FEDERAL UNIVERSITY OF TECHNOLOGY MINNA

MALARIA: THE USE OF PHYTOMEDICINES AS VIABLE ALTERNATIVE MANAGEMENT STRATEGY FOR AN AFRICAN AND THIRD WORLD TRAGEDY

By

ALI AUDU JIGAM
BSc (ABU Zaria), MSc (UNIJOS), PhD (FUT Minna)
Professor of Biochemistry

INAUGURAL LECTURE SERIES 49

15TH DECEMBER, 2016

FEDERAL UNIVERSITY OF TECHNOLOGY MINNA

MALARIA: THE USE OF PHYTOMEDICINES AS VIABLE ALTERNATIVE MANAGEMENT STRATEGY FOR AN AFRICAN AND THIRD WORLD TRAGEDY

By

ALI AUDU JIGAM
BSc (ABU Zaria), MSc (UNIJOS), PhD (FUT Minna)
Professor of Biochemistry

INAUGURAL LECTURE SERIES 49

15TH DECEMBER, 2016

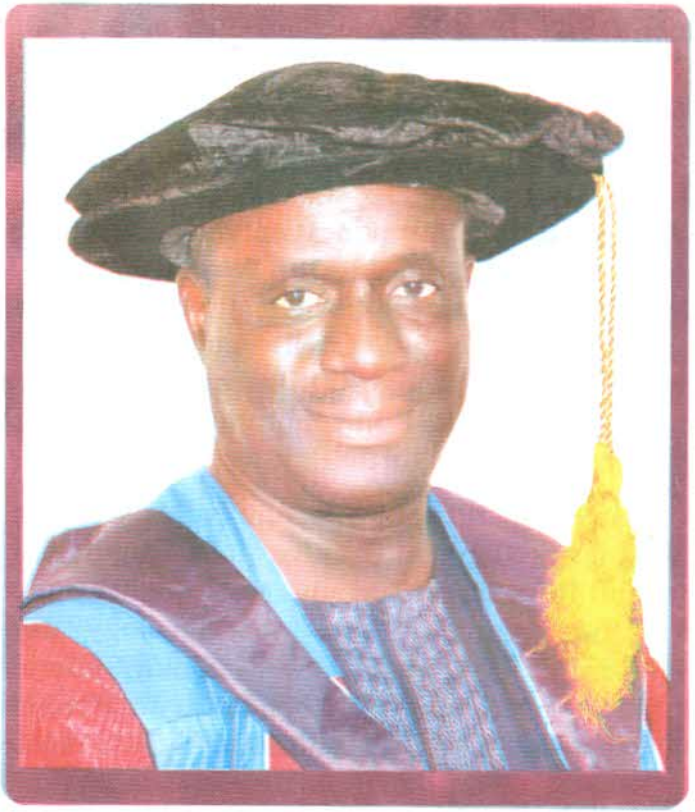
This 49th Inaugural Lecture was delivered under the Chairmanship of:

Professor M. A. Akanji, FNSMBM, FAS
Vice-Chancellor
Federal University of Technology, Minna

Published by:
University Seminar and Colloquium Committee
Federal University of Technology, Minna.

15th December, 2016

Design + Print:
Global Links Communications, Nigeria
✆: 08056074844, 07036446818



ALI AUDU JIGAM

B.Sc (ABU, Zaria), M.Sc (Unijos), PhD (FUT, Minna)

Professor of Biochemistry

Preamble

Mr. Vice Chancellor Sir, Deputy Vice Chancellors, Academic and Administration, the Registrar, Bursar, University Librarian, Deans of Schools, Professors, Directors, Heads of Academic Departments, Unit Heads of Academic Departments, Unit Heads, Erudite Scholars, Members of the University Community, invited guests, great FUT Minna students, great life sciences students, greatest Biochemistry students, distinguished ladies and gentlemen.

It is with absolute humility, adoration and gratefulness to the providence of ALLAH SUBHANAHU WA TA'ALA that I stand before you today to deliver the **49th** inaugural lecture of this great citadel of learning. This is the **SECOND** inaugural lecture from the School of Life Sciences, the **SECOND** from the department of Biochemistry and the **FIRST** on application of natural products, specifically phytochemicals in the fight against malaria.

Mr. Chairman Sir, the title of my lecture is "Malaria: The Use of Phytomedicines as Viable Alternative Management Strategy for an African and Third World Tragedy". Most would wonder why a biochemist has wandered into pharmacology, pathology, toxicology, drug development, even botany, microbiology, natural products etc. Simply put, biochemistry is at the interface of all life sciences and as specialization sets in especially in advanced learning taking into cognizance also limitations in our operational environment in terms of high-tech equipments and expertise, most academics traditionally relapse into basic research which in fact serves as the fulcrum of ground breaking work in all spheres of science. I have also chosen this topic because millions of people especially in sub-Saharan Africa and the third world continue to be devastated even now in the 21st Century by this debilitating ailment. Indeed malaria has been aptly tagged as "a disease of poverty" among others. The number of easily available, affordable and effective antimalarial drugs is

few. Viable multi-stage vaccines are unavailable and not envisaged until some decades into the future. This situation is further exacerbated by the rapid spread and intensification of drug resistance by certain malaria parasites. Therefore, whilst waiting for a "silver bullet cure', active antimalarial principles can be isolated and standardized from indigenous plant species with reputation among herbalists against fevers and the disease which can be used as alternative treatments. A few of such products have been developed and deployed with high success rates in some malaria endemic regions of the world. Moreover natural products or herbal medicines generally termed as **nutraceuticals** hit a global market value of up to 100 billion U.S. dollars in 2015. This could be a veritable national source of revenue for our country if properly utilized through the development of herbal treatments not just for malaria but the plethora of afflictions of mankind.

The lecture will now lay emphasis on chemotherapy, biochemistry of drug resistance by malaria parasites, my humble contributions, conclusion and suggestions.

Introduction

Malaria is a protracted disease burden with ravaging effects. It has compromised improved healthcare and life expectancy especially among the poor in tropical regions of the world including Africa, Asia, Central and South America. (Amoa-Onguene, 2013). Malaria with AIDS and tuberculosis is one of the three major communicable diseases linked to poverty. Recent WHO estimates indicate global malaria infection at over 300 million with up to 640,000 deaths annually (WHO, 2016; Abay *et al., 2015).* Indeed malaria is a disease experiencing a renaissance and is caused by *Protozoans* of the *genus Plasmodium*: *P.malariae, P. ovale, P.vivax* and *P. falciparum*, the latter being the most virulent and drug resistant specie responsible for about 80%

morbidity and mortality from the disease (Ntie-kang *et al.*, 2014; Amoa – Onguene *et al.*, 2013).

The situation has been aggravated by the unavailability of a viable vaccine and the spread of drug resistant *Plasmodium* species. This has resulted to a dramatic decline in the efficacy of the most common and affordable anti-malarial drugs (Del'Agli *et al.*, 2012). The screening of prevalent herbal medicines especially in endemic communities may yet offer some hope in the search for a new generation of cures for the disease. Such compounds should be active against chloroquine, Sulphadoxine-Pyrimethamine and Artemisinin resistant *P. falciparum* strains; resolve parasitaemia within a time frame of 24-72hrs; with high safety margin; be affordable and available in an appropriate formulation for oral use (Vale *et al.*, 2015).

The variability and sustainability of plants as sources of antimalarials is best exemplified by the fact that the alkaloid quinine isolated from *Cinchona ledgeriana* (*Rubeaceae*) has been the fulcrum of chemotherapy for the disease for over two centuries. Similarly, artemisinin, a Sesquiterpene lactone with potent antimalarial action was more recently isolated from the Chinese antipyretic herb, *Artemisia annua* (Abay *et al.*, 2015).

The widespread use of plants as medicines is well documented with some literature indicating that 80% of the health care needs of the rural poor in developing countries depend on this source (Amoa–Onguene, *et al., 2013).* Plant derived natural products have been exploited as Antimalarials (quinine, artemisinin, chinconine), analgesics and antipyretics (ipecac), transquilizers (reserpine), cardiac stimulants (digitoxin), anti-cancer (taxol, vincristine and vinblastine), AIDS (+) Calanolide A and (-) calanolide B) (Hay *et al.*, 2003).

Africa has a rich floral diversity which provides materials for the treatment of fevers and malaria and thus should afford the next

generation of drugs or templates necessary for their synthesis (Bashir *et al.*, 2015). Such pharmacologically important compounds could be found in bitter medicinal plants which contain high levels of alkaloids and terpenoids (Oliviera *et al.*, 2009). Alkaloids are intensely bitter, basic, nitrogenous secondary chemical constituents existing naturally in large proportions in the seeds, roots, leaves and stem bark of plants often in combinations with vegetable acids. More than 12000 alkaloids are known to exist in about 20% of plant species alone out of which only a few have been exploited for medicinal purposes (Doughari *et al.*, 2012).

Plant derived alkaloids in clinical use include the analgesics morphine and codeine, the muscle relaxant (+)tubocurarine, the antibiotics dangiunafine and barberine, anti-cancer agent vinblastine, anti- arrhythmic ajmaline, pupil dilatory atropine and the sedative scopolamine. Others are the addictive stimulants caffeine, nicotine, codeine, atropine, morphine, ergotamines, cocaine and ephedrine (Madziga *et al.*, 2010).

A search of the literature has indicated a host of alkaloids with anti-malarial properties derived from indigenous plants. These include indole alkaloids, naphthoisoquinolines, furoquinolines, acridones, amides and cryptolepines.

Other phytochemicals of non alkaloidal origin have also shown potentials as antiplasmodial agents thus could serve in malaria treatment. Such compounds include flavonoids, flavanones, isoflavones, chalcones, rotenoids, phenolics, polytylenes, quinones, coumarins, xanthones, sterols, lignans, tannins, glycosides, etc. Many more exist and are awaiting identification (Jigam *et al.*, 2013; Bashir *et al.*, 2015). The utility of such compounds as antimalarials can only be enhanced when their empirical parasitological, pharmacological and toxicological evidence and profiles have been ascertained. Chemometrics post structural elucidation of bioactive principles could generate

synthetic structural analogues with better activity and less toxicity as was the case with the 4, 8 and 9 aminoquinolines from quinine.

Herbal remedies for malaria are widely acceptable in poor rural African and Asian communities due to their easier accessibility, lower costs, lack of awareness about modern drugs and belief that the use of traditional medicine is more safe and effective. With the prevalence of drug resistance and threat to Artemisinin, emerging trends in malaria mitigation involves commercialization of standardized phytomedicines as is the case with Qinghao (*Artemisia annua*), Totaquina (*Cinchona* spp), Phyto–Laria (*Cryptolepis sanguinolenta*) and Azadirachtin A (*Azadirachta indica*) (Abay *et al.*, 2015).

Malaria is most devastating in Sub-Saharan Africa, where about 90% of global cases and deaths occur. Human malaria is transmitted by female *Anopheles* mosquitoes and is caused by four species of *Plasmodium*. Most cases of the disease and deaths are caused by *P. falciparum*. The development of resistance to mainstay drugs such as chloroquine and sulphadoxine and the threat to Artemisinin based Combination Therapies has necessitated the search for novel pharmacophores against the disease (Kaur *et al.*, 2009).

The life cycle, immunological defense mechanisms, and clinical development of malaria are characterized by periodic fever which follows the lysis of infected red blood cells and caused mainly by the induction of cytokines interleukin-1 and tumor necrosis factor. *P. falciparum* infection can have deleterious effects such as anemia, cerebral complications (coma or convulsions), hypoglycemia and glomerulonephritis. The disease is most acute in non-immune individuals including children, pregnant women and tourists (Kumar *et al.*, 2002).

Nature remains an ever evolving source for compounds of medicinal importance. Several compounds isolated from nature

also form a rich source of diverse structures for optimization to obtain improved therapeutics (Kaur *et al.*, 2009).

Natural products are the origin of approximately two-thirds of all drugs introduced in the past three decades (Newman and Craig, 2011). The connection between medicinal plants and antimalarial drugs date back to 1820 when quinine was first isolated from the bark of *Cinchona* spp. and continued to the present era with the isolation of artemisinin, a highly oxygenated sesquiterpene lactone from *Artemisia annua* (Achan *et al.*, 2011; Abay *et al.*, 2015).

In order to forestall the problem of drug resistance, artemisinin based combination therapy (ACT) is currently employed in the management of malaria. The fixed dose combinations involve artemisinin and various quinine based drugs e.g. primaquine, which has an impact on circulating mature gametocytes in humans while artemisinin blocks the transmission of *Plasmodium* parasites to humans from mosquitoes (Abay, 2013).

Despite the advantage of primaquine in the stated combination, a viable alternative to this drug is urgently needed because it can provoke hemolytic anemia in patients with Glucose-6-Phosphate Dehydrogenase deficiency (Abay *et al.*, 2015).

Artemisia annua is a Chinese antipyretic herb with an ancient history. Artemisinin was isolated in 1971 and recommended for the treatment of cerebral malaria and control of drug-resistant *P. falciparum* malaria.

Artemisinin derivatives in use include arteether, artesunate and artemether. The antiplasmodial activity of the drug involves its unique endoperoxide structure. Iron from digested haemoglobin reduces the endoperoxide bridge releasing highly reactive free radical iron oxo species which destroys the parasites. Artemisinin interferes with protein synthesis in growing parasites. It also acts on parasite membrane by lipid

peroxidation. Dihydroartemisinin the active metabolite alters ribosomal organization, endoplasmic dilation of nuclear envelope and disintegration of food vacuoles (White, 1997).

Quinine the original antimalarial together with its dextrorotatory isomer quinidine, are fluorescent alkaloids derived from the stem bark of Peruvian *Cinchona* tree. It is useful in treating other conditions e.g. arthritis, lupus, babesiosis and is even a frequent constituent of bitter tonics and stomach ache preparations (Cechinel-Filho, 2012). The crude drug was used for about 200 years before its alkaloids were isolated in 1820.

Laboratory synthesis of total quinine has been achieved by several methods but none of which can compete in economic terms with isolation of the alkaloid from natural sources (Okpako, 1991). Crude extracts are assumed to be more efficacious because of the possible synergism of the over 36 different alkaloids *Cinchona* contains (Lewington, 1990).

