OBAFEMI AWOLOWO UNIVERSITY, ILE-IFE, NIGERIA.

INAUGURAL LECTURE SERIES 326

AS IT WAS IN THE BEGINNING, NOW AND FOREVER: PHYTOMEDICINE AS PANACEA FOR HUMAN HEALTH

By

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Drug Research and Production Unit

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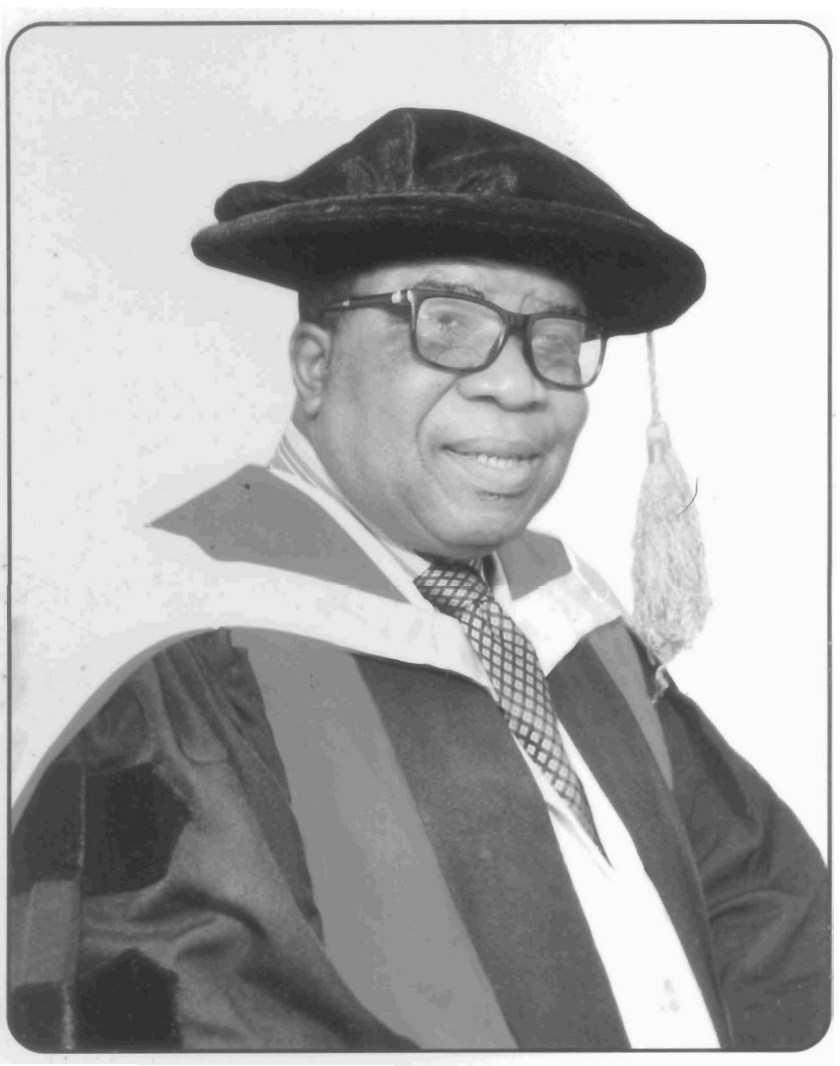

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AS IT WAS IN THE BEGINNING, NOW AND FOREVER: PHYTOMEDICINE AS PANACEA FOR HUMAN HEALTH

Introduction

Mr. Vice Chancellor sir, members of the Governing Council, members of the Senate and Congregation of this great University, all other non-academic members of staff and students of this great citadel of learning, Eminent personalities here present, spiritual and royal fathers here present, gentlemen of the press ladies and gentlemen. I give the Almighty God the honour and glory for giving me the grace to deliver this 326 inaugural lecture of our University. This is the third inaugural lecture to be delivered in the Drug Research and Production Unit, Faculty of Pharmacy but the first to be delivered by a Professor of Phytomedicine since the creation of the Unit in 1979. This lecture could not have come at a more auspicious time than today 25th September when the world celebrates the world Pharmacy day.

I have chosen the topic; **As it was in the beginning now and forever: Phytomedicine as panacea for human health** to draw our attention to the fact that we receive our good health from plants. This started right from the creation of mankind as made known to us by the Holy Bible and all the important books passed down to us from generations. Actually it is not only human beings that derive her source of life from plants other animals do likewise. We have the herbivorous and omnivorous animals. So it is a misconception for some people to adduce that they don't use herbal drugs. In this lecture I will attempt to prove to you that food is medicine and some medicines are foods. I will also attempt to prove that most medicines that had been in existence *ab. initio* and till date are either derived from plants or have their templates derived from chemicals isolated and characterized from plants or through structural modifications plants chemical constituents. Now genetic engineering is playing great roles in drug discovery and delivery however the template of most drugs be they through tissue culture or otherwise has their origin in plant.

In the beginning

The origin of most commonly used drugs predates history. Relevant verses in the Holy Bible showed that herbal remedies were ordained by God. In the Book of Genesis chapter 1 verse 29, God said, *"Behold, I have given you every plant yielding seed that is on the face of all the earth, and every tree with seed in its fruit. You shall have them for food. Every moving thing that lives shall be food for you and as I gave you the*

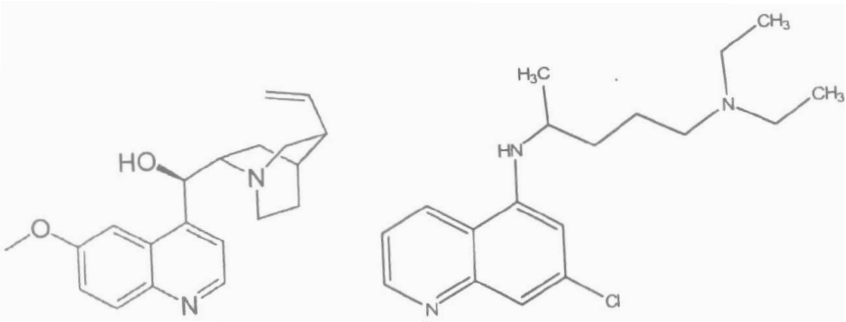
green plants, I give you everything. (Genesis 9: 3) *Then the angel showed me the river of the water of life, bright as crystal, flowing from the throne of God and of the Lamb through the middle of the street of the city; also, on either side of the river, the tree of life with its twelve kinds of fruit, yielding its fruit each month. The leaves of the tree were for the healing of the nations.* (Revelation 22:1-21).

In the book of Ezekiel 47: 12, it is written that *"their leaves will not wither, nor their fruit fail, but they will bear fresh fruit every month, because the water for them flows from the sanctuary. Their fruit will be for food, and their leaves for healing."*

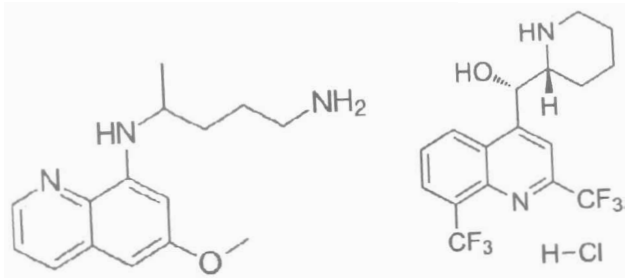
The Apostle Paul in his letter to the Romans in Chapter 14 verse 2 advised the weak to eat herbs. God created herbs for the services of man Psalm 114:14. These show that the remedial properties of herbs have been recognized and appreciated from time immemorial, but as time went by, people's attention was diverted and the advent of science finally relegated herbal remedies into the background.

Shaul moogra oil from a species of *Hydnocarpus* Gaertn. is one of the earliest recorded use of herbal medicine which had been known to be effective in the treatment of leprosy. Such use was recorded in the Pharmacopeia of the Emperor Shen Nung of China between 2730 and 3000 BC. Similarly, the seeds of Opium puppy (*Papaver somniferum* Linn.) and Castor oil seed (*Ricinus communis* Linn.) were excavated from some of ancient Egyptian tombs which indicated their use in that part of Africa as far back as 1500 BC. Hippocrates was regarded as the first Greek to regard medicine as a science in 460 BC.

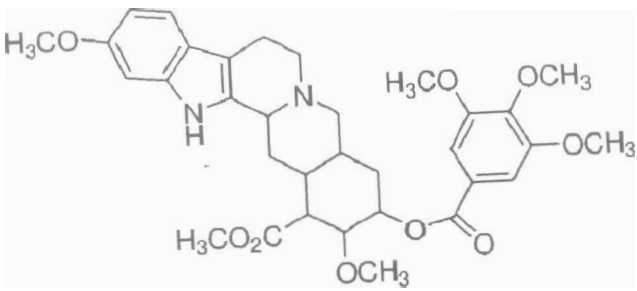
One of the earliest pharmaceutically accepted drugs was **quinine [I]** which was first identified in the early 17th century and isolated from *Cinchona* tree bark by Pelletier and Caventou in 1820. The discovery stimulated further research for new drugs and finally led to the synthesis of many antimalarial drugs such as **chloroquine [II]**, **primaquine [III]**, **mefloquine [IV]**, etc. They were derived from the knowledge of quinine. The important cardiovascular drug **reserpine [V]** is obtained from the *Rauwolfia* species. The antineoplastic drugs **vincristine [VI]** and **vinblastine [VII]** from *Catharanthus roseus.* These are used in their salt forms in the treatment of cancer. In short, many pharmacologically active drugs have been obtained from plants.



I **Quinine** **II** **Chloroquine**

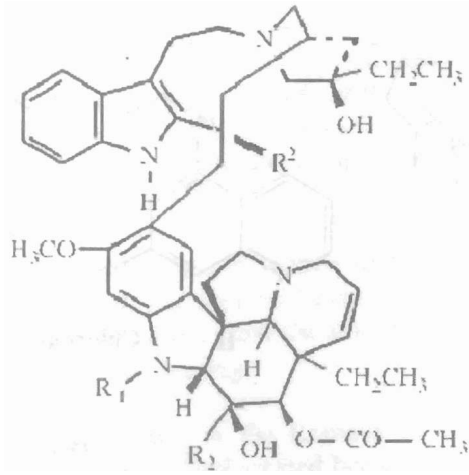


III **Primaquine** **IV** **Mefloquine**



V **Reserpine**

Figure 1: Structures of earliest pharmaceutically acceptable drugs from medicinal plants



Vinblastine: $R^1=CH_3$, $R^2=COOCH_3$

Vincristine: $R^1=CHO$, $R^2=COOCH_3$ **VII**

Figure 2: Structures of earliest pharmaceutically acceptable drugs from *Catharanthus roseus*

AFRICAN INDIGENOUS MEDICINE

African indigenous medicine is based on the cultural beliefs of the African. These gods and goddesses are part of their culture as such folkloric medicines differ from one culture to the other. According to the World Health Organization, African Traditional Healers (ATH) or African Traditional Medical Practitioners (ATMP) are defined as – a person who is recognized by the community in which he lives as competent to provide health care by using plant, animal, mineral substances and certain other methods. The methods are based on social, cultural and religious backgrounds as well as the knowledge attitudes and beliefs that are prevalent in the community regarding physical, mental and social well-being and the causes of diseases and disability. Traditional Medicine (TM) according to the World Health Organization definition can be defined as the total combination of knowledge and practices, whether explicable or not used in diagnosing, preventing or eliminating a physical, mental or social disease which may rely exclusively on past experience and observation handed down from generation to generation verbally or in writing (Sofowora, 2012).

Indigenous Knowledge of African Medicine: Theory and Origin

According to the Yoruba mythology, *Orunmila* was the father of medicine. He was endowed by this knowledge by God. *Orunmila* was the younger brother of *Osanyin*. These two were believed to be legendary men to first practice herbalism in Nigeria. Herbalism is a traditional form of medicine whose basis is the use of herbs to treat various ailments. A herbalist is expected to be knowledgeable in the efficacy, toxicity, dosage and compounding of herbs.

Some anthropologists believe that early man lived in fear, in order to allay this; he indulged in mystical and religious rituals. As such origin of selection of medicinal plants was influenced by religion. Some believed that knowledge of plant was gained accidentally. Some believe that knowledge of such medicinal plants was communicated to their ancestors in various ways (Lambo, 1979; Sofowora, 2012).

It is also believed that knowledge of medicinal plants was obtained by early men by watching the effects produced by various plants when eaten by domestic animals. There was the story of a woman that bought mushrooms *(olu)* in order to determine if it was poisonous or not, she first gave the soup prepared with the mushroom to her dog. After hours of consumption of the soup and no visible effect on the dog, she now dished it to her household. No sooner afterwards than the dog started foaming. Meanwhile, the family had eaten the mushrooms soup. Also those that keep domestic animals like dog or fowl could notice the animals consuming some leaves to alleviate dysentery. So knowledge of medicinal plants could be acquired from domestic animals even in our contemporary time. This method of determining toxicity of medicinal plants is still being practiced by some traditional healers till date. Another source of knowledge of medicinal plants is believed to be obtained from witches and wizards (Ogunyemi, 1979). Hunters in African countries have been reported as the original custodian of some effective traditional herbal recipes. Information on the use of medicinal plants through dreams and trance are believed to be passed on by the spirit of an ancestor who practiced herbalism. There is the doctrine of signature which is another source of knowledge of medicinals. In this doctrine it is believed that herbs resembling various parts of the body can be used by herbalists to treat ailments of those body parts. For example, a sliced carrot looks like human eye, the pupils, iris and radiating lines look just like the human eye. Science now shows that carrot greatly enhances blood flow to the eye thus enhance its function.

Tomato has four chambers and is red; research has shown that tomatoes are indeed good for the heart. It has vitamin A which is carotene which is good for the eye. Avocado or pear is shaped like the heart, and the womb (protruding the cervix) of a woman, research has shown that they are good for the heart, they also promote the health and function of the womb and cervix of the female, helps to balance hormone and prevent cervical cancer. Walnut looks like little brain with a left and right hemisphere, upper cerebrum and lower cerebellum. Research has now shown that walnut helps to develop over 3 dozen neurotransmitters for brain function. Kidney beans, as well looks like human kidney and it is believed to help maintain kidney functions (Pearce, 2008).

Concept of diseases and treatment

In African Traditional Medicine (ATM) the causes of disease have been classified into five categories according to Lambo in 1979. Traditional Medicine considers man as an integral somatic and extra material entity. It is believed that disease can be due to supernatural causes arising from the displeasure of ancestral gods, evil spirits, the effect of witch crafts, effect of spirit possession, or the intrusion of object into that body. TM places great emphasis on psychological causes of disease. It is often part of the culture of the people that use it, as such; it is closely linked to their beliefs.

According to Lambo (1979), categories of causes of diseases in ATM are:

(1) **Physical ailment**: These are disease caused by injurious elements entering the human system through food, drink skin etc. This is in agreement with cause of diseases in WM which believes that disease is caused by physiopathologic agent including micro-organism and noxious substances in food and the environment. This is the only area of aetiological agreement in the two systems.

(2) **Psychological causes:** There are diseases caused to man when his will is not in harmony with the laws of nature. It is believed that the diseased body is affected by the state of the mind. Some people tend to believe that they are sick when in actual fact nothing is wrong with their system (hypochondria).

(3) **Astral influences**: This is disease caused by radiations from cosmic agents e.g. sun, moon and the planets. It is believed that

these agents influence human beings either for good or evil. The moon is believed to influence the brain as such lunatics become wild and act abnormally when the new moon appears. The appearance of new moon is not in itself known to cause mental disturbance.

(4) **Spiritual causes**: Evil thoughts, desires and machination of enemies (i.e. by influences) including soul projection or evil telepathic messages are all grouped together as spiritual causes of diseases. Diseases caused by witchcraft also fall into this category.

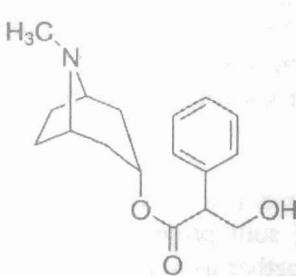
(5) **Esoteric Causes:** This is a disease originating from the soul or those caused by deeds of any individual in his former life (before reincarnation).

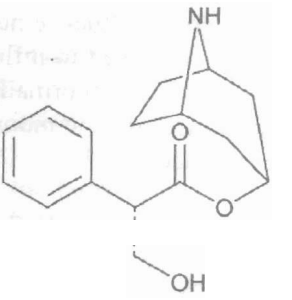
Rationalization of indigenous medical practice

There are scientific evidences to support indigenous medical practices.

(I) Collection of some plants at night:

There are evidences supporting collection of some plants at night rather than during the day for them to have desired therapeutic effect. It is now known in science that there is diurnal variation in the composition of some plant metabolites. Time of collection must therefore be put into consideration. For example, "Queen of the night" emits sweet odour at night which is not perceived at noon. As such if the volatile oil that produces the sweet odour is needed for perfume industry, it must be collected and extracted at night and not at noon. Also the volatile oil containing plant *Eupatorium odoratum* loses its oil content at noon, but high concentration of the oil is at the peak from sunset to midnight. It has also been found that there is interconversion of **atropine [VIII]** and **hyoscinamine [IX]** (Tropane alkaloid) which are isomers within a day.





