD may demonstrate raised blood pressure, glucose, and lipids as well as being overweight and obese. Studies have identified hypercholesterolemia, hypertriglyceridemia, high LDL- cholesterol, abnormal-body mass index, atherogenic index and coronary risk index as major factors in the aetiology of cardiovascular diseases (Yakubu *et al*., 2008; Sebastian and Valter, 2019; Mohammad, 2021).

My Research Contributions

My research team investigated the biochemical relationship between diet and CVDs. The goal of our studies was to understand the beneficial effect of plant-based diets in the prevention of cardiovascular diseases, establish the mechanisms by which sugar-based diet may predispose to cardiovascular diseases, and to also identify plants that may be of phytotherapeutic importance in the management of CVDs. One interesting fact from our studies is the evidence that a plant extract may contain two or more different pharmacotherapeutic properties and may show efficacy against different forms of cardiovascular disease risk factors. A single plant which for example may function as anti-diabetic may at the same time also serve as anti-hyperlipidemia and as anti-hypertensive.

In one of the studies, we assessed the effect of various concentrations of sucrose (table sugar) on predisposition of weanling rats to cardiovascular diseases (Salau *et al*., 2012). Our findings indicates that sucrose diet at 20% energy supply and above, increased energy density, plasma total cholesterol, LDL cholesterol, VLDL cholesterol, atherogenic risk index and coronary risk index but decreased HDL cholesterol level. In another study, we again investigated the effect of sucrose diet on some haematological and hemorheological parameters (Salau *et al*., 2013). Our findings revealed that inclusion of sucrose in the diet at concentrations above 20% energy supply increases blood viscosity, plasma viscosity, fibrinogen level, erythrocyte sedimentation and white blood cell count. ***The***

outcome of these studies is a clear indication that sugar plays a prominent role in the development of CVDs and that sucrose diet at the present level of consumption (above 25% energy consumption) will increase predisposition to cardiovascular diseases. This is because excessive absorption of sugar causes an increase in its concentration in the blood. Free sugar can be transformed in the liver to free fatty acids which can cause obesity, dyslipidemia and insulin resistance (Akanji *et al*., 2009). Imbalance of hypertension, dyslipidemia and insulin resistance can induce type-2 diabetes, cardiovascular diseases and metabolic syndrome (Figure 3).

When we placed albino rats on diet regimen supplemented with high cholesterol and then simultaneously administered extracts of different selected plants (based on ethnobotanical report) to validate their therapeutic effect on predisposition to cardiovascular diseases, our findings revealed that the leaves of *Amaranthus spinosus* (tete elegun) (Faponle *et al*., 2015a), *Rauvolfia vomitoria* (asofeyeje) (Faponle *et al*., 2015b), *Hydrocotyl bonariensis* (karo) (Ajani *et al*., 2012) and *Loranthus micranthus* (African mistletoe) (Ajani *et al*., 2014a) were all efficacious in reducing predisposition to cardiovascular disease risk. Data from our studies showed that the effectiveness of these plants lies in their ability to modulate plasma lipid, plasma lipoproteins and oxidative stress. Extracts prepared from the plants elicited significant reduction in atherogenic and coronary risk indices.

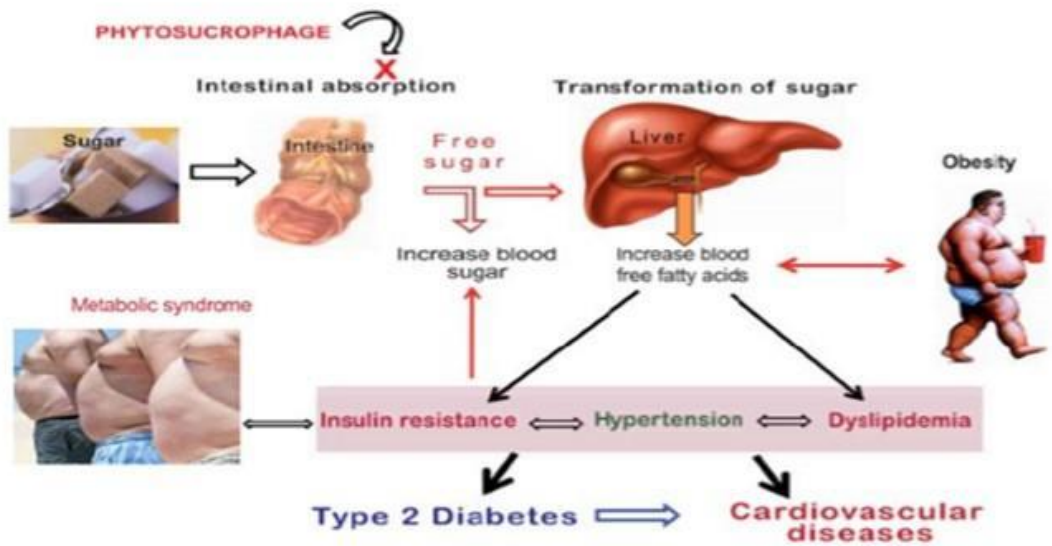


Figure 3: Role of sugar absorption and its impact on metabolic syndrome and obesity

Myocardial infarction (MI), characterized by the hypoxic state of myocardial tissue sequel to uneven perfusion of coronary blood supply compared to demand, is a leading cause of cardiovascular morbidity and mortality in men. My research team (Suleiman *et al*., 2021), investigated the cardioprotective effects of aqueous extract of ripped *Musa paradisiaca* (plantain) peel in isoproterenol (ISO) induced myocardial infarction rat model. Pre-treatment with the peel promoted

restoration of cardiomyocytes (cells responsible for generating contractile force in the intact heart) with no side effect. The extract improved antioxidant status of the heart and decreased the level of biomarker of inflammation (cytokines, IL-1β, IL-6, and TNF-α) and heart damage (cardiac troponin). Results from the histopathological study support the cardioprotective effects of the peel (Figure 4). The group administered ISO alone showed marked necrosis and infiltration of inflammatory cells. However, pre-treatment with plantain peel extract reduced the level of myonecrosis and lowered the level of inflammatory cells in a dose-dependent manner. The effect of the peel in offering protection to the myocardium, we opined may be attributed to its antioxidant and anti-inflammatory effect.

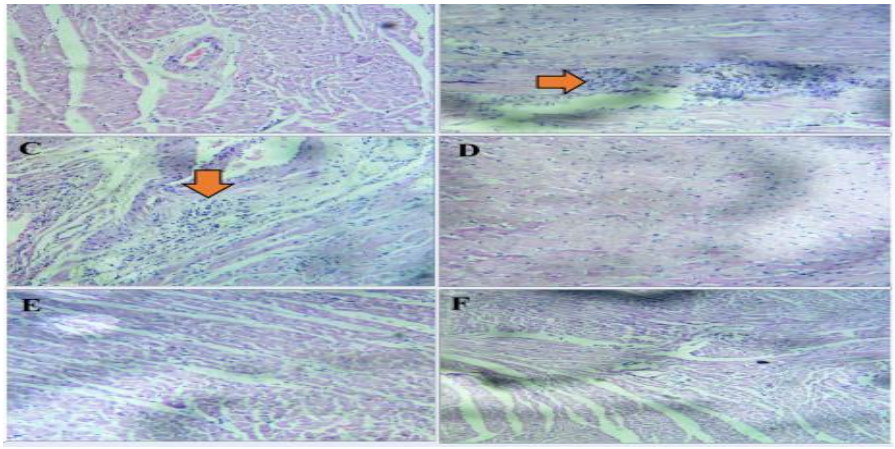


Figure 4: Effect of aqueous extract of *Musa paradisiaca* peels on cardiaomyocytes

In another study, we prepared wine from sweet potatoes and compared its effect in rats placed on high cholesterol diet with that of commercially available red wine (Ajani *et al*., 2021a). Our results indicate that sweet potato wine restores abnormalities in lipid profiles in the cholesterol fed rats and does not significantly alter the renal function biomarkers. Findings from this study suggest that sweet potato wine would be beneficial in restoring lipid profiles in cardiovascular diseases.

*2.1.1 **Phytotherapeutic Treatment of Hypertension***

We evaluated hypertensive patients randomly selected from the cardiovascular clinic of Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu. The patients were served edible portions of fairly ripe fruits (banana, pawpaw, grape fruits, tangerine and pineapple) mixed together in equal weight fruits salad with edible green leafy vegetable (fluted pumpkin leaf, spinach and waterleaf) after moderate cooking. The hypertensive subjects (after the study period) showed significant reductions in serum lipid parameters and blood pressure (Adebawo *et al*., 2006). The conclusion that may be drawn from these studies is that many plants that are readily available for consumption as functional foods, if explored, will provide immense benefits for patients suffering from cardiovascular diseases risk factors such as hypertension.

Hibiscus sabadariffa (Figure 5) commonly called "isapa", is an important multipurpose plant, native to West Africa and known to supply a range of foods, medicines and other products. It has been grown as a food crop for around 6,000 years and is still widely cultivated in both tropical and sub-tropical zones both for food and for its fibre. Decoctions of *Hibiscus sabdariffa* L. calyces are very popular for the preparation of homemade refreshing drinks known as zoborodo or simply zobo.



Figure 5: ***Hibiscus sabdariffa***

In our study on zoborodo using spontaneously hypertensive and non-hypertensive rats (Onyenekwe *et al*., 1999; Ajani *et al*., 1999), we demonstrated that the infusion lowered both systolic and diastolic blood pressure, reduced the total body weight and at the same time modulate other hypertensive and CVD related biomarkers such as total triglycerides (TG), Total Cholesterol (TC), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL) levels and urine output. Given the established association between weight change, urine production, lipoprotein levels and blood pressure status, we opined that the mechanisms by which zoborodo works as antihypertensive agent could be by reductions in insulin resistance, enhanced sodium retention, alterations in vascular structure and function, changes in ion transport, enhanced stimulation of the rennin-aldosterone-angiotensin system and increased activation of sympathetic nervous system.