Quinine acts as a blood schizontocide although it also has gametocytocidal activity against *P. vivax* and *P. malariae*. As with other quinoline antimalarial drugs, the mechanism of action of quinine has not been fully resolved. The most widely acceptable hypothesis is based on the well-studied and closely related quinoline drug, chloroquine. Because it is a weak base, quinine localizes to a non-acidic compartment within the food vacuole of *falciparum* malaria parasite and inhibits heme polymerase enzyme thereby blocking hemozoin biocrystallisation in the heme detoxification pathway. Free cytotoxic heme thus accumulates and is lethal to the parasite. Quinine has also been reported to inhibit *Plasmodium* phosphoenol pyruvate carboxylase or carboxykinase (White, 1997).

Several workers have analyzed different plants for antimalarial activity; *Bidens polisa* a medicinal plant has been shown by Andrade-Neto *et al* (2004) to be effective against chloroquine

and mefloquine resistant *P. falciparum* in vitro. This activity was attributed to flavonoid and acetylene compounds (Brandeo *et al.*, 1998). Interestingly extracts from plants cultivated under standardized conditions were less active compared to the wild plants (Andrade – Neto *et al.*, 2004). Tasdemir *et al.* (2005) evaluated some Turkish plants for inhibition of *plasmodium* enoyl-ACP reductase (Fab I), a crucial enzyme involved in fatty acid biosynthesis. The extracts of leaves of *Rhododendron ungernii* and *R. Smirnovii* strongly inhibited the Fab I enzyme, an effect attributed to some polyphenolic compounds.

The extracts of some Kenyan medicinal plants including *Toddalia asiatica* and *Rhamnus staddo* in combination with chloroquine improved parasitaemia suppression from 38-66% and resulted in longer survival of mice indicating synergistic interactions. This was also attributed to the immune-modulatory role of the plant extracts in the host during early days of infection (Muregi *et al.*, 2007). *Azadirachta indica* (neem), *Khaya senegalensis* and *Vernonia amygdalina* are among many plants used in treating many diseases including malaria among indigenous African tribes. Leaf, seed and stem bark extracts of *A. indica (meliaceae)* have been demonstrated in many studies to inhibit *P. falciparum* asexual stages *invitro* (Udeinya *et al.*, 2008; Lu Cantoni *et al.*, 2010). *Invitro* screening of purified limonoids from Neem revealed that gedunins and nimbolides are the most active molecules against *P. falciparum* (Bray *et al.*, 1990). *Vernonia amygdalina* leaves are used as vegetables in soups after the bitter principle has been extracted and discarded; the stem is useful as a chewing stick in the prevention of dental decay among Nigerians. The leaf extracts are however used in Sub-Saharan African countries for the treatment and prevention of malaria. The anti-plasmodial activity of the shrub has been confirmed by several *invitro* and *invivo* studies. Sesquiterpene lactones, steroidal saponins and flavonoids have been isolated from the

leaves and found to be effective against *P. falciparum* (Abay *et al.*, 2015).

Khaya senegalensis is another "cure all" in African herbal practice with severally reported effects against *Plasmodium* parasites (Jigam and Atunde, 2001).

It is interesting to note that apart from the well-known classes of phytochemicals such as alkaloids, glycosides, etc other groups e.g. plant peptides are presently gaining recognition and being proven to be effective against malarial parasites. Panseeta *et al* (2011) isolated and demonstrated the anti-plasmodial efficacy of the cyclopeptide alkaloids nummularines B and Hemesine A from the roots of *Zizipus mauritani*.

A vast array of alkaloids have been isolated from many plant species and shown to have potent antimalarial effects. The outstanding example is quinine from *Cinchona* spp. which has been used for the treatment of malaria for more than three centuries. Alkaloid based antimalarials derived from plants can be classified as indole alkaloids, Naphthoisoquinolines, furoquinolines, Acridones, amides and cryptolepines (Amoa-Onguene *et al.*, 2013).

Dioncopeltine A, dioncophylline B and dioncophylline C isolated from the extracts of *Triphyophyllum peltatum* (*Dioncophyllaceae*) were highly effective against *Plasmodium* parasites (Kaur *et al.*, 2009). The list of such effective alkaloids is enormous.

Global acceptability, application and efficacy of phytomedicines have proportionately exposed millions of users to the underlying but seldom reported hazards of medicinal plant toxicity and mis-adventuring. Most herbal treatments are in the forms of crude or partially purified extracts often administered over a few days or weeks with the likelihood of cumulative organ intoxication and even death among recipients (Jigam *et al.*, 2012a).

The Chinese traditional herbal antimalarial, *Dichorea febrifuga* (*Saxi frabaceae*) which active principle febrifugine is clinically effective against *P. vivax* and *P. ovale.* Its hepatic toxicity has rendered the drug unacceptable. In vitro anti-plasmodial activity has been established for a number of quassinoids. These are bitter tasting, biosynthetically degraded triterpenes characteristic of the family *Simaroubaceae.* Sergolide, one of the 14 quassinoids is acutely toxic with LD_{50} of 1.8mg/kg hence counterproductive and inimical as a chemotherapeutic agent. The medicinal plant *Symphytum officinale L.* contains hepatotoxic pyrrolizidine alkaloids (Ramadhani *et al.,* 2015; Gamaniel, 2000).

Thus, the need for in vitro and in vivo toxicological profiling of such drugs as an integral component in their development is imperative (Jigam *et al.,* 2012b). Such routine evaluations include acute toxicity studies which are critical as they provide a good idea about the nature of the medicinal extract in addition to determining safe doses for clinical use. Sub-chronic and Chronic studies are necessary in the elucidation of target organs of toxicity and demonstration of dose-response relationships. Some toxicological indices often evaluated using laboratory animals include organ and body weights, feed utilization, haematological parameters, clinical biochemistry, gross and histologic pathology of tissues (Gamaniel, 2000).

Table 1: Mechanisms of Action of Some Antimalarial Drugs

Drug	Targets
1. Quinolines (4, 8 and 9 NH_2 Quinolines) - Quinine - CQ - Amodiaquine - Mefloquine etc	Heme polymerase: Heme conversion to hemozoin (non toxic) Heme (toxic to *Plasmodium*) Inhibition of Plasmodium PEP carboxylase or Carboxykinase
2. Antifolates (a) Type I: Dapsone and Sulphadoxine (b) Type II: Pyrimethamine, Proguanil and Chlorproguanil a. and b used in Combination	Dihydropterate Synthetase (DHPS) Denovo Folate Synthesis DiHydro Folate Reductase (DHFRS) Folate Salvage Nucleotide and Methionine Biosynthesis
3. Artemisinins - Artesunate - Artemether - Dihydroarte misinin	Cleavage of endoperoxide bridge by heme from Hb digestion – releasing free radicals (FR) FR: alkylates proteins, Damages membranes, Inhibit hemozoin formation by formation of adducts with heme. Recent hypothesis: inhibition of calcium – dependent Atpase of *P. falciparum* Ca important in all stages of *Plasmodium* Short $t^1/_2$thus combination therapy (ACTs) advocated.
4. Napthoquinones e.g. Atovaquone	Electron Transport Chain: Disrupts regeneration of Ubiquinone the e-acceptor of DiHydroorotate DH in Pyrimidine Synthesis
5. Phytochemicals a) Flavonoids	Not fully elucidated (i) Inhibition of FAS II (F.a. biosynthesis). (ii) Inhibition of the influx of L – G/n and Myoinositol into infected Rbc
b) Cryptolepine alkaloids	i) DNA intercalation ii) Stabilization of topoisomerase II DNA covalent complex thus stimulating the scission of DNA by Topoisomerase
c) Polyphenolics	Enoyl-ACP Reductase (Fab1) Biosynthesis of Fatty acids
d) JIG1 (Polygalloyltannin) *Jigam et al., 2010	Action similar to 1,2,3,4,6- pentagalloylglucose from *Entandrophragmaangolense* and antimicrobials Tetracycline and clindamycin against *Plasmodium*
Others: Immune: modulatory role of certain extracts hence enhancing CQ action e.g. *Rhamnus staddo*	

Malaria Chemotherapy and Drug Resistance

Chemotherapy remains the fulcrum of malaria management but this is compounded by the absence of new drugs with novel mechanisms of action. The fact is that all existing antimalarial

drugs are actually only derivatives of certain core structures which can be grouped into three main classes; the **quinolines** (quinine, chloroquine, mefloquine, primaquine), the **anti-folates** (sulfadoxine, pyrimethamine) and the most recent, **artemisinin** derivatives (artemisinin, artemether, dihydroartemisinin) (Na-Bangchang & Karbwang, 2009). Certain antibiotics also have antimalarial properties. There is an increasing spread of drug and insecticide resistance due to the evolutionary pressure on mosquitoes and the parasites (Noedl *et al*, 2008). The development of resistance to currently used drugs may be due to several factors that include the overuse of antimalarial drugs, inadequate therapeutic treatments of infections, parasite adaptability at genomic and metabolic levels and fast proliferation rates of the parasites that allows new generations to be formed in a very short time (Hyde, 2007). The mechanism of resistance to these drugs involve the modification of drug transport systems, increased synthesis of inhibited enzymes (Nirmalan *et al.*, 2004) and increase in enzymes that can inactivate the drug and also the use of alternative metabolic pathways (Vangapandu *et al.*, 2007). Unfortunately, mode of action as well as the mechanism of resistance is poorly understood except for the folate drugs (Na-Bangchang & Karbwang, 2009).

Vaccines

Another step towards the eradication of malaria is through the development of an effective multistage vaccine. The ideal vaccine must be able to provide complete immunity against the disease or prevent severe disease and death. Unfortunately, genetic variability of the parasite is hampering vaccine development. Four stages of the parasite life cycle have been targeted as possible vaccine candidates including the pre-erythrocytic (when infected with sporozoites), the human hepatic stage, the erythrocytic and the gametocyte stages (Graves & Gelband, 2006). Vaccines directed towards the pre-erythrocytic stages

aim to completely prevent infection while blood stage vaccines aim to reduce and hopefully eliminate parasites to the vector. The most advanced pre-erythroytic vaccine to date is the RTS, S/ASO1 vaccine developed by GlaxoSmithKline in the process that started in 1984 at the Walter Reed Army Institute of Research (Ballou, 2009). It consists of the antigenic C-terminus of the parasite's circumsporozoit protein (CSP). The ASO2 oil-in-water adjuvant system was used and showed promising protection by RTS, S against malaria infection. The AS02 adjuvent was replaced with the RTS, S/ASO1 which contains liposomes as adjuvant RTS, S/ASO1 Vaccine has been finally approved for use by EU Regulators in 2015 (Regules et al; 2016). It is thus the only vaccine available for protozoans, a process that lasted 36 years. Other vaccine candidates have also been pursued over time but with less success to date than that obtained with RTS, S/ASO1. Asexual blood stage vaccines aim to protect against malaria disease rather than the infection, but has been less successful to date. Various MSP's have been investigated as vaccine candidates with little success in clinical trials. Another vaccine, the combination B vaccine (MSP/RESA), consisting of two merozoite surface proteins together with a ring infected erythrocyte surface antigen (RESA) shows good immunogenicity and is being investigated further (Graves & Gelband, 2006). Another research by GlaxoSmithKline and Walter Reed Army Institute of Research resulted in the FMP2.1(AMA-1/ASO2) vaccine candidate which showed host immunity and safety (Spring *et al.*, 2009). Another approach to vaccine development is transmission blocking vaccines that are based on the prevention of sporozite development in the mosquito salivary glands. Various surface protein antigens are in development but are hampered by the problematic protein expression of these proteins. The use of irradiated *P. falciparum* sporozoites was undertaken in trials but posed safety, technical and logistical problems (Ballou, 2009).

Targets for Antimalarial Drug Development

Metabolic pathways in the malaria parasite offer a rational basis

for drug development. Enzymes of pathways that are unique for the parasite are thought as evident targets. In glycolysis, recent molecular studies have indicated that lactate dehydrogenase and triose phosphate isomerase could serve as specific targets; purine and pyrimidine syntheses, the regulation of the cell cycle, protein trafficking and secretion, mitochondrial functions, cytoskeleton maintenance, proteasome and ubiquitin – mediated protein degradation, phospholipid metabolism, transport of substrates and waste products and signal transduction are all potential targets (Ginsburg, 2004). It is hoped that modern approaches in drug development such as functional genomics, proteomics and screening of combinatorial libraries that are becoming useful in drug development, will transcend into malaria research. The malaria genome project not only provides the expected information about genes that code for elements involved in the various processes described above, but also some surprises. Such are the genes that are related to the synthesis of amino acids (the parasite was considered hitherto to get amino acids from globin degradation or from the host) to the synthesis of ATP by mitochondria (the parasite was considered to depend exclusively on glycolysis for ATP production) and to the synthesis of fatty acids (considered to be supplied from the host). These apparent "inconsistencies" as well as the myriad of supposedly redundant genes (*rifin, stevor, ser/thr* protein kinase etc.) must await the verification of their expression (Newbold, 2003; Anthony *et al.*, 2012). It should be remembered that gene expression varies with parasite stage and progression through the life cycle, and the elucidation of the functional meaning of the genes at each phase in conjunction with their use as potential drug targets will hopefully get a refreshed impetus (Ginsburg, 2004; Ntie-Kang *et al.*, 2014). Thus, basic research has indicated possible targets as: Haemoglobin degradation, detoxification of ferriprotoporphyrin IX, redox and glutathione metabolism, the methionine cycle, methylation and polyamines, folate metabolism, ribonucleotide reductase and iron chelators, the apicoplast and shikimate pathway, biosynthesis of

ferriprotoporphyrin IX (Jigam *et al.*, 2011; Ntie-Kang et al., 2014).

Phytochemicals

Phytochemicals are secondary metabolites in plants. Some are responsible for color and other organoleptic properties, such as the deep purple of blueberries and the smell of garlic. Phytochemicals posses biological significance and have been attributed with many medicinal potentials and applications (Jigam *et al.*, 2012). They are produced as defence against insects and other organisms. They can be alkaloids or non-alkaloids.