VIII Atropine **IX Hyoscyamine**

Figure 3: Structures of the two naturally occurring tropane alkaloids

(II) The use of chewing sticks by Africans:
Plants such as Fagara (*Zanthoxylum zanthoxyloides* 'Orin ata' in Yoruba are used as chewing stick. The plant possesses antimicrobial constituent which can inhibit the activities of the mouth microflora thereby preventing teeth decay. It also contains fluoride which can strengthen the teeth.

Limits of African Traditional Medicine (ATM)

There are some similarities and wide differences between ATM and Western orthodox medicine (WOM). These are mainly based on the differences in the concept of causes of diseases and treatment in the different form of medicines. It is a common feature among the ATMPs that they make bogus claims that they can treat all forms of ailments. Actually they lack the scientific knowledge to support such claims. They boast on their prowess until the condition becomes worse and life threatening. They should learn to do quick referral once they realize that they are not competent to handle such cases. The referral could be among them or to the conventional health facilities. With advancement in science and availability of pathophysiological infrastructures, tests could easily be carried out to assist in diagnosis and appropriate treatments are prescribed. This is lacking in ATM.

In the area of compounding of herbal drugs, there is the need for the ATMP to improve on hygiene, standardization of herbal remedies through the use of appropriate measures and weights. They should pay adequate attention on dosages and toxicity. The incidence of renal failure is becoming increasingly rampant. This could be due to habitual

utilization of herbal drugs which are not subjected to adequate biochemical and histopathological toxicological tests

What is Phytomedicine?

The literal meaning of Phytomedicine is plant medicine. The basic human exploitation of herbal remedies and their clinical usage can be referred to as phytotherapy. Herbal medicine, or botanical medicine, is also known in Europe as *Phytomedicine*. The prefix "Phyto" is derived from Greek word meaning "plant." It is otherwise known as Alternative Medicine in the developed world but more correctly and more acceptably as "Herbal medicine" It can also be referred to as botanical medicine. It has been used over the centuries in almost all cultures. There is a close relationship between Phytomedicine and Pharmacognosy. While the former is the medicine of plant, the latter is derived from *pharmakon* meaning "drug" and *gignosco* meaning "the knowledge of". So Pharmacognosy is the knowledge of crude drugs of vegetable, animal and mineral origin, treated scientifically (Wallis, 2005).

Human Health

It is the will of the Almighty that one is in good health and if your body is the sanctuary of the Lord it is mandatory to keep it healthy.

God said, "*Behold, I have given you every plant yielding seed that is on the face of all the earth, and every tree with seed in its fruit. You shall have them for food. And to every beast of the earth and to every bird of the heavens and to everything that creeps on the earth, everything that has the breath of life, I have given every green plant for food.*" No matter how good a drug or physician is without faith especially if one is dispirited, the patient cannot receive healing. The scriptures says, *is anyone among you sick? Let him call for the elders of the church, and let them pray over him, anointing him with oil in the name of the Lord. And the prayer of faith will save the one who is sick, and the Lord will raise him up and if he has committed sins, he will be forgiven.* James 5:14-15. It is only the Lord that heals and He can heal all illnesses.

Here are other Bible quotations that will substantiate that healing comes from God. Behold, He says, I will bring them to health, I will heal them and reveal to them abundance of prosperity and security. **Jeremiah 33:6** Is there no balm in Gilead? Is there no physician there? Why then has the health of the daughter of my people not been restored? **Jeremiah 8:22**. I have seen his ways, but I will heal him; I will lead him, restore comfort

to him and his mourners, creating the fruit of the lips. Peace, peace, to the far and to the near," says the Lord, "and I will heal him. **Isaiah 57:18-19**

David said, Bless the Lord, O my soul, and all that is within me, bless his holy name! Bless the Lord, O my soul, and forget not all his benefits, who forgives all your iniquity, who heals all your diseases, who redeems your life from the pit, who crowns you with steadfast love and mercy, who satisfies you with good so that your youth is renewed like the eagle's. Psalm 103: 1-22. In contemporary times Fig tree is known to have medicinal value. It is recorded in the scriptures that Isaiah said, "Bring a cake of figs. And let them take and lay it on the boil that he may recover." And Hezekiah said to Isaiah, "What shall be the sign that the Lord will heal me, and that I shall go up to the house of the Lord on the third day?" And Isaiah said, "This shall be the sign to you from the Lord, that the Lord will do the thing that he has promised: In many verses of the scripture we are informed that, it is only God that gives good health. Human being can try his beat; it is only God that heals. Healing comes by faith in the Lord 1 Cor.12:9. And he said to her, "Daughter, your faith has made you well; go in peace, and be healed of your disease." **Mark 5:34** Jesus said, "The Spirit of the Lord is upon me, because he has anointed me to proclaim good news to the poor. He has sent me to proclaim liberty to the captives and recovering of sight to the blind, to set at liberty those who are oppressed, **Luke 4:18** Jesus went throughout all Galilee, teaching in their synagogues and proclaiming the gospel of the kingdom and healing every disease and every affliction among the people. **Mathew 4:23. Jesus** bore our sins in his body on the tree, that we might die to sin and live to righteousness. By his wounds we have been healed. **1 Peter 2:24.**

Food and Human Health

A large population of educated Christians and Moslems goes with the erroneous idea that every herbal drug is either fetish and unholy. As such any herbal drug prescribed will be discarded. Such individuals are ignorant of the fact that they, being an omnivore consume both plants and animals in their diet and such plants consumed as foods are medicine. Naturally, human beings have been endowed with different substances that help in their sustainance and maintenance of good health. The consumption and digestion of food has been the source of the elements and vitamins required to repair body tissues and provide energy for the body. Food with its therapeutic qualities prevails in the treatment

and prevention of different ailments. Fruits, vegetables, tomatoes, palm oil, cabbage, walnut, berries etc have been of high therapeutic values. Traditional diets whch comprises of carbohydrates, proteins, fat and oil contain macronutrients. Specific amounts are required for heathy well being while vitamins and minerals obtained from fruits and vegetables provide the micronutrients required by the body.

In as much as food is beneficial to the body unhealthy eating by consumption of animal fat, salt, refined sugar, artificial additives and to some extent genetically modified food can precipitate irreparable damage to the vital organs such as kidney, heart and liver. These substances can precipitate heart diseases, circulatory problems, cancer, aging, neurodegenerative disorders such as Alzheimers and Parkinson diseases. These unhealthy food substances are the causative agents for the generation of free radicals.

Free radicals are molecules containing unpaired number of electrons. They are formed when oxygen reacts with certain molecules. Once these free radicals are formed, they are unstable and very reactive. They initiate cascade of reactions by abstracting electron from nearby molecules. These free radicals are dangerous when they react with important cellular components such as DNA and cell membranes to reduce or eliminate their functions. Free radicals are generated continuously in the body due to metabolism and diseases. The body is able to minimize the effect of free radicals by using the complex system of antioxidant enzyme present in the body and those obtained from diets rich in fruits and vegetables (Yeum *et al.*, 2003).

Antioxidants

Antioxidants are molecules that safely interact with free radicals to end the cascade of reactions before vital molecules are damaged. They are able to reduce oxidative damage to cells. Examples of endogenous antioxidants which are naturally present in cell membranes include catalase, uric acid, superoxide dismutase, and gluthathione and the thioredoxine system. Exogenous antioxidants which consist of phytochemicals found in plants include lycopene found in ripe red tomatoes, ascorbic acid found in oranges (*Citrus* fruits) flavonol in onions and tea (especially green teas), sulphoraphane and dithiothiones in cruciferous vegetables. High concentration of tocophrol is present in kernel, to mention a few. Consumption of diets containing these phytochemicals reduce incidence of diseases especially that of vital

organs. This is achieveable by neutralizing free radicals, thus boosting celluar antioxidant defense and the maintenance of healthy immune function (Tripathi, 2003).

Fate of Carbohydrates

The fate of carbohydrate from *Dioscorea* spp. (Yam), *Zea mays (Corn)*, Oryza sativa (Rice), *Sorghum bicolor* (Millet), etc., consumed by man and after digestion, is absorbed into the mammalian system as sugar units, essentially utilized for the catabolic and metabolic processes in the body. Excess sugar is converted to fat which is stored in the body. When such sugar is required by the body, the fat deposit is reconverted to sugar again through a process of gluconeogenesis. Excess of sugar in the body is deleterious since it causes *Diabetes mellitus* and obesity which represent two of the most common global health challenges of our time. Other disease conditions, related to carbohydrates, include galactosemia (milk or lactose consumption), it is a hereditary disorder. The child cannot digest milk, being an in-born error of metabolism.

Fate of Proteins

Protein consumed in the diet undergoes series of chemical changes in the gastrointestinal tract (GIT). The physiology of protein digestion is complex; the enzymes pepsin and renin from the stomach trypsin from the pancreas and erepsin from the intestine do hydrolyse proteins into their component amino acids. Most of the amino acids are absorbed into the blood stream from the small intestine on their ways to the liver and to other parts of the body. Surplus amino acids lose the amino groups to form urea which is excreted as urine. The other components of the molecule are transformed into glucose sugar. Evidences have shown that certain little intact protein is taken up by certain cell linings of the small intestine.to play important role in the passive immunity conveyed by mother to her newborn child. Some unabsorbed proteins combine with amino acuds, together with the intestinal flora, contributing to the nitrogen molecules found in faeces. Most of the proteins found in the body are located in the muscle.

Fate of Fats and oils

Fats and oils are stored as triglycerides in the mammalian system. They are important sources of energy because they are both reduced and anhydrous. Triglycerides break down into fatty acids and monoglycerides by pancreatic lipase enzyme. Triglycerides are absorbed as free Fatty acids and 2- monoglycerides but small proportions are

absorbed as free glycerol and as diglycerides. When blood sugar is low, decreased insulin levels will signal the adipocytes to activate hormone sensitive lipase to convert triglycerides into free fatty acids (Andrews, 1999). The Free fatty acids have very low solubility in the blood. However, serum albumin binds with the free fatty acids, thereby increasing their effective solubility while the resultant serum albumin transports the fatty acids to organs in the body e.g. muscle and liver for oxidation at any time the blood sugar is low. The disorder of fatty acid metabolism is hypertriglyceridemia (excessive level of triglyceride) or other types of hyperlipidemia.

Fate of Minerals and Vitamins

Besides these three basic classes of food the roles of minerals and vitamins in human health are highly significant and equally very important. They have a number of functions in the body. Sodium, potassium and chlorine are present as salts in body fluids to maintain osmotic pressure. Calcium and phosphorous are present in the bone to maintain rigidity. Chlorine is present in hydrochloric acid which plays important role in the stomach for the digestion of protein. Iodine is an essential component of thyroxine a hormone produced by the thyroid gland. The above mentioned minerals play very important roles in human health e. g. iron in the red blood cells (mainly as a component of haemoglobin and myoglobin found in the muscles), among others. Iron is conserved in the body as a nutritional requirement of healthy male and postmenopausal requirement in healthy female. Tannins and phosphate in the food can reduce iron absorption. Women of child bearing age must replace lost iron resulting from the monthly blood loss. Deficiency of Iron leads to anaemia in the body.

Sulphur, manganese, magnessium, flourine are some of the other macro-elements needed by the human body. Many of these minerals are sourced from plants. Sulphur is consumed in human diet and its deficiency is linked with protein deficiency. Calcium is present in serum of the blood and extra- cellular fluid particularly in the blood plasma. So deficiency of Calcium especially among elderly women affects their skeleton thus causing osteoporosis and physiological fluids.

My contribution to the study of "Food as Medicine"

The afore-mentioned showed the importance of food which are mainly derived from plants. So, plants in nutrition serve both as food and

medicine. There is therefore little wonder in the saying of the Yorubas that "*Onje lore awo*" meaning that healthy skin results from good food.

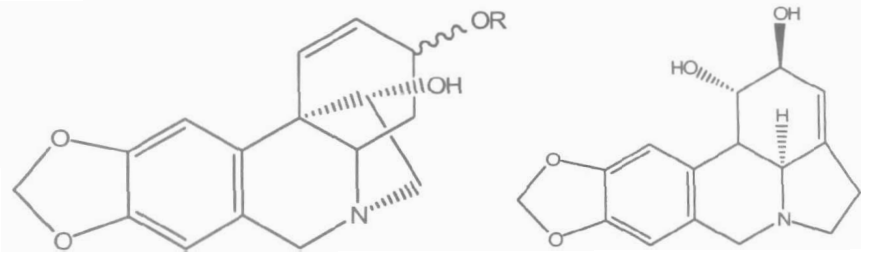
Food and Neurodegenerative disorder

My voyage into neurodegenerative disorder studies particularly acetycholine esterase and butyryl choline esterase inhibition as a means of developing drugs that can be used in the management of Alzheimers disease was as a result of my research visits to King's College London in 2003, 2004 and 2007 under the tutelage of Professor Peter Houghton. The Royal Society United Kingdom under her Developing World Study Visit (DWSV) award gave me the grant on two different occasions 2003 and 2007 to embark on the study. This opportunity had enabled me to train undergraduates, Masters and Doctor of Philosophy students in this area of study. Dr. (Mrs) Taiwo Elufioye whom I supervised her B.Pharm, M.Sc. and PhD research in this area is now a world acclaimed scientist in this area of study. She won the Elsevier Foundation award for early – career women scientist in the developing world in the field of chemical science in sub –Sahara Africa in 2014 based on her PhD thesis on the Phytochemistry of four Nigerian medicinal plants *(Peltophorum pterocarpum, Pycnanthus angolensis, Spondias mombin,* and *Morinda lucida)* based on ehnomedicinal survey we carried out.

Cholinesterase enzymes (AChE) are responsible for the hydrolysis of the neurotransmitter acetylcholine (Tougu, 2010). They are important therapeutic target for the management of Alzheimer's disease (AD), the current standard of care for mild to moderate AD being treatment with acetylcholinesterase inhibitors to improve cognitive function. (Citron, 2010), AChE inhibitors boost the endogenous levels of acetylcholine in the brains of AD patients thereby improving cholinergic neuronal transmission. (Talesa, 2001) AD is a chronic neurodegenerative disorder that leads to dementia, cognitive impairment, and memory loss accompanied by deficiency in choline acetyltransferase activity in the hippocampus and cerebral cortex (Li *et al.*, 2009; Nadri *et al.*, 2013) It is the fourth leading cause of death in developed countries following heart disease, cancer, and stroke (Li *et al.*, 2009). Hence, the search of new and active cholinesterase inhibitors is of great interest for AD treatment (Lee, 2011).

As part of my contribution to the Alzheimer's disease (AD) research, I reported the choline esterase inhibition properties of some Nigerian medicinal plants. Acetycholinesterase is a major inhibitor of acetycholine,

a neurotransmitter found in the synapse of cerebral cortex. Inhibition of acetycholine is one the major causes of Alzheimer's disease. As such, Houghton, Agbedahunsi and Adegbulugbe (2004) reported the cholinesterase inhibitory properties of alkaloids from Two Nigerian *Crinum* species. *Crinum jagus, Crinum glaucum* **Haemanthamine [X]** *and* **Hamayne [XI]**. Two other *Crinum* alkaloids are **Crinamine XII** and **Lycorine XIII** isolated from the same species.



X R = β-OCH_3 **Haemanthamine**
XI R = β-OH **Hamayne**
XII R = α-OCH_3 **Crinamine**

XIII **Lycorine**

Figure 4: Structures of Crinum alkaloids isolated from two Nigerian *Crinum* species with cholinesterase activity

The muscarinic, Ca++ antagonist and specific butyrylcholinesterase inhibitory activity of dried ginger extract was evaluated by Gayur, Agbedahunsi and other (2008). The muscarinic Ca^{++} antagonist and specific butyrylcholinesterase inhibitory activity of dried ginger extract might explain its use in dementia. Gayur was a doctoral student from Pakistan that I put through the study of cholinesterase inhibitory activity at the Kings College London.

I investigated the cholinesterase activity of eight different glucosinolates. Structural activity relationship was established for the range of the glucosinolates. This was an unpublished work which was meant for patenting. This is the first report of glucosinolates having this activity and is of interest because of the use of glucosinolate containing members of Brassicaceae in the diet e.g. cabbage. Also, onion, white and dark mustard contains sinigrin and sinalbin which had been found to possess this isothiocyanate glycoside.

Elufioye, Agbedahunsi and others (2010) evaluated the acetycholinesterase and butyrylcholinesterase inhibitory activities of some selected Nigerian medicinal plants. In our effort to reflect the philosophy of food as medicine, Cyril-Olutayo, Agbedahunsi and others in 2011 determined the acetycholine esterase inhibitory and toxicity effects of *Carica papaya* (pawpaw) seeds. Based on the report, pawpaw fruit can be recommended to be eaten, both as food and as medicine to manage Alzheimers disease.

The methanolic extract of *Picralima nitida* seed gave acetycholinesterase inhibition of 50.76 %. The petroleum spirit partitioned fraction gave 49.15 % out of which alkaloidal base took 47.20 %, alkaloidal acidic sub-fraction took 35.91 % while the remaining residue took 33.11 %. The enzyme kinetic studies showed that there was competitive inhibition between 50 µL and the control. It is not clear while uncompetitive inhibition occurred between 30 µL, 10 µL and control. The above results have shown that the seed of *P. nitida,* which is currently a component of the evidence-based, NAFDAC-approved MAMA Powder, a herbal antimalarial drug of the Drug Research and Production Unit, equally possessed acetylcholinesterase inhibitory activity which can also be exploited in the management of Alzheimers' disease (Dada and Agbedahunsi, 2008).

