A FOREST FOR NOVEL DRUGS: NATURAL PRODUCT CHEMISTRY

An Inaugural Lecture

By

CHUKWUNONYE MOSES OJINNAKA
B.Sc, PhD, C.Chem, MICCON, FCSN
Professor of Chemistry
Department of Pure and Industrial Chemistry
University of Port Harcourt
Nigeria

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Donald E. U. Ekong
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INTRODUCTION

It is a great honour to me to present the first inaugural lecture from the Department of Pure and Industrial Chemistry, University of Port Harcourt, Nigeria. I am also very happy to present the fifth inaugural lecture from Faculty of Science.

The first inaugural lecture from Faculty of Science was delivered by Professor Francis A. Onofeghara in 1986. Professor Onofeghara set the pace with "Botany in Human Affairs" discussing the role of plants and the science of botany as well as the place of plant physiology in human affairs. Professor Emmanuel O. Anosike (1987), "in praise of emzymes"[2], surveyed the involvement of enzymes in fermentation processes and the central role enzymes could play in heath-care delivery, nutrition and industrial processes. Professor Gabriel I. Ekeke (1997) recalled, in "Blood is thicker than water"[3], the application of the biochemistry of blood in health and disease.

In continuation of the inaugural lecture series from Faculty of Science, I shall correlate the "botany of human affairs" and the chemistry of secondary plant metabolites to the important role these plant metabolites play in health-care delivery. The choice of a title that will vividly describe this correlation has not been easy. The chemistry of plant metabolites has made great progress during the last decades as a result of our better comprehension of enzymatic processes,

and the development of biogenetic and biosynthetic theories which logically classify and link together an immense variety of compounds[4]. The underlying biosynthetic principles and enzyme mechanisms have had a great impact on imagination of many organic chemists and imitation of bio-organic processes in the laboratory has led to important advances in medicine. Since this concept involves a correlation between botany, chemistry and medicine, I have chosen for this inaugural lecture the title **A Forest for Novel Drugs: Natural Product Chemistry.**

I wish to inform the audience that the lecturer is a chemist, to be precise, a natural product chemist! Before I step further, I must retrace my steps to chemistry. It is not necessary to bore you with the definition of chemistry. However, it is necessary to inform this audience that chemistry is important in a range of related subjects as illustrated in figure 1. Anyone working in the fields shown requires at least some knowledge of chemistry, so chemistry must form part of the curriculum for a wide range of professional scientists[5]. Further, it is possible to devise research projects which involve interactions between chemistry and each of these related areas. For example, knowledge of chemistry is important in understanding that the crucial process in leather manufacture involves filling the spaces created by separation of the swollen collagen fibres with astringent tanning agents[6]. A wide range of examples could be given where chemistry is indispensable in all human endeavour. Look around you!

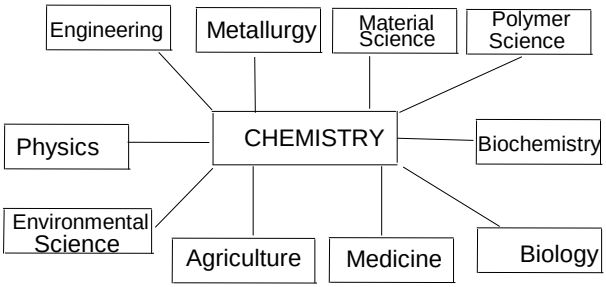


Figure 1. The central place of Chemistry

Look at your dress. Look at your shoe. Look around the building housing you. Whenever you enter any modern car, you will observe that many components which include interior, exterior and under the hood applications such as steering wheel, bumpers, fascia panels, car radiators, battery casing et cetera are polypropylene products[7]. This is chemistry at work! Knowledge of chemistry is important in automobile, petroleum and petrochemical industries, household management, medicine and health-care delivery. Chemistry is worth studying because it provides a valuable educational experience, there are surprises in store and more importantly in chemistry a clear distinction is made between what we know for sure (experimental facts) and what we know only provisionally (theories, models, hypothesis).

Having summarized the importance of chemistry in engineering, science and medicine, let me again retrace my step to the topic of this inaugural lecture. I shall, during this lecture, convey to the dignitaries here present, the great pleasure of our ancestors that their descendants have at last found it fit to retrace their hitherto hurrying and disdainful steps to enquire

into the chemistry, efficacy and therapeutic applications of our traditional trees and herbs. My discussion, therefore, will centre on how chemistry, specifically, natural product chemistry, recently enhanced the search for novel and prototype drugs. For a coherent discussion, the topic is summarized under three headings: In the beginning, the journey so far and the future.