Alkaloids

Alkaloids are one of the major classes of natural products that exhibit antimalarial activity. Hundreds of alkaloids from higher plants were reported to demonstrate significant antimalarial activity in studies published from 1990 till date; some of these

Table 2. Invivo anti-malarial activities of some West African medicinal plants

Plants	Part	Dose (Mg/kg)	% Inhibition	Survival days	
Pyrenacantha staudtii	Leaf	100/200/500	61/63.4/58.0		
Morinda lucida	Root	400	-	29	
Phytolacca dodecandra	Leaves	100/200/400	18/50/55		
Olea europaea	Leaves	40/80/120	30/55/80	-	
Acacia auriculiformis	Leaves	350/ 700/1050	69/72/76	15/18/20	
Acacia nilota	Roots	300	71/50/66	-	Jigam *et al.*, 2010
Adansonia digitata	Stem bark	100	60.47/32.90	20	
Ageratum conyzoides	Leaf	100/200/400	70.49/82.20/89.87		
Ageratum conyzoides	Leaves	400	89.87/ 61.74/52.61		
Alstonia boonei	Root back	200	62.2/58.8/66.4	-	
Amaranthus spinosus	Stem	200	789.36	-	
Anthocleista grandiflora	*Stem bark*	*300/500/700*	14/32/68		
Anthocleista vogelii	Stem	100/200/400	48.5/78.5/ 86.6%		
Artocarpus altilis	Stem bark	ED50	ED50214.2/227.2/310.2	-	
Aspilia Africana	Leaf	100/200/400 mg/kg	79.42/84.28/92.23	22/25/28 days	
Aspilia Africana	Leaf	100/200/400	*22/25/28*	-	
Azadiracta indica	Leaf/back	800	79.6/68.2	-	

Bombax buonopozense	Leaf	200/400/600	65/78/86	25/28/29	
Bridelia Ferruginea	Bark	400	-	26/16/27	
Byrsocarpus coccineus	Leaf	100,200 and 400	81/88/92	20/22/26	
Calpurnia aurea	Leaf	60	51.15, 47.77 and 36.8%	9.6/10/8	
Canthium glaucum	Root	100 mg/kg/day	31.98/43.76	20	
Cassia singueana	Root	50/100/150/ 200	48.22/66.51/79.06/ 80.45		
Cassia singueana	Roots	50/100/200	48/66/79	-	
Cassia Singueana	Bark	200/400/800	37/72/90		
Catha edulis	Leaf	1000	13.7		
**Chrozophora senegalensis*	Whole	75	51.80%,	-	Jigam *et al.*, 2011 *
Chrysophyllum albidum	Bark	1000/1500	74.20/62.90%		
Cissampelos Mucronata	Leaf	200	68.4/60.0/73.7 %	-	
Clerodendrum violaceum	Leaf	13	100 after 21 days		
Crateva Adansonii	Leaves	200/400/600	0.00/37.71/ 40.41		
Croton macrostachyus	Leaf	200/400	39/69	6/7 days	
Croton zambesicus	Root	81/57/57	86.18/57.88/75.39	-	
Cryptolepis sanguinolenta	Leaf	36	25	-	
Cymbopogon Citrates	Leaf	200/400/800	82,84,99/66,74,83/ 43,56,70	-	
Cymbopogon Citrutus	Bark	200/400/800	50/77/100	-	
Dicliptera verticillata	leaf	290/580/870	59.14 /70.67/83.66	--	
Dodonaea Angustifolia	Seed	600	62.02/86.21%	11.3/11.25	
Dodonaea Angustifolia	Seed	100 mg/kg	35.79/48.6		
Eleucine indica	Leave	600	64.67/56.34	27	
Enantia chlorantha	Stem bark	-	317.9	-	
Entada abyssinica	Leaves	600	39.2/66.4	11.45/11.65	
Faidherbia albida	*Stem bark*	*100/200/400*	*24/72/89*	-	
Ficus platyphylla	Stem Bark	300	43.50	28	
Flacourtia indica	Leaves	100	0.2/87	7/8.6	
Hoslundia opposita	Roots	100	90/41	9.2/9.6	
**Lippia multiflora*	Leaf	200/400	13.35% and 50.94		Jigam *et al.*, 2009 *
**Momordica balsamina*	Leaf	200/600	13.78 and 9.41/28.08 and 27.29/45.21 and 53.07		Jigam *et al.*, 2012 *

Source: Bashir et al., 2015

are more potent than chloroquine (Saxena *et al.*, 2003). Herein, some of the active reported alkaloids are grouped according to their structural classes.

Bisbenzylisoquinolines

Are a large and diverse group of alkaloids that occur in many plant species, particularly in members of the *Menispermaceae,*

Berberidaceae, Ranunculaceae, Annonaceae and Monimiaceae. Many of the plants that contain these compounds have reputations as medicinals in the folklore of various cultures. In an effort to discover new antimalarial agents from natural sources, Angerhofer *1999* and co-workers tested 53 bisbenzylisoquinoline alkaloids that were isolated via phytochemical studies and bioassay-directed fractionation.

Aporphine-benzylisoquinoline

These are phenolic alkaloids isolated from the roots of *Thalictrum faberi* Ulbr. (*Ramunculaceae*) and shown to be more active against CQR *P. falciparum* clones (W2; IC50 <25ng/ml) than against CQS clones (D6; IC50 >100 ng/ml). Selectivity indexes ranging from 9.4 to 65.7 were observed for 3-hydroxy-6'-desmethylthalifaboramine (A), 3-hydroxythalifaboramine (B) and 6'-desmethylthalyfaboramine (C) , whereas these indexes were>540 and >1, 800 for quinine against the *P. falciparum* clones W2 and D6, respectively (Lin *et al.*, 1999).

Morphinans

A morphinan alkaloid which was biogenetically derived from benzylisoquinolines via aporphines, was isolated from *Strychnopsis thouarssi* (a Menispermaceae plant species that is endemic to Madagascar) and it was named tazopsine (tazo = malaria) (Carraz *et al.*, 2006). This plant is the only ingredient in a widely used remedy that is reputed to provide specific protection against malaria. Stem bark decoction has shown weak activity against the FcB1 strain of *P. falciparum* erythrocytic stages *in vitro* (IC50 34.0 ±9.4µg/ml). The traditional use of this plant to prevent malaria led to the *in vitro* evaluation of its effect on liver stages of *P. yoelli* and *P. falciparum*. Bioassays of plant decoction in cultured mouse primary hepatocytes infected with *P. yoelli* sporozoites produced an IC50 of 8.5 ± 0.7µg/ml with hepatic forms that were completely eliminated at concentrations of 20µg/ml or higher. Bioguided isolation of active compounds led

to the identification of tazopsine, which is the major constituent of the plant material.

Napthylisoquinolines

A class of structurally unique acetate biogenetically-derived alkaloids that have been isolated from tropical lianas belonging to the families *Dioncophyllaceae* and *Ancistrodaceae* (Bringmann and Feineis, 2001). Plant species of these families are widely used in the traditional medicine of West African countries, and Southern and Southeast Asia to treat malaria and other diseases, such as dysentery, leprosy, fever, and measles. Good correlations between *in vitro* (CQR *P. falciparum* NF54 strain) and *in vivo* (*P. berghei*, Anka strain) antimalarial activities were observed for representatives of this group of alkaloids. Dioncophylline C, dioncophylline B and dioncopeltine A caused complete clearance of parasites after oral administration to *P. berghei*-infected mice, without noticeable toxic effects (Bringmann *et al.*, 2003, Francois *et al.*, 1997).

Cryptolepine

An indoloquinoline alkaloid is the major constituent (this alkaloid constitutes over 1% of its weight) and the most potent antiplasmodial compound derived from *Cryptolepis sanguinolenta*. A decoction of the roots of this climbing shrub is used in West Africa for the treatment of malaria. Furthermore, its major constituent, cryptolepine, has potent effects against both CQS (D6 IC50 27.0 ± 0.3 ng/ml) and CQR *P. falciparum* strains *in vitro* (K1 IC50 33.0 ± 0.1 ng/ml, W2 IC50 41.0 ± 0.5 ng/ml); however, cytotoxic effects have been observed. It has been demonstrated that cryptolepine intercalates with DNA and stabilizes the topoisomerase II-DNA covalent complex; thus, the scission of DNA by topoisomerase is stimulated (Cimanga *et al.*, 1997).

Mono- and bis-indole alkaloids

This group has been isolated from several plants that are

traditionally used to treat malaria in different continents. The most active compounds are those that originate from plants that belong to the genera *Strychnos* (*Loganiacae*) and *Alstonia* (*Apocynaceae*). A review covering the indole alkaloids that have high antiplasmodial activities *in vitro* and *invivo*, and favourable selectivity indices (SI=CC50/IC50) have been published (Frederich *et al.*, 2008).

Benzofenantridine

Alkaloids isolated by bioassay-guided fractionation of the trunk bark of *Zanthoxylum rhoifolium*; this specie was traditionally used in French Guienea to treat and prevent malaria. The antiplasmodial activity was concentrated in the alkaloid fraction, which comprised seven benzophenantridine alkaloids, of which nitidine was the most potent against *P. falciparum* (IC50 <0.27μM). The investigation of a trunk bark decoction that was employed as a traditional remedy revealed the presence of alkaloids, including nitidine; therefore the traditional use of *Z. rhoifolium* for the treatment of malaria was justified (Julian *et al.* 2006). *Zanthoxylum* species are frequently used to treat malaria in Madagascar. *Z. tsihamimposa* is used either alone or in combination with other plants to relieve malarial symptoms, such as tiredness and muscular aches. Five alkaloids that were isolated from the stem bark were assayed *in vitro* for antiplasmodial activity against *P. falciparum* (FCM 29); IC50 values in the range of 459.1 to 87.7μM were obtained. The most potent alkaloid was the quinolone γ - fagarine, which had an IC50 of 98.4μM (Randrianarivelojosia *et al.* 2003). Nitidine was also isolated by biossay-guided fractionation of extracts from *Toddalia asiatica*, a Rutaceae used by the Pokot tribe of Kenya as the major antimalarial component.

Acridone

Alkaloids derived from species that belong to the genera *Citrus* (*Glycosmis* and *Severimia*) and are members of the family *Rutaceae* were tested for antimalarial activity *in vitro* against *P.*

yoelli and *in vivo* against *P. berghei* - and *P. vinckei*-infected mice. At a concentration of 10µg/ml *in vitro*, seven out of the 30 tested alkaloids inhibited 90% or more of the parasite growth. Against *P. yoelli*, they were shown to be either equally or more effective than chloroquine *in vitro* (94% ±4 growth inhibition). Of the seven or more active alkaloids, atalaphillinine was the only one to be tested for *invivo* activity. A daily dose of 50 mg/kg of this alkaloid was injected i.p. into mice for a period of three days. Marked prophylactic activity against *P. berghei* - and *P.vinckei*-infected mice was observed by days 4 and 5 after infection (Fujioka *et al.*, 1989).

Furoquinoline and acridine

Are Alkaloids that have been isolated from plants that belong to the Rutaceae family. The *in vitro* and *in vivo* activities of acridones against rodent malaria (Fujioka *et al.* 1989) and the *in vitro* effect of 23 furoquinoline and acridone alkaloids against CQR (W2) and CQS (HB3) clones of *P. falciparum* have been reported (Basco *et al.*, 1994). The assayed alkaloids included isolates from three New Caledonian plants (*Geijera balansae, Sarcomelicope glauca* and *Sarcomelicope dogniensis*) and derivatives that were obtained by chemical modifications and the dimerization of acronycine. Fourteen alkaloids had IC50 < 10µg/ml against the W2 strain.

Tetrahydroquinoline

Are alkaloids isolated from the trunk bark of *G. officinalis*. This traditional medicinal plant from Venezuela, commonly named angostura bark, is reputed to be the source of a tonic and stimulant that is used against fever (Jacquemond - Collet *et al.*, 1999). Hexane, chloroform extracts and pure alkaloids were tested for their *in vitro* activity against *P. falciparum* strains. The IC50 values ranged from 1.8 to 40.0µg/ml against a CQS strain (Nigerian) and 0.09 to 38.0µg/ml against CQR strains (FcB1 and FcM29). With an IC50 of 0.09 to 0.9µg/ml, against CQR strains,

galipinine was the most active alkaloid. (Jacquemond-Collet *et al.*, 2002).

Naturally Occurring Antiplasmodial Non-Alkaloids

Flavanoids

Chemically, they have the general structure of a 15-carbon skeleton, which consists of two phenyl rings (A and B) and heterocyclic ring (C). This carbon structure can be abbreviated C6-C3-C6. According to the IUPAC nomenclature, they can be classified into: flavonoids or bioflavonoid; isoflavonoids and neoflavanoids. Invitro research work has indicated medicinal roles of these compounds as antioxidant, anti-inflammation, anti-cancer, treatment of cardiovascular diseases and antibacterial effects. Recent researches also indicate flavanoids have anti-plasmodial action by inhibiting fatty acid synthesis (Jigam *et al.*,2013) Different types of bioactive flavonoids have been derived from medicinal plants growing in Africa. Even though the molecular mechanism of action of anti-malarial activities of flavonoids is not fully elucidated, it is believed that flavonoids act by inhibiting the fatty acid biosynthesis (FAS II) of the parasite (Freundlich *et al.*, 2005). Some flavonoids have also been shown to inhibit the influx of *L*-glutamine and myoinositol into infected erythrocytes (Elford *et al.*, 1986).

Chalcones

Chalcone is an aromatic ketone and an enone that forms the central core for a variety of important biological compounds, which are known collectively as chalcones or chalconoids. Benzylidene acetophenone is the parent member of the chalcone series. Chalcones and their derivatives demonstrate a wide range of biological activities such as anti-diabetic, anti-neoplastic, anti-hypertensive, anti-retroviral, anti-inflammatory, anti-parasitic, anti-histaminic, anti-malarial, anti-oxidant, anti-fungal, anti-obesity, anti-platelet, anti-tubercular, immunosuppressant, anti-arrhythmic, hypnotic, anti-gout, anxiolytic, anti-spasmodic, anti-

nociceptive, hypolipidemic, anti-filarial, anti-angiogenic, anti-protozoal, anti-bacterial, anti-steroidal, cardio protective, etc(Jigam *et al.*, 2013).

Flavanones

The antiplasmodial and cytotoxic activities of flavanones and arylbenzofuran derivatives from *Morus mesozygia* were investigated by Zelefack *et al.*, 2012. This plant is used in treating many diseases, including malaria and fever. Fractionation of the methanolic extract of its stem bark led to the isolation and identification of two flavonoids: artocarpesin and kushenol E. These compounds were active against the FcB1 strain of *Plasmodium*

Isoflavones

The acetone extracts of the root and stem bark of *Erythrina sacleuxii* showed antiplasmodial activities against the D6 and W2 strains of *P. falciparum*. Further chromatographic separation of the acetone extract of the root bark afforded a new isoflavone, 7-hydroxy-4′-methoxy-3′-prenylisoflavone, named 5-deoxy-3′-prenylbiochanin A along with known isoflavonoids as the antiplasmodial principles (Andayi *et al.*, 2006).