Annona senegalensis and *Xylopia aethiopica* were evaluated for acetychlinesterase (AChE) and butychlinesterase (BuChE) inhibitory activities. The leaf, stem-bark and root-bark extracts demonstrated 66 %, 79 % and 78 % AChE inhibition, respectively. On the other hand, while the leaf was not active in the BuChE inhibitory activity experiments, the stem-bark and root-bark gave 18 % and 19 % activities, respectively. *Xylopia aethiopica* gave 33 %, 37 % and 70 % AChE inhibition for the leaf, stem-bark and root-bark extracts, respectively while there was no BuChE inhibitory activity in any of the extracts (Agbedahunsi and Okwoli, 2008).

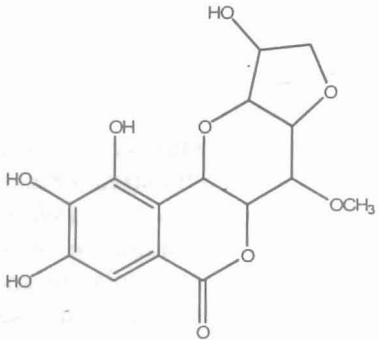
Twenty two Nigerian medicinal plants which are used as memory enhancers in Sagamu, South Western Nigeria were evaluated for their cholinesterase inhibitory activities. We reported that some of the plants showed selective acetycholinesterase and butyryl cholinesterase activities (Elufioye, Agbedahunsi and others, 2012).

Morinda lucida (Oruwo in Yoruba) is a common medicinal plant popularly used in Nigeria for the treatment of malaria and a component of MAMA Decoction, another evidence-based, NAFDAC-approved

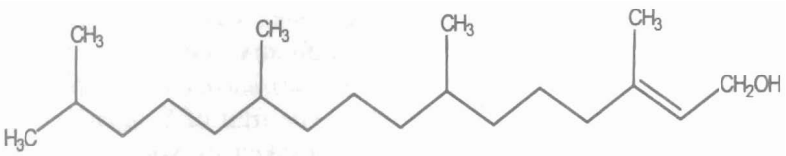
herbal antimalarial drug of the Drug Research and Production Unit. However, we have discovered that *Morinda lucida* possessed cholinesterase inhibitory activity (Elufioye, Agbedahunsi and others, 2013a). The cholinesterase constituents were reported in 2015 (Elufioye, Agbedahunsi and others, 2015). Similarly, the acetycholinesterase and butylcholinesterase inhibitory activities of *Peltophorum pterocarpum* (DC) Baker ex Heyne, family Leguminosae, was reported (Elufioye, Agbedahunsi and others, 2013b). The isolation and characterization of berginin from the leaf of this and its cholinesterase inhibitory activities was equally reported by Elufioye, Agbedahunsi and others (2016). The cholinesterase activity of a new phytol derivative, its structural elucidation and a new cinnamic acid ester were reported by Elufioye, Agbedahunsi and others (2016), from the leaves of *Pycnanthus angolensis*. In 2017, the cholinesterase inhibitory constituents from the leaves of *Spondias mombin* (Iyeye in Yoruba) leaves were reported by Elufioye, Agbedahunsi and others (2017). The fruit of *S. mombin* which is also rich in Vitamins A and C are often taken by young and old in Yoruba land for pleasure. It is one of the plants that possessed anti-aging property from our ethno-medicinal survey. We hereby recommend its consumption by the senior citizens of this campus and elsewhere.

Table 1: The AChE ans BuChE of compounds isolated from medicinal plants reported by Elufioye (2012)

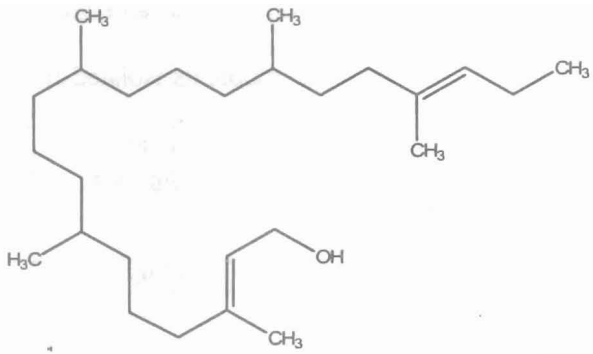
Plant Extract	Compounds Isolated	AChE (µg/mL)	BuChE (µg/mL)
Peltophorum pterocarpum	**Peltocourin [XIV]** **Phytol [XV]**	4.32 12.93	4.79 24.90
Morinda lucida	**Phytol**	12.93	24.90
Pycnanthus angolensis	**Nansol[XVI]** **Angolensate [XVII]**	22.26 6.51	34.61 9.07
Spondias mombin	**Phytol** **Mombinstinrol[XVIII]** **Campesterol [XIX**	12.93 0.88 1.89	24.90 4.67 4.08



XIV **Peltocourin** isolated from *Peltophorum pterocarpum*

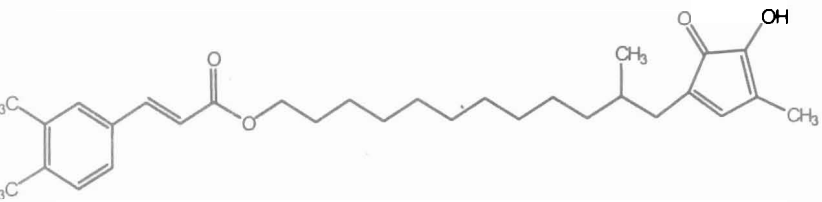


XV **Phytol** from *Morinda lucida*

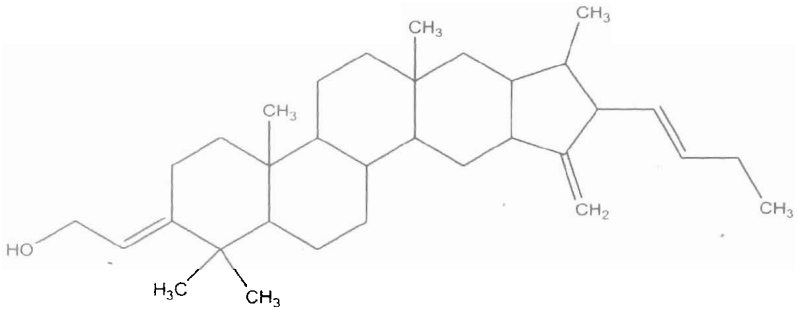


XVI **Nansol** isolated from *Pycnanthus angolensis*

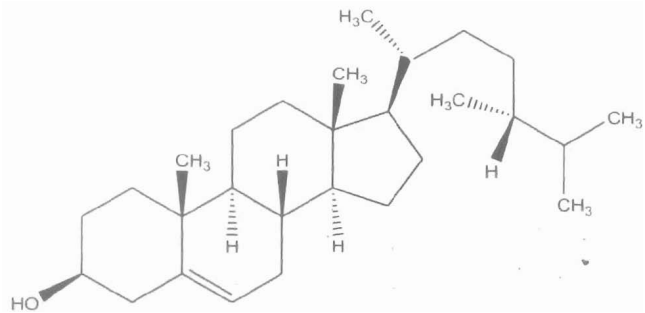
Figure 5: Structures of the isolated compounds



XVII **Angolestoate** isolated from *P. angolensis*



XVIII **Mombinstinrol** isolated from *Spondias mombin*



XIX Campesterol isolated from *S. mombin*

Figure 6: Structures of the isolated compounds with cholinesterase activity

Maytenus senegalensis fruit which is edible and the root extract which we studied. Agbedahunsi Elufioye and Houghton 2007 The chloroform partitioned fraction (Ms/CF) gave the highest AChE inhibitory activity of 73.54 % at a concentration of 47.62 µg/ml. The plant was further purified to yield a glycoside, thus validating the ethnomedicinal uses of the plant and can also help in restoring ailing memory.

Agbedahunsi and Fadahunsi (2008) reported the *in vitro* acetycholinesterase inhibitory and antioxidant activities of the fresh leaf of *Brassica olaraceae var capitata*, family Cruciferae (Cabbage) by adopting an activity-guided fractionation approach. This involved: obtaining an ethanolic extract of the leaf; partitioned fractionation of the crude extract successively, between water and: petroleum spirit, chloroform, ethyl acetate to obtain the corresponding fractions and final aqueous residue. The extracts and fractions were subjected to qualitative

antioxidant (TLC bioautography), quantitative antioxidant and anti-cholinesterase activities (spectrophotometric assay methods). The results showed that the aqueous fraction demonstrated the highest antioxidant activity with IC_{50} values of 1.55 mg/mL compared to quercetin, the positive control with 5.43 µg/mL. The aqueous fraction also exhibited the best anti-cholinesterase activity with a 95.12 % inhibitory effect at 60.0 µg/mL. The study concluded that Cabbage contains antioxidants and anti-cholinesterase constituents which could be utilized by Alzheimer's patients to restore their cognitive functions, representing another example of "food and medicine". As stated earlier, Cabbage is a common ingredient in the preparation of salad, containing isothiocyanate glycoside which possessed cholinesterase inhibitory activity.

MALARIA

The theme chosen by the World Health Organization for the World malaria day 2018 is "Ready to Beat Malaria" (WHO, 2018). The theme underscores the commitment of the global world in the eradication of Malaria worldwide. Unfortunately, it appears the world is losing the battle. Statistics has shown that there appears to be an upsurge in the incidence of Malaria in 2016 compared to previous years. According to WHO (2018) report in 2016 there were 216 million cases of malaria in 91 countries, 5 million more than 211 million cases as it was the case in 2012. However, the Global Technical Strategy for Malaria projected a 40% reduction of Malaria between 2016 and 2030. It is however noteworthy that those countries with ongoing transmission are increasingly falling into one of two categories. These are those moving towards elimination and those with a high burden of the disease that malaria is significantly increasing. WHO also reported that Malaria continues to claim a significant number of lives? In 2016, 445,000 people died from malaria globally, compared to 446,000 estimated deaths in 2015. It is not surprising that Africa with high level of poverty and poor hygiene had 194 million cases of malaria and 407,000 malaria deaths. Africa is followed by South –East Asian countries 14.6 million malaria cases and 27,000 deaths, what a big gap between Africa and Southeast Asia! The incidences of malaria in other parts of the world are rather insignificant. Based on the aforementioned, the African Region bears 90% of malaria cases worldwide and 91% of malaria deaths. The above scenario calls for concerted efforts by the governments of Africa, South of Sahara and the scientists, social scientists, environmentalists, etc. should join hands in fighting the scourge of malaria in Africa.

Mr. Vice Chancellor sir, prior to the advocacy by the Honourable Minister, at the 2018 World Malaria Day in Abuja, Nigeria, Agbedahunsi and others had been investigating the anti- malarial effects of many Nigerian plants with a view to developing antimalarial drugs that will combat the multidrug resistance of *Plasmodium falciparum*. This study has spanned a period of 33 years. Ethno-medicinal compilation of plants used in the management of malaria were carried out with a view to determining the plants that are commonly used in Nigeria for the management of the disease. (Fateru and Agbedahunsi, 1997).

Table 2: Plants with documented Antimalarial activity

S/N	Plant Scientific Name	Family	Local Name	Part Used
1.	*Dracaena fragrans* (L) Ker-Gawl	Agavaceae	Peregun (Yoruba)	Leaves Agbedahunsi *et al* 2000
2.	*Achyranthes aspera* Linn	Amaranthaceae	Aboro (Yoruba)	Root Gessler *et al*., 1994
3.	*Mangifera indica* Linn	Anacardaceae	Mangoro (Yoruba)	Leaves Iwu, 1988
4.	*Enantia chlorantha* Oliv.	Annonaceae	Osopupa (Yoruba)	Stem bark Agbaje, 1991; Moody *et al*., 1992
5.	*Alstonia congensis* Engl.	Apocynaceae	Ahun or Awun (Yoruba)	Bark Makinde and Obih, 1998
6.	*Picralima nitida* Thand Hel. Dum	Apocynaceae	Erin	seed, fruit, rind, stem bark Iwu, 1992
7.	*Rauwolfia vomitoria* Afz	Apocynaceae	Asofeyeje	Root
8.	*Aristolochia albida* Duch	Aristolochiaceae	Gidakuka (Hausa)	Root and Leaves Farnsworth, 1966; Iwu, 1988
9.	*Spathodea campanulata* Beauv.	Bignonaceae	Oruru (Yoruba)	stem bark Makinde *et al*., 1988
10.	*Bauhinia rufescens* Lam	Caesalpiniaceae	Jiga (Hausa)	Root Allen and Allen, 1981; Iwu, 1988
11.	*Cassia occidentalis* Linn	Caesalpiniaceae	Rere (Yoruba)	Leaves Etkin and Ross, 1983
12.	*Dialium guineense* willd	Caesalpiniaceae	Awin (Yoruba)	Bark and Leaves Allen and Allen, 1981
13.	*Carica papaya* Linn	Caricaceae	Ibepe (Yoruba)	Leaves and roots of male plant Iwu, 1988
14.	*Momordica foetida* Schum and Thonn	Cucurbitaceae	Ejirin (Yoruba)	Leaves Gessler *et al*., 1994
15.	*Jatropha*	Euphorbiaceae	Lobotuje, Lapalapa	Leaves Gbessor *et*

	gossypiifolia Linn		pupa	*al.*, 1989
16.	*Ocimum gratissimum* Linn	Labiatae	Efinrin (Yoruba)	Leaves Grieve, 1974
17.	*Abrus precatorius* Linn	Leguminosae	Oju Ologbo (Yoruba)	Leaves Iwu, 1988
18.	*Cajanus cajan*	Leguminosae	Otili (Yoruba)	Leaves Sodeinde, 1995
19.	*Pisum sativum* L.	Leguminosae	Awin	Pods Abatan *et al.*, 1986 Sodeinde, 1995

My contributions to Antimalarial Research

The development of Anti-malarial Drug from a Nigerian Medicinal Plant: *Khaya grandifoliola* stem bark

Nigerian flora still harbors several herbs that can remedy the scourge of malaria in the country. The recurring incidents of multi drug resistant *Plasmodium* parasites have necessitated the search for potent anti-malarial drugs from medicinal plants.

My major first contribution to science is in the area of anti- malaria research. This is because of the continuous scourge of malaria which is still endemic in tropical Africa south of Sahara. The incidence of resistance to available anti-malarial drugs has made the search for newer drugs especially from medicinal plants inevitable. As a result of this, I investigated the anti-malaria properties of a number of medicinal plants particularly, *K. grandifoliola* (**Oganwo** in Yoruba and commonly called **Mahogany**). We found out that the plant has anti-malarial activity even against chloroquine resistant *P. falciparum* strain *in vitro* (Makinde, Awe and Agbedahunsi, 1988, Agbedahunsi and Elujoba, 1998). **Grandifolin [XX]** a mexicanolide type of limonoid was isolated from the malaria active NH-2 fraction of *K. grandfoliola*. This gave IC_{50} of 1.4 µg/ml against the multi-drug resistant strain (Agbedahunsi *et al.*, 1998). The anti-malarial principle of *K. grandifolia* gave 91% chemosuppression of plasmodial parasite and an IC_{50} value of 1.7µg/ml for the multidrug resistant clone W2 strain and 0.8 µg/ml for the Nigerian *Plasmodium falciparum* isolates (Agbedahunsi *et al.*, 1998).

The effect of *K. grandifoliola* on red blood cells and bones was studied. It gave increase in red blood cell count (RBC), packed cell volume (PCV), haemoglobin and plasma iron contents in rats. There was a general trend of reduction in bone minerals (Ca, P, Mg and Cu) at 500 mg/kg dose. However, there was a dose dependent increase in bone

potassium and iron (K and Fe) contents. The alkaline phosphatase (ALP) decreased. *K. grandifoliola* showed positive effect on erythropoesis and no significant effect on bone mineral content at therapeutic doses of 100 mg/kg (Bumah, Agbedahunsi and others, 2004). *K. grandifoliola* had also been shown to have hypoglycaemic, hypoproteinaemic and hypocholesterolaemic effects on rats there was reduction in the Liver protein content and glutathione (GSH). The concentration of free fatty acid in the plasma was not significantly reduced nor was there any significant increase in the liver malondialdehyde (MDA) in the extract treated rats (Bumah *et al.*, 2005). From the toxicological and biochemical studies carried out and reported, it was found out that the plant was generally safe at low doses with $LD_{50} > 1000$ mg/kg, but could be toxic at high doses if administered sub-chronically at doses above 500 mg/kg. (Bumah and Agbedahunsi, 2007). Histopathological studies revealed that morphological abnormalities were found only within the white matter of the cerebral cortex at high doses in subchronic oral administration of the extract which reversed after the ceasation of the drug administration after 14 days. It also showed moderate anti-inflammatory activity 69.43 % at 200 mg/kg (Agbedahunsi Fakoya and Adesanya, 2004).