IN THE BEGINNING

From the earliest days, man has relied on natural products for sustenance of life. However, what led to primitive man to select certain plant materials for the treatment of various diseases is still debatable. Some people relied on the African folklore that most plants reveal their medicinal uses to the traditional healer whenever he (the traditional healer) passes through the forest[8]. This belief was strengthened by the "Doctrine of Signatures" in which Paracelsus asserted that plants were the gift of the gods and argued that God-his catholic God had given to certain plants such distinct morphological signs-e.g., shapes, colours, number, habitat etc.-that they clearly indicated the diseases for which they should be used. The religious belief of that time notwithstanding, the use of plants as food and medicine is ordained of God. God gave us "every herb bearing seed" as food and ordered "their fruit be used for food and their leaves for healing". There is also this belief that ancient man had little or no knowledge of the medicinal values of natural products but discovered them by trial and error or by accident or observation of the instinctive discrimination of plants by animals. The knowledge so acquired was tried and when found successful was formulated into traditional medicine[9]. The knowledge

acquired from traditional medicine was repeatedly used over centuries and resulted in accumulation of information on the medicinal values of herbs which became the foundation upon which modern medicine was built. The accumulated information documented in many books[10-21], dealt with either the ethnobotanical, ethnomedicinal or traditional uses of the African plants. Ethnobotany[22] is the study of plants used by the primitive and aboriginal people while ethnomedicine is the use of plants or animals by members of an indigenous culture for which there is no organized medical system. Whereas traditional medicine[23] refers to the use of plants or animals in the treatment or amelioration of diseases within an organized indigenous system, the person who provides health-care to the community by using vegetable, animal and mineral substances is the traditional healer. In folkloric medicine, ethnobotany (also called herbal medicine), ethnomedicine, traditional medicine and traditional healer are recognized by the community.

The ethnomedicinal uses of many African plants are documented but the active principles responsible for the therapeutic applications of most of these plants are not yet identified. Medicinal plants are used basically in two different forms;

(i) as complex mixtures containing broad range of constituents and

(ii) as pure chemically defined active principles[8].

Whereas herbal medicine involves the use of plants as complex mixtures, the process that leads from the plants to a pure bioactive substance is very long and

tedious and requires a multidisciplinary collaboration of botanists, pharmacognosists, chemists, pharmacologists, and toxicologists[24]. Multidisciplinary approach for obtaining active principles from plants involves the steps shown in figure 2.

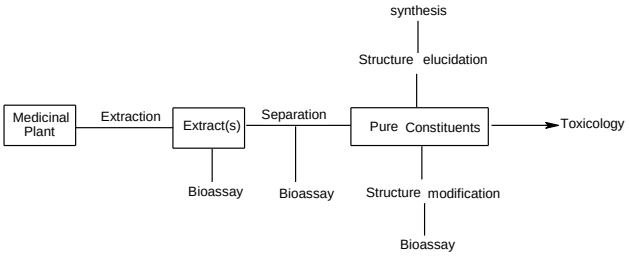


Fig. 2. Procedure for obtaining active principles from plants

It could have been ideal, if a natural product chemist is a scientist well-schooled in the classic techniques and principles of botany, chemistry and pharmacology. Research projects that go easiest to completion are those where everyone on the project is a chemist or where everyone is a pharmacologist or where everyone is a botanist. This happy situation is impossible in natural product research because a multidisciplinary team is necessary if the project is to be both efficient and successful[25]. This is also the reason why publications on natural product research are co-authored since no author could hold claim to the entire publication. The function of ethnobotanist in natural products project is to identify the plant species and provide information on their ethnomedicinal uses. The ethnopharmacologist searches for new prototype drugs-molecules with new mechanisms of action that will change a course of

therapeutics – by carrying out a dose-response activity and testing the activity of the crude and isolated drug. The natural product chemist, in this team, isolates active principles using a bioassay as a guide. The ultimate aim is to isolate pure crystalline materials so as to answer a very important question – has a new plant principle been isolated? Plant materials are used in medicine and pharmacy because of the special properties – therapeutic or physical – of the constituents in such a plant and since the constituents are chemical entities, the subject has a chemical basis.

Natural product chemistry is the study of secondary plant metabolites (that is phytochemistry) or the scientific study of those substances which are used or have been used in medicine and pharmacy (pharmacognosy or materia medica). The study of crude drugs was first referred to as pharmacognosy by Professor Jonathan Pereira during his inaugural lecture on September 27, 1843, though the word had been introduced in this context by Seydler in 1817. However, it was many years before the term was officially used as the name of the subject taught to pharmacy students[26]. There is a little confusion in the use of the terms pharmacognosy, phytochemistry and Natural Product chemistry in many British University colleges of pharmacy. For example, at the School of Pharmacy, University of London, Pharmacognosy is taught as a subject, Strathclyde University teaches Phytochemistry whereas at Herriot-Watt University, natural product chemistry is taught. This subject, taught in different universities with different names, has almost the same course content. No matter what name this subject is called, there is a distinction

between a natural product chemist, a phytochemist and a pharmacognosist. The natural product chemist and the pharmacognosist deal with the isolation of active principles from plants and animals and important factors related to their structure which influenced the therapeutic activity of this group of drugs. Whereas the pharmacognosist is a pharmacist, the natural product chemist is an organic chemist. Apart from providing much that is still relevant in terms of subject matter as well as the opportunity of applying techniques ranging from extraction, separation and structure elucidation of compounds, natural product chemistry affords plenty of scope of training in mental and manipulative skills which, in the long run, are more important than the mere amassing of factual information.