Rotenoids

Milletia usaramensis ssp. *usaramensis* is a plant growing in East Africa, which is reported to contain anti-malarial flavonoids, particularly rotenoids (Yenesew *et al.*, 2003). Seven rotenoids have been reported from this species, including usararotenoid C, usararotenoid A, (+)-usararotenoid B and (+)-12a-*epi*-millettosin. These compounds exhibited moderate to weak antiplasmodial activity against the D6 and W2 strains of *P. falciparum*.

Carotenoids

Carotenoids, also called tetraterpenoids, are organic pigments that are found in the chloroplasts and chromoplasts of plants and

some other photosynthetic organisms, including some bacteria and some fungi. There are over 600 known carotenoids; they are split into two classes, xanthophylls (which contain oxygen) and carotenes (which are purely hydrocarbons, and contain no oxygen). All are derivatives of tetraterpenes, meaning that they are produced from 8 isoprene molecules and contain 40 carbon atoms. In general, carotenoids absorb wavelengths ranging from green light. This causes the compounds to be deeply colored yellow the dominant pigment in autumn leaf. Coloration of about 15-30% of tree especially reds and purples, are due to other classes of chemicals.

Phenolics

p-hydroxy-cinnamic acid along with other compounds, atranorin, specicoside, 2β,3β,19α-trihydroxy-urs-12-20-en-28-oic acid were isolated from the stem bark of *Kigelia africana* and the drug interactions of the isolated compounds was carried out as well as their combination effects with quinine and artemether (Zofou *et al.*, 2011).The Ethiopian medicinal plant *Combretum molle* was reported to possess genuine anti-malarial activity. The fractionation of the stem bark extract yielded punicalagin as the active compoun d(Cheplogoi *et al.*, 2007).

Polyacetylenes

Polyacetylenes have unique chemical structures which make them rare and often unstable and very reactive. They thus have wide variety of biochemical and pharmacological uses. The root bark extract of *Cussonia zimmermanii* is commonly used to treat malaria, fever and epilepsy (Senn *et al.*, 2007).

Coumarins

Two isomeric 5-methylcoumarins from the roots of *Vernonia brachycalyx*; 20-*epi*-cycloisobrachycoumarinone epoxide and cycloisobrachycoumarinone epoxide were identified by Cubukcu *et al.*, 1990. The results of the antiplasmodial assays against the chloroquine-susceptible 3D7 and chloroquine-resistant Dd2

strains of *P. falciparum*, showed that 20-*epi*-cycloisobrachycoumarinone epoxide was weakly active, with IC_{50} values of 160 µM and 54 µM, while for cycloisobrachycoumarinone epoxide, the IC_{50} values were 111 µM and 54 µM, respectively. Cycloisobrachycoumarinone epoxide was also isolated from the ether extract of *Exostema caribaeum* but with moderate activity (Noster *et al.*, 1990).

Tannins

A tannin (or tannoid) is an astringent, polyphenolic biomolecule that binds to and precipitates proteins and various other organic compounds including amino acids and alkaloids. The tannin compounds are widely distributed in many species of plants, where they play a role in protection from predation, and perhaps also as pesticides, and in plant growth regulation. The astringency from the tannins is what causes the dry and puckery feeling in the mouth following the consumption of unripened fruit or red wine. Jigam *et al.*, 2010a isolated 1,3,6-digalloyl-2,4-monogalloytannin with efficacy against *Plasmodium berghei* in mice from the roots of *Acacia nilotica.* This appeared to be an early indication of the potentials of tannins in malaria therapy.

Xanthones

The anti-malarial xanthones; 5-hydroxy-3-methoxyxanthone and 3-hydroxy-5-methoxyxanthone were isolated from stem bark of *Hypericum lanceolatum*. These compounds exhibited an IC_{50} of 13.56 µg mL^{-1}, and 8.28 µg mL^{-1}, respectively, on the multidrug-resistant W2mef strain of *P. falciparum* (Zofou *et al.*, 2011). Six other anti-malarial xanthones; allanxanthone C, garciniafuran, tovophyllin A, rubraxanthone, norcowanin and mangostin were isolated from the methanolic extract of the stem bark of *Allanblackia monticola* (Azebaze *et al.*, 2006).

Sterols

The steroid, ergosterol-5,8-endoperoxide, isolated from the aerial parts of *Ajuga remota*, exhibited high antiplasmodial

activity against the chloroquine-sensitive FCA 20/GHA strain of *P. falciparum*, with an IC_{50} value of 8.2 μM (Kuria *et al.*, 2002). Steroidal saponins with anti-malarial activity have also been isolated from the leaves of *Vernonia amygdalina.* The isolation of vernonioside A1, A2, A3, A4 and B1, was also reported. These saponins had weak antiplasmodial activity against the multidrug-resistant K-1 strain of *P. falciparum*, with IC_{50} values of 139.7, 94.1, 245.1, 81.8 and 46.1 μg mL^{-1} respectively. These saponins are also reported to be the bitter compounds in the leaves of *V. amygdalina* (Ohigashi *et al.*, 1994).

Lignans

Lignan is the generic term for a large group of aromatic polymers resulting from the oxidative combinatorial coupling of 4-hydroxyphenylpropanoids (Ralph *et al.*, 2004). *Pycnanthus angolensis* is a plant used in traditional medicine against several diseases. The anti-malarial effect of dichloromethane extract of the bark of *Pycnanthus angolensis* was investigated and an activity against 3D7 *P. falciparum* strain with IC_{50} of 1.6 μg mL^{-1} was observed (Ramalhete *et al.*, 2007). This was further subjected to chromatographic bioguided fractionation yielding the lignans, (−)-dihydroguaiaretic acid, 4′-hydroxy-3,3′,4-trimethoxylignan, 4,4′-diacetyl-3,3′-dimethoxylignan, hinokinin, and heliobuphthalmin, along with the labdane diterpene ozic acid and the steroids stigmast-4-en-6β-ol-3-one, stigmasterol and β-sitosterol. *Asparagus africanus* is used in Kenya to treat malaria. A bioassay-guided fractionation of the root extract led to the isolation of the lignan nyasol, along with the sapogenin muzanzagenin, as the bioactive compounds responsible for the anti-malarial activity of this plant (Oketch-Rabah *et al.*, 1997).

Quinones

A quionone is a class of organic compounds that are formally "derived from aromatic compounds (such as benzene or naphthalene) by conversion of an even number of –CH= groups into –C(=O)- groups with any necessary rearrangement of

double bonds", resulting in "a fully conjugated cyclic dione structure". The class includes some heterocyclic compounds.

The prototypical member of the class is 1, 4-benzoquione or cyclohexadienedione, often called simply 'quionone' (thus the name of the class). Other important examples are 1, 2-benzoquione (ortho-quionone), 1, 4-naphthoquione and 9, 10-anthraquionone.

Derivatives of quinones are common in biologically active molecules. Some serve as electron acceptors in electron transport chains such as those in photosynthesis (plastoquinone, phylloquinone), and aerobic respiration (ubiquinone). Phylloquinone is also known as Vitamin K_1 as it is used by animals to help form certain proteins, which are involved in blood coagulation, bone formation, and other processes.

Natural or synthetic quinones show a biological or pharmacological activity, and some of them show anti-tumoral activity. They embody some claims in herbal medicine. These applications include purgative (sennosides), antimicrobial and antiparasitic (rhein-and saprorthoquinone, atovaquone), anti-tumor (emodin and juglone), inhibition of PGE2 biosynthesis (arnebinone and arnebifuranone) and anti-cardiovascular disease (tanshinone). Quinones also exhibit diverse pharmacological properties, including anti-malarial activity. Four quinones have been isolated from the root bark of *Hoslundia opposite*, including 3-*O*-benzoylhosloppone, 3-*O*-cinnamoylhosloppone, 3-*O*-benzoylhinokiol, and 3-*O*-benzoylhosloquinone. *Cassia siamea* was identified from southwest Nigerian ethnobotany as a remedy for febrile illness. This led to the bioassay-guided fractionation of stem bark of the plant extract for assessing the *in vitro* anti-malarial activity. Emodin and lupeol were isolated from the ethyl acetate fraction. Both compounds were found to be the active principles

responsible for the antiplasmodial property with IC_{50} values of 5 $\mu g\, mL^{-1}$ respectively (Ajaiyeoba *et al.*, 2008).

Phyto-Antimalarial Analysis – My Humble Contributions

Analysis for bioactive principles with utility against malaria could be tasking, time consuming but very interesting and sometimes addictive. Such procedures necessarily incorporate antiplasmodial, analgesic/antipyretic and anti-inflammatory protocols as the WHO defined malaria as the presence of *Plasmodium* parasites and fever. Host-parasite interactions result in red blood cell destruction hence anaemia and also host inflammatory response with cytokine activation resulting also in fever chill, pains, rigors, lasitude and even cough (Jigam *et al.*, 2009). Drug resistance especially by *P.falciparum* and *P. vivax* necessitates direct screening of plant extracts against such parasites using standard *invitro* and in *vivo* techniques. Furthermore, the acceptability of any drug is a function of its safety hence the inclusion of safe dose, LD_{50}, IC_{50}, subchronic and chronic toxicological evaluations as core components (Jigam and Niwoye 2013).

Generally the required Qualities for a good antimalarial drug include; activity against CQ, sulphadoxine and even artemisinin resistant *P. falciparum,* Resolution of parasitemia within 24-72hrs, High safety margin, Affordability and Availability in appropriate formulation especially for oral use.

In consonance with the above observations, I undertook a PhD research work between 2001 and 2008 from which at least 6 articles were generated. Also within the period from 2000 to date I supervised many undergraduate, masters and doctoral projects coupled with a few research grants all with the same theme of plants with antimalarial potentials. Most of the work have been published in reputable journals. My PhD work for example involved twenty-six medicinal plant species (Table 3) which

were extracted with suitable solvents and analyzed for antimalarial, pharmacological and toxicological properties. Crude extract yields from the plants ranged between 8.00%-21.25%. Over 70% of the plants had LD_{50} values greater than 1000mg/kgbw due probably to the fact that the species are widely consumed in folk medicine and as vegetables and spices among the indigenous population (Benoit-vical, 2013; Suleiman and Jigam, 2013). A variety of phytochemicals were identified in the extracts with tannins as the most prevalent while cyanophoric glycosides were least incident further buttressing their safe nature.

Analysis of Antimalarials from Plants (Simplified)

a. Selection and Authentication of plant specie, organs etc (Reputation, voucher samples)
b. Preparation/Isolation of Extracts (appropriate solvents, crude, alkaloidal, non-alkaloidal)
c. Qualitative and Quantitative phytochemical analysis
d. Invitro antiplasmodial analysis*
e. Determination of Safe Dose and LD50 of Extracts in mice (*in vivo*).
f. Determination of antiplasmodial effects (preliminary, suppressive, curative, prophylactic)
g. Bioguided activity determination (purification with chromatography, partitioning etc).
h. Spectral Analysis of active isolate (NMR, ESI-MS)
i. Analgesic and Anti-inflammatory activities of extract(s).
j. Toxicological screening (sub-chronic, chronic): Enzymes, kidney, liver functions, haematology and histopathology.

Table 3: Some Plant Species Analyzed

Plant	Hausa	Organ used
Ficus ingens	Kawari	Stem bark
Ficus polita	Durumi	Leaves
Ficus ovate	Cediya	Stem bark
Cassia accidontalis	Majamfari	Roots
Centaurea perrottetti	Dayi	Whole
Cyperus articulatus	Kajiji	Roots
Momordica balsamina	Garahunu	Whole
Pipe guineense	Masoro	Fruits
Psidium guajava	Gwaiba	Leaves
Acacia nilotica	Bagaruwa	Roots
Agelanthus dodoneifolius	Kauci	Whole
Artemisia maciverae	Tazargade	Whole
Diospyrus mespiliformis	Kanya	Leaves
Erthrina senegalensis	Minjirya	Roots
Feretia apodanthera	Kurukuru	Leaves
Sorghum species	Dawa	Roots
Securinega virosa	Tsatsagi	Leaves
Syzgium aromaticum	Kanumfari	Cloves
Thonningea sanguinea	Kulla	Roots
Xylopia aethiopica	Kimba	Fruits
Zingiber officinale	Cittar kaho	Rhizome
Azadirachta indica	Darbejiya	Leaves, bark, roots
Lippia multiflora	Bunsurunfadama	Leaves
Cochlospermum tinctorium	Rawaya	Roots
Guiera senegalensis	Sabara	Leaves
Chrozophora senegalensis	Damagi	Whole

Fifty percent of the plant extracts analyzed had activity against *Plasmodium berghei* in mice compared with only 27% against *P.chabaudi.* The latter had correspondingly lower mice survival period. This discrepancy can be rationalized on the basis that *P. berghei* has a mild clinical course hence ideal for chemotherapeutic research but *P. chabaudi* is more virulent hence better employed in drug resistance studies (NIPRD, 2000; Jigam *et al.,* 2011b). Parasitological drug response analyses further distinguished the active extracts as either plasmodicidal i.e. effective against both tissue and blood forms of the parasites hence potential radical cure for malaria or plasmodistatic which

clears only circulating parasites without effect against hypnozoites or tissue forms that could emerge and result in recrudescence (Jigam *et al*; 2010C). The work established that crude extracts of *Acacia nilotica, Momordica balsamina, Lippia multiflora* and *Azadirachta indica* as the most active among the initial 26 plants in the study in terms of antiplasmodial, analgesic and anti-inflammatory effects.