What is evident from our study is that zoborodo may not just be a refreshing drink, but more importantly will provide therapeutic benefit for patients suffering from hypertension. When we presented the outcome of our study at the 23rd Annual Conference of the West African Society of Pharmacologist (WASP), held at National Institute for Pharmaceutical Research and Development, Idu, Abuja (Iwunayanwu and Ajani, 1996), it was recognized as a novel study on the antihypertensive efficacy of zoborodo. It will interest you, Mr Vice Chancellor sir, that although numerous other reports on zoborodo and its therapeutics efficacy have been published after our initial study, yet scientists are still actively working on exploring the therapeutic properties of this refreshing infusion. Under the umbrella of the African Centre for Herbal Research, Ilorin (ACHRI), my research team has produced teabag from zobo powder (Figure 6) which is now available commercially.

Considering the popularity of zobo as a readily taken refreshing drink and in order to maximize its therapeutic advantage, we saw the need to investigate the safety of the infusion. Both our earlier study (Ajani *et al*., 1999) and our other recent studies (Njinga *et al*., 2020, Ajani *et al*., 2021b) showed that the infusion is safe for consumption. Presently, we are researching into combining *Hibiscus sabdariffa* calyx extract with some spices for the phytotherapeutic management of cardiovascular diseases. The team consists of Horticulturists, Pharmacists, Biochemists, Chemists and Microbiologists from different Universities in Africa.

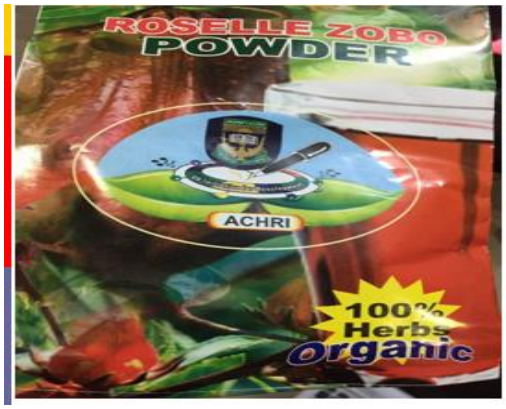


Figure 6: Roselle teabag by ACHRI

2.1.2 *Phytotherapeutic Treatment of* Diabetes

Mr Vice Chancellor sir, diabetes mellitus, commonly known as diabetes, in the last decade has become a serious global public health issue and has gain recognition as the most challenging health problem of this century (Marsha *et al*., 2016). Diabetes mellitus is a condition in which the body is unable to control blood glucose levels adequately, resulting in high blood glucose levels (hyperglycaemia). The global incidence of diabetes has dramatically increased from an estimate of 151 million people in 2000 (IDF, 2000, Zimmet *et al.*, 2016) to 424.9 million people worldwide in 2017. This is estimated to increase by 48 % to 628.6 million by 2045 (Standl *et al*., 2019). Type 2 diabetes is the more common form of the disease, affecting 90–95% of diabetics and is characterized by a loss of ability to respond to insulin (there is insulin resistance, also termed as insulin insensitivity). Today, type 2 diabetes, which a few decades ago was regarded as a relatively uncommon and low-profile disease is fast becoming a major international public health problem. The disorder may yet be the greatest chronic disease epidemic in the history of human existence.

Glucose, also refer to as sugar is a main source of energy for the cells that make up muscles and other tissues. In healthy individuals, blood glucose levels range between 3.5 and 5.5 mmol/l before meals. This range is maintained by the actions of hormones (primarily insulin and glucagon) as required

following meals, during fasting and exercise. Insulin produced by the pancreatic cell moves glucose from the blood into the cells (Figure 7) to be stored or used for energy.



Figure 7: Insulin's role in diabetes mellitus

With diabetes, the body either does not make enough insulin or cannot effectively use the insulin it makes. Consequently, the body now relies on alternative energy sources in the tissues, muscles, and organs. This forces the pancreas to work harder to make more insulin. Over time, this can damage cells in the pancreas and eventually the pancreas may not be able to produce any insulin and leads to glucose building up in the bloodstream thereby leaving the body's cells starved for energy. This can be rightly referred to as "**being hungry in the midst of plenty.**" What triggers this series of events? It may have to do with cell dysfunction in the pancreas or with cell signalling and regulation. In some people, the liver produces too much glucose. There may also be a genetic predisposition to developing type 2 diabetes. Diabetes manifests in a variety of symptoms such as lack of energy, fatigue, weight loss, excessive thirst, frequent urination, dry mouth, itchy skin and blurry vision.

The preferred first line of treatment of diabetes is lifestyle intervention with diet and exercise (ADA, 2020). Although this approach has proven to be quite effective, the success has only been reported in a minority of people with type 2 diabetes (Zimmet and Alberti, 2012). The discovery of insulin did not perform the curative magic. This fact was emphasized by Dr. Grant Banting himself when in his Nobel lecture following the discovery of insulin, admits thus: **"Insulin is not a cure for diabetes, it is a treatment. It enables the diabetic to burn sufficient carbohydrate so that protein and fats may be added to the diets in sufficient quantities to provide energy for economic burdens in life**" (Awuchi, 2020). This is why pharmacological intervention is almost inevitable. But even with an increasing number of new drug therapies in the market, the treatment of type 2 diabetes remains unsatisfactory. Zimmet *et al*., (2012) noted that although there is an arsenal of anti-diabetic conventional drugs in circulation, yet, this disorder besides not being cured continues to expand in prevalence and incidence. The reason for this may be because of the several reaction pathways and

body organs involved in diabetes and the potential number of metabolic defects that result from the disease. Thus, not a single therapeutic agent, let alone a combination of agents is enough to provide the answer to metabolic control. This is why intervention targets in-terms of treatment become multiple and thus conventional drugs may not be able to offer lasting help. Plants, however, contain a variety of phytochemical ingredients that are thought to act on a variety of intervention targets by various modes and mechanisms and therefore have the potential to provide maximum therapeutic efficacy with minimum side effects.

Mr Vice Chancellor sir, my research studies on phytotherapeutic management of diabetes mellitus started in 2010 and since then, my team has investigated several plants with potential antidiabetic efficacies.

I. *Musa sapientum*

Although the efficacy of different parts of *Musa sapientum* (banana or ogede wewe) as antiulcerogenic, antihelminthic and antidiabetics has been previously reported, the attention of previous researchers was focused on the fruit of banana (Figure 8a) and not on the sucker (Figurer 8b). Our study with alloxan induced diabetic rats (Salau *et al*., 2010) showed that the sucker reduced fasting blood glucose level in diabetic rats. We demonstrated with the histoarchitecture of the pancreas of the rats, the effectiveness of banana sucker in restoring the pancreatic cell and the weight catchup.



Figure 8a: *Musa sapientum* Fruit



Figure 8b: *Musa sapientum* Sucker

Alterations in plasma lipid profile are common occurrences in diabetes and uncontrolled hyperlipidaemia is a predisposing factor to cardiovascular diseases. We showed in one of our studies (Salau and Ajani, 2012) that *Musa sapientum* sucker improves lipid profile in alloxan-induced diabetes and also lowers the atherogenic and coronary risk indices. The study suggests that administration of *Musa sapientum* sucker extracts will be of immense therapeutic benefits to diabetic patients.

II. *Cyperus esculentus*

Cyperus esculentus L (Figure 9), commonly known as tiger nut or "imumu" (Yoruba) is a plant widely cultivated and used as dietary supplement in the Arabian Peninsula, Spain, East Africa, and many West African countries including Nigeria. The tubers of *C. esculentus* (CE) are edible, with characteristic sweet nutty flavour. In Nigeria, the fresh tuber is either roasted, baked, dried, eaten raw, or prepared as 'kunnu'.



Figure 9*: Cyperus esculentus* tubers

In the management of diabetes mellitus, carbohydrates-metabolizing enzymes; the alpha (α)-glucosidase and alpha (α)-amylase represent the most crucial of the pharmacological targets. These enzymes are the two key enzymes involved in the digestion of carbohydrate. Inhibitors of these enzymes can slow down the liberation of absorbable monosaccharides from dietary complex carbohydrates and thus prevent any sudden rise in meal induced blood glucose level.

We investigated the α-amylase and α-glucosidase inhibitory activities of *Cyperus esculentus* (Ajani *et al*., 2016a, Sabiu *et al*. 2017a). Findings from our study showed that tiger nuts have inhibitory effect on the specific activities of α-amylase and α-glucosidase. Judging by the IC_{50} values obtained, our study demonstrated that tiger nuts elicited a stronger inhibition on the activity of α-glucosidase than α-amylase. The therapeutic significance of the findings from the study is that tiger nuts will not only serves as an effective antidiabetic agent, but it will also be effective in abolishing the adverse effects consistent with the conventional α-glucosidase and α-amylase inhibitors. Our investigation further revealed that tiger nuts contained phytoconstituents that has been previously reported to have capacity to aid regeneration of pancreatic β-cells and inhibit the specific activities of α-glucosidase and α-amylase (Kunyanga *et al*., 2011; Madhusudhan and Kirankumar, 2015). This clearly explains why *C. esculentus* was shown in our study to be efficacious in treating diabetes. Based on their structure, the phytoconstituents were grouped as tannins, alkaloids and saponins. I*n vivo* study with

albino rats showed that the extract does not elicit any damage to the liver nor the kidney. It is therefore recommended as a non-toxic therapeutic plant for treating diabetes.

III. *Solanum incanum*

Solanum incanum (African garden egg) is a plant (Figure 10) commonly referred to as "Igbo" or "Ikan" (Yoruba). Our study demonstrated inhibitory effect of *Solanum incanum* fruit on alpha amylase and alpha glucosidase activities, suggesting that the fruit is a pharmacologically potent inhibitor of carbohydrate metabolizing enzymes implicated in diabetes (Sabiu *et al*., 2018). We showed in one of the studies, a reduction in the values of Km and Vmax of these enzymes with the extract, thus predicting its uncompetitive modulatory action on the activity of alpha-amylase. The implication of this finding is that there is a higher affinity of the enzyme for garden egg extract than the substrate, suggesting that it can strategically regulate further hydrolysis of systemic carbohydrate and thereby lead to less production of glucose.



