FEDERAL UNIVERSITY OF TECHNOLOGY MINNA

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BSc (ABU Zaria), MSc (UNIJOS), PhD (FUT Minna)
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INAUGURAL LECTURE SERIES 49

15TH DECEMBER, 2016

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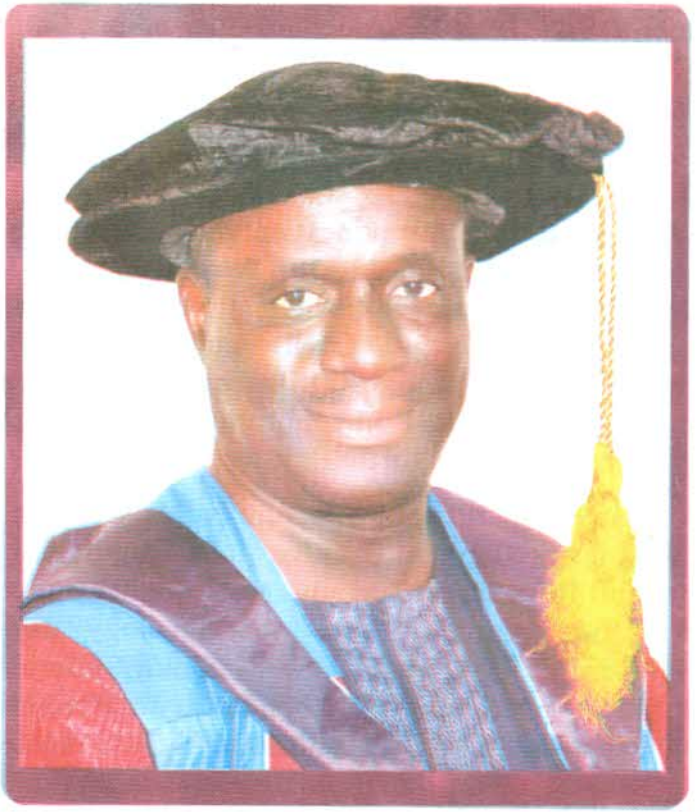

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Preamble

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