A bioguided activity approach was used to further fractionate and purify *A. nilotica* and in the process isolated the bioactive principle (JIG 1). Spectral characterization using NMR and ESI-MS of JIGI indicated a large M-1 signal at M/Z 1395 consistent with the molecular formula ($_{62}H_{43}0_{38}$). Further analyses of the mass spectrum data showed progressive signals that differed by m/z 152 synonymous with the galloyl moiety ($C_7H_40_4$). These spectra confirmed JIGI as constituted of one glucose centrol unit bound to eight gallic ester groups. A structure in which the JIGI molecule is least strained was thus postulated corresponding with 1, 3, 6-digalloyl-2,4-monogalloltannin (Jigam *et al.*, 2010a). Chronic toxicological screening of crude *A. nilotica* extract was undertaken due to the fact that herbal treatment utilizes such preparations. The study indicated that *A. nilotica* at 300mg/kg body weight of mice resulted in weight gain, significant ($P<0.05$) elevations in serum triglycerides, aspartate and alanine transaminases and chloride ions. Packed cell volume depreciated with the absence of any significant ($P>0.05$) variations in serum glucose, total proteins, alkaline phosphatase and potassium ions. Histopathology indicated lack of lesions in lung, cardiac, pancreatic, spleen and intestinal tissues. A feathery degeneration of the liver and destruction of nephrons in the kidneys were however noted which are indicative of some toxicity to the organs in question hence some necessary precaution against protracted intake of *A. nilotica* root extracts in the course of medicinal use (Jigam, *et al*, 2011c).

In summary therefore, my contributions could be listed thus:

a. Over 60 medicinal plants analysed for antimalarial and toxicological effects.
b. Isolation and identification of a novel polygalloyltannin with potential against *Plasmodium* parasites.
c. Training of over 80 Undergraduate and Post Graduate students in phytoantimalarial analysis contributory to the critical mass required in the fight against malaria.
d. Pioneering efforts in phytochemical analysis in FUT Minna.

The excitement and exhilaration of medicinal plant research is at times due to unexpected and dramatic findings often not as part of the primary research goals. One such example in question was earlier in this research in which the acutely toxic nature of *Chrozophora senegalensis* came to the fore. It killed many mice within a few minutes of administration (Jigam *et al.*, 2011b). Secondly, is the fact that serial passage of *P.berghei* in successive generations of mice resulted in the parasites loosing virulence (Jigam *et al.*, 2012b). Indeed natural products and their corresponding pharmacological effects are so vast and varied.

Table 4. LD_{50} Values of plant extracts in mice

Plants	LD_{50} (mg/kgbw i.p.)
Chrozophora senegalensis	90
Ferretia apodanthera	90
Centaurea perrottetti	178
Cassia occidentalis	340
Securinega virosa	340
Guiera senegalensis	800
Azadirachta indica	900
Ficus ingens	1000
Ficus ovata	1480
Psidium guajava	1500
Artemisia maciverae	1840
Piper guineense	2000
Sorghum species	3000
Thonnningea sanguinea	3000
Acacia nilotica	3000
Agelanthus dodoneifolius	3000
Cochlospermum tinctorium	3000
Syzygium aromaticum	>3000
Ficus polita	>3000
Lippia multiflora	>3000
Momordica balsamina	>3000
Xylopia aethiopica	>3000
Zingiber iofficinale	>3000
Diospyros mespiliformis	>3000
Cyperus articulatus	3600
Erythrina senegalensis	3600

bw = body weight
i.p = intraperitoneal

Table 5. Preliminary antiplasmodial effects of plant extracts

Plant	*Plasmodium berghei*		*Plasmodium chabaudi*	
	a	*b*	*a*	*b*
A. nilotica/ L. multiflora (1:1)	+	-	+	+
Azadirachta indica	+	-	*	+
Lippia multiflora	+	+	+	++
Acacia nilotica	++	-	+	+
Momordica balsamina	++	+	+	+
Diospyros mespiliformis	++	+	+	+
F. polita/ F. ovata (1:1)	+	++	+++	*
Syzygium aromaticum	+	++	*	*
Guiera senegalensis	++	+	++	++
Ficus polita	++	+	*	*
Psidium guajava	++	++	*	*
Ficus ovata	++	++	*	*
Zingiber officinale	++	++	*	*
Thonningea sanguinea	++	++	*	*
Artemisia maciverae	++	++	*	*
Erythrina senegalensis	+++	++	+	+
Ferretia apodanthera	+++	++	*	*
Xylopia aethiopica	+++	++	*	*
Cassia occidentalis	+++	++	*	*
Cochlospermum tinctorium	+++	+++	*	*
Centaurea perrottetti	+++	+++	*	*
Cyperus articulatus	++	*	*	*
Chrozophora senegalensis	+++	*	*	*
Piper guineense	+++	*	*	*
Agelanthus dodoneifolius	+++	*	*	*
Ficus ingens	+++	*	*	*
Sorghum species	*	*	*	*
Securinega virosa	*	*	*	*
Chloroquine phosphate	+	-	+	+
Normal saline	+++	*	*	*

- = absent; + = slightly present; ++ = moderately; present;
+++ = highly present; * = died; a = male mice; b = female mice

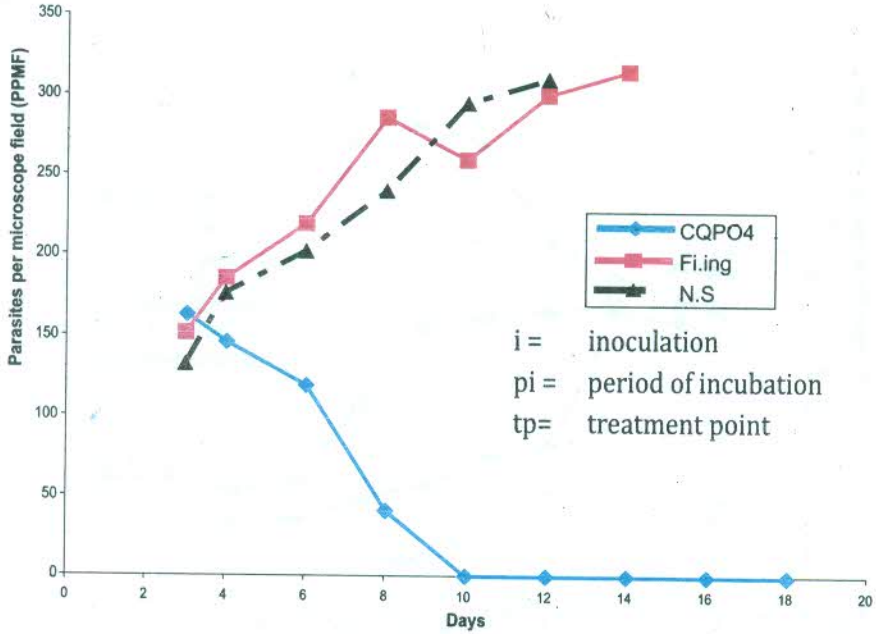


Fig. 1: Activity of *F. ingens* in *P. berghei* infected mice

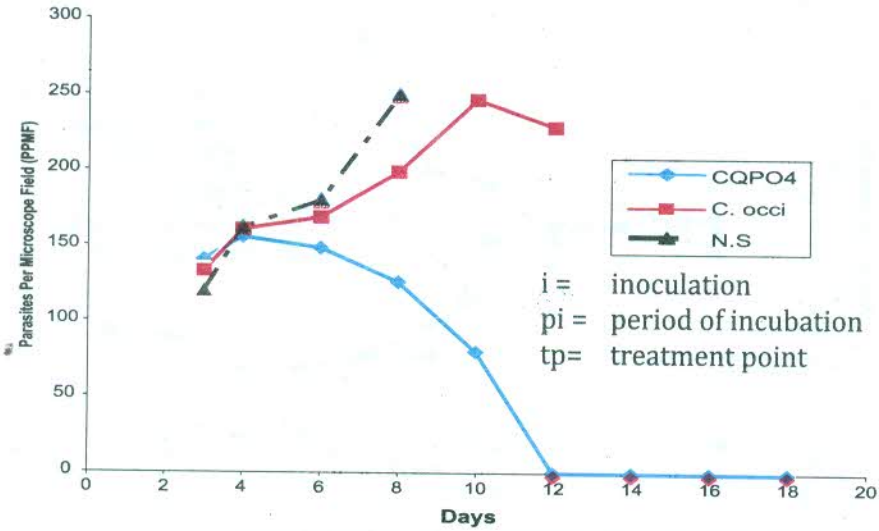


Fig. 2: Activity of *C. occidentalis* in *P. berghei* infected mice

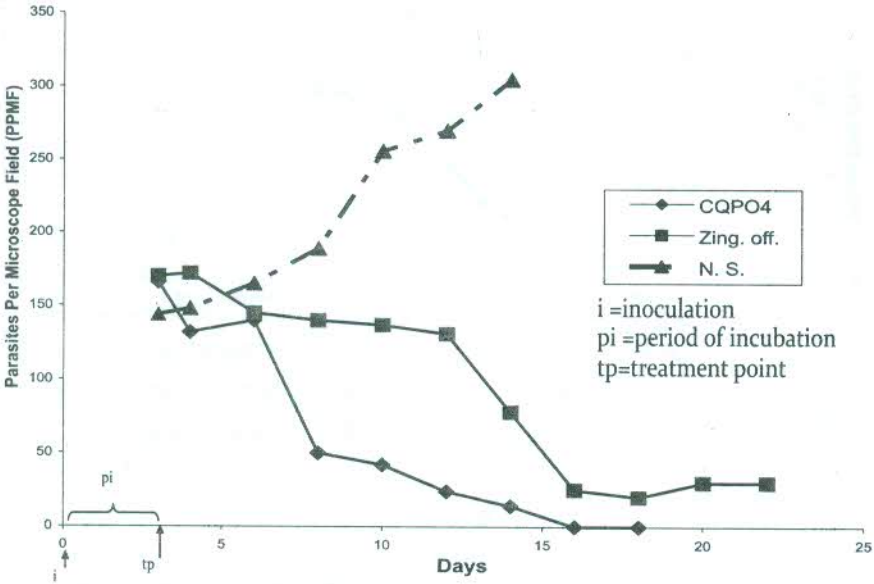


Fig. 3: Activity of *F. polita* in *P. berghei* infected mice

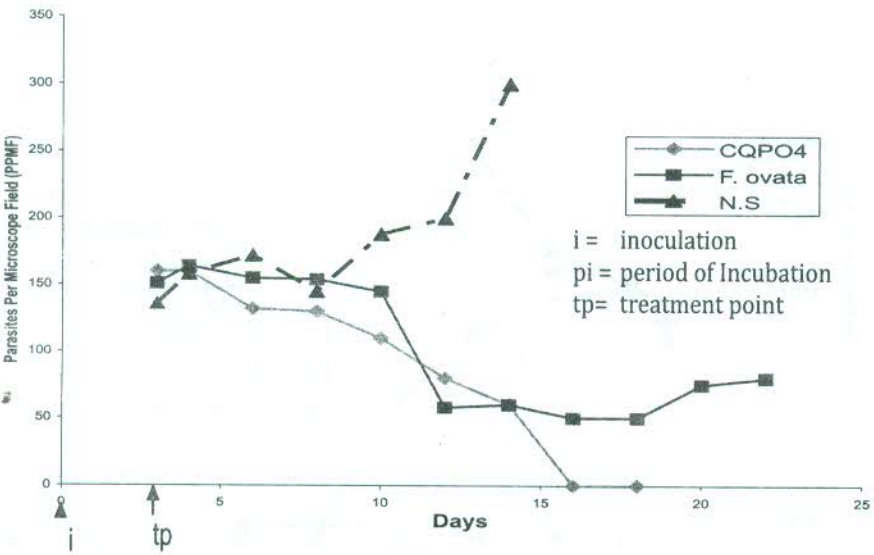


Fig. 4: Activity of *F. ovata* in *P. berghei* infected mice.

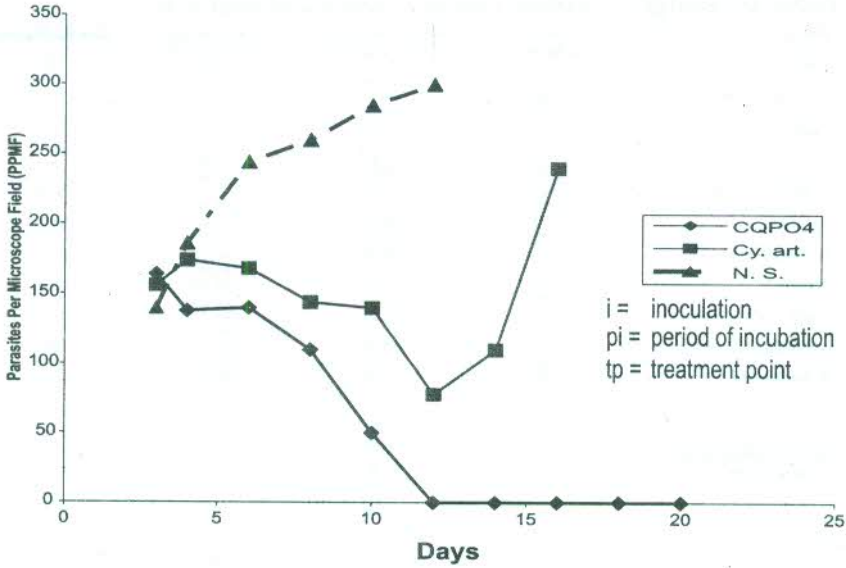


Fig. 5: Activity of *C. articulatus* in *P. berghei* infected mice.