THE JOURNEY SO FAR

The emphasis on natural product chemistry is to discover prototype drugs from natural sources. A prototype drug, in a chemist's view is defined as the drug that has a wholly different chemical structure from existing agents and wholly different medical applications. Discovery of a prototype drug brings forth changes in the practice of medicine – consider the impact of curare on the art of surgery, the impact of penicillin G on mortality from infectious disease, the impact of reserpine on the treatment of mental disease. It must be recognized that these three drugs alone have completely changed our life expectancy and the quality of life on earth.

In this inaugural lecture, my business is not to discuss the numerous ethnomedicinal plants and the bioactive substances isolated from them but to highlight how

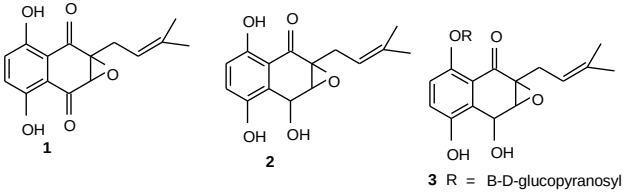
secondary metabolites from medicinal plants have aided in changing the course of health-care delivery. In doing this, different organic molecules are classified according to their biological activity and discussed as a group under the following sub-heading: Antifungal and antiviral, antimalarial, Hypoglyceamic, anticancer and molluscicidal compounds.

Antifungal And Antiviral compounds

Traditional healers in West Africa have claimed success in treatment of several infectious diseases including fevers, bronchitis, venereal diseases, skin disorders and worm infestations. Often, information obtained from traditional healers is very helpful for the selection of plants species by a natural product chemist who wishes to identify the constituents responsible for the plant's therapeutic effect or for the toxicity. Some examples of medicinal plants used in ethnomedicine whose constituents have been shown to exhibit antifungal properties include *Sesamum angolense* (Pedaliaceae), *Garcina kola* (Guttiferae), *Piper guineense* (Piperaceae) and *Buchholzia coriacea* (Capparaceae).

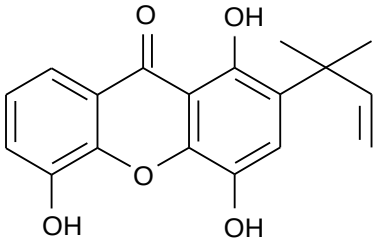
Sesamum angolense is a tropical African plant more predominant in Malawi. The plant is used ethnomedicinally as a remedy for respiratory troubles. Extracts from *Sesamum angolense* exhibited antifungal activity as well as growth-inhibiting activity against a human colon carcinoma cell line. The antifungal active components were two naphtoxirene derivatives (1) and (2). The fungicidal activity seems to require the presence in the molecule

of an OH group in the peri position to a carbonyl function.



It was discovered that naphtoxirene (1) in which two such functional groups are present exhibited the strongest activity; compound (2) which contained only one OH peri to a carbonyl was about 10 times less active while (3) which did not possess this arrangement was inactive. This is an example of structure-activity relationship (SAR) which is an attempt to correlate chemical configuration with biological activity. The greatest numbers of new drugs are presently being developed with this method.

Garcina kola is used ethnomedicinally to prevent or relieve cough and is considered effective against bronchitis and throat troubles. The root sap is applied to cure parasitic skin diseaes[12]. The extracts of *Garcina kola* seeds possess remarkable antihepatotoxic and hepatotropic properties. From the root bark extract of *Garcina gerrardii.* A fungicidal active pyranoxanthone (4) was isolated. This compound was tested for its activity against the plant



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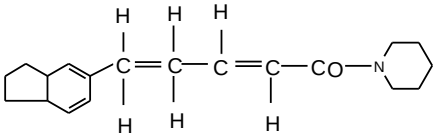
pathogenic fungus in a TLC bioassay and shown to prevent growth of the fungus at 0.2μg.

Traditionally, *piper guineense* has been used in several formulations which are used for the treatment of cough, gastro-intestinal disorders, cold, bronchitis, venereal diseases and rheumatism and as a preservative in indigenous medicinal preparations[14]. Constituents of piper *guineense* include piperine (5) and dihydro piperine (6) which showed antimicrobial activity against *Mycobacterium smegmatis* at concentration of 100 ppm.



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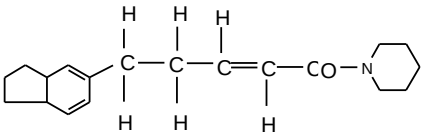

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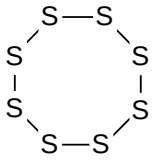
In addition, piperine exhibited antimicrobial activity against *Candida albicans* while dihydro piperine showed activity against *Klebsiella pneumonia.*

Buchholzia coriacea is known for its ethnomedicinal uses. The young leaves are used as a poultice for boils, the seeds, which have peppery taste, are used as condiments or as cough medicine. The crushed seeds are used on skin eruptions while the bark is made into stuff to relieve headache and nasal congestion. The bark decoction is also used to wash persons with small-pox[27]. Cyclooctasulphur (7) was isolated from the seed kernels and investigation into the antimicrobial activity of the isolated cyclooctasulphur showed significant antifungal activity[28].