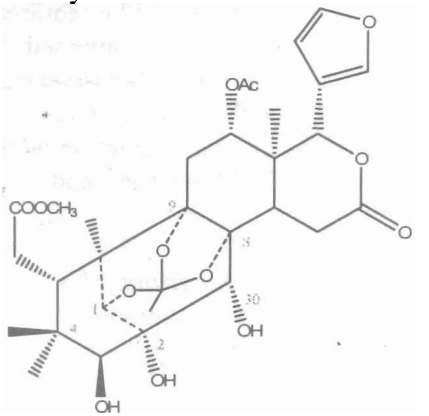
Combination therapy is one of the ways through which resistance is combated as such in a pharmacodynamic evaluation, the interaction of *K. grandifoliola* with two standard antimalarial drugs, chloroquine and halofantrine, using murine mammalian models were evaluated. It was observed that *K. grandifoliola*: halofantrine combination elicited synergistic effect at sub-optimal dose of each agent. The mean survival period of the parasitized animals was also enhanced by the combination. Very low dosage of halofantrine would be required to potentiate parasite clearance when the two drugs were combined. This would constitute great advantage to halofantrine which is associated with cardiotoxicity at high doses (Ijarotimi, Agbedahunsi and others, 2010). Agbedahunsi *et al.* (2013) also reported the *in vivo* interaction between extracts of *Khaya grandifoliola* (Welw) CDC (Meliaceae) and artemisinin in a murine malaria model.

In view of the above report *K. grandifoliola* is a potential plant for further development through formulation into appreciable dosage forms and clinical trials for the management of malaria in Nigeria.

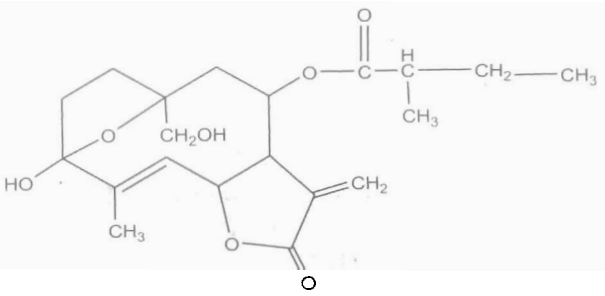
A number of other Nigerian medicinal plants have been investigated by me and my research collaborators for their anti-malarial activities. The

antimalarial potentials of *Eugenia uniflora* (Agbedahunsi and Aladesanmi, 1993), *Dracaenia fragrans* (Agbedahunsi *et al.*, 2000). Repository activity of *Cassia occidentalis* by Osinoiki and Agbedahunsi in 2002 reported a dose-dependent antimalarial activity with 85.6 % of the crude ethanolic leaf extract at 400 mg/kg, while pyrimethamine gave 92 % activity at 1.2 mg/kg. Schizonticidal activity of *Curcuma longa* on early malaria infection using Swiss albino mice was also reported by Soyemi and Agbedahunsi (2002). The average suppression of parasitaemia of 43.13 % was obtained at 400 mg/kg, while chloroquine at 5 mg/kg, on resistant *P. berghei* malaria parasite, gave 57.6 % suppression. *Tithonia diversifolia* and *Crossopteryx febrifuga* (Elufioye and Agbedahunsi, 2004). Their levels of antimalarial activities were evaluated. *Tithonia diversifolia* was extensively studied and we reported a new molecule, 8-(2- methoxybutanoyl)-3, 10 Epoxy-3,8'-dihydroxyl - 4,11 (13)-germacradien-12,6- olide **[XXI]** we isolated – a sesquiterpene lactone from the antimalarial active fraction (Elufioye, Agbedahunsi and Adesanya, 2004). The toxicity of *Tithonia diversifolia* was evaluated; the histology of the kidney and liver showed that the ethanolic extract of *T. diversifolia* has cytotoxic effect on rapidly dividing cells. The plant can be useful as antimalarial if used as single dose (Elufioye, Agbedahunsi and others, 2009).

Therapeutic Effects of various solvent fractions of *Alstonia boonei* (Apocynaceae) stem bark on *Plasmodium berghei*-induced Malaria was reported by Olanlokun, Agbedahunsi and others (2012), Agbedahunsi *et al.* (2016) reported the antimalarial properties of *Morinda lucida* and *Alstonia boonei* on Sulphadoxine-Pyrimethamine and *Curcuma longa* in Mice.



XX **Grandifolin,** a mexicanolide type of limonoid isolated from the stem bark of *Khaya grandifoliola* for the first time by me

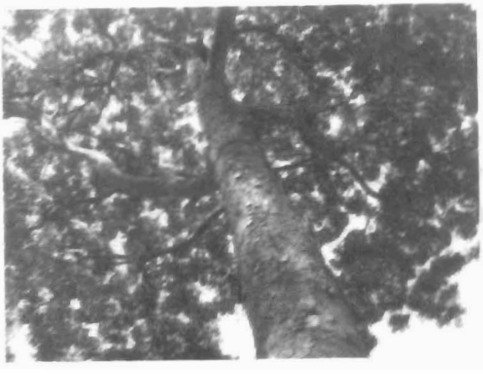


XXI A new Sesquiterpene lactone, 8-(2-mehylbutanoyl)-3, 10 Epoxy-3, 8-dihydroxyl-4, 11 (13)- germacradien-12, 6-olide we isolated for the first time from the aerial part of *Tithonia diversifolia*

Figure 7: Structures of compounds isolated with anti-malaria activities

Khaya ivorensis

K. grandifoliola



K. senegalensis

Picralima nitida **Seeds**

Eugenia uniflora

Cymbopogon citratus

Plate 1: Some of the Antimalarial Research Plants Collected at the O.A.U., Ife Campus

Mr Vice Chancellor sir, at a programme to mark the world antimalarial day in Abuja, Nigeria, the Nigerian Health Minister advocated the return to herbal therapy to manage malaria (Daily Trust Newspaper, 27th May 2018), I am pleased to inform you and the general public that under my watch as the Director of DRPU the Unit successfully got two of her antimalarial herbal drugs- (MAMA Herbal® decoction and MAMA herbal® powder) listed by NAFDAC. This was in tandem with the desire of the Honourable Minister. This is therefore a call for medicinal plant scientists and physicians to join the Minister and the WHO in saying that Nigeria is "Ready to Beat Malaria". In the same vein Mr. Vice-

Chancellor sir, may good things continue to surface in your time at OAU. With the first two antimalarial herbal drugs, approved by NAFDAC for the University and with high potentials for marketability, we request that the Management join the Dean and the entire family of the Faculty of Pharmacy with DRPU to say that OAU is "Ready to Beat Malaria".

SICKLE CELL DISEASE

The term *sickle cell disease* (SCD) describes a group of inherited red blood cell disorders. People with SCD have abnormal hemoglobin, called *hemoglobin S or* sickle hemoglobin, in their red blood cells. Hemoglobin is a protein in red blood cells that carries oxygen throughout the body. SCD is an inherited disease. "Inherited" means that the disease is passed by genes from parents to their children. SCD is not contagious. A person cannot catch it, like a cold or infection, from someone else. People who have SCD inherit two abnormal hemoglobin genes, one from each parent. In all forms of SCD, at least one of the two abnormal genes causes a person's body to make hemoglobin S. When a person has two hemoglobin S genes, Hemoglobin SS, the disease is called *sickle cell anemia*. This is the most common and often most severe kind of SCD. Hemoglobin SC disease and hemoglobin Sβ thalassemia (thal-uh-SEE-me-uh) are two other common forms of SCD.

There are six common forms of Sickle Cell Disease; these are Hemoglobin SS, Hemoglobin SC, Hemoglobin $S\beta^0$ thalassemia, Hemoglobin $S\beta^+$ thalassemia, Hemoglobin SD and Hemoglobin SE Cells in tissues need a steady supply of oxygen to work well. Normally, hemoglobin in red blood cells takes up oxygen in the lungs and carries it to all the tissues of the body. Red blood cells that contain normal hemoglobin are disc shaped (like a doughnut without a hole). This shape allows the cells to be flexible so that they can move through large and small blood vessels to deliver oxygen. Sickle hemoglobin is not like normal hemoglobin. It can form stiff rods within the red cell, changing it into a crescent, or *sickle* shape.

Sickle-shaped cells are not flexible and can stick to vessel walls, causing a blockage that slows or stops the flow of blood. When this happens, oxygen can not reach nearby tissues.

Normal Red Cells and Sickle Red Cells

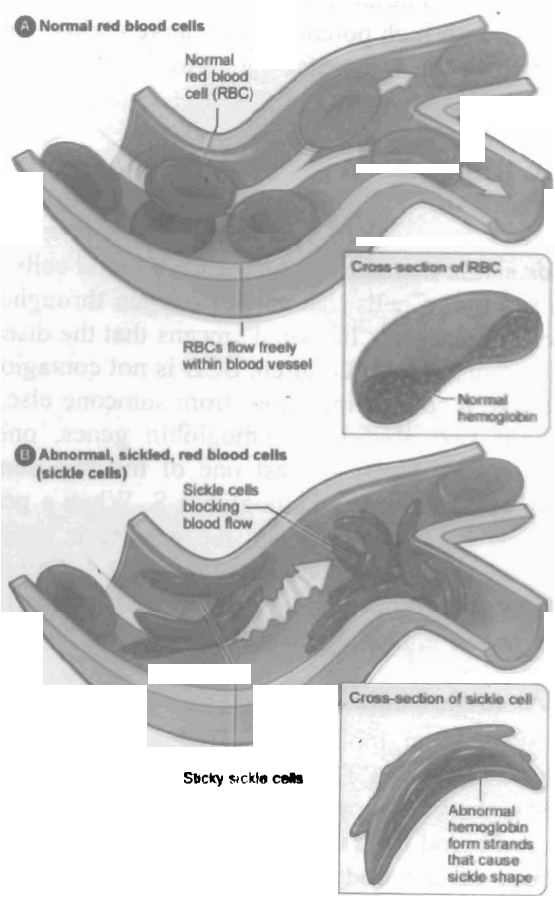


Plate 2: *shows normal red blood cells flowing freely in a blood vessel. The inset image shows a cross-section of a normal red blood cell with normal hemoglobin. Figure B shows abnormal, sickled red blood cells blocking blood flow in a blood vessel. The inset image shows a cross-section of a sickle cell with abnormal (sickle) hemoglobin forming abnormal stiff rods.* Culled from NHLBI (2008).

The lack of tissue oxygen can cause attacks of sudden, severe pain, called pain crises. These pain attacks can occur without warning, and a person often needs to go to the hospital for effective treatment. Most children with SCD are pain free between painful crises, but adolescents

and adults may also suffer with chronic ongoing pain. The red cell sickling and poor oxygen delivery can also cause organ damage. Over a lifetime, SCD can harm a person's spleen, brain, eyes, lungs, liver, heart, kidneys, penis, joints, bones, or skin. Sickle cells can not change shape easily, so they tend to burst apart or *hemolyze*. Normal red blood cells live about 90 to 120 days, but sickle cells last only 10 to 20 days. The body is always making new red blood cells to replace the old cells; however, in SCD the body may have trouble keeping up with how fast the cells are being destroyed. Because of this, the number of red blood cells is usually lower than normal. This condition, called *anemia*, can make a person have less energy.

Sickle cell disease is a life-long illness. The severity of the disease varies widely from person to person. An A to T transversion in the 6th codon of human β-globin gene. This change causes a polar glutamic acid residue to be replaced by a non-polar valine in the S-globin chain on the surface of HbS ($\alpha_2B^S_2$) tetramers. The valine creates a hydrophobic projection that fits into a natural hydrophobic pocket formed on Hb tetramers after deoxygenation (Platt *et al.*, 1994).

The highest frequency of SCA disease is found in Africa South of Sahara. It is also found among the African Americans, India and the Middle East. Migration from the SCD endemic region to Europe has increased the incidence of the disease in recent decades. As such SCD has now overtaken more familiar genetic conditions such as hemophilia and cystic fibrosis (Weatherall and Clegg, 2001).

The World Health Organization (WHO) reported that the carrier frequency ranges from 10% to 40% across equatorial Africa. Around 2% of newborns in Nigeria are affected by SCA (WHO, 2010). Based on the estimated population of Nigeria of 190 million, about 3.8 million children are affected annually.

The health implication of SCA is significant. Its effect is prominent among children 6 months – 5 years of age. There is high incidence of morbidity and mortality. The social implication of the disorder on families with individual carrying the HbSS gene is enormous. It ranges from financial burden, care for the patient and uncertainty of life expectancy are few of the traumas that family members undergo.

SCA is a genetic disease as such no chemotherapeutic cure has been found for the disorder. However, several therapeutic strategies have been involved in the management of SCD. These include pharmacological modulation of fetal Hb (Olivieri and Weatherall, 1998), blood transfusion (Ballas, 1999), opiod analgesics to deal with pain crisis (Ballas, 1999), erythrocyte membrane acting agent (Asakura, 1980), and reduction of iron overload using chelating agents (Inati *et al.*, 2010).

Life expectancy is shortened, with studies reporting an average life expectancy of 42 and 48 years for males and females, respectively.
At the present time, hematopoietic stem cell transplantation (HSCT) is the only *cure* for SCD. Unfortunately, most people with SCD are either too old for a transplant or don't have a relative who is a good enough genetic match for them to act as a donor. A well-matched donor is needed to have the best chance for a successful transplant. The goal of Stem Cell Transplant (HSCT) is to eliminate the sickle erythrocyte and its cellular progenitors and replace them with donor hematopoietic pluripotent stem cells that give rise to erythrocytes that expresses no HbS thereby reducing HbS level in the blood. (Johnson *et al.*, 1984; Bernaudin *et al.*, 2007).

The Knowledge of SCD is relatively recent in Africa. It could be safely regarded as a disease associated with the Negroid race based on its incidence in the tropical regions of Africa. As such Africans must have 'ways of managing the disease, hence ethno-botanic survey was carried out by the Drug Research and Production Unit, on the management of the disorder in South Western Nigeria in 2012

Incidence of SCD
Nigeria has the highest prevalence rate in the world with a rate varying between 1.5-3%. According to the Nigerian Sickle cell Foundation (NSF) and the World Health Organization (WHO), twenty five million Nigerians are with sickle cell gene, out of which 4 million suffers from the disease. About 150,000 infants are born with SCD annually and out of which 100,000 of them die from this genetic disorder in spite of improved medicare. Nigeria accounts for 75 % of infant SC cases in Africa.

Part of the mission statement of the Obafemi Awolowo University (OAU), Ile-Ife is to advance frontiers of knowledge that are relevant to National and global development, Promote and nurture the African

culture and tradition (including its medicine). In view of the aforementioned, the University has included advocacy and sourcing of new drugs for the management of SCD in her strategic plan, was with a view to deepening research that will contribute substantially to innovation for the national economy and peoples well being.

My Contributions to Sickle Cell Research

A number of medicinal plants had been worked upon by graduate students under my supervision and reported in many international and local journals.

Amujoyegbe, Agbedahunsi and others in 2012 evaluated in vitro and reported the membrane stabilizing activities of leaf and root extracts of *Calliandra portoricensis* (Jacq) Benth on sickle and normal human erythrocytes. The percentage membrane stabilizing activities of these extracts were found to be concentration dependent. Both extracts protection capability competes favourably with the standard drug (Ibuprofen) but the exthanolic root extract exhibited the best membrane stabilizing activity. From this result, it could be inferred that *C. porticensis* exhibited human erythrocyte membrane stabilizing activity which could be useful in the management of sickle cell related ailment.

Amujoyegbe, Agbedahunsi, Akinpelu *et al.* (2013) reported the *in vitro* antisickling activities of the aqueous leaf and fruit extracts of Yellow Passion *(Passiflora edulis* F. Flavicarpa Deg), using inhibitory and reversal methods. The results demonstrated a concentration-dependent linear increase in the inhibitory and reversal of the sickled HbS gene. The aqueous extract of the leaf at 4 mg/mL exhibited the highest inhibitory and reversal activities at 93.99 % and 92.66 % respectively. The inhibitory activity of the leaf extract (97.81 %) was relatively higher than that of the fruit juice extract (93.99 %). It was concluded that the leaf extract possesses more putative compounds than the fruit juice extract.

Amujoyegbe, Agbedahunsi and Akanmu (2014) reported the *in vitro* antisickling properties of two *Calliandra* species: *C. portoriscensis* and *C. haematocephala* (Fabaceae). A 70% ethanol extracts and aqueous extracts of the leaf and root of the two plants were evaluated, using the inhibitory and reversal methods. It was observed that there was concentration-dependent linear increase in the inhibitory and reversal activities of the ethanolic and aqueous extracts of the leaf and root. At a

concentration of 4 mg/mL, the ethanolic extract of the root of *C. portoricensis* exhibited the highest activity for inhibitory at 90.19 % and reversal activity at 92.63 % among all the plant part extract tested. It was concluded that *Calliandra portoricensis* is an antisickling plant that can play essential role in the management and treatment of sickle cell disorder.