Figure 10: *Solanum incanum* fruit

However, because it competitively inhibited the activity of α-glucosidase, it is suggestive of a stronger structural resemblance of the major constituent of the extract to that of the substrate. This favourably facilitated the binding of the extract on the enzyme's active site at the expense of the substrate. As a result, the rate of starch hydrolysis to free glucose is either effectively reduced or abolished.

The study also demonstrated that garden egg extract elicited marked antioxidant activities, indicating that the plant has the tendency to regulate or stall free radicals chain reactions associated with diabetes complications. It also conferred marked stabilization potential on the RBC against haemolysis, suggesting the ability of the constituents of the extract to adhere to the erythrocyte membrane and prevent deleterious attacks on the membrane as well as promote dispersion of ions as normally observed in erythrocyte haemolysis. The overall effects elicited by garden egg extract as demonstrated in our study could be attributed to its adaptogenic phytonutrients. We identified twenty (20) bioactive compounds in the GC-MS study which were grouped as either alkaloids, saponins,

carotenoids, flavonoids, glycosides, flavones, and cinnamic acids. What our study therefore suggests is that diabetic patients can overcome the disorder by regularly eating African garden egg.

IV. *Cochlospermum planchonii*

Cochlospermum planchonii (Figure 11) is commonly known as "Ghehutu", Feru" or "Oboyo". We demonstrated that the leaves of "Oboyo" repressed the hepatic α-amylase activities in streptozotocin-induced diabetic rats, thereby resulting in lowering plasma glucose concentration (Bamisaye *et al*., 2017a). It also normalized the glucose -6-phosphate dehydrogenase (G6PDH) activities. The decrease in the activity of this enzyme in the diabetic condition diminishes the reducing equivalent and increases oxidative stress, leading to diabetic complications. The extract increased the flux of glucose into the glycolytic pathway and hexose monophosphate shunt. The consequence of this, Mr Vice Chancellor sir, is an increase in the glucose degradation through an alternative pathway and a reduction in the levels of glucose in blood resulting in an increased production of the reducing agent, NADPH, with a concomitant decrease in oxidative stress.



Figure 11: ***Cochlospermum planchonii***

Our study further demonstrated that *C. planchonii* leaves induces reduction in total cholesterol, triglyceride, LDL and VLDL-cholesterol with a corresponding increase in HDL-cholesterol suggesting that the leaf is a good and safe remedy in diabetes management and prevention of the upsurge of atherosclerosis and coronary artery disease. We further demonstrated in another study, the non-toxicological effect of administration of the extract (Bamisaye *et al*., 2017b).

V. Striga-resistant Yellow-Orange Maize Hybrids

Striga hermonthica (purple witch weed) is a root hemi-parasitic plant (Figure 12) which causes yield loss as high as 100% under severe infestation. To mitigate the losses in the yield and quality of maize occasioned by *S. hermonthica* infestation, the best control method used is to plant Striga-resistant maize genotypes. We evaluated some bioactive constituents and carbohydrate profiles of sixteen Striga-resistant hybrids. Our findings indicate that the Striga-resistant yellow-orange maize hybrids

have a good combination of bioactive constituents (Elemoso *et al*., 2020). We also observed that extracts of the maize hybrids scavenged free radicals and inhibited α-amylase and α-glucosidase (Elemoso *et al*., 2021) enzymes. These findings indicate that, the striga-resistant yellow-orange maize hybrids will be beneficial in alleviating oxidative stress and postprandial hyperglycaemia. This thus represents a good clinical strategy for managing obesity and type 2 diabetes.



Figure 12: Striga infested maize plant

2.2 Phytotherapeutic Treatment of Lens Cataract

Vision is the most dominant of our senses and in a world built on the ability to see, vision plays a critical role in every facet and stage. Though we often take vision for granted, but without vision, we only struggle to learn, walk, read, participate in school, and work. Globally, at least 2.2 billion people have vision impairment, and of these, at least 1 billion people have vision impairment that could have been prevented or is yet to be addressed (WHO, 2019). This burden is not borne equally. It weighs more heavily on low- and middle-income countries, on older people, and on rural communities. Most worrisome is the fact that projections show that global demand for eye care is set to surge in the coming years due to population growth, ageing, and changes in lifestyle. The leading causes of vision impairment are cataract, uncorrected refractive errors, age related macular degeneration, diabetic retinopathy, corneal opacity and trauchoma (Bourne *et al*., 2017).

Cataract is defined by the presence of any lens opacities or loss of transparency. In cataract, there is the progressive loss of optical quality of the eye lens (Figure 13), which is caused by the formation of crystals (crystalline lens). The lens is made up of cells packed with structural proteins called crystallins. The lens can suffer structural changes due to metabolic problems or simply due to aging. Mr Vice Chancellor sir, in spite of the technological advancements in eye surgery in the last two decades, cataract is still recognized as the leading reason of blindness worldwide (WHO, 2019) (Figure 14).

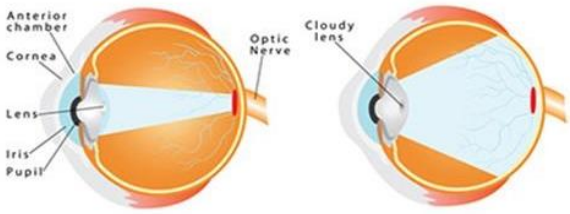


Figure 13: Normal (a) and cataractous (b) lens

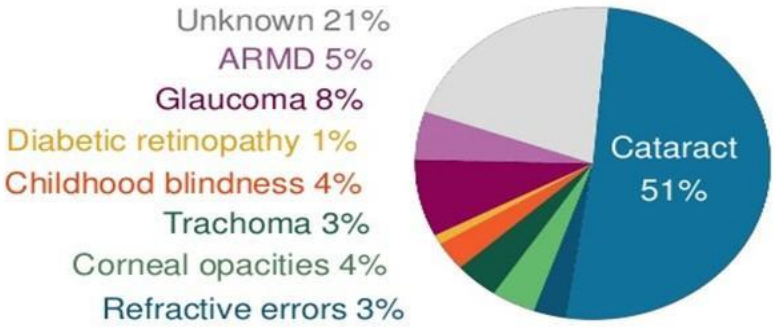


Figure 14: Distribution of blindness by cause. Source: WHO (2019)

Globally, among 7.79 billion people living in 2020, an estimated 49.1 million were blind (indicating a 42.8% increase from 34.4 million in 1990) (Rupert *et al*., 2020; GBD, 2021). Results from the Nigeria National Blindness and Visual Impairment Survey showed that the prevalence of blindness was 4.2 % and increases significantly with increasing age (National Survey of Blindness, 2008). How then can we fight this menace? Strategies must target human resource, infrastructural development, and effective disease control. At present, there is no definitive pharmacological therapy available for cataract and thus, the only solution for any patient with advanced cataract is surgery, which sometimes may result in serious complications and irreversible loss of vision. Moreover, there is a significant lack of access to surgery, especially in the developing world. After the surgery, the mobility of the lens is lost and correcting glasses are usually necessary. This will only increase the expense and the discomfort for the patient.

Biochemically, cataract in most cases is triggered by free radicals, which cause severe oxidative stress (Figure 15) thereby, leading to lens protein modifications (Thiagarajan and Manikandan, 2013). Since oxidative stress is the main mechanisms involved in the development of age-related cataract, it therefore suggests that antioxidant agents will be effective in ameliorating the condition. Another treatment modality is by targeting the blocking of enzymes such as aldose reductase which is involved in another biochemical reaction that leads to cataract.

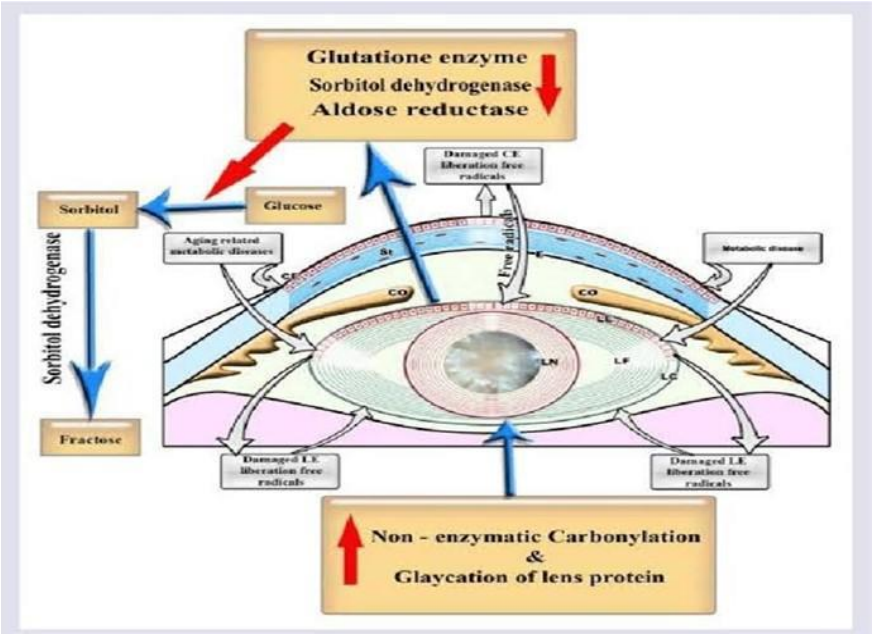


Figure 15: Aetiology of cataracts

Source: Wong *et al.*, (2019)

My Research Contributions

2.2.1. *Hydrocotyl bonariensis*

Hydrocotyl bonariensis also known as large-leaved pennywort is a creeping herbaceous plant (Figure 16) common on sea shores of tropical Africa and America. It is native to many countries including Nigeria and commonly referred to as "karo" among the Ijebu's in South West Nigeria. Mr Vice Chancellor sir, I developed interest in the anticataract efficacy of the plant in 2005 following my interaction with Professor Julius Bamikole, a Professor of Botany who informed me of how his aunt had successfully managed cataract by the application of the leaves of the plant. We developed a rat model of age related (senile) cataract by feeding weanling rats with high galactose diet and thereafter monitored the prophylactic and remediation effect of administration of aqueous leaves extract of *Hydrocotyl bonariensis* (Ajani *et al*., 2009).