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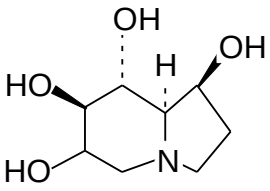
The search for antiviral compounds has been stimulated by the rapid spread of AIDS. The identification of the human immunodeficiency virus (HIV) as the causative agent of AIDS enhanced the impetus for the search for novel antiviral agents. Development of anti-HIV drugs led to the isolation of two plant derived compounds, castanospermine (8) and hypericin (9). Castanospermine, a



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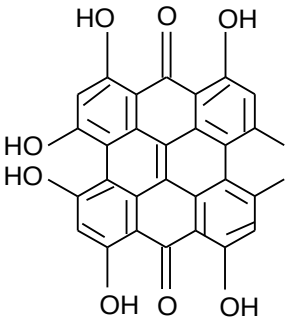

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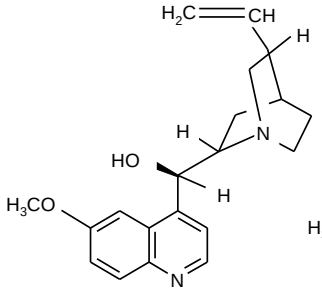
tetrahydroxyindolizidine alkaloid, isolated from the seeds of *Castanospermum australe* (Leguminosae)[29] is a potent inhibitor of ß-glucosides[30] and thus inhibits the replication of HIV[31]. Without the proper glycoprotein coating, the HIV- virus is unable to spread to non-invested cell. Hypericin, an aromatic polycyclic anthraquinone derivative, isolated from *Hypericum perforatum* (Guttiferae), has antiretroviral activity and it inhibits the propagation of Friend leukaemia virus (FLV) [32].

Antimalarial Compounds

The use of medicinal herbs for malaria treatment is perhaps as old as man. The extracts and infusion from *Cymbopogon citratus* (Gramineae), *Cryptolepis sanguinolenta* (Periplocaceae), *Morinda lucida* (Rubiaceae), *Picralima nitida* (Apocynaceae), *Cinchona officinalis* (Rubiaceae), *Azadirachta* indica (Meliaceae), *Carica* papaya (Caricaceae) and *Mangifera indica* (Anacardiaceae) are used by rural inhabitants of Nigeria as remedy against malaria attack. These plant species in addition to their antimalarial activity are shown to possess antipyretic,

analgesic and anti-inflammatory properties. *Azadirachta indica* is a plant indigenous to India but it is now widespread in West Africa. The leaves and bark are used against malaria and fever. Available evidence in support of its antimalarial activity[33-35] has been provided. Although many bitter principles[36-37] have been isolated, the actual antimalarial principle has not been identified.

Natural product chemistry owes an abundant debt to folkloric evidence. The use of quinine as an antimalarial is reputed to have its origin in an accidental discovery of a South American Indian who, thirsty and febrile, drank from a pond into which a *cinchona* tree had fallen and was thereby miraculously cured. The most important alkaloid isolated from the bark of *cinchona officinalis*, which grows wild in South America, is quinine (10)[38].



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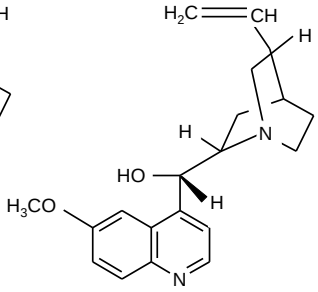

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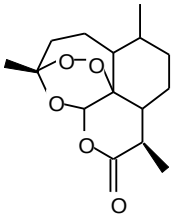
Quinine still remains the most potent antimalarial drug discovered. This is a serendipic example of how therapeutic application of a plant is correlated to its

chemical constituent. It is possible, therefore, to postulate that knowledge of the traditional uses of a plant species may aid a correlation between the plant's therapeutic application and its chemical constituents. Quinidine (11), a dextro-rotary stereoisomer of quinine, was also isolated from the bark of *Cinchona officinalis*. Quinidine is a cardiac depressant (antiarrhythmic). It is interesting to note how the difference in stereochemistry of quinine and quinidine changed the activity of both compounds, one acting as antimalarial and the other a cardiac depressant.