Oyekunle, Soriyan and Agbedahunsi (2015) evaluated the knowledge of herb sellers in the diagnosis of SCD in Osun and Oyo States Southwestern Nigeria. Structured interviews were carried out on a total of ninety herb sellers. A total of sixty herbsellers were interviewed using close-ended questionaires while the remaining thirty were interviewed using open-ended questionaires. A spreadsheet packagae were used for the data analysis and the response from these herb sellers revealed that the most important symptoms of SCD includes pain, reduced stamina, anaemia, stunted growth, jaundice, and increase in abdominal girth. The survey showed clearly that herb sellers have a vast knowledge of the diagnosis of SCD which were acquired over time.

Fatokun, Agbedahunsi and Elujoba (2015) reported the antisickling activities of some Nigerian Medicinal Plants. Varying degrees of antisickling activities were observed from the ten medicinal plants studied. *Anthocleista vogelii* Planch gave 61% reversal activity, ripe fruit of *Cassia sieberiana* DC gave 54 % and 90 % reversal activities inhibitory while the pericarp of the fruit gave 71 % inhibitory and 54 % reversal activities among others.

Cyril-Olutayo and Agbedahunsi (2015) reported the effects of the ethanolic extract of *Cnidoscolus aconitifolius* (Mill) I.M. Johnst on sickled haemoglobin red blood cells *in vitro*. The ethanolic extract of the dried leaves gave antisickling, cell membrane stability and antioxidant activities. The plant extract gave antisickling activity which was significantly ($P< 0.05$) higher than that of Ciklavit, the positive control. It gave 96.82±0.01 %. The extract caused a concentration dependent membrane stability of HbS and blood cell *in vitro*. It also gave increase in free radical scavenging activity as the concentration increased.

Oyedapo, Agbedahunsi and Cyril-Olutayo (2016) reported the anti-sickling activities of the stem bark of three *Khaya* species found in Nigeria: *K. senegalensis* A. Juss., *K. grandifoliola*, (Welw) Cdc., and *K. ivorensis* A. Chev. These three species have same common name –

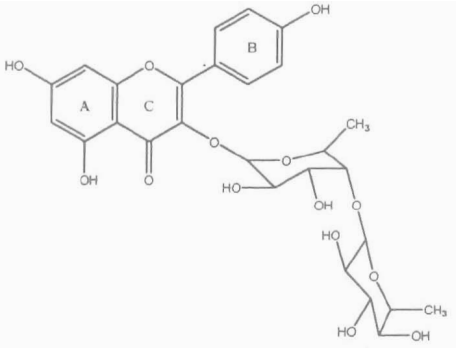
Mahogany and local name (Oganwo) among the Yorubas. Fall *et al.* (1999) reported the anti- sickling activity of *K. senegalensis.* Awe *et al.* (1991) estimated the antimalarial activities of the three species found out that *K. ivorensis* gave the best antimalarial activity followed by *K. grandifoliola* and the least was *K. senegalensis.* It is interesting that our result on the anti-sickling potential of *Khaya* species followed the same sequence as that of Awe *et al.* (1991) on antimalarial activities!

Sickle Cell Disease (SCD) is an ailment with enormous social and economic burden for patients and care givers. Amujoyegbe, Agbedahunsi and others (2016) investigated the *in vitro* antisickling and antioxidant properties of aqueous and ethanol extracts of fifty selected plants used in the management of sickle cell disease (SCD), with the aim of justifying their use in the management of the disease in southwestern Nigeria. Aqueous and 70% ethanol extracts of the selected plants were subjected to *in vitro* antisickling activities and forty plants giving values above 50% activity levels in both inhibitory and reversal models were later tested for their antioxidant assay involving four tests namely DPPH, FRAP, Fe^{2+} chelating and total antioxidant contents, using standard methods. Significant mean values were separated using the Least Significant Difference at 0.05 % level of probability. Among all the plants with above 50% activity levels in both inhibitory and reversal models, three plants, extracted in ethanol, *Gongronema latifolium, Cymbopogon citratus and Piper guineense* had the highest values of 89.81, 89.72 and 84.48 %, respectively. The least activity for both aqueous and ethanol extracts was found in *Amaranthus spinosus* and *Amaranthus viridis (Tete elegun and Tete jije* in Yoruba*).* It can be inferred from the result of the study that 80 % the plants evaluated possessed high antisickling and antioxidant activities and might justify their use in the management of SCD in the South – West, Nigeria.

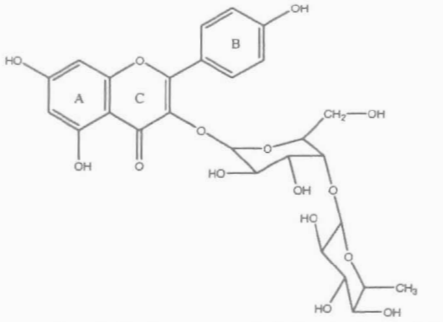
Akinpelu, Agbedahunsi and others (2017) evaluated the anti-inflammatory and antisickling potentials of *Archidium ohioense* (Schimp. ex Mull) extracts. The study investigated the possible anti-inflammatory and antisickling potentials of a moss plant *A. ohioense.* The phytoconstituents in acetone, chloroform and ethylacetate extracts of the plant were analysed using standard methods. Membrane stabilizing, antisickling, xanthine oxidase and lipooxygenase inhibitory activities of the extracts of the plants on sickle and normal erythrocytes were conducted. The acetone and ethyl acetate extracts of the plant stabilized red blood cell membrane of normal and sickle erythrocytes at various

concentrations except at 2.0 mg/ml while the chloroform extract exhibited profound protective effect on both normal and sickle erythrocytes at highest concentration used (2.0 mg/ml). All the *A. ohioense* extracts showed mild anti-lipoxygenase and xanthine oxidase inhibitory activities. As the concentrations of the *A. ohioense* chloroform and acetone extracts increased, the percentage inhibition of sickling significantly increased and compared favorably with para-hydroxybenzoic acid, a known reversal antisickling reference compound. These two extracts also demonstrated significant ($p \leq 0.0001$) dose dependent increase in antisickling reversal activities. This study indicates that *A. ohioense* could be valuable source of anti-inflammatory and antisickling agents.

Plant-derived foods, particularly vegetables and fruits, are generally considered to be highly beneficial components of the human diet, providing wide range of nutrients, vitamins and other compounds which widen the therapeutic arsenal (Newman, 2003). Cyril-Olutayo and Agbedahunsi (2015), Cyril-Olutayo, Agbedahunsi and others (2018a and 2018b) reported the antisickling properties of three medicinal plants: *Telfairia occidentalis* (Ugwu), *Moringa oleifera* (Moringa) and *Cnidoscolus aconitifolius* (Iyana Ipaja – Tree spinach). These three plants are edible vegetables rich in nutrients, vitamins, proteins, antioxidants and are being used in the management of sickle cell anaemia ethnomedicinally. The study authenticated the use of these plants for use as antisickling plants. The properties are due to their high antioxidant contents, free radical scavenging abilities, abilities to protect red cell membranes by inhibiting potassium ion efflux thereby preventing loss of cellular deformability and promote flexibility of sickle red blood cells. The plants possess high erythropoeitic abilities, reduced percentage dense cells and increase the mean cell volume of Hb SS red blood cells *in vitro*. Pure compounds Kaempferol-3-rhamnosyl-1→4-rhamnoside and Kaempferol-3-rhamnosyl-1→4-glucoside with high antisickling activities were isolated from *Telfairia occidentalis* (Cyril-Olutayo, Agbedahunsi and others, 2018b).



XXII Kaempferol-3-rhamnosyl-1→ 4-rhamnoside



XXIII Kaempferol-3-rhamnosyl-1→ 4-glucoside

Figure 8: Structures of thr Antisickling compounds from *Telfairia occidentalis*

Drug Development for the Management of Sickle Cell Disease

In order to fulfill the mandate and as the Director of Drug Research and Production Unit, in 2012, I led a University Research Committee (URC) project as Principal Investigator to develop new drugs for the management of Sickle cell disorder and carried out advocacy programme in South west Nigeria. We secured a TETFund grant of about ten million Naira in 2012 for the studies with the approved research objectives as follows, to:

- develop herbal drugs of potential benefit in the management of SCD and
- create awareness of the disorder in the community and develop strategies to reduce its prevalence in the country.

Indigenous knowledge (IK) of the people from two States, in the South Western Nigeria Zone were surveyed through distribution of

questionnaires with a view to acquiring and documenting dietary/herbal remedies used in the management of SCD. We conducted systematic scientific studies through interdisciplinary research in order to validate the information from the IK obtained and to develop herbal drugs of potential benefits in the management of SCD.

Methodology

Based on the etnobotanical survey, we made compilation of common medicinal plants used by the local communities in three Senatorial districts each, in Osun and Ondo States of Nigeria. We randomly picked two local governments from each of the Senatorial districts for the survey. The report of the medicinal plants used for the management of the disease is given below.

In fulfilment of the Research Objectives of the grant, we evaluated eighty nine plants from about thirty-eight families with ethnomedicinal anti-sickling values from Osun State, and One have been documented from our survey in Osun State and eighty three medicinal plants from Ondo State. The results of these ethnobotanical surveys are as shown in Tables 3- 6.

Table 3: Medicinal plants used in ethnomedicine for the management of Sickle cell disorder in Osun State, Nigeria

S/N	*VERNACULAR NAMES*	*SCIENTIFIC NAMES*	FAMILY	PART USED
1	Egbo Ewuro	*Vernonia amygdalina*	Asteraceae	Roots
2	Ibepe	*Carica papaya*	Caricaceae	Ripe seeds
3	Ewe Imi-esu	*Ageratum conyzoides*	Asteraceae	Leaves
4	Ewe olojogbura	*Heliotropium indicum*	Boraginaceae	Leaves
5	Ewe olojogbodu	*Solenostemon monostachyus*	Labiatae	Leaves
6	Ewe ologbokiyan	*Ritchiea capparoide*	Capparidaceae	Leaves
7	Eso abere	*Parinari sp.*	Chrysobalanacea e.	Fruits
8	Pandoro	*Kigelia africana*	Meliaceae	Fruits
9	Esan abo (ekuro)	*Criestis ferruginea*	Cyatheaceae	Fruits
10	Ewe arojoku	*Cycnium camporum*	Scrophulariaceae	Leaves
11	Epo emi	*Butyrospermum* paradoxum	Sapotaceae	Bark
12	Ewe mangoro	*Mangifera indica*	Anacardiaceae	Leaves
13	Ewe pepe	*Alchornea laxiflora*	Euphorbiaceae	Leaves
14	Ata ire	*Aframomum meligueta*	Zingiberaceae	Fruits
15	Eeru	*Xylopia aethiopica*	Anonaceae	Fruits
16	Egbo akogun	*Aristolochia repens*	Aristolochiaceae	Roots
17	Egbo ahun	*Alstonia boonei* *Alstonia congensis*	Apocynaceae	Roots
18	Egbo seyo	*Caesalpinia bonduc*	Fabaceae	Roots
19	Oju Ologbo	*Abrus precatorius*	Fabaceae	Seeds

20	Ewe patanmo	*Biophytum petersianum*	Oxalidaceae	Leaves
21	Ukaliptu	*Eucalyptus root*	Myrtaceae	Roots
22	Egbo Inabiri	*Plumbago zeylanica*	Plumbaginaceae	Roots
23	Osan-wewe	*Citrus medica var. acida*	Rutaceae	Fruits
24	Ugwu leaf	*Telfairia occidentalis*	Cucurbitaceae	Leaves
25	Ginger	Zingiber officinale	Zingiberaceae	Rhizomes
26	Ewe Igbale	*Moringa oleifera*	Moringaceae	Leaves
27	Iyere leaf & root	*Piper guineense*	Piperaceae	Leaves & roots
28	Alubosa elewe	*Allium ascalonicum*	Liliaceae	Bulbs
29	Oori	*Syzygium guineense*	Myrtaceae Alliaceae	Gums
30	Ogede ibile or ogede odo	*Crinum jagus*	Amaryllidaceae	Bulbs
31	Alubosa Ayu	*Allium sativum*	Liliaceae, Alliaceae	Bulbs
32	Ope oyimbo	*Ananas comosus*	Bromeliaceae	Fruits
33	Ewe asunwon	*Cassia podocarpa*	Caesalpiniaceae	Leaves
34	Efinrin	*Ocimum gratissimum*	Labiatae	Leaves
35	Orin Ata	*Fagara*	Rutaceae	Roots
36	Osan ganinganin	*Citrus aurantium*	Rutaceae	Fruits
37	Igi osun	*Pterocarpus osun*	Papilionaceae	Tree
38	Oganwo	*Khaya ivorensis*	Meliaceae	Stem bark
39	Ogbo leaf & root	*Parquetiana nigrescens*	Asclepiadaceae	Leaves & roots
40	Iroko root	*Chlorophora excels*	Moraceae	Roots
41	Alovera	*Aloe vera*	Liliaceae	Leaves
42	Ewe kakasela	*Paullinia pinnata*	Sapindaceae	Leaves
43	Egbo ologbotuje	*Jatropha cucas*	Euphorbiaceae	Roots
44	Epo igi igba	*Lagenaria siceraria*	Cucurbitaceae	Bark
45	Ikunmu ogano	*Khaya senegalensis*	Meliaceae	Gums
46	Omo onigelegele	*Cassytha filiformis*	Lauraceae	Leaves
47	Awo iki	*Paspalim conjugatium*	Poaceae	Bark
48	Agogo igun leaf & root	*Heliotropium indicum*	Boraginaceae	Leaves & roots
50	Ewe Oparun	*Bambusa vulgaris*	Poaceae	Leaves
51	Ata-ile	*Zingiber officinale*	Zingiberaceae	Rhizomes
52	Opon oyinbo	*Ananas comosus*	Bromeliaceae	Fruits
53	Epo obo	*Erythrophleum suaveoleus*	Caesalpiniaceae	Bark
54	Egbo ogbo	*Parquetina nigrescens*	Asclepiadaceae	Roots
55	Ewe asunwon	*Cassia alata*	Caesalpiniaceae	Leaves
56	Ewe rinrin	*Perperomia pellucid*	Piperaceae	Leaves
57	Ewe odundun	*Bryophyllum pinnatum*	Crassulacae	Leaves
58	Igi agbalumo	*Chrysophyllum albidum*	Sapotaceae	Tree

59	Igi ako	*Brachyestegia eurycoma*	Asteraceae	Tree
60	Ewe Asofeyeje	*Rauvolfia vomitoria*	Apocynaceae	Leaves
61	Ewe isepe agbe	*Chassalia kolly*	Rubiaceae	Leaves
62	Tagiiri	*Adenopus breviflorus*	Cucurbitaceae	Fruits
63	Egbo inabiri	*Plumbago zeylanica*	Plumbaginaceae	Roots
64	Ewon agogo	*Acacia ataxacantha*	Fabaceae	Leaves
65	Allubosa onisu	*Allium ascalonicum*	Liliaceae	Whole bulb
66	Eso arin pupa	*Dioclea reflexa*	Fabaceae	Seeds
67	Egbo arun pale	*Chenopodium ambrosoides*	Chenopodiaceae	Roots
68	Egbo agbaboje	*Motandra guineensis*	Apocynaceae	Roots
69	Dongoyaro bark	*Azadirachta indica*	Meliaceae	Bark
70	Atetedaye	*Amaranthus hybridus*	Amaranthaceae	Leaves
71	Ogede Agbagba (unripe)	*Musa sapentum var paradisiacal*	Musaceae	Bulbs
72	Ewe Rekureku	*Indigofera nummulariifola*	Fabaceae	Leaves
73	Ewe iyere osun	*Baphia nitida*	Leguminosae	Leaves
74	Epo sapo	*Anthocleista djalonensis*	Loganiaceae	Bark
75	Egbo/epo kasia	*Cassia alata*	Caesalpiniaceae	Roots & bark
76	Ewe taba	*Nicotiana tabacum*	Solanaceae	Leaves
77	Bara	*Colocynthis citrullus*	Cucurbitaceae	Leaves
78	Egbo oora igbo	*Grewia pubescens*	Tiliaceae	Roots
79	Oruwo	*Morinda lucida*	Rubiaceae	Leaves
80	Egbo tude	*Calliandra portoricensis*	Mimosoideae	Roots
81	Ewe aka	*Cynometra megalophylla*	Fabaceae	Leaves
82	Ewe awoyoyo	*Gisekia pharnaceoides*	Aizoaceae	Whole plant
83	Lapa lapa pupa	*Jatropha officinale*	Euphorbiaceae	Leaves, stem & bark
84	Laali	*Lawsonia inermis*	Lythraceae	Dried leaves & roots
85	Papasan	*Portulaca oleraceae*	Portulacaceae	Leaf decoction
86	Guava	*Psidium guajava*	Myrtales	Leaves, fruits & bark
87	Aridan	*Tetrapleura tetraptera*	Mimosaceae	Fruits
88	Ifon	*Olax subcorpiodea*	Olacaceae	Leaves
89	Tanna poso	*Mirabilis jalapa*	Nyctaginaceae	Roots

Table 4: Medicinal plants used in ethnomedicine for the management of Sickle cell disorder in Ondo State, Nigeria