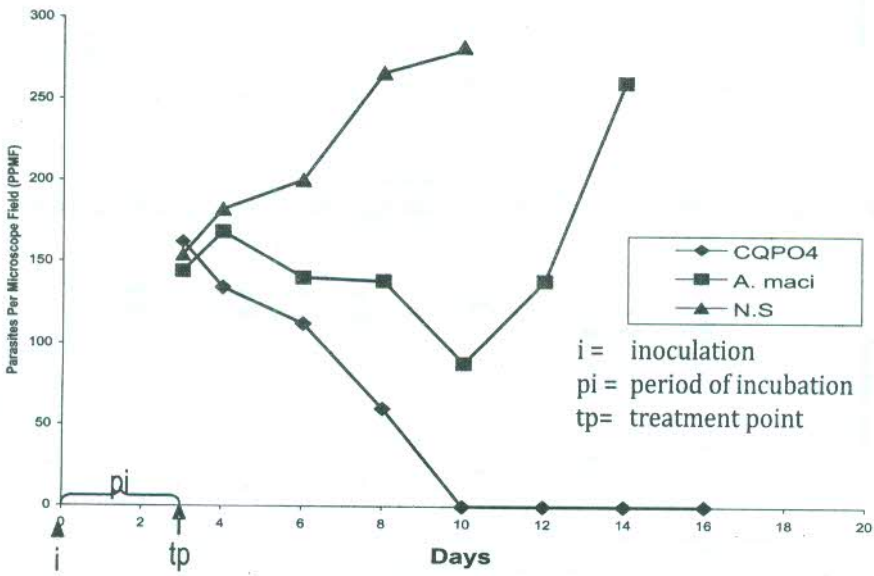


Fig. 6: Activity of *A. maciverae* in *P. berghei* infected mice

Table 6. Analgesic potentials of some plant extracts

Plants	Dose (mg/kg bw i.p)	Mean abdominal constriction	Percentage inhibition (% i)	ASA equivalent
F. ovate	150	40.60	0.00	0
	300	39.40	0.00	
S. aromaticum	150	44.60	0.00	0
	300	39.40	0.00	
P. guajava	150	46.60	0.00	0
	300	40.40	0.00	
C. tinctorium	150	52.60	0.00	0
	300	52.20	0.00	
D. mespiliformis	150	49.20	1.20	38.10
	300	36.40	26.91	
F. polita	150	48.80	0.00	24.76
	300	45.20	6.61	
G. senegalensis	150	23.00	43.35	2.54
	300	22.40	44.83	
A. indica	150	24.40	45.29	1.91
	300	52.60	71.30	
Z. officinale	150	14.80	59.12	1.89
	300	12.20	66.30	
L. multiflora	150	19.40	59.58	1.87
	300	11.20	76.67	
M. balsamina	150	13.00	71.86	1.72
	300	8.20	82.25	
A. nilotica	150	12.40	70.33	1.70
	300	9.80	76.56	
Acetyl Salicylic Acid (ASA) (150mg/kg bw i.p)	150	7.88	86.88	0.00
Normal Saline	20ml	43.47	0.00	

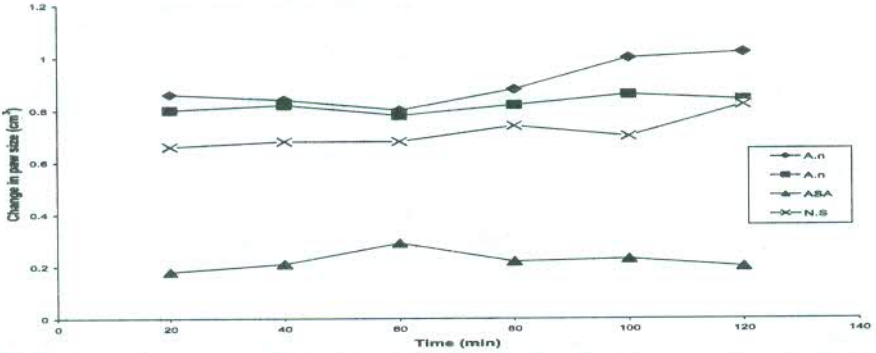


Fig.7: Anti-inflammatory effect of *A. nilotica* in egg-albumin induced oedema in mice

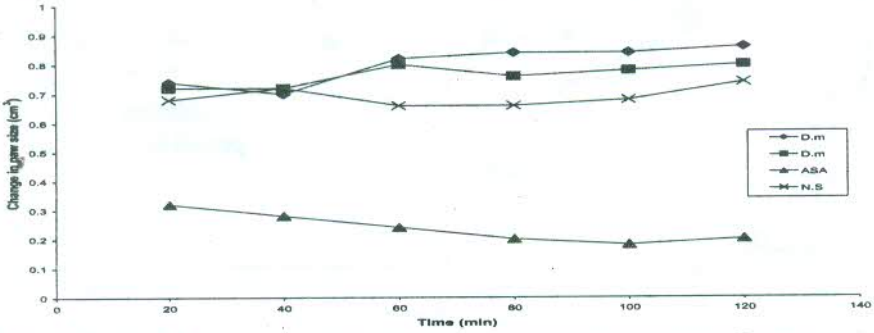


Fig. 8: Anti-inflammatory effect of *D. mespiliformis* in egg-albumin induced oedema in mice

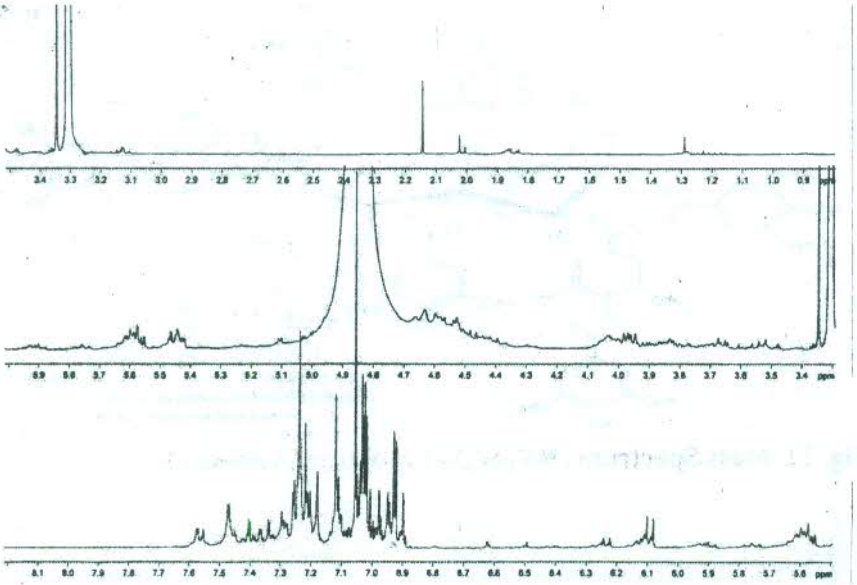


Fig. 9: NMR of JIG1

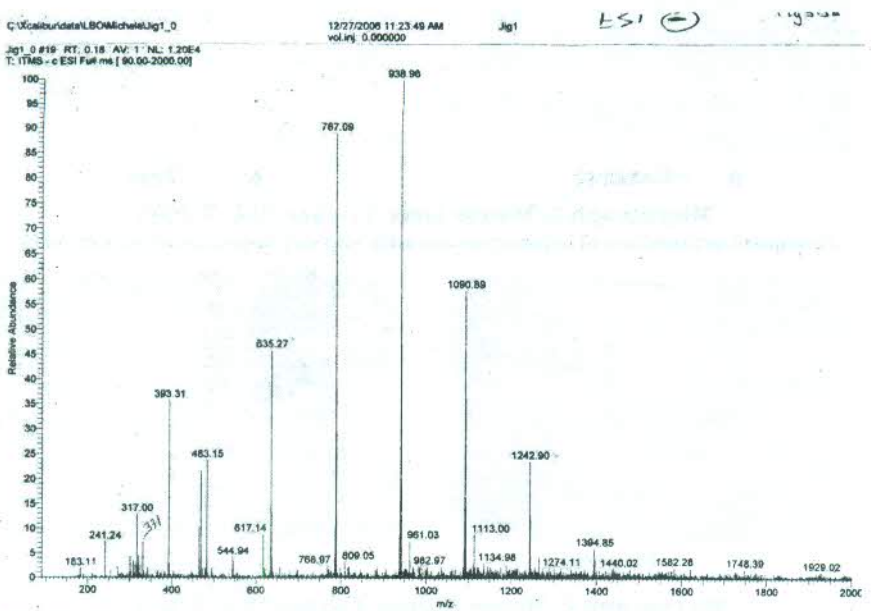


Fig. 10: Mass Spectrum (MS) of JIG1 Fraction (*A.nilotica*)

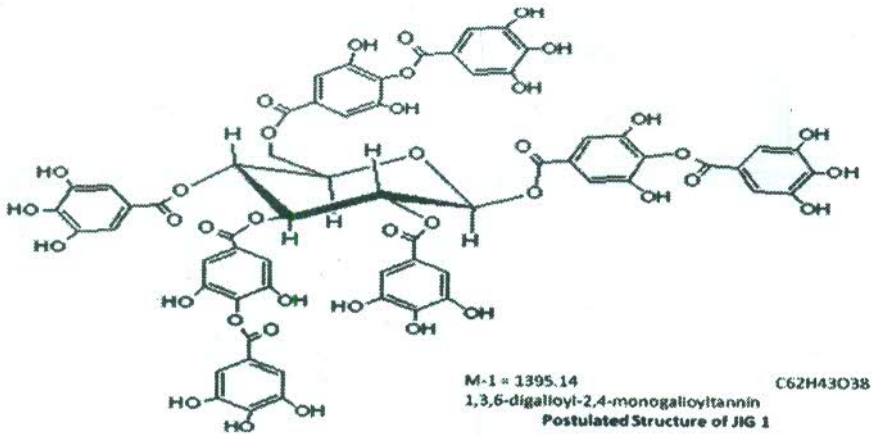
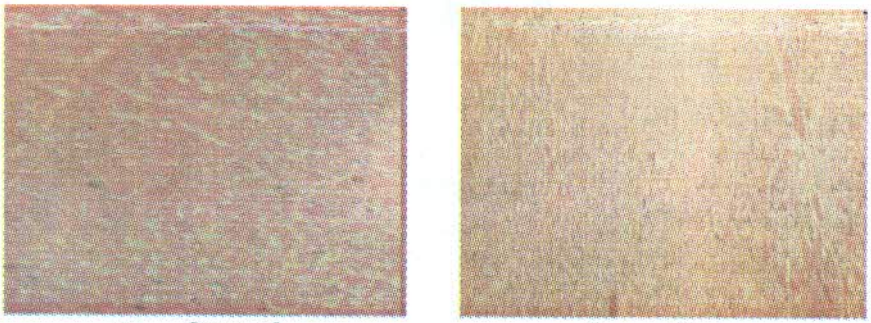


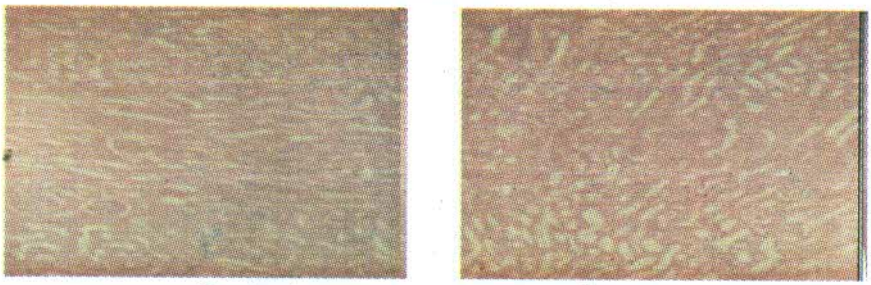
Fig. 11: Mass Spectrum (MS) of JIG1 Fraction (*A.nilotica*)



a Control b Test

Micrograph 1: Mouse Liver Tissues (H.E. X 400)

Hexagonal architecture of hepatocytes but with feathery degeneration in test tissue



a Control b Test

Micrograph 2: Mouse Kidney Tissues (H.E. X 400)

Glomeruli with ghost-like myelin material in test

Conclusion

The widespread use of plants as medicines is well documented with some literature indicating that 80% of the health needs of the rural poor in developing countries depend on this source. Even such, the urban rich in the west have a new found belief in the use and efficacy of supplements in the form of nutraceauticals derived chiefly from plant products. This has been reflected in the recent report estimating the market share of these products at over US$100 billion globally in 2015 alone. Plant derived natural products have been exploited as antimalarials (quinine, artemisinin), analgesics/antipyretics (ipecac), tranquilizers (reserpine), cardiac stimulants (digitoxin), anticancer (taxol, vincristine and vinblastine), AIDS (+) calanoide A and (-) calanolide). Some of our efforts above have demonstrated that some natural products e.g. tannins that were hitherto not closely associated with antimalarial activity do in fact have potentials against the disease. Again most of the plants analysed have high safety margins.

Apart from pure compounds, crude extracts with efficacy against malaria are currently being employed especially in endemic environments. However, limitations such as toxicity, low bioavailability and/or poor solubility have restricted the scope of use for several natural products in humans. Nevertheless, nature provides novel leads, templates which can be developed into safe drugs by synthetic strategies as exemplified by artemether and quionline class of antimalarials. The goal is to obtain products active against resistant strains of *Plasmodium*.

Since nature has been generous in providing several remedies for malaria, the vast unexplored flora should be systematically explored to provide new leads and drugs for malaria therapy as vaccines are still being awaited.

Recommendations

This lecture set out to draw attention to the diversity of plants

and phytochemicals therefrom that can be employed to tackle the ravaging effects of malaria and simultaneously earn enormous capital needed by the economy.

However, stumbling blocks exist that require resolution if these potentials are to be actualized:

a. Government should formulate and execute an integrated ethnomedicinal policy to involve traditional practitioners, academics, technocrats, health workers, the business community and other stakeholders.

b. Medical and allied institutions such as National Institute for Pharmaceutical Research and Development, Raw Materials Research and Development Council, National Institute for Medical Research, National Agency for Food and Drug Administration and Control, Standards Organisation of Nigeria etc should be re-oriented to posses the capacity to contribute more in ethnomedical research.

c. A national educational agenda to include ethnomedicine in the curricula from primary to tertiary levels.

d. Government to partner the business sector in the provision of enabling environment in terms of equipments, staff training and motivation/incentives for robust ethnomedical research at the tertiary level of education with focus on application not publication.

e. Sustainable use of medicinal plants, cultivation and planting of exotic species and overall protection of the biodiversity.

ACKNOWLEDGEMENT

Mr. Vice Chancellor Sir, this lecture shall not be complete without appreciating people who played different roles whether directly or indirectly in my life: First and foremost, is my utmost sense of gratitude and glorification to ***Allah Subhanahu wataala***, for divine favours in giving me the opportunity to deliver this lecture today, ***Alhamdulillah***!

Words alone cannot convey my utmost gratitude for the love of my late parents: Mallam Audu Jigam, Mrs. Hauwa Naakwii and Mrs. Hadiza Naakrom. My father could neither read nor write but had such fervent passion that I acquire Western education. It is very painful that they are gone but my prayer to God is that they be granted ***Aljannah FirDausi***, ***Ameen***. My siblings late Mohammed Darabo, Zainab Briskila, Ado, Kabiru, Lami and Maria, Adieu to you all but those alive including Aishatu Naanchin, Alhaji Garba, Usman, Jibrin, Yusuf, Rabi and Suleiman; are all appreciated.

I was sort of a foster child to almost every family and elders within the Hausa Community in my village Panyam. As a result the women would contribute a bar of soap, a pair of socks, toothpaste, 20 kobo, you name it here and there anytime my holidays were over and was about to go back to Government Secondary School, Katsina-Ala in far away Benue State. Most are no more alive but to all of them I pray Allah reward you in the best manner possible. The families of Alhaji Isa Daika, late Mama Patu, Mama Hadiza; Late Alhaji Idi Sarkin Tasha, his wives Mama Alti, Mama Uwani, Maimuna, his brother late Alhaji Sabo and others too many to be mentioned will remain evergreen in my memory.