Resistance of *Plasmodium* strains to currently used antimalarial drugs has led to screening programmes aimed at isolating new antimalarial drugs of plant origin. Artemisinin (12) was isolated from the aerial parts of the plant *Artemisia annua* (Asteraceae) which was used in China as a febrifuge and in malarial therapy[39]. This sesquiterpene lactone endoepoxide



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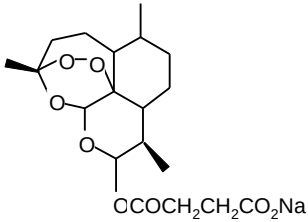

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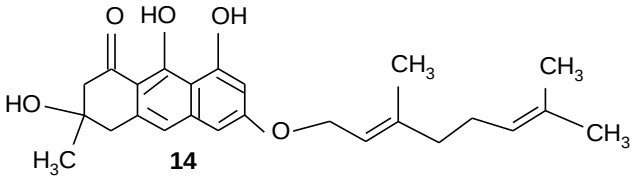
represents a completely new chemical class of antimalarial compounds with a high level of blood schizontocidal activity against *plasmodium* strains resistant to all known antimalarials. Preliminary biochemical studies indicate that artemisinin has a

mode of action quite different from currently used synthetic antimalarials[24]. As artemisinin is highly lipophilic, there are problems with its administration as a drug. This problem is now overcome by synthesizing a derivative, sodium artesunate (13), which has been clinically tested for the intravenous treatment of *Plasmodium falciparum* infections. Because chemical synthesis of artemisinin only results in a very low yield[40], the plant is the most profitable source of production.

From *Psorospermum febrifugum* (Guttiferae), vismione D (14) was isolated. Vismione D is a very active antimalarial drug with IC_{50} = 0.095 ppm comparable to the activity of quinine.



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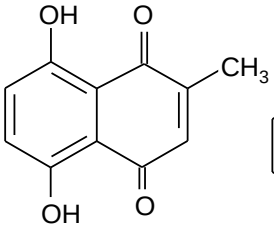
A prototype of a new class of drugs derived from naphthoquinones is discovered to be excellent antimalarial. Isoshinanolone (15) and 2-methylnaphthazarin (16) were isolated from the roots of *Nepenthes* thorelii Lec. (Nepenthaceae). These naphthoquinones have structures different from known antimalarial drugs and their IC_{50} values are found to be between 0.05-40 ppm.



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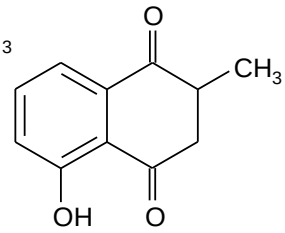

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With malaria causing organisms beginning to develop resistance to chloroquine, there is urgent need for more novel type of antimalarial compounds. In searching for such novel antimalarial drugs, it must be noted that certain parasites are species specific thus making cross infection difficult except between closely-related hosts. An experimental chemotherapist who is unable to work with malaria in man, for example, may find it difficult to obtain a cheap and suitable host for human *plasmodia* and if his aim is to discover a drug for use in man and not fundamental research, he can be misled by the reaction of both parasite and hosts to his compound.

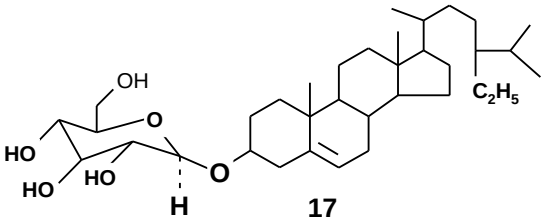
Hypoglyceamic Compounds

The discovery of useful oral agents for decreasing the concentration of glucose in the blood is a great advance in the therapy of diabetes. During the last forty years some 1000 sulphonamide derivatives and a few compounds of different chemical structure have been studied in respect of blood sugar lowering activity. Since plants have been used as sources of medication, it is not surprising that some of these were associated with hypoglyceamic activity. Various

ethnic groups have all had their favourable remedies, real or imaginary, for diabetes. Among the more recent were leaves of *Bridelia Ferruginea* (Euphorbiaceae), unripe fruits of *Momordica charantia* and *Momordica foetida* (Cucurbitaceae), the leaves as well as the bark of *Myrianthus arboreus* (Cecropiaceae).

The antidiabetic properties of *Bridelia Ferruginea* were established by the isolation from the leaves of antidiabetic coumestan.

Fruits of *Momordica charantia* have been successfully used by diabetic patients and crude extracts have shown hypoglyceamic activity when screened in rabbits. A polypeptide, p-insulin[42] or v-insulin[43] and charatin[44] were isolated from fruits and seeds of *Momordica charantia.* Charantin was later shown to be identical with foetidin[45,] a neutral constituent of *Momordica foetida* consisting of equal parts of ß – sitosterol glucoside (17) and 5, 22-stigmastadiene-3-o1 glucoside (18). Both charantin[46] and foetidin[47] were shown to decrease the blood glucose level only in normal rabbits but not in the alloxan-diabetic animals. It was, therefore, concluded that charantin acts not only by direct insulin-like action but also by stimulating the release of insulin. It was probably due to this reason that the drug was more potent in normal rabbits.