Figure 16: *Hydrocotyl bonariensis*

The study demonstrated that *H. bonariensis* reduced cataract index significantly in pre-treated rats and also reduced cataract progression when administered after cataract onset. It also lowered the level of lens lipid peroxidation, increased the level/activities of lens endogenous antioxidants [reduced

glutathione (GSH), catalase and superoxide dismutase] and prevents protein insolubilization. These findings suggest that *Hydrocotyl bonariensis* will effectively protect against cataract onset and also reduced cataract progression. As a novel study in cataract management with plant extract, the outcome of this finding when presented at the 2009 Experimental Biology Conference held at San Diego, USA generated much interest. This was a motivation for me to carry out further studies on the plant so as to fully explore its potentials as anticataract agent.

In one of such studies, we compared the lens aldose reducatase inhibitory activities of the aqueous and organic extracts of *H. bonariensis* leaves and also investigated the mode of inhibition of its bioactive principles (Ajani *et al*., 2011). The study demonstrated that aqueous extract was the most active, suggesting that water is more effective as the extractive solvent. The mode of inhibition was shown in the study to be uncompetitive, suggesting that the phytoconstituents of the extract binds only to enzyme–substrate complex at locations aside the catalytic site of the enzyme leading to a modification of the enzyme structure. This invariably renders the inhibitor-binding position accessible. The implication of this is that inhibition of aldose reductase by *Hydrocotyl bonariencis* cannot be reversed by increase in substrate concentration.

In another study, my research team fractionated the *Hydrocotyl bonariencis* leaf extract and evaluated the aldose reductase and antioxidant activity of the fractionates *in vitro*. We thereafter characterized the isolated bioactive constituents of the active fraction and elucidated the structure by spectroscopic study and chemical shifts. The most active fraction yielded one (1) known compound, quercetin (Figure 17a) and an unknown anticataract compound, 3-O-β-D-glucopyranosyl-sitosterol (Figure 17b) (Ajani *et al*., 2017a). The study implies that *H. bonariensis* leaves can be exploited as a potential source of a new aldose reductase inhibitor and a phytotherapeutic agent against cataract.

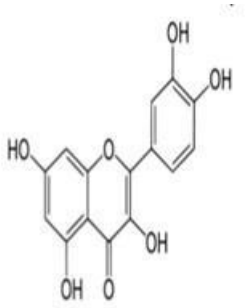


Figure 17a: Quercetin

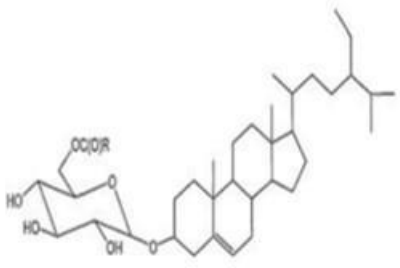


Figure 17b: 3-O-β-D-glucopyranosyl-sitosterol

2.2.2 *Lonchocarpus cyanescens* and *Chromolaena odorata*

Lonchocarpus cyanescens, (Figure 18) commonly known as "elu" (Yoruba) is a species of shrub from the family Fabaceae. *Chromolaena odorata*, also known as "Awolowo" or "Akintola" weed (Yoruba) is a perennial weedy shrub (Figure 19) native to the America and which has reached alarming proportions in Nigeria. Our study demonstrated that aqueous fraction of this plant was the most active and showed an uncompetitive inhibition of the aldose reductase whereas the crude methanol extract showed mixed inhibition (Ajani *et al*., 2016b and Ajani *et al*., 2017b).



Figure 18: ***Lonchocarpus cyanescens***



Figure 19: ***Chromolaena odorata***

The mixed type inhibition observed indicates the presence of an array of constituents in the crude extract which may act differently. All the fractions showed antioxidant capacities but this was also strongest with aqueous fractions. Phenol, flavonoids, tannins and phlobatannins were detected in the crude methanolic extract of *Lonchocarpus cyanescens* whereas in addition to these compounds, we detected alkaloid, saponin, terpenoid and quinones in *Chromolaena odorata*. These compounds were hypothesized to be responsible for the observed bioactivity. The study indicates that the phytochemical constituents of crude methanolic extract of *Lonchocarpus cyanescens* and *Chromolaena odorata* bind to the enzyme and also the enzyme substrate complex whereas the aqueous fraction phytoconstituent binds only to enzyme–substrate complex at locations aside the catalytic site of the enzyme. The result of these findings suggests that *Lonchocarpus cyanescens* and *Chromolaena odorata* are effective phytotherapy against cataract and that water is the best extractive solvent for the anticataractogenic principle. These studies support the ethnobotanical use of these plants for the treatment of cataract.

Other plants that we have demonstrated in our studies to be efficacious as anticataract agents are *Rauvolfia vomitoria* (asofeyeje) (Figure 20) and *Hyptis suaveolens* (Figure 21), known commonly as bush mint, bush tea, or "jogbo" (Yoruba). Both plants are considered as weed and are commonly found along roadsides and farmsteads in different parts of the world. *Rauvolfia vomitoria* has a history of being commonly used traditionally for the management of psychiatric conditions in Nigeria (Akpanabiatu *et al*. 2006). The extracts of the plant have been reported to have anti-inflammatory (Kato *et al*. 2009) and antipyretic (Amole *et al*., 2009) properties.



Figure 20: ***Rauvolfia vomitoria***



Figure 21: ***Hyptis suaveolens***

In the Northern part of Nigeria, a decoction of *Hyptis suaveolens* leaves is traditionally used for treating boils, eczema and diabetes mellitus. Crushed leaves are applied on the forehead to treat headaches. Infusion made from the leaves and the inflorescence are used as stimulant, carminative, diuretic, antipyretic and treatment of eyes related disorders (Danmalam, *et al*., 2009). Our studies demonstrated that both plants inhibit lens aldose reductase in an uncompetitive manner and also reduce lens free radicals. The highest aldose reductase inhibition and antioxidant capacities were obtained with aqueous fractions of both plants (Ajani *et al*., 2016 c and d). With these studies, we recommended both plants as potential sources for the identification of novel and effective AR inhibitors and as phytotherapeutic plants for cataract.

2.3 Phytotherapeutic Treatment of Reproductive Dysfunction

Mr Vice-Chancellor Sir, another area of research concern where my studies have found plants to be very effective is reproductive dysfunction. Human beings generally practice sexual reproduction. This is a form of reproduction which involves the fusion of the male gamete (sperm cells) and the female gamete (ova or egg cell) to form zygote. This form of reproduction takes place in stages:

1. **Sexual intercourse**: This is the stage at which semen is expelled into the female via male ejaculation with the aid of the penis';
2. **Conception/fertilization**: This describes the fusion of sperm with the egg and its attachment to the walls of the uterus;
3. **Pregnancy/gestation/gravidity**: At this stage, the developing embryo or foetus is carried within the female body;
4. **Parturition/giving birth/delivery**: This is a forceful expulsion of the foetus from the uterus of the mother after the gestation period.

Reproductive dysfunction is any disturbance in the normal functioning of a reproductive system. Diseases and conditions that affect the testes, epididymis, seminal vesicles, prostate, vas deferens and penis in males and the uterus, ovaries, vulva, cervix, fallopian tubes and vagina in females are included in this category. Common reproductive dysfunction includes sexual dysfunction, erectile

dysfunction, uterine fibroids, endometriosis, infertility, pregnancy related, menopause related, prepubescent and polycystic ovary.

My Research Contributions

2.3.1 *Cyperus esculentus*

My team demonstrated the efficacy of *Cyperus esculentus* tubers (tiger nut) in boosting sexual competence (Sabiu *et al*.,2016). Our study demonstrated restoration and improved sexual behaviour and libido in sexually dysfunction rats treated with tiger nuts. Tiger nuts - treated sexually dysfunction rats showed increase frequencies of mount (the number of mounts without intromission from the time of introduction of the female until ejaculation), intromission frequency (the number of intromissions from the time of introduction of the female until ejaculation), ejaculation and ejaculatory latency (time lag between the first intromission and ejaculation). In addition, the latencies of mount, intromission, and post-ejaculation were significantly reduced. Testicular activities of alkaline phosphatase, acid phosphatase, lactate dehydrogenase and the concentrations of protein, cholesterol, glycogen, testosterone, luteinizing hormone, follicle stimulating hormone and testes: body weight were all restored in rats treated with the extract. Using GC-MS chromatogram, we identified 25 bioactive principles in the tiger nuts (Figure 22) and we opined that the observed aphrodisiac properties were due to the activities of some of these phytoconstituents. Our study thus suggests that men with low sexual desire, penile erection problem, prolong or early release of sperm will have enhanced activities by regularly consuming tiger nuts.

In another study, we investigated the toxicity implication of the consumption of this tuber as a fertility enhancing agent. We demonstrated in our study that the extract elicited no treatment-related toxicity or mortality. This confirmed that it is unlikely to be toxic to the investigated organs and thus indicates that the use of tiger nuts as an aphrodisiac or as a base for the development of aphrodisiac drug is safe and poses no toxicity threat (Ajani *et al*., 2016a).