I have been lucky to find divine favour in circumstances that appeared hopeless; this would be the case with my in-laws who took me in on the first day of my relationship with their daughter and sister instantly transforming a total stranger into a bon-afide

member of their large family. Allah would reward you Sir, Baba Alhaji Nuhu Yusuf with good health; Late Mama Hajiya Ruqqayyatu, Mama Hajiya Khadijat (Maman Palo), Hajiya Hadiza Yayan Shiroro, Baban Shiroro Alhaji Abubakar Madakin Buddong, Baba Alhaji Mallam and other departed uncles and aunties with the prayer that Allah grant you *Aljannah Firdausi*. I am also grateful to Alhaji Sadiq Nuhu Yusuf, Alhaji Datti Nuhu Yusuf, Hajiya Halima Nuhu Yusuf, Alhaji Sani Nuhu Yusuf and Alhaji Tukur Danladi Nuhu Yusuf.

Mention and also appreciation is hereby made of my teachers at all levels of my academic pursuit. Professor (Mrs.) H. O. Akanya taught me at the undergraduate level in ABU Zaria and also supervised my Ph.D. Her husband the former Director General of Standards Organisation of Nigeria, Prof. A. Akanya has not only been my teacher but also my mentor to whom I am much indebted, God shall indeed reward you mightily! Former Minister of Science and Technology, Prof. Abubakar Kaoje of Usmanu Danfodiyo University, Sokoto; Alhaji Datti Usman, the immediate past Registrar are among many of my mentors to whom I shall always be grateful

I want to deeply appreciate our matriarch Mama Lami Rosaleen Makun, late Pa Peter Ojongbede, Great Granny Mado and the entire Makun family of Bosso for giving a stranger his first shelter as it is the family I stayed with on assumption of duty at FUT Minna in October of 1992. I cannot also forget the late Chief of Bosso Alhaji Abubakar Lolo for his fatherly care very early in my stay in Bosso. History indeed has a way of repeating itself as I was being fostered again by yet another community even in my adult life!

I also thank my superiors, colleagues and friends in the defunct Department of Biological Sciences which comprised of Biology, Biochemistry and Microbiology Units from 1992 and now metamorphosed into the School of Life Sciences.

These include Prof. S. A. Garba, Prof. T. A. Gbodi, Prof. Oladimeji, the late Prof. J. A. Abalaka, Prof. (Mrs.) H. O. Akanya, Prof. U. J. J. Ijah, Prof. M. Galadima, Prof. S. B. Oyeleke, Prof. E. O. Ogbadoyi (incidentally my classmate in 1979 at the undergraduate level at ABU Zaria), Prof. H. A. Makun, Dr. A. Y. Kabiru, Dr. E. C. Evans, Drs. Abdulkadir A, Hadiza, Tosin, Adefolalu, Adeyemi and all others not mentioned. Prof. Falusi and Dr. Faruk Kuta are also appreciated. My friendship with Prof. A. N. Saidu is special and on many levels. He was our class representative at the University of Jos in 1989 during my Masters Programme; he introduced me to then Vice Chancellor of Federal University of Technology Minna, Prof. Suleyman Adeyemi in 1991 upon our graduation and which led to my invitation, interview and subsequent employment into the services of this university (coincidently again is the fact that both Profs. Adeyemi and Akanji held from the same locality: the former employed me while the later midwifed my Professorship! *AllahuAkbar*!!); critically and most momentous indeed is that the very Prof. Saidu introduced me to then my wife to be, **Hajiya Hauwa Nuhu Yusuf,** and the rest as being said is now history! Our elders not in Life Sciences but pivotal to my success including, Prof. G. D. Mommoh, Prof. K. R. Salami, Prof. E. Okosuns, Prof. M. A. T. Suleiman, Prof. B. E. N. Dauda, Prof. J. M. Baba, Prof. (Mrs.) I. N. Mogbo and others not mentioned are hereby acknowledged and appreciated. Some of my former classmates in ABU Zaria such as Prof. J. A. Noks and Alhaji Abdullahi Rilwanu Azara have a special place in my heart and I am indeed grateful. In the course of my career, I supervised many students such as Dr. Rabiat Unekwu Hamza, Dr. Sambo M. Dantsugwai, Dr. Talatu Bala Bosso, Dr. Fabunmi, Arc. Abdulwasiu Jimoh, the CEO of West Field Global Construction Ltd., Engr. Hamza Abdullahi, Dami-Dami, Jones Nwanjoku etc; who I hereby fully acknowledge all.

I have never forgotten my village Panyam, Mangu L.G.A. in Plateau State all through my academic and Professional sojourn

which included Government Secondary School, Katsina-Ala, Benue State (1974-1979); Ahmadu Bello University, Zaria (1979-1983); Cross River State (NYSC, 1983-1984); Plateau State Polytechnic, Barkin Ladi (1986-1992); University of Jos (1989-1991-Masters) and Federal University of Technology, Minna (1992-Date). I am still therefore nostalgic and appreciative of all my childhood and adulthood friends such as the late Mallam Lawal Mohammèd and Mallam Tanimu Sura; relatives and the community as a whole specifically, the present chief of Panyam, His Royal Highness, Engineer Aminu Derwan whom incidentally has been a friend since childhood. It is noteworthy that the chiefdom under his nascent leadership most recently conferred on me the title of "**TURAKIN PANYAM.**" I am indeed grateful. In this regard my family also remains indebted to the Wazirin Panyam, Chief S. D. Lot and other chiefs for their efforts in taking a *"prodigal"* son back to his roots.

I thank the amiable Prof. M. A. Akanji, our Vice Chancellor and other members of management, Prof. S. O. E. Sadiku, Prof. W. Morenikeji, Mrs. V. N. Kolo, Mrs. H. Kuso and Dr. A. J. Alhassan; all have worked tirelessly to provide the most conducive working environment in recent memory at F.U.T. Minna. The immediate past DVC, academics Prof. Abdullahi Bala is also hereby appreciated for all the support.

I remain most grateful to Prof. J. O. Okogun of NIPRD Abuja for linking me with his associates in Italy with regards to the spectral analysis of my PhD work, appreciation also to Mr. T. Zakkarayya for most of the parasitological and toxicological analysis over the years. All my friends and associates both within and outside FUT Minna whose names are too numerous to mention and have played different roles in my life are not forgotten, only Allah can reward you, thank you from the bottom of my heart.

My immediate family members have been my pillars of support. In this regard **Hajiya Hauwa Nuhu Yusuf** whom I first met in

1993 here in FUT Minna and then became my wife in [illegible] deserves special commendation. Meeting her totally changed [illegible] life: perhaps apart from my biological parents no single individual has positively impacted on me as she has done. Allah will reward you. My love for you shall remain evergreen. [illegible] children, Rukkayyah Ameerah, Amina Mufeedah and Fat[illegible] Eemann remain our sources of joy and may Allah raise them [illegible] His obedience and glory.

Finally, I thank all members of the University Seminar [illegible] Colloquium Committee ably headed by Prof. Bisi Ayanwa[illegible] their tireless efforts in organising this lecture. Equally, everyone who has honoured me and has come to grace [illegible] occasion today, I am grateful. May Almighty God grant you journey mercies back to your places of abode.

Vice Chancellor Sir, this draws the curtain on our discussion [illegible] the reminder that academics, researchers and experts on ma[illegible] especially in the third and developing world must champion [illegible] elimination of this disease and other afflictions of the poor, [illegible] then our global partners will remain at best only on the sidelines while the tragedy forges on!

Sir, thank you once again, **Alhamdulillah**.

REFERENCES

Abay S. M., Lucantoni L., Dahiya N., Dori, G., Dembo E. G., (2015). *Plasmodium* transmission blocking activities of *Verninia amygdalina* extracts and isolated compounds. *Malaria Journal*, 14: 288

Abdullahi A., Hamza R. U., **Jigam A. A.**, Yahya A, Kabiru A. Y., Muhammad H, Sakpe S, Adefolalu F. S., Isah M. C., Kolo MZ (2012). Inhibitory activity of Xanthine oxidase by fractions of *Crateva adansonii. Journal of Acute Disease* 1(2): 1-4 www.jadweb.com.

Achan J., Talisuna A. O., Erhart A., Yeka A., Tibenderana J. K., Baliraine F. N. *et al.* (2011). Quinine, an old anti-malarial drug in a modern world: role in the treatment of malaria. Malaria Journal 10:144.

Ali A. Jigam, Helmina O. Akanya, Emmanuel O. Ogbadoyi, Bukar E. N. Dauda and Egwim C. Evans (2009). In vivo antiplasmodial, analgesic and anti – inflammatory activities of the leaf extract of *Lippia multiflora mold. Journal of Medicinal Plants Research 3(3): 148-154. Published Online:www.academicjournals.org/JMPR*

Ali A. Jigam, Helmina O. Akanya., Bukar E. N. Dauda., and Okogun J. O. (2010). Polygalloyltannin isolated from the roots of *Acacia nilotica Del. (Leguminoseae)* is effective against *Plasmodium berghei* in mice. *Journal of Medicinal Plants Research. 4(12); 1169-1175 .Published Online: www.academicjournals.org/JMPR*

Ali A. Jigam, Samuel T. Olorunfemi, Florence I. Obiokpa (2012). Plasmodistatic, Anti-inflammatory and Analgesic Effects of different fractions of *Mormodica balsamina* extracts in Rodents. *Asian journal of Biochemical and Pharmaceutical Research* 2(4), 116-125 www.ajbpr.com/issue8.php ISSN: 2231-2560

Ali A. Jigam, Usman T. Abdulrazaq and Martins N. Egbuta (2011).

Invivo antimalarial and toxicological evaluation of *Chrozophorasenegalensis* A. Juss (*euphorbiaceae*) extracts. *Journal of Applied Pharmaceutical Science.* 01(10): 90-94 ISSN 2231-3354. www.japsonline.com

Ali A. Jigam, Usman T. Abdulrazaq, Halima A. Mahmud and Falilat O. Tijjani (2012). Efficacy of *Thonningia sanguinea* vahl, (Balanophoracea) Root Extract against *Plasmodium berghei, P. Chabaudi,* Inflammation and Nociception in Mice. *Journal of Applied Pharmaceutical Science.* 02: 47-51.

Ali A. Jigam, Usman T. Abdulrazaq, Rukkaya S. Suleiman, and Patience S. Kali (2012). Effect of Sub-Chronic administration of *Diospyros Mespiliformis Hochst* (Ebenaceae) Root Extracts on Some Biochemical Parameters in Mice. *Journal of Applied pharmaceutical Science* 02(05):60-64 www.japsonline.com ISSN: 22-31-3354.

Ali A. Jigam, Usman T. Abdulrazaq, Halima, A. Mahmud and Falilat, O. Tijani (2012). Efficacy of *Thonningiasanguinea* Vahl. (*Balanophoraceae*) Root Extract Against *plasmodiumberghei, Plasmodiumchabaudi,* inflammation and nociception in mice. Journal of Applied pharmaceutical Science 02(01):47-51 www.japsonline.com ISSN:22-31-3354.

Ali A. Jigam, Helmina O. Akanya, Bukar E. N. Dauda, Emmanuel O Ogbadoyi. (2011). Antiplasmodial, Analgesic and Anti-inflammatory Effects of *Guiera senegalensis* leaf extracts in mice infected with *Plasmodium berghei. Journal of Pharmacognosy and Phytotherapy.* 3(10):150-154 ISSN 2141-2502 *www.academicjournals.org/JPP*

Ali A. Jigam, Helmina O. Akanya, Emmanuel O. Ogbadoyi and Bukar E. N. Dauda. (2010). In vivo antiplasmodial, analgesic and anti-inflammatory activities of the root extracts of *Acacia nilotica Del. Asian Journal of Experimental Biological Sciences. 1(2); 315-320. Published Online: www.ajebs.webnode.com*

Ali A. Jigam, Hadiza L. M., Adefolalu F. S., Abdulkadir A. and Jimoh T. (2011). Effects of crude *Acacia nilotica* DEL. Root Extracts in mice. *International Journal of Applied Biological Research.* 3 (1): 56-68. www.ijabr.com

Andrade-Neto V. F., Goulart M. O., da Silva Filho J. F. da Siva M. J., Pinto Mdo A. V., Zalis M. G., Carvalho L. H., Kretlli A. U. (2004) Anti-malarial activity of phenazines from lapachol, beta-laphacone and its derivatives against Plasmodium falciparum *in vitro* and Plasmodium berghei *in vivo.* Bioorg. Med. Chem. Lett. 08; 14(5):1145-9

Anthony M. P., Burrows J. N., Duparc S., Moehrie J. and Wells T. N. C. (2012). The global pipeline of new medicines for the control and elimination of malaria. *Malaria Journal* 11: 316.

Bashir, L., Oluwatosin, K. S., Adamu, Y. K., **Ali A. Jigam**., Maimuna, B. Umar, Eustace, B. Berinyuy and Blessing U. Alozieuwa (2015). Potential Anti-malarials from African Natural Products: A Review: *Journal of Interculture and Ethnopharmacology*, 4(4):318-343

Brandeo M. G. L., Nery C. G. C., Mamao M. A. S. and Kretili A. U. (1998). *Phytochemistry*, 48: 397

Bray D. H., Warhust D. C., Connoly J. D., O'Neill J. D. (1990). Phillipson plants as sources of antimalarial drugs. Part 7. Activity of some species of meliacea plants and their constituent limonoids. *Phytotherapy Research.* 4: 29-35.

Bringmann, G., Menche, D., Bezabih, M., Abegaz, B. M. and Kaminsky, R. Antiplasmodial Activity of Knipholone and Related Natural Phenylanthraquinones. Planta Med. 2003, 65: 757-758. 10.1055/s-2006-960859.

Cechinel-Filho (2012). Plant Bioactives and Drug Discovery: Principles, Practice and Perspectives, Hoboken, New Jersey. John Wiley and Sons. Pg 2.

Cheesbrough, M. (2000). District Laboratory Practice Manual in Tropical Countries pt. 2. Cambridge University Press.