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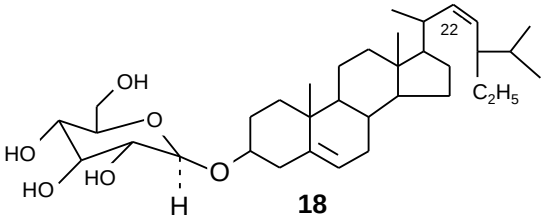

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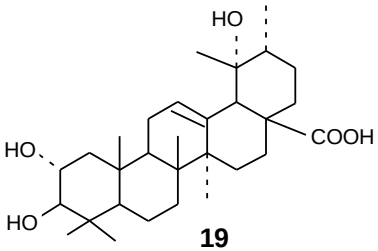
The stem of *Myrianthus arboreus*, a plant widespread in tropical West Africa[48], was shown to possess hypoglyceamic properties[49] while the leaves had antitussive properties[50]. Phytochemical studies on *Myrianthus arboreus* (rootwood and stems) afforded alkaloids[51], pentacyclic triterpenes[52, 53] and ß – sitosterol glucoside[54]. The components containing tormentic acid (19) and ß – sitosterol glucoside exhibited hypoglyceamic activity.



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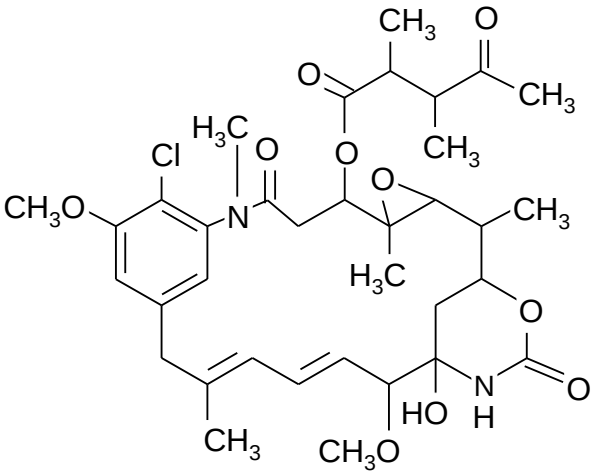
Anticancer Compounds

A strong effort has been put into the search for novel anticancer agents since the last four decades. The emphasis is to discover new drugs from plants but experience has shown that new drugs may not be beneficial to the discoverer as the isolated drug may be replaced, within a short time, by a superior synthetic analogue. For example, the antileukemic ansa macrolide, maytansine (20), was first isolated by Kupchan from an Ethiopian species of *Maytenus ovatus* (Celastraceae) in a poor yield[55]. Better yield of maytansine was obtained from the Kenyan species of *Maytenus buchnanii* while the best yield was extracted from the South African plant, *Putterlickia verrucosa.* In 1980, Corey and his co-workers[56] successfully carried out a total synthesis of maytansine. Neither Ethiopia nor Kenya will derive any economic benefit from the discovery of the drug in a plant in their country because subsequent commercial production would be either by total



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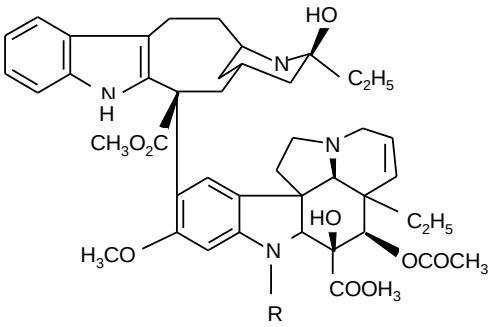
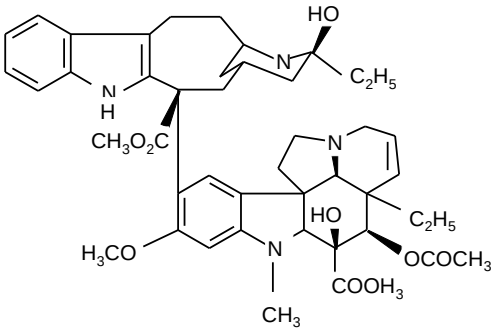
synthesis or at worst by extraction from a South African plant[57]. Unfortunately, Kupchan died of cancer in October 1976 before maytansine was shown in 1977, to be clinically very promising as an antileukemia drug.

The story is similar with vinblastine (21)[58] and vincristine (22)[59] - antineoplastic drugs - first isolated from the pink and white Madagascan rose periwinkle, *Catharanthus roseus* G. Don (Apocynaceae). We have recently started the phytochemical study of the Nigerian species of *Catharanthus* in our laboratory. Vinblastine and vincristine differ in their clinical utility and toxicity. The major use of vinblastine is the treatment of patients with Hodgkin's disease,



	R
21	CH_3
22	CHO

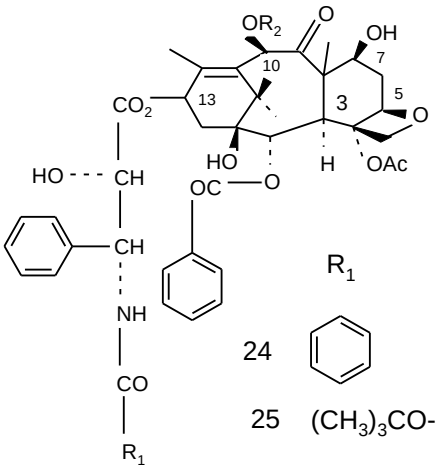
non-Hodgkin's lymphomas, renal, testicular, head and neck cancer. Vincristine is widely used, in combination with other anticancer agents, in the treatment of acute lymphocytic leukemia in childhood, small cell lung cancer, cervical and breast cancer[60]. Structural variants of vinblastine and vincristine, called 5'-noranhydrovinblastine (23) was synthesized[61, 62] and developed to an anticancer drug that has been recently introduced in France[24].