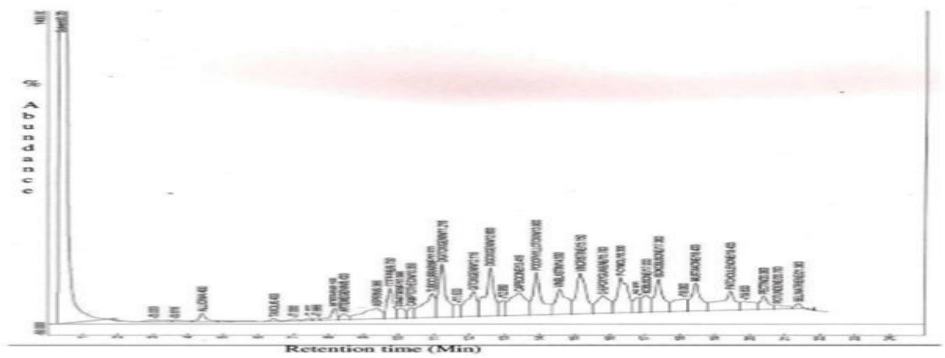


Figure 22: GC-MS chromatogram of crude aqueous extract of *Cyperus esculentus*
Source: Sabiu *et al*., (2016)

Our investigation of the biochemical mechanism of action of standardized fraction of tiger nuts showed that it has a potent membrane stabilization potential. We observed a significant improvement on the testes-body weight ratio, quality and viability of sperm cells as well as testicular concentrations of proteins, cholesterol, glycogen, testosterone, follicle stimulating hormone and luteinizing hormone. Consequent upon the significant androgenic and membrane stabilization activities of *Cyperus esculentus* demonstrated in the study, we concluded that the plant is endowed with phytotherapeutic constituents that justifies its use as aphrodisiac (Sabiu *et al*., 2018b).

2.3.2 *Nigella sativa* (Black seed)

Nigella sativa (Figure 23) is an annual flowering plant in the family, Ranunculaceae, native to the Indian Subcontinent and West Asia. *N. sativa* and its seed are variously called black caraway, black seed, black cumin, nigella, nutmeg flower and Roman coriander. It is widely used in Asian traditional medicine and some part of Africa where it is traditionally applied as preventive supplement against numerous diseases including inflammation, hypertension, infertility, diabetes and depression. We investigated the efficacy of the seed in preventing reproductive dysfunction in rats exposed to environmental reproductive dysfunction agents (battery leachate).



Figure 23: ***Nigella sativa***

We used signalling molecule (acetylcholinesterase, AChE) and purinergic cascade markers (ATP, ADP and AMP) to investigate the effect of dietary supplementation from black seed flour (D-BSF) on male reproductive disorder following exposure to environmental mixed metals in experimental animal model (Akintunde *et al*., 2018). We observed that treatment with D-BSF inhibited the upsurge in lipid peroxidation, ATP, ADP and AMP as well as adenosine deaminase, and AChE hydrolysis activities in leachate- exposed rats' testes. We opined, based on the results from our study that the possible mechanisms by which D-BSF elicit spermatogenesis could be through inhibition of testicular lipid peroxidation, nucleotides hydrolysis and modulation of purinergic metabolizing enzymes. We showed the presence of gallic acid, catechin, chlorogenic acid, caffeic acid, orientin, rutin, quercitrin, quercetin and luteolin in the black seed. Findings from our study indicate that people predisposed to

reproductive disorder by reason of been exposed to battery leachate may enjoy normal sexual function if their diet is well supplemented with *Nigella sativa* seed. When we carried out further investigations, we showed that leachate intoxication inhibits testicular steroidogenic enzymes activities, declined follicle stimulating hormone (FSH), leutenising hormone (LH) and testosterone levels whereas diet supplemented with BSF normalized these parameters in intoxicated rats and also prevented the alterations associated with spermatogenesis (Akintunde *et al*., 2019). Based on findings from our studies, we concluded that diet supplemented with black seed improves sexual performance via increase in the hormones of spermatogenesis and protection against free radical damage. We thus, recommended based on the study, that black seed flower may be incorporated in diet to reverse reproductive disorder and that black seed may be used in developing pharmacological compound against reproductive dysfunction.

2.3.3 *Tamarindus indica*

Tamarindus indica Linn commonly called Tamarind or "*Ajagbon*" (Yoruba) is a leguminous tree (family Fabaceae) bearing edible fruit that is indigenous to tropical Africa. The tamarind tree produces pod-like fruits (Figure 24) containing brown, edible pulp used in cuisines around the world. The pulp is also used in traditional medicine and as a metal polish.



Figure 24: *Tamarindus indica*

We investigated the prophylactic and ameliorative effect of ethanolic fruit pulp extract of *T. indica* on sodium fluoride-induced animal model of reproductive dysfunction and observed that the extract improved sperm count and restore sperm motility, morphology and viability. Follicle stimulating hormone, progesterone, testosterone and oestrogen also compared favourably with the control. The histopathological studies of the testes of rats pre-treated with the extract showed the presence of large interstitial space in the seminiferous tubules with a relatively normal histomorphological representation. Our study clearly demonstrated that infertile couples will benefit from regular consumption of *Tamarindus indica* fruit pulp in the management of infertility (Ajani and Usman, 2020).

Our study on *Phyllanthus amarus (*Eyin Olobe), a pantropical weed that grows well in moist, shady and sunny places, (Ogunlabi *et al*., 2015) demonstrated that the leaves of the plant stalls dyslipidaemia and uterine toxicity in monosodium glutamate administered rats. We also observed that the extract preserved the final body weights, uterine weight ratio and uterine histoarchitecture. This finding indicates the probable benefits of *Phyllanthus amarus* leaves in uterine fibroid. Preliminary results from an on-going study have also shown the efficacy of African wall nut (awusa) in the prevention and reversal of uterine fibroid. We are also investigating the efficacy of oyster mushrooms in treating uterine fibroid. Our choice of investigating these plants is based on our previous ethnobotanical survey which showed that the plants are widely used in Nigerian Traditional medicine practice to treat uterine fibroid but without sufficient scientific data.

2.4 Phytotherapeutic Treatment of Stomach Ulcer

Ulcer is an open sore of the biological membrane characterized by sloughing of inflamed dead tissue. More specifically, it could either occur as a lesion on the surface of the skin or a mucous membrane with significant superficial loss of tissue. Although, ulcers may be encountered at almost any part of the body, they are mostly found on the skin of the lower extremities and in the gastrointestinal tract. Peptic ulcer (PU), the most prevalent ulcer is erosion of lining of either the stomach or duodenum. The biochemical mechanism of occurrence of peptic ulcer disease (PUD) has been attributed to the imbalance between gastric mucosal protective and destructive factors. Under normal conditions, a physiologic balance exists between gastric acid secretion and mucosal defence. However, when there is disequilibrium between offensive (acid, pepsin, and *Helicobacter pylori*) and defensive factors (mucin, prostaglandin, bicarbonate, nitric oxide, and growth factors), the pathophysiological features of stomach ulcer become evident (Wenji *et al*., 2020). Although patients with SU have normal or diminished acid production, yet ulcers may occur even in complete absence of acid. In some cases, stomach ulcer can be life threatening with symptoms like bloody stool, severe abdominal pain, and cramps coupled with blood vomiting. Drugs that may be used against ulcers are proton pump inhibitors (PPI) that block acid-producing cells, H_2-receptor antagonists which prevent the stomach from producing excess acid, antacids and drugs that protect the stomach lining. A number of such drugs are available but clinical evaluation of these drugs indicates high relapse rate, side effects and drug interactions. These complications necessitated the development of new antiulcer drugs and the search for novel molecules from the drug basket of nature, which is plant.

My Research Contribution

2.4.1. *Parkia biglobossa*

Parkia biglobossa (West African locust bean) is an arboreous West African plant known for its nutritional and medicinal properties and commonly referred to in Yoruba as “Igba”. The fermented

seed product is known as “iru”. Mr Vice Chancellor sir, my interest in antiulcerative efficacy of *Paria biglobossa* arose from some personal experiences growing up as a young farmer in the early 80’s. While in the farm then, whenever I complained of stomach upset (which in most cases were feigned out of the desire to escape farm work), my father will cut the bark of *Parkia biglobossa* tree and instruct me to chew it. Years later as a young lecturer, I developed an animal model of stomach ulcer with the administration of indomethacin. The study showed that administration of *P. biglobossa* stem bark extract to the ulcerative rats significantly reduced ulcer score and Paul’s ulcer index in a dose dependent manner (Ajani *et al*., 2003a; Solahdeen *et al*., 2006). The extract also decreased gastric acid secretion and increased the pH value of the stomach. Administration of the extract does not compromise the biochemical markers of liver, kidney and cardiac functions (Ajani *et al*., 2003b). Based on findings from these studies, we recommend the use of stem bark of *Parkia biglobossa* as a safe phytotherapy for the treatment of stomach ulcer.

2.4.2 *Langenaria breviflora*

Lagenaria breviflora, (Figure 25) commonly called ‘Tagiri’ in the South-Western part of Nigeria, is an important plant belonging to the family, Cucurbitaceae (Yasuyuki, *et al*., 2005; Oridupa *et al*., 2011). The potency of its fruits against a wide range of gastrointestinal disorders and measles in experimental animal models has been documented (Ajayi *et al* 2002).



Figure 25: *Lagenaria brevifolia*

We demonstrated that *Lagenaria brevifolia* leaves attenuate the increase in ulcer index, gastric acidity, malondialdehyde level and pepsin activity in indomethacin-induced stomach ulcer (Ajani *et al*., 2015). The study also showed that it attenuated the reduced activity of catalase, stomach pH and mucin content in the ulcerated rats. These findings are indicative of gastroprotective and antioxidative potentials of the plant and imply that *L. breviflora* could be harnessed as preventive therapy for gastric ulcer related disorders. In a previous study, we showed that the leaves of *L. breviflora* protect against liver damage (Ajani *et al*., 2014). The overall findings from these studies suggest that *L. breviflora* have electron donating potential and consequently halts free radical chain reactions. This could be the

basis for its gastroprotective properties and justifies its use as a safe and effective phytotherapeutic agent for the treatment of gastric ulcer.