S/N	VERNACULAR NAMES	SCIENTIFIC NAMES	FAMILY	PART USED
1	Igi Agbao	*Musanga cecropiodes*	Cecropiaceae	Roots
2	Igi Osun	*Diospyros alboflavescens*	Ebenaceae	Roots
3	Eeru	*Xylopia aethiopica*	Annonaceae	Fruits
4	Igi Ifon	*Olax subscorpioidea*	Olacaceae	Roots
5	Ogede Agbagba (ripe)	*Musa sapientum* var *paradisiaca*	Musaceae	Bulbs
6	Ewe fruit	*Terminalia catappa*	Combretaceae	Leaves
7	Epo Agbon	*Cocos nucifera*	Palmae	Bark
8	Epo Mangoro	*Mangifera indica*	Anacardiaceae	Bark
9	Ewe gbegbe	*Icacina trichantha*	Icacinaceae	Leaves
10	Ewe owu	*Gossypium arboretum*	Malvaceae	Leaves

11	Ewe ewuro	*Vernonia amygdalina*	Asteraceae	Leaves
12	Ewe Ogbo	*Pargentina nigrescens*	Asclepiadaceae	Leaves
13	Ewe Awogba arun	*Petiveria alliacea*	Phytolaccaceae	Leaves
14	Epo Aroje	*Harrisonia abyssinica*	Simaroubaceae	Bark
15	Epo (podi) cocoa	*Theobroma cacao*	Malvaceae	Bark
16	Poropo baba	*Sorghum bicolor*	Poaceae	Leaf sheaths
17	Iseremedu (lsawewe)	*Stronphanthus preusii*	Apocynaceae	Leaves
18	Egunsi white (ogirisi)	Cucumis melo	Cucurbitaceae	Seeds
19	Odofin igbo	*Trichilia prieureana*	Meliaceae	Leaves
20	Ewe epin	*Ficus asperifolia*	Moraceae	Leaves
21	Ata ire	*Aframomum melegueta*	Piperaceae	Fruits
22	Ata wewe	*Capsicum frutescens*	Piperaceae	Fruits
23	Asofeyeje	*Rauvolfia vomitoria*	Apocynaceae	Leaves
24	Egbo Ayin	*Anogeissus leiocarpus*	Combretaceae	Roots
25	Egbo ogbarasi	*Nauclea latifolia*	Rubiaceae	Roots
26	Egbusi Bara	*Colocynthis citrullus*	Cucurbitaceae	Seeds
27	Ewe Ayoo	*Caesalpinia bonduc*	Caesalpiniaceae	Leaves
28	Ewe Ako	*Brachyestegia eurycoma*	Leguminosae	Leaves
29	Egbo Botuje	*Jatropha curcas*	Euphorbiaceae	Roots
30	Ewe tangiri	*Adenopus breviflorus*	Cucurbitaceae	Leaves
31	Epo obi abata	*Cola acuminata*	Malvaceae	Bark
32	Epo cocoa	*Theobroma cacao*	Malvaceae	Bark
33	Ewe ogbo	*Parquetina nigrescens*	Apocynaceae	Leaves
34	Ewe ugwu	*Telfairia occidentalis*	Cucurbitaceae	Leaves
35	Ewe laali	*Lawsonia inermis*	Lythraceae	Leaves
36	Ewe cashew	*Anacardium occidentale*	Anacardiaceae	Leaves
37	Epo ora	*Grewia pubescens*	Tiliaceae	Bark
38	Epo ahun	*Alstonia boonei*	Apocynaceae	Bark
39	Epo osopupa	*Enantia chloranta*	Mimosaceae	Leaves
40	Ewe ibepe	*Carica papaya*	Caricaceae	Leaves
41	Egbo ijegun	*Solanum torvum*	Solanaceae	Roots
42	Ewe oriji	*Hannoa undulate*	Quassia Amara	Leaves
43	Egbo tude	*Calliandra portoricensis*	Fabaceae	Roots
44	Egbo ipeta	*Securidaca longepedunculata*	Polygalaceae	Roots
45	Ewe ajekobale	*Croton lobatus*	Euphorbiaceae	Leaves
46	Alubosa elewe	*Allium ascalonicum*	Liliaceae	Bulbs
47	Ibepe dudu	*Carica papaya*	Caricaceae	Fruits
48	Ewe oruwo	*Morinda lucida*	Rubiaceae	Leaves
49	Orin ata	*Zanthoxylum zanthoxyloides*	Rutaceae	Roots
50	Epo Eki	*Lophira alata*	Ochnaceae	Bark
51	Patanmo	*Momosa pudica*	Mimosoideae	Leaves
52	Igo oke/ewe oko	*Aeglopsis chevsheri*	Rutaceae	Roots
53	Eru	*Croton lobatus*	Euphorbiaceae	Leaves
54	Ireke omode	*Costus afer*	Costaceae	Leaf sheaths
55	Ata ijosi	*Capsicum annuum*	Zingiberaceae	Fruits
56	Epo agbonyin	*Piptadeniastrum*	Leguminosae	Bark

		africanum		
57	Osan wewe	*Citrus medica var.acida*	Rutaceae	Leaves & Roots
58	Ogede wewe	*Musa sapientum*	Musaceae	Suckers
59	Asunwon	*Cassia podocarpa*	Caesalpiniaceae	Leaves
60	Eyin olobe	*Phyllanthus amarus*	Euphorbiaceae	Leaves
61	Osan ganinganin	*Citrus aurantium*	Rutaceae	Leaves & Roots
62	Mangoro bark	*Mangifera indica*	Anacordeaceae	Bark
63	Oganwo	*Khaya ivorensis*	Meliaceae	Roots
64	Ogbesi	*Nauclea latifolia*	Rubiaceae	Roots
65	Feeru	*Cochlospermum tinctorium*	Cochlospermaceae	Leaves
66	Oso pupa	*Enantia chlorantha*	Annonaceae	Leaves
67	Poporo baba/oka-pupa	*Sorghum bicolor*	Poaceae	Leaf sheaths
68	Efirin	*Ocimum gratissimum*	Lamiaceae	Leaves
69	Ejirin	*Momordica charantia*	Cucurbitaceae	Leaves
70	Igi sagere	*Strophantus hispidus*	Apocynaceae	Roots
71	Ewe Epepe	*Alchornea laxiflora*	Euphorbiaceae	Roots & Bark
72	Aka	*Cynometra mannii*	Leguminosae	Leaves
73	Mafowokanmi	*Argemone Mexicana*	Papaveraceae	Leaves
74	Ema	*Desmodium gangeticum*	Fabaceae	Leaves
75	Dagunro	*Acanthospermum hispidum*	Asteraceae	Leaves
76	Osomolu	*Enantia chlorantha*	Annonaceae	Leaves
77	Egbure	*Talinum portulacifolium*	Portulacaceae	Whole plant
78	Ojiji	*Dalbergia ogea*	Fabaceae	Leaves
79	Opoto	*Ficus capensis*	Moracea	Leaves
80	Abere	*Parinari* spp.	Chrysobalanaceae	Leaves
81	Aridan	*Tetrapleura tetraptera*	Fabaceae	Fruits
82	Alubosa elewe	*Allium ascalonicum*	Liliaceae	Bulbs
83	Unripe pawpaw	*Carica papaya*	Caricaceae	Fruits

Table 5: Frequency olf occurrence of medicinal plants used in the management of SCD in Osun State

S/N	*VERNACULAR NAMES*	*SCIENTIFIC NAMES*	FAMILY	PART USED	FREQU-ENCY OF OCCUR-RENCE	PERCENTAGE (%)
1	Ewuro	*Vernonia amygdalina (Del)*	Asteraceae	Root	5	6
2	Ibepe	*Carica papaya(Linnaeus)*	Caricaceae	Ripe seed	4	5
3	Imi-esu	*Ageratum conyzoides (Lantana camara)*	Asteraceae	Leaves	2	3
4	Olojogbura	*Heliotropium indicum* (Linn.)	Heliotropium	Leaves	1	1

5	Olojogbodu	*Solenostemon monostachyus* (P. Beauv.)	Asclepiadaceae	Leaves	1	1
6	Ologbokiyan	*Ritchiea capparoide* (Andr.)	Capparidaceae	Leaves	2	3
7	Abere	*Parinari sp.*	Rosaceae	Fruit	2	3
8	Pandoro	*Kigelia Africana (Benth)*	Meliaceae	Fruit	6	8
9	Esan abo (ekuro)	*Criestis ferruginea*	Cyatheaceae	Fruit	1	1
10	Arojoku	*Cycnium camporum*	Scrophulariaceae	Leaves	1	1
11	Emi	*Butyrospermum* paradoxum	Sapotaceae	Bark	2	3
12	Mangoro	*Mangifera indica*	Anacordeaceae	Leaves	4	5
13	Pepe	*Alchornea laxiflora*	Euphorbiaceae	Leaves	1	1
14	Ata ire	*Aframomum meligueta*	Zingiberaceae	Fruit	7	9
15	Eeru	*Xylopia aethiopica*	Anonaceae	Fruit	13	16
16	Akogun	*Aristolochia repens*	Aristolochiaceae	Root	1	1
17	Ahun	*Alstonia boonei Alstonia congensis*	Apocynaceae	Root	1	1
18	Seyo	*Caesalpinia bonduc*	Caesalpiniaceae	Root	1	1
19	Oju Ologbo	*Abrus precatorius*	Leguminosae	Seed	1	1
20	Patanmo	*Biophytum petersianum*	Oxalidaceae	Leaves	1	1
21	Ukaliptu	*E ucalyptus root*	Myrtaceae	Root	2	3
22	Inabiri	*Plumbago zeylanica*	Plumbaginaceae	Root	3	4
23	Osan-wewe	*Citrus medica var. acida*	Rutaceae	Fruit	7	9
24	Ugwu	*Tefalaria*	Cucurbitaceae	Leaves	1	1
25	Ginger	Zingiber officinale	Zingiberaceae	Rhizo me	1	1
26	Igbale	*Moringa oleifera*	Moringaceae	Leaves	1	1
27	Iyere	*Piper guineense*	Piperaceae	Leaves & root	4	5
28	Alubosa elewe	*Allium ascalonicum*	Liliaceae	Bulb	6	8
29	Oori	*Syzygium guineense*	Myrtaceae Alliaceae	Gum	4	5
30	Ogede odo	*Crinum jagus*	Amaryllidaceae	Bulb	1	1
31	Alubosa Ayu	*Allium sativum*	Liliaceae Alliaceae	Bulb	5	6
32	Ope oyimbo	*Ananas comosus*	Bromeliaceae	Fruit	1	1
33	Asunwon	*Cassia podocarpa*	Caesalpiniaceae	Leaves	2	3
34	Efinrin	*Ocimum gratissimum*	Labiatae	Leaves	1	1
35	Orin Ata	*Zanthoxylum zanthoxyloides*	Rutaceae	Root	3	4

36	Osan ganinganin	*Citrus aurantium*	Rutaceae	Fruit	1	1
37	Osun	*Pterocarpus osun*	Papilionaceae	Tree	1	1
38	Oganwo	*Khaya ivorensis*	Meliaceae	Stem bark	3	4
39	Ogbo	*Parquetiana nigrescens*	Asclepiadaceae	Leaves & root	4	5
40	Iroko	*Chlorophora excels*	Moraceae	Root	4	5
41	Alovera	*Aloe vera*	Aloaceae	Leaves	1	1
42	Kakasela	*Paullinia pinnata*	Sapindaceae	Leaves	1	1
43	Ologbotuje	*Jatropha cucas*	Euphorbiaceae	Root	1	1
44	Igba	*Lagenaria siceraria*	Cucurbitaceae	Bark	1	1
45	Ikunmu ogano	*Khaya senegalensis*	Meliaceae	Gum	1	1
46	Omo onigelegele	*Cassytha filiformis*	Lauraceae	Leaves	1	1
47	Awo iki	*Paspalim conjugatium*	Poaceae	Bark	1	1
48	Agogo igun	*Heliotropium indicum*	Boraginaceae	Leaves & root	1	1
50	Oparun	*Babusa vulgaris*	Poaceae	Leaves	1	1
51	Ata-ile	*Zingiber officinale*	Zingiberaceae	Rhizo me	1	1
52	Opon oyinbo	*Ananas comosus*	Bromeliaceae	Fruit	1	1
53	Obo	*Erythrophleum suaveoleus*	Caesalpiniaceae	Bark	1	1
54	Sese	*Cajanus cajan* (L) Millsp.	Fabaceae	Seed	1	1
55	Asunwon	*Cassia alata*	Caesalpiniaceae	Leaves	2	3
56	Rinrin	*Perperomia pellucida*	Piperaceae	Leaves	2	3
57	Odundun	*Bryophyllum pinnatum*	Crassulacae	Leaves	2	3
58	Agbalumo	*Chrysophyllum albidum*	Sapotaceae	Tree	1	1
59	Akoo	*Brachyestegia eurycoma*	Asteraceae	Tree	1	1
60	Asofeyeje	*Rauvolfia vomitoria*	Apocynaceae	Leaves	3	4
61	Isepe agbe	*Chassalia kolly*	Rubiaceae	Leaves	1	1
62	Tagiiri	*Adenopus breviflorus*	Cucurbitaceae	Fruit	2	3
63	Aka	*Cynometra megalophylla*	Fabaceae	Root	1	1
64	Ewon agogo	*Acacia ataxacantha*	Fabaceae	Leaves	1	1
65	Allubosa onisu	*Allium ascalonicum*	Liliaceae	Whole bulb	1	1

66	Arin pupa	*Dioclea reflexa*	Leguminosae	Seed	1	1
67	Arun pale	*Chinopodium ambrosoides*	Chenopodiaceae	Root	1	1
68	Agbaboje	*Motandra guineensis*	Apocynaceae	Root	1	1
69	Dongoyaro	*Azadirachta indica*	Meliaceae	Bark	1	1
70	Atetedaye	*Amaranthus hybridus*	Amaranthaceae	Leaf	1	1
71	Ogede Agbagba	*Musa sapentum var paradisiacal*	Musaceae	Bulb (unripe)	1	1
72	Rekureku	*Indigofera nummulariifola*	Fabaceae	Leaves	1	1
73	Iyere osun	*Baphia nitida*	Leguminosae	Leaves	1	1
74	Sapo	*Anthocleista djalonensis*	Loganiaceae	Bark	1	1
75	Kasia	*Cassia alata*	Caesalpiniaceae	Root & bark	4	5
76	Taba	*Nicotiana tabacum*	Solanaceae	Leaves	1	1
77	Bara	*Colocynthis citrullus*	Cucurbitaceae	Leaves	2	3
78	Oora igbo	*Grewia pubescens*	Tiliaceae	Root	1	1
79	Oruwo	*Morinda lucida*	Rubiaceae	Leaves	1	1
80	Tude	*Calliandra portorisensis*	Mimosoideae	Root Leaves	1	1

Table 6: Frequency of occurrence of Medicinal Plants used in the Management of SCD in Ondo State

S/N	VERNACULAR NAMES	SCIENTIFIC NAMES	FAMILY	PART USED	FREQUENCY OF OCCURRENCE	PERCENTAGE (%)
1	Epo & Egbo Eki	*Lophira alata*	Ochnaceae	Bark	2	4
2	Ewe Patanmo	*Momosa pudica*	Mimosoideae	Leaves	1	2
3	Igo oke/ewe oko	*Aeglopsis chevsheri*	Rutaceae	Roots	1	2
4	Unripe pawpaw	*Carica papaya*	Caricaceae	Fruits	1	2
5	Ireke omode	*Costus afer*	Costaceae	Leaf sheaths	1	2
6	Ata ijosi	*Capsicum annuum*	Zingiberaceae	Fruits		4
7	Epo & Egbo agbonyin	*Piptadeniastrum africanum*	Leguminosae	Bark	2	4
8	Osan wewe	*Citrus medica var.acida*	Rutaceae	Leaves & roots	2	4
9	Ata ire	*Aframomum*	Zingiberaceae	Fruits	2	4

		meligueta				
10	Ewuro	*Vernonia amygdalina*	Asteraceae	Leaves	2	4
11	Ina	*Cremaspora triflora*	Rubiaceae	Leaves	1	2
12	Ogede wewe	*Musa sapientum*	Musaceae	Suckers	1	2
13	Asunwon	*Cassia podocarpa*	Caesalpiniaceae	Leaves	1	2
14	Eyin olobe	*Phyllanthus amarus*	Euphorbiaceae	Leaves	1	2
15	Osan ganinganin	*Citrus aurantium*	Rutaceae	Leaves	1	2
16	Mangoro bark	*Mangifera indica*	Anacordeaceae	Bark	1	2
17	Eru	*Xylopia aethiopica*	Anonaceae	Fruits	3	6
18	Oganwo	*Khaya ivorensis*	Meliaceae	Roots	1	2
19	Egbesi	*Nauclea latifolia*	Rubiaceae	Roots	1	2
20	Feeru	*Cochlospermum tinctorium*	Cochlospermaceae	Leaves	1	2
21	Oso pupa	*Enantia chlorantha*	Annonaceae	Leaves	2	4
22	Poporo baba/oka-pupa	*Sorghum bicolor*	Poaceae	Leaf sheaths	2	4
23	Efirin	*Ocimum gratissimum*	Lamiaceae	Leaves	1	2
24	Ejirin	*Momordica foetida*	Cucurbitaceae	Leaves	1	2
25	Igi sagere	*Strophantus hispidus*	Apocynaceae	Roots	2	4
26	Epepe	*Alchornea laxiflora*	Euphorbiaceae	Roots & Bark	1	2
27	Aka	*Cynometra mannii*	Leguminosae	Fruits	1	2
28	Mafowoka nmi	*Argemone Mexicana*	Papaveraceae	Leaves	1	2
29	Ema	*Desmodium gangeticum*	Fabaceae	Leaves	1	2
30	Dagunro	*Acanthospermum hispidum*	Asteraceae	Leaves	1	2
31	Egbure	*Talinum portulacifolium*	Portulacaceae	Whole plant	1	2
32	Ojiji	*Dalbergia ogea*	Fabaceae	Leaves	1	2
33	Opoto	*Ficus capensis*	Moracea	Leaves	1	2
34	Abere	*Parinari sp.*	Chrysobalanaceae	Leaves	1	2
35	Aridan	*Tetrapleura tetraptera*	Fabaceae	Fruits	1	2
36	Alubosa elewe	*Allium ascalonicum*	Liliaceae	Bulbs	1	2

We have screened fifty of these plants for their ability to inhibit or reverse sickle RBC and the results are presented in Table 7.