23

Taxol (24)[63] has become one of the most important compounds to emerge from the screening of natural

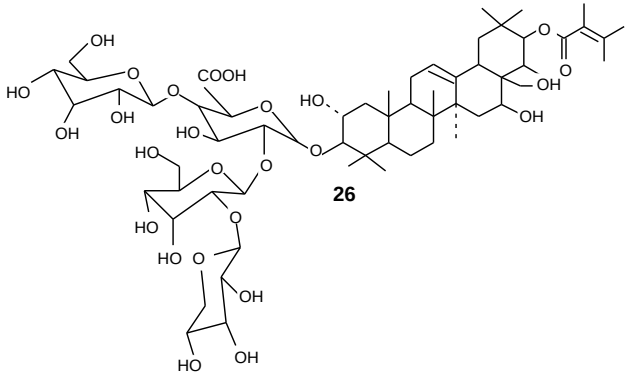
products in recent years. It was first isolated in 1971 by Wall and his collaborators from the stem bark of *Taxus brevifolia* (Taxaceae) [64]. Taxol showed significant activity against various leukemias, the Walker 256 carcinosarcoma, sarcoma 180, Lewis lung tumour and other cancers[65]. It is a mitotic inhibitor which has a very unusual mechanism of action in that it stabilizes microtubule and prevents disaggregation in contrast to other agents like maytansine, *vinca* alkaloids and colchicine which inhibit microtubule formation[66]. To avoid *Taxus brevifolia* being extinct as a result of the use of the plant, taxol analogue (25) was produced by partial synthesis from a congener found in the leaves in appreciable amounts[67] and was shown to have greater chemotherapeutic potential than taxol itself[68].



Molluscicidal Compounds

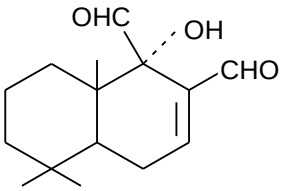
Schistosomiasis (or bilharzia) is a disease that affects millions of people living in Africa and it is transmitted through certain species of freshwater snails – *Biomphalaria glabrata* – which serve as intermediate hosts to the parasite. One way of controlling schistosomiasis is by chemotherapy with orally administered anti-schistosomal drugs, such as metrifonate, oxamniquine and biltricide. Molluscicidal or snail-killing activities of plants are of special importance for the control of schistosomiasis as they seem to be less expensive than synthetic compounds.

Of the natural products with the most potential in the fight against schistosomiasis, the triterpene glycoside appears to be in the forefront at the moment especially as some plant parts can contain as much as 30% saponin[69]. A highly promising plant molluscicide, napoleonaside (26), was isolated from the fruits of a Nigerian plant, *Napoleonaea imperialis* (Lecythidaceae) [70]. Napoleonaside was tested for its molluscicidal properties against *Biomphalaria glabrata* and was found to be one of the most potent naturally occurring plant molluscicides with activity of 0.4 ppm (observed after 24 h)[71]



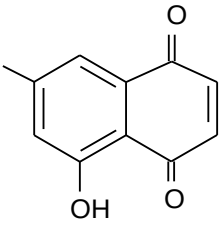
26

Several sesquiterpenes and sesquiterpenes lactones are potent molluscicidal agents. Warburganal (27)[72], from the bark of the East African tree *Warburgia ugandensis* (Canellaceae), kills *Biomphalaria glabrata* snails at 2 ppm within 24h.



27

From the root bark of *Diospyros usambarensis* (Ebenaceae)[73], used in Malawi as a traditional schistosomiasis cure, were isolated 7- methyljuglone (28) and plumbagin (29) with activity of 5 ppm and 2 ppm respectively.



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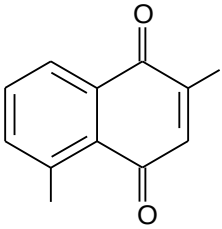
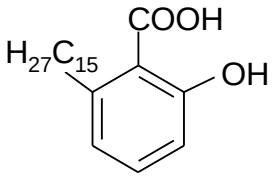


29

An unsaturated anacardic acid (30) was isolated from the shells of cashew nuts *(Anacardium occidentale*, Anacardiaceae*).* Anacardic acid is among some of the most potent naturally occurring molluscicides having high toxicity (LC_{50} 0.35 ppm) [74].



30

THE FUTURE

In the beginning we believed in the traditional and ethnomedicinal use of plants for healing. The journey so far reveals that plants are sources of novel and prototype drugs. What is the future of drug development from natural sources of Nigeria?