2.4.3 *Spondias mombin* Linn and *Ficus exasperata* Valh

Spondias mombin (SM) commonly known as "Iyeye" (Yoruba) is a fructiferous tree in the Family Anacardiaceae. The plant (Figure 26) grows in rain forests and coastal areas. It is reportedly used in folk medicine to cure many diseases (Ayoka *et al*., 2008, Maduka *et al*., 2014). *Ficus exasperata* Valh (Figure 27), commonly known as "Epin" (Yoruba) or 'sand paper tree' belong to Moraceae Family. The South-Western people of Nigeria use the decoction and infusion of the plant for the management, control and treatment of hypertension, diabetes mellitus and cardiovascular dysfunction (Odiba *et al*., 2012). Leaves of *Ficus exasperata* cooked with bananas are eaten for the treatment of gonorrhea (Anowi *et al*., 2012).



Figure 26: *Spondias mombin*



Figure 27: *Ficus exasperata*

Our study demonstrated modulation of ulcer index, gastric volume, malondialdehyde level, and pepsin activity in ulcerated rats treated with the plants (Sabiu *et al*. 2015a). Extracts from both plants increased the activity of superoxide dismutase, stomach pH and mucin content in ulcerated rats. Findings from this study are indicative of gastroprotective and antioxidative potentials of the plants and this is also evident in the degree of percentage inhibition against ulceration. Our investigation further indicates that the phytoconstituents of the plants acts by scavenging free radicals and regulate mucosal membrane permeability, thereby countering the effect of indomethacin on gastric acid secretion.

2.4.4 *Gossypium barbadense* L

Gossypium barbadense L. (Malvaceae) is a perennial shrub, 1–3 m high (Figure 28), native to South America and now widely cultivated in the tropics with significant presence in Nigeria. The plant is commonly known as "cotton" or in Yoruba as "owu" (Brubaker *et al*., 1999). Our study demonstrated that the indomethacin-mediated elevations in the ulcer index, gastric volume, pepsin activity and

mucosal level of malondialdehyde were dose dependently attenuated in rats treated with extract from the plant. The extract also significantly modulated and improved the stomach pH, mucin content, glutathione (reduced) as well as gastric activities of superoxide dismutase and catalase in the ulcerated rats (Sabiu *et al*., 2017d).



Figure 28: ***Gossypium barbadense***

The observed effects of the extract are suggestive of the capability of the plant to prevent mucosal damage and preserve gastric functions. GC-MS analytical chromatogram revealed the presence of 19 phytoconstituents earlier hypothesized to have gastroprotective activities. Based on our investigations and findings, we also proposed that the antiulcerative effect of *Gossypium barbadense* are via antioxidative and proton pump inhibition (Figure 29).

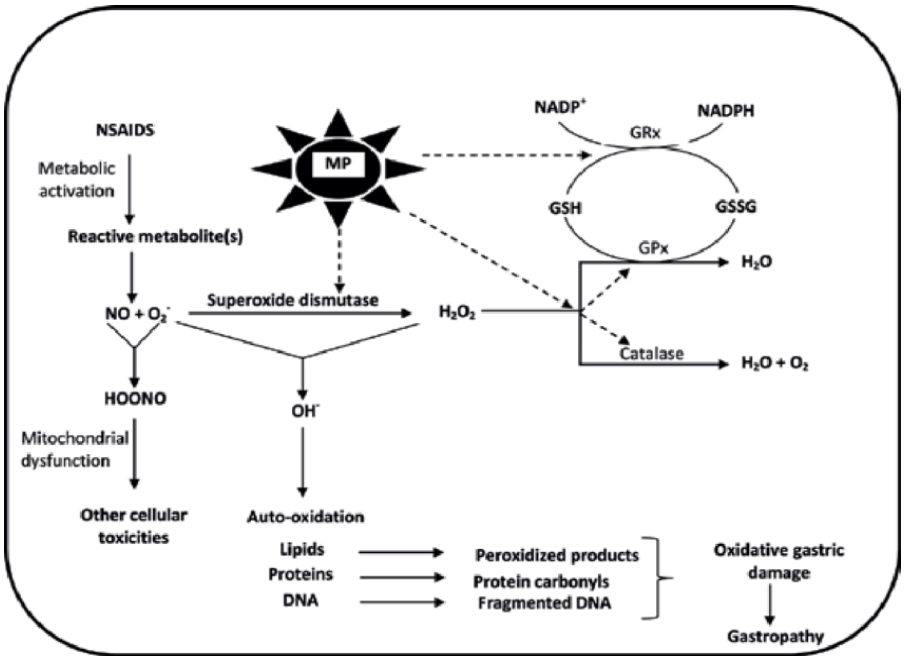


Figure 29: Probable mechanism of antioxidative and gastroprotective capabilities of medicinal plants. The dotted arrows represent sites of induction and optimization by the plants that consequently promote scavenging of O^{2-} and OH^{-}.

Source: Sabiu *et al*., (2018c)

2.5 Phytotherapy and Organ Toxicities

Although all organ systems can be targets of toxic exposures, the liver and kidneys are common organs primarily affected by chemical toxicity. Drug damage to the liver or kidneys can be particularly catastrophic as these organs are needed for the proper "cleaning" of the body. If they are compromised, this leads to further accumulation of potentially toxic metabolites which can do further damage to organs in the body. Hepatotoxicity is a term that refers to chemical-driven liver damage. In addition to certain medicinal agents, other chemicals used in laboratory and industries, and herbal remedies can induce hepatotoxicity (Akanji *et al*., 2008, Pandit *et al*., 2012).). These chemicals that cause liver injury are generally referred to as hepatotoxins.

We carried out investigation on the protective role of some medicinal plants against chemical induced liver injury. In an ethnobotanical survey of Nigerian Traditional Medicine, we observed the use of *Eucalyptus obliqua* L.Her. (Messmate stringy bark), an ornamental plant (Figure 30) both as antimalarial and in the treatment of inflammation and liver disorders. We investigated the hepatoprotective effect of *E. obliqua* leaves extract in CCl_4-perturbed hepatotoxicity (Sabiu *et al*., 2017b). Our study demonstrated that the leaves normalized all the biomarkers of hepatic functions altered with administration of CCl_4 in a dose-dependent manner. The extract also improved the activities of superoxide dismutase, catalase, glutathione reductase and glutathione peroxidase as well as total protein, albumin and reduced glutathione concentrations in the hepatotoxic animals.



Figure 30: ***Eucalyptus obliqua***

We attributed the observed hepatoprotective effect to the isolated phytochemical constituents of the leaves as revealed by GC-MS analysis. Our *in vitro* antioxidant potential and *in vivo* toxicological investigation of the leaf extract via acute and 28-day once daily treatments in Wistar rats, showed that the plant is safe. Our evaluation of the sub-chronic administration showed that there was no alteration of the biochemical and haematological indices of the treated subjects (Sabiu *et al*., 2017c and Sabiu *et al*., 2017d). Based on these findings, we recommended aqueous leaf extract of *E. obliqua* as a non-toxic and practically safe (at the investigated doses) antihepatotoxic agent.

Citrullus lanatus (family Cucurbitaceae) also known as water melon or "ẹ̀gúsí agbè" (Figure 31 a and b) is an annual plant which originated from the southern part of Africa. The antioxidant activities, anti-inflammatory effects and several essential nutrients of *C. lanatus* fruits have been previously reported (Abdelwahab *et al*., 2011; Huang *et al*., 2016).



Figure 31a: *Citrullus lanatus*

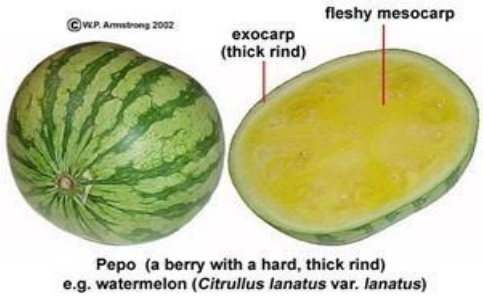


Figure 31 b: *Citrullus lanatus* rind

The juice or pulp of *C. lanatus* is consumed by people, while the rind and the seeds are usually discarded as agro-wastes. We demonstrated the antioxidative efficacy of the mesocarp rind of *C. lanatus* by the reversal of the hepatic oxidative damage in CCl_4 treated albino rats (Bamisaye *et al*., 2017b). The implication of our findings is that the mesocarp rind of *C. lanatus* should not be treated as waste when taking water melon because in addition to its phytotherapeutic effect, it will also protect the liver against toxic damage.

Corn silks (*Stigma maydis*) is a plant part often regarded as waste but which has been widely reported as useful in traditional medicine. It is an elongated stigma from the female flowers of maize which look like a tuft of hairs (Figure 32). Corn silk has long been used traditionally by the Chinese and Native Americans to treat many diseases.



Figure 32: Corn silk

Many traditional healers have also reported its potential healthcare benefits as anti-fatigue, anti-depressant, anti-diabetic, and as hypoglycaemic agent as well as its efficacy in the treatment of cystitis, edema, kidney stones, prostate disorder, urinary infections, bedwetting and obesity (Farsi *et*

al., 2008; Jianyou *et al*., 2009; Zhao *et al*., 2012). Despite the acclaimed phytotherapeutic attributes of *Stigma maydis* in folkloric medicine, there is paucity of information on its toxicity profile. Our study demonstrated that the extract did not alter red blood cells, haematocrit, haemoglobin, mean corpuscular volume, mean corpuscular haemoglobin concentration, and mean platelet volume at all the tested doses (Sabiu *et al*., 2015a). Our findings are indicative of non-haematotoxic potential of the extract. Based on our findings, we recommended that corn silks can be considered as a safe phytotherapeutic agent at the investigated doses.

Ethnobotanical survey of Nigerian Traditional Medicine indicates the use of *Spondias mombin* L. ("iyeye") leaf as excellent analgesic and anti-inflammatory remedy against stomach ache associated with child birth in women. Although we had earlier demonstrated its therapeutic significance as antiulcerogenic agent in one of our studies (Sabiu *et al*., 2015b), we further investigated the effect of 'iyeye' on acetaminophen-mediated oxidative onslaught in rats' hepatocytes (Sabiu *et al*., 2017c). Our study revealed that the extract dose-dependently scavenged free radicals. It also normalized the activities of liver enzymes and reversed the acetaminophen-enhanced reduction in the specific activities of antioxidative enzymes as well as attenuated the observed elevated concentrations of autoxidized products and rived DNA. Our findings suggest that 'iyeye' is capable of ameliorating acetaminophen-induced hepatic damage via enhancement of antioxidant defence systems.
Silymarin (Figure 33) is a standardized constituent of the milk thistle plant (*Silybum marianum*) which also contains silybin, silybinin, silydianin and silychristin.