Chinedu E., Arome D. and Ameh F. S. (2013). A new method for determining Acute Toxicity in Animal Model. *Toxicity International.* 20(3): 224-226

Dell'Agli M., Sanna C., Rubiolo P., Basilico N., Colombo E., Scaltrito M. M., Ndiath O., Maccarone L., Taramelli D., Bicchi C., Ballero M. and Bosisio E. (2012). Anti-plasmodial and insecticidal activities of the essential oils of aromatic plants growing in the Mediterranean area. *Malaria Journal*, 11: 219

Demissie A. G. and Lele S. S. (2013). Bioactivity-Directed Isolation and Identification of Novel Alkaloid from *Jatropha curcas* (Linn.). *Research Journal* of *Chemical and Environmental Sciences*, 1(2): 22-28.

Dougharib B., Eziefula A. and Gosling R. (2012). Improved Traditional Phytomedicines in Current Use for the Clinical Treatment of Malaria. *Planta Medica*, 77: 662-671

Evans E. (1997). *Mormodica balsamina L:* Properties and Medicinal Uses. Horticultural Services, North Carolina State University, U.S.A. pp3-6

Farnworth N. R., and Bingel A. S. (1977). Problems and prospects of discovering new drugs from higher plants by pharmacological screening. In *New Natural Products and Plant Drugs with Pharmacological, Biological or Therapeutical Activity. (eds.* Wagner, H., and Wolff P.). Springer Verlang, Berlin, p. 1-22.ss

Farnworth, N. R. (1980). Rational approaches applicable to the search for and discovery of new drugs from plants, *First Latin America and Caribbean Symposium on Natural Occuring Pharmacological Agents.* Havana, Cuba, 23-28 June

Frederich, M., Jacquier, M. J., Thepenier, P., Mol, P. D., Tits, M., Philippe, G., Delaude, C., Angenot, L., and Zèches-Hanrot, M.

(2002). Antiplasmodial activity of alkaloids from various *Strychnos* species. J Nat Prod 65, 1381–1386.

Fujioka, H., Nishiyama, Y., Furuka, W. A .H., and Kumadan. (1989). *In vitro* and *in vivo* activities of atalaphilline and related acridone alkaloids against rodent malaria. Antimicrob Agents Chemother 33: 6–9.

Gamaniel K. S. (2000). Toxicity from medicinal plants and their products. *Nigerian Journal of Natural Products and Medicine.* 04: 4-8

Hamzah R. U., **Jigam A. A,** Makun H. A. and Egwim E. C. (2014). Phytochemical screening and antioxidant activity of methanolic extract of selected wild edible Nigerian mushrooms. *Asian Pacific Journal of Tropical Biomedicine.* 4(1): 930- 934. www.elsevier.com/locate/apjtb.

Harborne J. B. (1998). Phytochemical Methods: A Guide to Modern Techniques of Plant Analysis. Chapman and Hall London. Pp. 49-188.

Hay S., Guerra C., Taretew A., Noor A. and Slow R. (2003). The Global Distribution and Population at Risk of Malaria: Past, Present and Future. *Lancet of Infectious Disease* 4 (6): 327-336

Jigam A. A., Niwoye A. A. (2013). Assessment of some Enzyme and Haematological parameters in Malaria patients resident in Minna, Nigeria. *International Journal of Biology, Pharmacy and Applied Sciences* 2(1), 125-137 www.ijbpas.com ISSN: 2277-4998

Jigam A. A., Olorunfemi S. T., Niwoye A. A., (2013). Evaluation of the effects of *Mormodica balsamina Linn.* Extracts on some biochemical parameters in mice. *International journal of Biology, Pharmacy and Applied Sciences* 2(1), 59-71 www.ijbpas.com ISSN: 2277-4998

Kaur K., Jain M., Kaur T., Jain R., (2009). Antimalarials from nature Bioorganic and medical chemistry, 02: 050

Kelechi E. Okunji, Musa Galadima and **Ali A. Jigam** (2012). Toxicological Evaluation of Five Herbal Drugs Hawked in Minna, Niger State. *Journal of Applied Pharmaceutical Science* 2(12): 167- 171 www.japsonline.com ISSN 2231-3354.

Kumar S., Epstein J. E., Richie T. L., Nkrumah F. K., Soisson L., Carucci D. J., Hoffman S. L. (2002). Trends parasitol. 18:129

Lewington J., (1990). Plant for man. 1st edition. Natural history museum publication, London pp 136-145.

Lin L. Z., Hu, S. F., Chu, M., Chan, T. M., Chai, H., Angerhofer,. C K., Pezzuto, J. M., and Cordell, G. A. (1999). Phenolic aporphine-benzylisoquinoline alkaloids from *Thalictrum faberi.* Phytochem 50: 829–834.

Lucatoni L., Yerbanga R. S., Lupidi G., Pascualini L. and Esposito F. H. (2010). Activity of Standardized Neem (*Azadirachta indica)* Seed extract on the Rodent Malaria Parasite *Plasmodium berghei* in its Vector *Anopheles stevensi. Malaria Journal*, 9: 66.

Madziga A. A., Delves M. J., and Leroy D. (2010). Potential of *Khaya iviriensis-Alstonia boonei* extract combination as antimalarial prophylactic Remedy. *Journal of Ethnopharmacology*, 137: 743-53

Muregi F. W., Ishih A., Suzuki T., Kino H., Amano T., Mkoji G. M., Myase T., Terada M., (2007). Phytotha. Res. 21: 337.

National Institute for Pharmaceutical Research and Development (NIPRD) (2000). Evaluation of the antimalarial properties of plant extracts. *NIPRD-AM-1.* Pp. 1-9

Newman D. J. and Cragg G. M. (2012). Natural Products as Sources of New Drugs Over the 30m years from 1981-2010. *Journal of Natural Products.* 75: 311-315.

Ngemenya M. N., Akam T. M., Yong J. N., Tane P., Fanso-Free S. N. Y.

Berzins K. and Titanji V. P. K. (2006). Antiplasmodial Activities of some Products from *Turrenthus africanus* (Meliacea). *African Journal of Health Sciences*, 13: 33-39. NNMA; Medicinal Plants of Nigeria, North Central Zone, Vol. 1, 120pp.

Ngouela, S., Lenta, B. N., Noungoue, D. T., Ngoupayo, J., Boyom, F. F., Tsamo, E., Gut, J., Rosenthal, P. J. & Connolly, J. D. (2006) Antiplasmodial and Antioxidant Activities of Constituents of the Seed Shells of *Symphonia globulifera Phytochemistry*. 67: 302-306. 10.1016.

Noster, S. and Kraus, L. (1990). *In vitro* Antimalarial Activity of *Coutarea latiflora* and *Exostema caribaeum* Extracts on *Plasmodium falciparum*. Planta Med., 56: 63-65. 10.1055/s-2006-960885.

Ntie-Kang F., Onguene P. A., Lifongo L. L., Ndom J. C., Sippl W. and Mbaze L. M. (2014). The potential of anti-malarial compounds derived from African medicinal plants, part II: a pharmacological evaluation of non alkaloids and non-terpenoids. *Malaria Journal*, 13: 81

Okpako D. T. (1991). Principles of pharmacology. A tropical approach. Cambridge University Press, Cambridge. Pp 228-313.

Olivera A. B., Dolabela F. M., Braga F. C., Jacome R. L. R. P., Povoa M. M., (2009). Plant-derived anti-malaria agents: new leads and efficient phytomedicines. Part 1Alkaloids. *An Acadbra Science*. 81:715-40

Oloyed O. I. (2005). Chemical Profile of Unripe pulp of *Carica papaya*. *Pakistan Journal of Nutrition*. 4: 379-381

Onguene P. A., Ntie-Kang P., Lifongo L. L., Ndom L. C., Sippl W. and Mbaze L. M. (2013). The potential of anti-malarial compounds derived from Africa medicinal plants, part I: a pharmacological evaluation of alkaloids and terpenoids. *Malaria Journal* 12: 449

Panseeta P., Lomchoey K., Prabpai S., Kongsaeree P., Suksamrarn A., Ruchirawat S., Suksamrarn S. (2011) Antiplasmodial and antimycobacterial cyclopeptide alkaloids from the root of *Ziziphusmauritania*. *Phytochemistry* 72(9): 909-15.

Ramadhani S., Nondo O., Mainen J. M., Erasto P., Zofou D., Njovendou J. A., Wanji S., Ngemenya M. N., Kidukuli A. W., Masimba P. J. and Titanji P. K. (2015). Evaluation of the Cytotoxic Activity of Extracts from Medicinal Plants used for the Treatment of Malaria in Kagera and Lindi Regions, Tanzania. *Journal of Applied Pharmaceutical Science*, 5(04): 007-012.

Schleiferbock S., Scheurer C., Ihara M., Itoh I., Bathurst I., Burrows J. N., Fantauzzi P., Lotharius J., Charman S. A., Morizzi J., Shackleford D.M., White K. L., Brun R. And Wittlin S. (2013). In vitro and in vivo characterization of the antimalarial lead compound SSJ-183 in *Plasmodium* models. *Drug Design, Development and Therapy*, 7: 1377-1384.

Regules, J. A., Cicatelli, S. B. and Bennett, J. W. (2016). Final results of RTS, S Vaccine. Lancet. 386(9988): 31-45.

Sha'a A., Oguche S., Watila I. and Ikpa T. F. (2011). In vitro Antimalarial Activity of the Extracts of *Vernonia amygdalina* commonly used in Traditional Medicine in Nigeria. *Science World Journal*. 6: (2).

Tasdemir D., Brun R., Perozzo R. and Donmezi A.A. (2005). *Phytotherapy Research* 19: 162

Trager W. (1990). On the establishment in culture isolates of *Plasmodium falciparum. Transaction of the Royal Society of Tropical Medicine and Hygiene.*

Trager W. And Jensen J. B. (1976). Human Malarial Parasites in Continuous Culture. *Journal of Parasitology*. 91: 484-6.

Trease G. E., and Evans, W. C. (1978). A *Textbook of Pharmacogosy,* 11th edn. Bailliere Tindall, London.

Udeinya J. I., Shu E. N., Quakyi I., Ajayi F. O., (2008). An antimalarial neem leaf extract has both schizonticidal and gametocytocidal activities. *American Journal of Therapy*. 15: 108-110

Vale V. V., Vilhena C. T., Trindade S. C. R., Ferreira C. R. M., Percario S., Soares F. L., Pereira A. L. W., Brandao C. G., Olivera B. A., Dolabela F. M., De Vasconcelos F. (2015). Anti-malaria activity and toxicity assesment of Himatanthus articulatus, a plant used to treat malaria in the Brazilian Amazon. *Malaria Journal* 14:132

White N. J. (1997). Assessment of the pharmacodynamic properties of Antimalarial Drugs *in vivo*. Antimicrobial Agents and Chemotherapy. 41: 1413-1422

WHO (2001). In vitro micro-test (Mark III) for the assessment of *P. falciparum* to chloroquine, mefloquine, quinine, amodiaquine, sulfadoxine/pyrimethamine and artemisinin. CTD/MAL/9720Rev2. Geneva, Switzerland.

WHO Malaria Policy Advisory Committee and Secretariat (2012). Malaria Policy Advisory Committee to the WHO: conclusions and recommendations of September 2012 meeting. *Malaria Journal*. 11: 424

Wilson R. J. (2008). Serotyping *Plasmodium falciparum* malaria with S-antigen. *Nature*. 3: 284 (5755): 451-452.

PROFILE OF THE INAUGURAL LECTURER

Professor Ali Audu Jigam was born in Panyam, Mangu LGA of Plateau State on 10th January 1962 to the family of late Mallam Audu Jigam Maigoro and Mallama Hauwa Naakwii Bigwan. He attended Panyam Local Education Authority Primary School at a very tender age and was by 1974 admitted into Government Secondary School Katsina-Ala in Benue State. He completed his secondary education in June 1979 and by August of the same year using the Mock WASC but awaiting result proceeded to the School of Basic Studies, Ahmadu Bello University, Zaria. He successfully completed the IJMB after earlier obtaining the required credits in WASCE was absorbed into the degree programme of Biochemistry (1980-1983). He went to the University of Jos (1989-1991) where be bagged an MSc (Biochemistry) and also Federal University Technology, Minna for a PhD (2008) in Biochemistry.

He joined the services of Federal University of Technology, Minna in October 1992 from Plateau State Polytechnic Barkin Ladi as Lecturer II and rose to the rank of Professor of Biochemistry in October 2013.

Professor A. A. Jigam served the University on different committees including: the Search Team for a new Vice Chancellor (2012), STEP-B Audit Committee of the Governing Council (2010), University Health Services Management Board, adhoc disciplinary panels on both staff and students and University intellectual property rights.

He also held several important positions of responsibility within and outside the university Such as: Examinations Officer, SIWES Coordinator, Time Table Officer and Head of the Department of Biochemistry. Within the community, Prof. Jigam has been adhoc electoral officer with INEC since the return to democratic governance in 1999 at Local Government and State levels. He was

in fact the Returning Officer for Niger East Senatorial district during the 2015 general elections. He is deeply involved with the Socio-cultural and economic advancement of his ancestral land resulting in his recent appointment to the exalted position of **TURAKIN PANYAM**.

In the academic sphere, Prof. Jigam has attended and actively participated in several conferences both at National and International Levels. He has to his credit over Eighty (80) scholarly publications in reputable journals, edited proceedings and conference reports. He is currently on the Editorial Board of five (5) Journals including Advances in Bioresearch, Scientific Speculation and Research, Elsevier, Research Journal of Chemical and Environmental Sciences and Nigerian Journal of Biochemistry and Molecular Biology. He has equally reviewed countless articles for many international journals.

Professor Jigam has for almost 25 years been enhancing the capacity of Biochemists through teaching and project supervision. To date he has supervised or co-supervised over a hundred (100) undergraduates, twenty three (23) Masters and Ten (10) Doctoral Students. He has served as external examiner at both undergraduate and Post graduate levels and Assessor for Professorial cadre to various universities. He is a member of many Professional bodies and also received several awards such as the University Servicom award for commitment to service involving punctuality and successful re-accreditation of the department of Biochemistry by National Universities Commission in 2012. Professor Jigam believes in mentoring and supporting younger academics, hence floated the Malaria Research Group with the express intention of attracting research grants, capacity building and training of mentees in the rudiments of malariology contributory to the WHO goal of the elimination of malaria globally. Professor Jigam has an innate passion for animal husbandry and is happily married with children.