Table 7: Plants that have been screened for anti-sickling activity

S/N	PLANT	FAMILY	PART(s) USED	LOCAL NAME	Antisickling Activity @ 4mg/ml	
					Inhibitory (%)	Reversal (%)
1.	*Mangifera indica* L.	Anacardiaceae	Stem bark and Leaf decoction	Mangoro	88.0	76.9
2.	*Parquetina nigrescense*	Periplocaceae	Leaf	Ogbo	52.2	66.0
3.	*Calliandra portoricensis*	Mimmooideae Leguminoseae	Leaf, Root	Tude	89.5 ± 2.1	76.5 ± 2.8
4.	*Alchonia laxiflora*	Euphorbiaceae	Leaf	Pepe/ Ijan	86.2 ± 3.0	65.3 ± 3.2
5.	*Olax subcorpiodea*	Olacaceae	Leaf	Ifon	75.8 ± 2.5	66.6 ± 4.9
6.	*Tetrapleura tetraptera*	Mimosaceae	Fruit	Aridan	36.1	51.5
7.	*Jatropha officinale*	Euphorbiaceae	Leaf and Stem bark	Botuje Pupa, lapa lapa pupa	53.3	69.1
8.	*Gisekia Pharnaceoides*	Molluginaceae	Whole plant	Ewe awoyoyo	14.3	46.8
9.	*Lawsonia inermis*	Lythraceae	Dried leaf, Root	Laali	50.3	83.2
10.	*Portulaca oleraceae*	Portulacaceae	Leaf decoction	Papasan	0.0	74.8
11	*Bryophyllum pinnatum*	Crassulaceae	Upper part	Abamoda	36.86 ± 10.68	2.86 ± 2.43
12	*Kalanchoe crenata*	Crassulaceae	Upper part	Odundun	43.54 ± 8.96	1.27 ± 1.91
13	*Peperomia pellucida*	Piperaceae	Whole plant	Erinrin	54.13 ± 3.45	0.09 ± 1.18
14	*Spondias mombin*	Anacardiaceae	Leaf	Iyeye	6.91 ± 5.71	22.81 ± 7.19
15	*Spondias mombin*	Anacardiaceae	Root	Iyeye	38.89 ± 7.25	29.31 ± 8.10
16	*Lecanodiscus cupanioides*	Sapindaceae	Leaf	Akika	41.93 ± 6.12	8.11 ± 2.33
17	*Senna alata*	Solanaceae	Leaf	Asunwon Oyinbo	16.15 ± 2.88	26.35 ± 2.18
18	*Anthocleista vogelli*	Loganiaceae	Bark	Sapo	12.40 ± 4.02	61.09 ± 5.68
19	***Morinda lucida***	Rubiaceae	Leaf	Oruwo	25.59 ± 12.72	28.92 ± 9.12
20	***Baphia nitida***	Leguminosae	Leaf	Igi Osun	16.08 ± 2.81	17.40 ± 3.11

21	*Mimosa pudica*	Mimosaceae	Whole plant	Patanmo	44.60 ± 1.68	9.29 ± 3.01
22	*Crinum jagus*	Amaryllidaceae	Bulb	Ogede Odo	11.02 ± 3.99	-
23	*Dioclea reflexa*	Leguminosae	Seed	Arin	44.65 ± 7.64	3.32 ±1.13
24	*Harungana madagascariensis*	Guttiferae	Leaf	Amuje	27.10 ± 11.79	15.59 ± 5.47
25	*Harungana madagascariensis*	Guttiferae	Bark	Amuje	Agglutination	agglutination
26	*Heliotropium indicum*	Boraginaceae	Leaf	Ogbe Akuko	2.20 ± 4.92	8.25 ± 4.85
27	*Drymaria villosa*	Caryophyllacaea	Whole plant		49.81 ± 11.72	-
28	*Cassia sieberiana*	Leguminosae	Leaf	Aridantooro	30.60 ± 1.33	6.12 ± 1.68
29	*Cassia sieberiana*	Leguminosae	Seed	Aridantooro	20.47 ± 5.78	9.78 ± 1.28
30	*Cassia sieberiana*	Leguminosae	Bark	Aridantooro	13.88 ± 2.19	14.12 ± 10.36
31	*Cassia sieberiana*	Leguminosae	Pod	Aridantooro	54.93 ± 8.70	5.90 ± 4.37
32	*Theobroma cacao*	Malvaceae	fruit pod 70% ethanol Aqueous	Koko	22.41 35.50	40.86 42.00
34	*Parquetina nigrescences*	Asclepiadaceae	Leaf and Stem 70% ethanol Aqueous	Ogbo	28.5761.20	40.00 82.50
35	*Alchornea laxiflora*	Euphorbiaceae	Leaf 70% ethanol Aqueous	Opoto	42.06 69.45	46.15 78.20
36	*Olax subscorpiodea*	Olacaceae	Leaf 70% ethanol Aqueous	Ifon	29.65 45.35	30.77 38.20
37	*Morinda lucida*	Rubiaceae	Stem and leaf 70% ethanol Aqueous	Oruwo	39.45 67.30	51.45 72.20
38	*Magnifera indica*	Anacardiaceae	Stem 70% ethanol Aqueous	Mangoro	30.45 58.40	34.55 62.50
39	*Vernonia amygdalina*	Asteraceae	Leaf 70% ethanol Aqueous	Ewuro	25.25 34.00	30.42 42.45
40	*Anacardium occidentale*	Anacardiacea	Stem 70% ethanol Aqueous	Guafa	17.45 59.65	18.65 23.20
41	*Cola acuminate*	Malvaceae	Bark	Obi		

			70% ethanol Aqueous		29.00 45.35	30.33 32.42
42	*Carica papaya*	Caricaceae	unripe fruit 70% ethanol Aqueous	Ibepe	60.20 73.00	62.45 89.65
43	*Croton zambesicus*	Euphorbiaceae	Leaf 70% ethanol Aqueous	Aje ko bale	50.35 70.35	54.55 74.45
44	*Spondias monbin*	Anacardiaceae	Leaf	Ewe Iyeye	56.61 ± 7.40	9.29 ± 2.70
45	*Lecanodiscus cupanioides*	Sapindaceae	Leaf	Akika	1.65 ± 1.03	1.73 ± 2.39
46	*Senna alata*	Solanaceae	Leaf	Asunwon oyinbo	18.49 ± 6.92	84.04 ± 4.65
47	*Anthocleista vogelli*	Loganiaceae	Bark	Sapo	47.48 ± 2.39	2.49 ± 1.77
48	*Mimosa pudica*	Mimosaceae	Whole plant	Patanmo	13.70 ± 1.48	9.03 ± 3.80
49	*Cassia sieberiana*	Leguminosae	Leaf	Aridantooro	26.30 ± 2.11	2.96 ± 2.59
50	*Cassia sieberiana*	Leguminosae	Seed	Aridantooro	55.59 ± 13.04	36.15 ± 3.29

Five of these plants have been evaluated to fractional levels. The resuls of this study is presented in Table 8.

Table 8: Antisickling Activities of fractions obtained from five antisickling plants

Plant	Crude extract		Pet. Spirit Frac		Ethyl acetate Frac		Aqueous Frac	
(4mg/ml)	Inhibitory	Reversal	Inhibitory	Reversal	Inhibitory	Reversal	Inhibitory	Reversal
Olax subscorpoideae (1mg/ml)	18.1	73.1	19.8	70.6	21.3	68.4	8.0	88.2
Moringa oleifera	88.0	76.9	88.2	94.7	94.3	94.0	94.6	69.2
Parquentina nigrescense	52.2	66.0	69.5	65.6	72.7	73.4	70.2	69.2
Alchornia laxiflora	86.2	65.2	11.5	3.1	21.0	16.1	51.3	61.0
Calliandra portoricensis	89.5	76.5	5.9	10.2	31.6	25.3	61.9	65.6

Calliandra portoricensis and *C. haematocephala* were found to have very good antisickling activities and as such, *C. portoricensis* was extensively studied with a view to developing a herbal drug which can be used by SCD patients to manage their crises. Thus, the extract of *C. potoriscensis* leaf was subjected to histological, biochemical, toxicology and cell membrane stabilization tests to determine its safety and possible mechanism of action.

The extracts of the plants were evaluated for anti-sickling potency. The relative antisickling activities of the leaves and roots of the two *Calliandra* species were determined to assess the most active fraction of the plants; and their effects on human erythrocyte cell membrane stability. The results of the anti-sickling findings have been delivered at International conferences and Seminars.

The biochemical, sub-chronic toxicological studies of *Calliandra portoricensis* (Jacq.) H.M.Hern (Mimosaceae) are being reported for the first time. The toxicological evaluation of the ethanolic extract of the leaf of this plant was investigated with a view to ascertaining its possible toxic effects. Thirty-six Swiss Albino mice of both sexes (20 g – 31 g *b.w*) were grouped into 4 comprising three treatment groups administered with doses of the extract (2, 4 and 8 mg/kg body weight *o.p.*), and one control group without treatment with the extract for 14 days. At the end of the 7 days, 14 days, and 28 days (after 14 days post-treatment/recovery period), the various groups of mice were sacrificed and assessed for tissue damage by measuring the enzyme activities in the serum and liver.

The result showed that at 7-day period, there was significant ($p<0.05$) increase in the activities of serum AST and ALT, and significant ($p<0.05$) decrease in serum ALP, liver AST and ALT when compared to control. Following 14 days post treatment, the observed changes were comparable with the control values. It can be concluded that the administration of the extract depressed the liver amino transferases in a dose dependent manner, with concurrent increased pattern of activity in the serum. This indicates that *C. portoricensis* extract could be toxic when administered sub-chronically but the enzyme activities can be restored on cessation of extract administration. It follows that the extract should not be administered chronically or continuously on daily basis. (Izuka and Agbedahunsi, 2011).

The histopathological evaluation of the leaf of *Calliandra portoricensis*

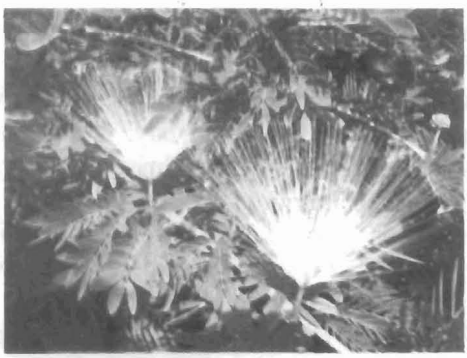
In a sub-chronic histopathological study, 70 % ethanolic extract of the leaf was administered orally to the animals, repeatedly daily, for 14 days after which the drug was withdrawn and the animals observed for additional 14 days. The toxicological effect of this administration was evaluated at dose range of 1- 8 mg/kg body weight (bw) dose on Swiss albino mice.

There was a general non-significant change ($P< 0.05$) in the relative organ weights of the animals. There was an increase in the liver weight monitored on the 7th and 14th day which was reversed after the withdrawal of the extract by the 28th day. There was no noticeable significant change ($P< 0.05$) in the weights of the brain, kidney, heart and spleen. The microanatomic features revealed dose dependent progressive degeneration upon administration and withdrawal of the extract. There was however irreversible damage in the liver and kidney at high doses particularly above 4 mg/kg bw dose (Adejuwon and Agbedahunsi, 2011). Both the biochemical and histopathology of the extract indicated that the dose should not exceed 4 mg/kg *bw*, which is the therapeutic dose.

In an attempt to determine the possible mechanism of action of *C. portoricensis* leaf extract, an *in vitro* evaluation of the membrane stabilizing activities of the leaf and root extracts of the plant was carried out on sickle cell and human erythrocytes (Amujoyegbe, Agbedahunsi and others, 2012). The result showed concentration dependent membrane stabilization property. The mode of protection of the leaf and root extracts compete favourably with the standard drug (Ibuprofen). The ethanolic root extract gave the best protection. The study concluded that *C. portoricensis* exhibited human erythrocyte membrane stabilizing property with the possibility of stabilizing the RBC of the HbSS cell membrane from becoming sickled even in hypoxia states.

Formulation of *IFESIKLIN*®: *Calliandra portoricensis* leaf extract as an anti-sickling agent

Based on the efficacy and relative nontoxic results at doses $\leq$ 4.0mg/kg bw we carried out formulation studies on the leaf extract and the formulated products tested at various doses at 1 – 4 mg/mL. The formulated products inhibited and reversed the HbSS RBC in manners comparable to vanillic acid for inhibitory activity (88.37 %) and para-hydroxyl benzoic acid (PHBA) for reversal (88.35 %) at 4.0 mg/mL while ***IFESIKLIN***® product gave 88.68 % for reversal and 93.32 % for inhibitory at 4.0 mg/mL. This research is currently undergoing patenting (Shaibu, Agbedahunsi, and Oladimeji, 2016).



Calliandra portoricensis

Cnidoscolus aconitifolius

Moringa oleifera

Carica papaya

Telfairia occidentalis

Plate 2: Some of our Sickle Cell Research Plants at the O.A.U. Campus

Other Research Contributions

Besides these three main research areas, I made some contributions to research in steroid industry. I investigated the steroidal release of sapogenins, particularly hecogenin from Nigerian *Agave* species and

Furcraea selloa. I reported that *F. selloa* gave better yield of hecogenin than the *Agave* species (Agbedahunsi, Elujoba and Adesina, 1987 and 1990). Similarly, in the area of anti-parasitic research, the hirudinicidal activities of some natural molluscicides used in schistosomiasis control was reported (Gibremedhin, Agbedahunsi and others, 1994) while the ecotoxicity and pharmacoepoeial standards were determined for a natural molluscicide, used in the control of schistosomiasis (Adewunmi, Agbedahunsi and other. 2001a). Some Nigerian medicinal plants have been screened for trypanocidal properties which are useful in both human and ethno-veterinary medicine (Adewunmi, Agbedahunsi and others, 2001b). Adelodun, Agbedahunsi and others (2013) studied the anti-trypanocidal and anti inflammatory activities of selected Nigerian medicinal plants. Agbedahunsi *et al.* (2006) studied the trypanocidal properties of *Terminalia ivorensis in vitro.* Adepiti, Adewunmi and Agbedahunsi (2014) reported the anti-trichomonal activities of *Acanthospermum hispidium.* As part of our studies in the environmental control of mosquitoes which are the vectors for malaria parasites and yellow fever virus, we studied the biological activities of the methanolic extract of *Lycopersicon esculentum* leaf from South West Nigeria (Adewoyin, Agbedahunsi and others, 2012). We also studied the larvicidal and ovicidal properties of 18 plants from the Asteraceae family against vectors that transmit Zika virus, Dengue fever and Chigunguya, the *Aedes aegypti* mosquito (Adediji, Agbedahunsi and Adewoyin, 2016). This was with a view to controlling the disease. Asteraceae family contains pyrethroids which is an active ingredient in DDT insecticide.

Mr. Vice Chancellor sir, I joined the service of this University as a Research Assistant in the Drug Research and Production Unit of the Faculty of Pharmacy in 1984. I was pursuing an M.Phil degree in Pharmacognosy then but by the grace of God and the assistance of the University, through the then staff training scheme, the University funded the completion of my M.Phil and Ph.D. in Pharmacognosy. Mr. Vice-Chancellor, I am very grateful sir.