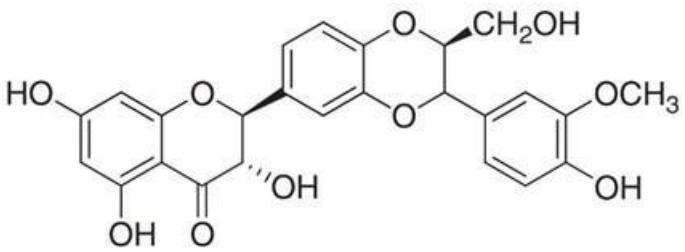


Figure 33: Silymarin

The seeds of *Silybum marianum* have been reported in ethnobotanical studies to be used for the treatment of liver and gall bladder disorders, including hepatitis, cirrhosis and jaundice. The seeds have also been used in traditional medicine to protect the liver against poisoning from chemicals, environmental toxins, snake bites, insect stings, mushroom poisoning and alcohol. We demonstrated in our study that significantly altered activities of liver function biomarkers, as well as levels of thiobarbituric acid reactive substances and antioxidants enzyme activities were normalized following

administration of silymarin (Sahiu *et al*., 2015c). These findings are indicative of hepatoprotective attributes of milk thistle plant, suggesting that the plant can be exploited in developing a remedy against liver damage.

Traditional medicine practitioners in Nigeria use decoction of *Cochlospermum planchonii* roots otherwise known as 'Gbehutu' or 'Feru' (Yoruba), (Figure 34) for the treatment of gonorrhoea and jaundice. Our study revealed that the leaves of *C. planchonii* contain alkaloids, cardenolides, cardiac glycosides, flavonoids, phenolics, saponnins, terpenoids and tannins. We demonstrated that the plant caused a dose dependent reduction of the serum electrolyte concentrations but increased bilirubin and blood creatinine concentrations (Bamisaye *et al*., 2017a).



Figure 34: *Cochlospermum planchonii*

When we carried out histopathological examination of the liver and kidney following treatment with extract of *C planchonii*, we observed a dose dependent dissociation of hepatic cords in the hepatic parenchyma of the liver with few foci of nephrosis (coagulative tubular necrosis) in their kidney (Figure 35 a and b). The implication of our study is that although *C. planchonii* may have the acclaimed medicinal properties but its administration may also predispose to liver and kidney toxicity at sub-acute administration.

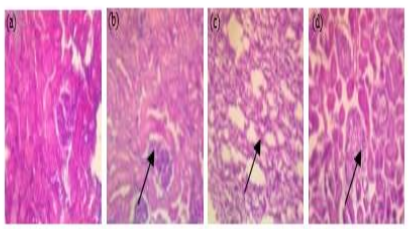


Figure 35a: Photomicrographs of kidney (400X)

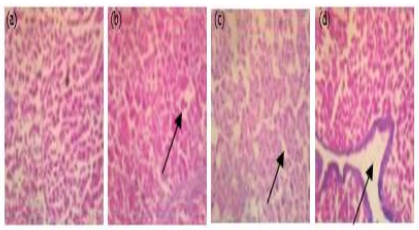


Figure 35b: Photomicrographs of liver (400X)

Mr Vice Chancellor sir, another growing concern in pharmacology is the toxicity of synthetic drugs. This is a common and significant health problem, yet it often goes undetected. Drug toxicity refers to the level of damage that a chemical compound can cause to an organism. Although drug toxicity usually occurs at doses that exceeds the therapeutic efficacy of a drug, our study of some routinely

used antimalarial drugs such as P- alaxin (Kareem *et al*., 2014), chloroquine (Ajani *et al*., 2004, 2009, 2013a, b), artemisinin combination (Ajani *et al*., 2014b) and phenobarbitone (Alabi *et al*., 2015) also demonstrated that toxicity and therapeutic effects may co-exist. We therefore investigated the phytotherapeutic benefit of some plants if administered into individuals placed on therapeutic drugs regimen.

Our study of *Garcina cola* (bitter cola) demonstrated that the plant is capable of protecting against amodiaquine induced hepatic damage (Ajani *et al*, 2007). The extract normalized the relative liver weight and observed liver mitochondria lipid peroxidation. What this suggests is that *Garcinia cola* is effective in preventing liver toxicity that may be associated with prophylactic administration of amodiaquine. We however did not observe similar cardioprotective effect with *Garcinia cola* (Ajani *et al*., 2008) in amodiaquine administered rats. The findings from this study indicated that people who may be pre-disposed to liver dysfunction through prophylactic use of amodiaquine will benefit from taking bitter cola but that bitter cola intake may not prevent pre-disposition to cardiac toxicity in prophylactic use of amodiaquine. My research team also observed similar protective effect with *Loranthus micranthus* Linn (African mistletoe) (Ajani *et al*., 2014c).

In another study, we investigated the protective effect of *Allium sativum* (garlic) in monosodium glutamate induced toxicity. Monosodium glutamate (MSG) is the sodium salt of glutamic acid, one of the most abundant naturally occurring non-essential amino acids. Trade names of monosodium glutamate include Aji-No-Moto, Vedan and Ve-Tsin. Although MSG was classified by the United States Food and Drug Administration and the European Union as a food additive, there are controversies on its tissue toxicity. We investigated the cardio toxicity effect of MSG and the protective effect of garlic. Findings from our study suggest that MSG intake will cause hyperlipidaemia and we therefore recommend caution in its usage. Again, our study showed that garlic will protect against MSG induced lipid alterations (Ogunlabi *et al.*, 2014).

My research team further compared the effect of monosodium glutamate-containing flavour enhancer (Maggi) with that of Vedan and locally fermented locust bean seed (iru). The three agents were administered to different groups of rats orally for 32 days after which we evaluated the effects on the liver and kidney function (Alabi *et al*., 2019). Results from our study showed that Vedan, fermented locust bean (Iru) and Maggi cubes consumed at 600 mg/Kg poses no adverse effect on the liver and kidney functions, generated no reactive species, increased enzymic antioxidant system and does not increase cholesterol deposition in the liver and kidney. The implication of our study is that these flavour enhancers are safe for consumption at the recommended dosages for use in cooking. However,

owing to the reported cardiac toxicity effect of MSG that we had earlier reported (Ogunlabi *et al*., 2014) at 200 mg/kg, we recommended that this flavour enhancer should be used with caution.

2.6 Plants as Functional Foods in Human Nutritional Diseases

The process by which food is obtained and thereafter used for obtaining energy, growth and body repair is generally referred to as nutrition. Mr Vice Chancellor sir, Nigeria today is a nation that is suffering from poverty, food insecurity and poor understanding of nutrition and dietary practices. We are confronted with increasing deaths and disabilities not only among children, but also among adults and these can be attributed largely to poor nutrition. Good nutrition has become a necessity in order to ensure that children develop physically and mentally, a requirement for normal human biological development.

A study by Uddin *et al*, (2010) and Nyaradi *et al*., (2013) reported that optimal brain development is associated with better academic ability and that cognitive development in children is synergistically enhanced by good nutrition. The narrative that best supports this assertion is the Biblical report of the test undergone by Daniel and his friends while in Babylon. For these young men who were slaves in the land to be brought under the services of the Babylonian king as advisers, they first must pass a test which includes eating the king's food for three years. This is supposed to make them fit to appear before the king. Daniel and his friends however requested that they be fed with vegetables and water. This does not seem to go well with the king's steward but he reluctantly agreed to allow Daniel and his friends try out their diet for just 10 days. Amazingly, few days later, it was observed that when compared to the king's men, Daniel and his friends appeared healthier- "**and *at the end of ten days, their countenances appeared fairer and fatter in flesh than all the children which did eat the portion of the king's meat*" (Daniel 1:15).** At the end of three years that Daniel and his friends had continued to live on vegetables and water, they were brought to be tested by the king and the king spoke with them to test their level of intelligence. Amazingly, what the king observed was far different from what one would have expected. The Bible reported in Daniel 1: 19-20 that: **"and the king spoke with them, and among all of them, none was found like Daniel, Hananiah, Mishael, and Azariah. Therefore, they stood before the king. And in every matter of wisdom and understanding about which the king inquired of them, he found them ten times better than all the magicians and enchanters that were in all his kingdom."**

Macronutrients (except water and fibre) are needed to provide energy. Carbohydrate, protein and fats are essential for growth, reproduction, immunity and healing (NGC, 2018) and taking less of these nutrients contribute to a number of major illnesses, such as heart disease, type 2 diabetes, cancer, and

osteoporosis. Japanese sailors (whose diets consisted almost entirely of white rice), developed *beriberi* (a disease that results in heart problems and paralysis), but British sailors and Japanese naval officers did not, because their food contained vegetables and meat which were able to prevent the disease. Similarly, a report observed that animals fed diet of white rice developed the symptoms of *beriberi* but remained healthy when fed unprocessed brown rice with the outer bran intact. Over two decades later, nutritionists learnt that the outer rice bran (which we still throw away as waste) contains vitamin B1, also known as thiamine (Oladiji, 2012). These observations suggest that food can cure diseases.

Mr Vice Chancellor sir, vegetables, fruits and nuts have emerged as food items which could address multiple problems at both ends of the socioeconomic spectrum. They can provide the 'micronutrients' usually deficient in the diets of poor communities and at the same time also provide the 'phytonutrients' which help to combat chronic diseases. These groups of foods, which in addition to their nutritional properties present additional benefits for health, are called functional foods. Functional foods are therefore any foods that have positive impact on an individual's health, physical performance, or state of mind, in addition to their nutritious value. Researchers are of the opinion that bioavailability of micronutrients from plant foods can be greatly assured if along with some other measures, there is improved cooking and processing procedures.

Child malnutrition includes under nutrition and over nutrition, both of which are diseases caused by inadequate nutrition. Undernutrition causes children to have less energy and less interest for learning. It also affects physical growth and maturation, thus affecting growth rate, body weight and height. Overnutrition on the other hand is a condition whereby the individual gets too much energy or too much of a given nutrient over time, causing obesity, heart disease, or nutrient toxicity. The most common form of childhood malnutrition is protein energy malnutrition (PEM). PEM is caused by a deficient intake of energy and usually protein. Secondary PEM can result from other complications like AIDS, chronic kidney failure, inflammatory bowel disease and other illnesses that impair the body's ability to absorb and / or utilize nutrients, or compensate for nutrient loss. The condition is usually almost always aggravated by repeated episodes of diarrhoea and other infections. The more severe ones are marasmus (Figure 36) and kwashiorkor (Figure 37).



Figure 36: Marasmus



Figure 37: Kwashiorkor

2.6.1 My Research Contributions

2.6.1.1 Protein Energy Malnutrition

We investigated the effect of protein deficiency on Ca^{2+}-ATPase activities and the modulation effect of *Moringa oleifera* (Nurain *et al*., 2013). Rats fed with protein deficient diet supplemented with *Moringa oleifera* leaves were compared with rats fed with protein deficient diet supplemented with fish. The results of our study indicated that *Moringa oleifera* leaf is a good modulator of the activity of Ca^{2+}ATPase. Our study showed that, intake of *Moringa oleifera* powdered leaves improved intracellular Ca^{2+} level which is an essential element for normal cellular activities. As a follow up to this study, we recruited malnourished primary school pupils and supplied them either with tea or *Moringa oliefera* in addition to their regular diet. Our study demonstrated that supplementation with *Moringa oleifera* leaves improves body mass index and some other biochemical and haematological indices of malnutrition (Nurain *et al*., 2015). We therefore recommended that *Moringa olifera* may be included as supplement in the diet of children particularly in the rural communities in order to alleviate the biochemical effect of inadequate nutrition.

We also studied the effects of fluoride nutrition on lipid peroxidation (LP) and antioxidant enzymes in the brain regions of protein undernourished (PU) and well-fed (WF) rats (Adebayo *et al*., 2013). Our study demonstrated that the body and brain weights of PU rats as well as rats given fluoride (both WF and PU) were reduced. We also observed in addition, increased lipid peroxidation in the cerebrum and cerebellum of PU rats. In another study, we observed a similar repression in antioxidant enzymes and an increase in lipid peroxidation during aging (Oyefuga *et al*., 2012) suggesting that ageing contributes to increased oxidative stress. We, however, demonstrated in the later study, that long term consumption of honey protects against this oxidative insult. By implication, we recommend that excessive fluoride intake should be avoided particularly in undernourished individuals so as to prevent brain oxidative stress and that consumption of honey should be encouraged as a protective agent against oxidative damage.

2.6.1.2 Iodine Deficiencies

Iodine is an essential mineral used by the thyroid gland to make thyroid hormones that control many functions in the body including growth and development. However, because human beings do not produce iodine, it needs to be supplied in the diet. Low or inadequate iodine intake will result in a series of functional and developmental abnormalities including hypothyroidism, endemic goiter and cretinism, endemic mental retardation, decreased fertility, increased prenatal death, and infant mortality. Major international efforts are directed at reducing the problem, mainly through the use of iodized salt and supplements. However, salt iodization alone may not be sufficient to assure adequate iodine nutrition, hence we evaluated vegetables, fruits and nuts as a good dietary source of iodine.

Our findings revealed that *Amaranthus hubridus* (Tete abalaye), *Ocimum canum* (Efirin wewe), *Chordorins spp.* (Ewedu), *Veronia amydalina* (bitter leaf or ewuro) and *Teleferia occidentalis* (ugwu) have high iodine content and are better sources of dietary iodine compared with other vegetables investigated (Salau *et al*., 2011). When we again compared the iodine content of different tubers and cereals, our study showed that among the tubers, *Ipomea batata* (sweet potatoes, white variety) had the highest iodine contents while *Glycine soja* (soybean) was the richest in iodine among the cereals (Salau *et al*., 2008). These findings indicate that some of the locally consumed vegetables, tubers and cereals, if well selected may be exploited as dietary sources to meet the daily iodine requirement. We however, further discovered that to retain the iodine content of these vegetables, care must be taken in selecting better cooking strategies. Our study demonstrated that when compared with some other processing techniques, fermentation leads to the greatest loss in iodine content of vegetables and tubers (Salau *et al*., 2010). The reduction could be attributed to leaking of iodine into the soaking water and also possibly by evaporation especially during drying. Our study also showed that boiling significantly reduced iodine content when compared with roasting.

3.0 WHAT NEXT?

Conclusion

Mr Vice Chancellor sir, many countries with good health care system are able to attain this feat because they incorporate Traditional Medical Practice into their health care practices. This lecture has drawn our attention to the fact that Nigeria also has the potential to join this league of countries if we make deliberate effort to maximize the medicinal potentials of many floras that exist in our nation. Mr Vice Chancellor sir, distinguished ladies and gentlemen, I wish to submit here that for Nigeria to truly eliminate a number of diseases by the year 2030 and ensure healthy lives through promotion of well-being for all at all ages, achieving universal health coverage (UHC), addressing health emergencies and promoting healthier populations (Sustainable Development Goal 3), closer

attention **must be paid to phytopharmacology**. Mr. Vice Chancellor Sir, *quod erat demonstradum* (Q.E.D)

Recommendations

General Public

1. Traditionally, plants are generally used in medical practices largely in the crude forms which are prepared in different herbal formulations such as tinctures, elixirs, poultices, powders, etc. To guarantee safety and minimize toxicity, users of herbal formulations should ensure that their choice of plants are guided by scientific validation through standardization, evaluation of purity and demonstration of its efficacy in animal model of diseases.
2. We often underestimate the toxicity of natural products believing that once it is natural, then it is safe. It is important to reiterate that it is the quantity that distinguishes between therapy and toxicity. Therefore, the use of herbal products must be guided by dosage.

Government

3. One of the main policies of the Nigeria Traditional Medicine practice is to develop mechanism for incorporating traditional medicine into the health care delivery system. However, since 2007 when this policy was formulated, no serious measure has been put in place for its realization. It is important to put this policy into effect now. This also should be done in line with patient's choice and expectations and consistent with evidence on quality, safety and effectiveness.
4. The Nigeria Government in 1989 established the National Institute for Pharmaceutical Research and Development, Idu, Abuja. The institute's mandate includes undertaking research and development work on drugs and to also serve as a reference centre for research on biopharmaceutics. It is however unfortunate that the Institute has not made the much-expected impact in natural product development. My personal experience with the Institute showed that if well supported, it has the capacity to translate Nigeria to a country that will not just be a dumping ground for less potent drugs but rather be in a better position to develop more potent drugs from our endowed natural resources. I therefore recommend that the Research Institute should be mandated and empowered to deliver on its mandate and that the Institute should serve as a coordinating centre for researchers who are working in various drug development fields but lack resources to follow up their investigations.

5. Researches in natural products development requires advanced analytical techniques. These techniques will make it possible to elucidate the molecular structures of complex natural products and make available valuable lead compounds and new drugs. The cost of these technique is enormous but that is where innovative science is. My appeal is to the Kwara State Government through its relevant agencies to facilitate the development of these techniques in Kwara State University through provision of Bioinformatics and Computational Biology Laboratory equipped with modern drug design and development equipment such as Computers equipped with necessary software's such as Scaffold Hunter software, PASS software, SPIDER software etc. (for Molecular Modelling, virtual screening and Docking, Database searching and computer-aided molecular designs). Other relevant equipment will include Nuclear Magnetic Resonance Spectroscopy, High Performance Liquid Chromatography, computational algorithms, DNA barcoding for genotyping, Mass-Spectrometry etc. This will serve to make KWASU a reference University in Medicinal plant research and development.
6. Many plants that are of medicinal importance are already going into extinction as a result of industrial development. Strategies should be put in place to manage and conserve Nigeria's indigenous plants. The development of a compendium of indigenous plants with potential and clinical benefits is highly recommended.
7. Sometimes in 2020, the Minister of Health, Dr. Osagie Ehanire inaugurated a 20-member committee to fine-tune modalities for the establishment of the National Institute of Traditional, Complementary and Alternative Medicine. While this is recognized as a step in the right direction, it is however important to ensure that this laudable effort comes to limelight by removing all bottleneck against its realization.

Kwara State University

8. The Vice chancellor in a bid to incorporate traditional medical practice into medical care in KWASU inaugurated the Centre for Complementary and Alternative Therapy. Mr Vice chancellor sir, I most sincerely commend this laudable effort of yours which is unique in Nigerian Universities. I would like to also recommend that the University management should put in place necessary infrastructure to facilitate the activities of this Centre.
9. The use of animals is a fundamental component of phytopharmacology research. I wish to appeal to the University administration under the leadership of our dynamic Vice Chancellor for the establishment of well-equipped small animal house for the use of Departments and researchers who may require animals.

10. The University Research Council, should intensify the on-going effort at facilitating the establishment of KWASU Research Ethics Committee. This will enhance the development of ethical policies on animal use in research and encourage quality research in phytopharmacology.

Researchers

11. Natural product drug discovery and development requires a multidisciplinary approach. Collaborative research among various specialties and cutting across Universities, Pharmaceutical companies and Research Institutes should be intensified.

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Mr Vice Chancellor sir, at this point, appreciation is very much in order. Foremost, all praise is due only to God, the I am that I am. That I can stand before you today as a Professor (of Biochemistry)- the dream of all University lecturers, is just a product of His Mercies and Grace- Indeed, "it is not of Him that willeth, nor of him that runneth but of the Lord who showeth Mercy". I give all glory and honour unto His name.

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