As an academic member of staff, I have won many laurels and grants such as the Royal Society U.K Developing World Study Visit (DWSV) Award, **Dec. 2000 - Mar. 2004; March – June, 2007.** Obafemi Awolowo University Research Grant in 1998 for Chemical and Anti-malarial Studies of *Khaya ivorensis* A. Chev. **URC/98/PHM/1: (₦218,210:00).** I was the Principal Researcher and my co-researchers were Prof. S.A. Adesanya and Dr. Vincent O. Makanju of blessed

memory (may his soul continue to rest in peace). Again, through the University Research committee, I got the Educational Trust Fund (TETFUND) Grant in **2012** for Advocacy and Development of Drugs for the Management of Sickle Cell Disorder in Southwest Nigeria. The sum of the grant was **₦9,868,488:00)**. I was the **Principal Researcher** and my Co-Researchers were Prof. Norah O. Akinola, Dr. Francis A. Oladimeji, Prof. Moses A. Akanmu and Dr. Olanike O. Olaogun. The outcome of the grant enabled us to carry out advocacy visits and ethnomedicinal surveys in two local government areas each, in the three senatorial zones of Ondo State (Okiti pupa, Igbokoda, Ile Oluji, Ondo, Owo and Ikare). In Osun State we carried out the survey in Ile Ife, Osu, Iwo, Ikire, Osogbo and Ila Orangun. We identified and compiled the plants which the Traditional Medical Practitioners (TMPs) use in the management of Sickle Cell Disease (SCD). We trained 3 PhD, and 6 M.Sc. students. We established a standard Sickle Cell Research laboratory in the Drug Research and Production Unit (DRPU) that serve the needs of students and staff that are interested in carrying out sickle cell research from within and outside our University. We have screened over 50 plants for their antisickling activities *in vitro*. We have also formulated a drug (IFESICKLIN®) which is undergoing preliminary clinical trials (Phase III). We have also trained SCD care givers and set up some SCD Support Groups in Akure, Ondo State, and Ile Ife, Osun State in collaboration with the Mustered Seed NGO.

I got the TWAS Grant for Scientific Meetings held in Developing Countries **09-025 SM/AF/AC/M/A - UNESCO_FR:3240206836 (11/5/2009). (US$3,000:00)** to organize an International Symposium on Drug Development from Medicinal Plants: Problems and Prospects hosted by DRPU, OAU, Ile-Ife in 2009. I won the 1st Prize Award as the Best Researcher in Life Sciences and Medicine at the 4th Nigerian Universities Research and Development Fair held in conjunction with the National Universities Commission at the University of Nigeria Nsukka, November 2010. I also won the award to participate at the Life Time Leadership training programme by the Haggai Institute Atlanta, U.S.A. I was in Maui Hawai from June to July 2001.

I am a member of some professional bodies: Nigerian Society of Pharmacognosy (1985 to date); I had once held the position of the Society's National Vice-President and the current Editor-in-Chief of the Society"s Journal: Nigerian Journal of Natural Products and Medicine (NJNPM), a position I have occupied since 2008. This Journal ranked

second according to the National University Commission ranking of Nigerian journals. The journal was one of the national journals that won the 5 million Naira TETFund grant for the development of Nigerian academic journals. Presently, the production of the 22nd volume (2018) is in progress. It is also one of the African Journals on-Line (AJOL), possessing both the DOI and ISSN numbers.

I am a member of the Nigerian Field Society (1985 to date); New York Academy of Sciences, from June 1999 and I am a member of the Research Board of Advisors of the American Biographic Institute (2002). I have been an associate member of the Third World Organization for Women in Science since 2000. I have held many positions in theWest African Network of Natural Products Research Scientists (WANNPRES) from 2004 to date. I am the current Nigerian National Coordinator for the West Africa sub–regional body which draws membership of natural product research scientists from the Francophone and Anglophone Countries in the subregion.

In my tenure as the Director of DRPU, we succeeded in registering three of our herbal drugs, with NAFDAC, namely: *JEDDY Decoction* (for flatulence and haemorrhoids), *MAMA Decoction* (antimalarial) and *MAMA Powder* (antimalarial). The Unit manufactured other herbal products such as *Schisto* herbal soap (Aridanin the putative compound is a natural molluscicide which kills the cercarea worms that are vectors of schistosomiasis Adewunmi, Agbedahunsi and others, 2001a), Avtola herbal soap (a bathing beauty soap), Chancellor and Tonic herbal teas (the former is very good in the management of asthma. It relaxes the guinea pig trachea muscles, while the latter is a blood tonic with proven erythropoietic effect - Oyedara and Agbedahunsi, 2006), along with the generic drug paracetamol produced by the Unit.

Professional Accomplishment

My research focus has primarily been on investigating medicinal plants used for the treatment or management of diseases such as malaria, alzheimer's and sickle cell disorder. My accomplishments in these areas of medicinal plant research have been well discussed in this lecture. I have chaired two sessions at a scientific conference on traditional medicine, organized by the Goeth Institute of the German Embassy in Lagos on 10 - 11th November 1997. I served as external examiner for undergraduate and postgraduate degree programmes in the department of Pharmacognosy in various pharmacy schools in Nigeria. I served as

external examiner for the oral examination of the PhD theses of three Ghanian students and I moderated the undergraduate examinations of the Department of Pharmacognosy, Kwame Nkuruma University of Science and Technology Kumasi (KNUST), Ghana. I serve on the editorial boards and have reviewed manuscripts for publications for some international journals. I have served as external assessors for professorial (PFQ) cases both within Nigeria and in Ethiopia. Also as external assessor at the KNUST, Kumasi, Ghana. I was invited as expert to develop curriculum for the M.Sc. programme in Kenya in 2017 for the Pan African University (PAU) in their Institute of Life and Earth Science. Pan African University is an African Union established University. Since 2010, I have led the University team to the National University Research Innovation Scientific and Development Fair (NURESDEF), organized by the National Universities Commission. The University had won prizes on various editions of the Fair. I have served on many occasions as the Director of the Drug Research and Production Unit (2007 - 2013 and 2016 - 2018), a position I relinquished in July 2018 in order to take up a Research Professor position at the National Institute for Pharmaceutical Research (NIPRD), Abuja on a one-year sabbatical leave.

Mr. Vice-Chancellor sir, I have travelled to many countries, projecting the image of our University. I became an expert on anticholinesterase inhibitory studies for the management of Alzheimers disease at the Kings College London School of Pharmacy, under the leadership of Professor Peter Houghton. I made oral presentation entitled "Anti-Malarial and Toxicological Studies on *Khaya grandifoliola*" at the Joint Scientific Meeting of Phyto-chemical Research Groups of (Kew Garden, Surrey – Kings College, London- London School of Pharmacy Brunswick Square) at the Royal Botanic Gardens (Kew Gardens), Surrey, London, on the 18th June, 2003. I attended the 50th Anniversary Conference of the Phytochemical Society of Europe, Cambridge, 11 - 14th April, 2007. I made a poster presentation on Non-alkaloidal Inhibitors of Acetycholinesterase (Professor Houghton, P.J., **Agbedahunsi, J.M.**, Masahiro, O., Mukherjee, P.K. and Govindarajan, R.).

I was at the 2nd WANNPRES sub-regional conference held in Elmina, Cape Coast, Ghana (August 2006), 3rd and 4th of the international regional conference in Ouagadougou, Burkina Faso, August 2008 and 2010, respectively. I was a member of the Local Organizing Committee that organized the 5th and 6th edition of the international conference held

in Nigeria 2012 and 2014, when the Secretariat of the international body moved to our University (OAU). I was also present at the 7th and 8th edition in Burkina Faso in August 2016 and 2018. I led the Nigerian delegates to the last two conferences as the Country National Coordinator. In all the editions of the international conferences, I made oral presentations. I was one of the national experts invited to the Research Continuum in Natural Products Drug Discovery, Abuja, Nigeria, jointly organised by National Institute for Pharmaceutical Research and Development (NIPRD), Federal Ministry okf Health, Nigeria, National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), and United States Department of Health and Human Services. 12 – 14th May, 2009. I participated in the African Journal Partnership Programme (AJPP) Workshop, Noguchi Memorial Institute for Medical Research, University of Ghana, Legon, 28th September, 2009. I also participated at the Naturally African Sub-Regional Consultative Workshop on Natural Products of Western and Central Africa, organized by SNV and World Agroforestry Centre (ICRAF) in Tamale, Northern Ghana, 27 - 29th October, 2009. These are just few of the Workshops and Conferences I participated.

My Administrative Services

Services within the Department: I have served in many capacities in the Unit especially as acting and substantive Director of the Unit as mentioned earlier in this lecture. I have also served on many Boards and Committees of the Faculty.I have served on two task forces in this University viz Task Force on Traditional Medicine (1997 -1998) and Task Force on the Activities of the Teaching and Research Farm of our University December 2016 to March, 2017. I was the Chairman of the Faculty Postgraduate Committee and subsequently a member of the Postgraduate College Board from 2007 – 2010. I was a member of the Ethical Committee of the Institute of Public Health (IREC) 2015- 2017. I have represented the Dean of Pharmacy on the Board of Natural History Museum and Institute of Cultural Studies of our University. I am also on the board Natural History Museum O.A.U., Ife.

Outside the University, I have been a member of the welfare and visiting committee of the Nigerian Prison, Ile Ife since 1995 and **Chairman**, Water Project Committee, I facilitated the sinking of deep well at the Prison in 2004 by the Osogbo Diocese of the Catholic Church. I was an associate diocesan coordinator of the Justice Development and Peace Commission of the Catholic Church from 1994 to 2000 thereafter I

served on the Board of the Commission. I have been a member of the Full Gospel Business Men's Fellowship International, Nigeria. I served as the President of the Ile-Ife Main Chapter from 2001 – 2005, and Field Representative of the fellowship since, 2005 to date. I am a 4th degree Knight of St. Mulumba (KSM) of the Catholic Church.

Conclusion and Recommendations

I hope I have been able to convince you that our existence is closely knitted to the plants. There is a great symbiotic relationship between man and plants. Actually man requires plant more than the otherwise. The diverse utilization of plants by man is beyond the scope of this lecture. I wish to end this lecture by making these few recommendations:

- that there is no mystification in the utilization of herbal drugs provided it is standardized, with assurance of non being toxic and correct dosage
- Utilization of imported food suppliments are not necessary, In Nigeria we have been blessed with abundance of fruits and vegetables virtually all the year round. We should cultivate the habit of eaten at least a fruit and vegetable daily.
- It is hereby recommended that all Nigerians should have medicinal garden and orchard at home where fruits such as Orange, Pawpaw, grape fruits, banana, plantain, guava, almond fruit and Avocado pear are cultivated. Constant consumption of fruits and vegetables will reduce your visit to the hospital.
- It is also recommended that our various researches be translated into finished formulated products which will be registered by NAFDAC for the wellbeing of our people especially in the management of chronic diseases such as diabetes mellitus, hypertension, sickle cell disorder Alzheimer 's disease etc.
- I also wish to charge our Natural Products Research Scientists to endeavor to take their researches to patentable level; else smart scientists abroad will complete the work and gain all the credit. The latter calls for the intervention of our Governments both at the Federal and State levels to fund researches. Many of our laboratories are begging for acquisition of cutting edge scientific equipment. Many of our Laboratories in the Country do not have hyphenated chromatographic/spectroscopic machines, and functional spectroscopic equipment which are essential tools for Natural products researches. Brain drain of our bright young scientists will continue except our Government addresses the above issues

I wish to recommend closer synergy between research scientists in our Universities, Polytecnics, Research institutes and the Industries in Nigeria as it is in developed countries. Many of our scientific outputs often end up on the shelves without contributing to the National economy or development

Acknowledgement
Mr Vice Chancellor sir, my voyage into the academic world at the Obafemi Awolowo University, Ile Ife was providential. I merely escorted Prof. Ayodeji Onayade (then Dr. Deji Onayade) to visit his wife, Dr. Olubunmi Onayade (nee Sontan) of blessed memory in October 1982. Bunmi was a great friend and classmate; may her gentle soul continue to rest in the Lord. There was an interview going on in the Faculty of Pharmacy on the fateful day. Bunmi had already started her Master of Philosophy programme in the Department of Pharmacognosy then. Deji challenged me on why embarking on a postgraduate programme had not appealed to me like his wife, Bunmi. I took up the challenge but since I was not aware of what providence had in store for me, I did not come with any of my credentials. It was Bunmi that went to the Postgraduate School to purchase the postgraduate form and later came to Lagos to collect the completed form along with my credentials and submitted on my behalf. Behold I was admitted. At that time, Prof. Anthony Elujoba was the Acting Head of Department of Pharmacognosy and he happened to have supervised my M.Phil. degree program; he also happened to have later supervised my doctoral degree thesis. Both late Dr. Mrs. Olubunmi Onayade and Professor Anthony Elujoba played significantly unforgettable roles in my academic and intellectual career; these roles will remain evergreen in my loving memory. It is most disheartening and unfortunate that Bunmi is not here today to witness this inaugural lecture but we are consoled that where she is today, no death can touch her any more. It is therefore my prayer on this occasion as always that, her lovely and gentle soul continues to find eternal rest in the bosom of Father Abraham. Amen.

Mr. Vice-Chancellor, distinguished Ladies and Gentlemen, when the pronouncement of my professorship became depressively intractable, God raised an Angel in the person of Professor Anthony Adebolu Elujoba, the then Acting Vice-Chancellor of this University, to escavate my papers from where they were kept and within a short while, the professorship was announced on the 6th October, 2016 and was backdated to October 2012, the effective date of my promotion.

Professor Elujoba sir, my teacher, my supervisor and my mentor, I will continue to thank God for your life sir. To all others, that have contributed to my academic career, particularly my former teachers; I am very grateful to you all.

I want to specially acknowledge all my Postgraduate students that accompanied me on this journey to the successful "Cannan Land", full of milk and honey. Briefly on the list of my graduate students: I have had the privilege of successfully supervising the Doctor of Philosophy theses of the following, namely: Dr. Taiwo O. Elufioye, Dr. Ololade O. Oyedapo, Dr. Mojisola C. Cyril- Olutayo, Dr. Chukwunwike N. Nwonu and Dr. David A. Adediji. I am grateful to you all. I am grateful to God that all of you are contributing your quota in the development of our father land. I have supervised ten Masters of Science students they are Dr. Taiwo Elufioye, Dr. Awodayo Adepiti, Dr. Olayinka O. Amujoyegbe, Tolulope A. Ajayi, Adeola Mary Fadeyi, Tawakalit O. Shittu, Adeola Oyekunle, Femi Emmanuel Shaibu, Tolulope O. Adeleye and Ibikunle O. Adeyiola. I will particularly want to acknowledge two of my former students but today are eminent Professors, they are Professor Clement Adebooye and Professor Seyi Fabiyi of our University. I am currently supervising 3 Ph.D. and 2 M.Sc. students. To others such as Dr. Violet V, Bumah University of Calabar, now in the USA), Dr. M.N. Gayur (at Kings College London, now in Canada), Dr. J.O. Olanlokun (University of Ibadan) and Dr. Ayodeji Oriola (Ife), that I contributed in their PhD studies, I give God the glory to impact positively in their lives. I am most grateful to my Inaugural Lecture orgarnizing committee led by Prof. I.B. Osho for their untiring effort to see to the success of this inaugural lecture. I also want to acknowledge my collagues at both the DRPU and the Faculty of Pharmacy for their moral support and age long comradeship.

I am particularly grateful to my father, late Gregorio, Bankole Francis Agbedahunsi who through thick and thin made sure he gave my siblings Engineer Babawale Agbedahunsi, Ms Aderonke Agbedahunsi and I good education. He believed in education, he would rather go hungry than forfeit our education. I am grateful to you sir. May your soul rest in peace. Words are inadequate to express my profound gratitude to my darling mother, Mrs Celestina A. Agbedahunsi who is here present to witness the academic crowning glory of her son. I am very grateful ma. I pray that God in His infinite mercy will grant you the grace to witness more auspicious occasions in your life. To my sibblings Wale and Ronke

I am very grateful to you for the love and kindness you have shown to me since our childhood. My prayer is that the Lord will bless your spouses and children. I am extremely grateful to my sisters-in-law and their spouses who are my brothers. Mrs Aderonke Adeniyi (my wonderful prayer partner) and her husband Professor Funso Adeniyi, Ayodele Akande and her husband Dr. Alaba Akande, Temitope Lakisokum and Abiodun Asabor with her husband Wale. The bond of Late Chief and Mrs Adeleke Lakisokun that bind us together will forever be strong.

The Scripture tells us that nothing is comparable to finding a virtuous wife (Prov. 31:10-12). Mine is an excellent wife. I found a sister, a mother, a companion and a soul-mate in my lovely beautiful wife, Chief Mrs. Abimbola Abidemi Anne Agbedahunsi, a retired Permanent Secretary from the service of the State of Osun. You bore me our four lovely and successful children, Barrister Mosunmola Adeolu-Adeoti, Mrs. Adedoyin Adeniyi-Faleye, Dr. (Engineer) Alex Oreoluwatomiwa Agbedahunsi and Barrister Flora Oluwatomisin Agbedahunsi. They have all been our pride with their spouses Adeolu Adeoti and Adeniyi Faleye. This acknowledgement will not be complete if I fail to mention our grand children, namely: Adedamola and Abake Adeolu-Adeoti; also Anne Mojolaoluwa and Anastasia Mofetoluwa Adeniyi-Faleye. You all have played great roles in my life and I pray that the Almighty that rewards good deeds will reward you (Col. 3:24).

Mr. Vice Chancellor sir, all the days of my life I will continue to give the Almighty the glory. It is neither by my power nor my might that I achieved this feat of standing before this august gathering this day to deliver my inaugural lecture. As such, I ascribe all power, all honour and all adoration to this great God who gave me life, intellect and grace. I commit the rest of my life to Him and humanity. I will continue to seek His guidance and protection in my journey of life. So as it was in the beginning, now and forever, He alone will be my God and that of my household.

I thank you for listening. God bless you all.

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