For future drug development, the Nigerian government and the pharmaceutical companies in Nigeria should collaborate in establishing a comprehensive National Institute for Natural Product Development (NINPD). NINPD will aim at acquiring and screening new bioactive substances from plants as well as conducting necessary preclinical development studies needed to bring active drugs to clinical trials. It will be the duty of NINPD to draw up a programme that should be a service to researchers in academia, research institutes and the pharmaceutical industry who are working in various drug development fields but lack resources to follow up their investigations. Enough information is needed for extensive rational drug design and it will be the duty of NINPD to provide the necessary information. Since natural products are excellent sources of complex chemical with a wide variety of biological activities, natural product extracts should form an important component of NINPD screening programme. The discovery of new active compounds from natural products will open up new areas for investigation of related compounds and provide new biochemical tools for cell biology. The screening of new materials must be an on-going process. If better equipped and upto date laboratories are established at the proposed NINPD, Nigeria will have advantage over developed countries who lack variety of plant species as are found in the rich forest of Africa. Well-equipped and upto date laboratories for natural product chemistry will facilitate natural products research and offer a new incentive to many researchers in this field who deviated from their original research programmes[75-79]. The deviation from original research programmes, aimed at isolating new bioactive substances, may be

associated with lack of proper funding. If there is improved funding for the harness of natural product resources, Nigeria will no longer be a dumping ground for less potent drugs as the country will be in a better position to develop more potent drugs from its endowed natural resources. Pharmaceutical industries in Nigeria should be encouraged to set up viable Research and Development programmes to solve problems associated with drug development from synthetic and natural sources. Companies should no longer be allowed to rush to parent companies abroad for solution to problems that should be solved in Nigeria by Nigerians.

If the problem of poor funding and ill-equipped laboratories is solved, the Nigerian natural product chemist will still be confronted with the problem of collaborative research. The isolation and subsequent development of bioactive compound into clinical acceptable drug requires a multidisciplinary approach. The quality of research can only be as good as the co-operation between botanists, natural product chemists and pharmacologists. A good collaboration between botanists and natural product chemists has developed over the years but the collaboration with pharmacologists in Nigerian Universities is of more recent date and definitely needs to be intensified.

CONCLUSION

"Living better through the magic of synthetic chemistry" is an old chemical adage. Synthetic chemistry has completely revolutionized the pattern and quality of life world-over. It is important to recognize that plants are miraculous in their synthetic

capacity. Plants take their energy from the sun rather than from petrochemicals. Their demand for raw materials is exceedingly modest and they do not have to be paid the wages of a chemist. The world is now energy conscious for many good reasons but plants acquire unlimited energy from the sun for their synthetic products. New drugs are biosynthesized as long as plants exist in a forest. This forest of novel drugs, which is exploited by man for a healthier human race, is made possible through the application of techniques in natural product chemistry.

I thank you for listening patiently.

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CITATION ON
PROFESSOR CHUKWUNONYE MOSES OJINNAKA
B.Sc (Ib), PhD (Ib), FCSN, MICCON

Professor Chukwunonye Moses Ojinnaka was born on 6th June 1946 at Akpulu in Ideato North Local Government Area of Imo State, Nigeria. He is the second surviving son of Late Chief Samuel Onyejekwe Ojinnaka (the Ezelefeanya of Akpulu) and Late Lolo Janet Abiazuba Ojinnaka. He attended St. James Central School, Akpulu (1956 -1958), St. Anne's Primary School, Ahiaeke, Umuahia (1959), Madonna High School, Ihitte (WASC, Division One, 1960 -1964) and Government Secondary School, Afikpo, (HSC, 1965-1966). In September 1970, Professor Ojinnaka gained admission into University of Ibadan, where he obtained the B.Sc. (Hons) degree in Chemistry (1973) and PhD (1977), specializing in Natural Product Chemistry. As a graduate student at University of Ibadan, late Professor D.E.U. Ekong, Professor J.I. Okogun and Professor D.A. Okorie variously supervised Professor Ojinnaka.

Throughout his university education in Nigeria, Professor Ojinnaka was sponsored by the Federal Government of Nigeria as a Federal Scholar (1970 - 1973) and by the University of Ibadan for the PhD degree as a University Scholar (1974 -1977).

After his formal education, Professor Ojinnaka had a rewarding working experience. Professor Ojinnaka taught Chemistry/Mathematics at St. Augustine's Seminary, Amechi, Ezzamgbo, Abakaliki (January 1967–August 1968) and Holy Child, Sharon, Abakaliki (January 1970–August 1970). He served at Christ School, Ado-Ekiti as a member of the first batch of the National Youth Service Corps (1973 – 1974) and worked briefly as a Research Officer at the Federal Institute of Industrial Research, Oshodi (July – October 1974) and Graduate Assistant in the Department of Chemistry, University of Ibadan in 1975. In 1978, he was appointed Senior Research Officer and Head of Research Division, Leather Research Institute of Nigeria, Samaru, Zaria. He held the post until August 1979, before assuming duties as Lecturer II, in School of Chemical Sciences, University of Port Harcourt. Through hard work and vigorous research, he rose steadily through the ranks: Lecturer I (1981); Senior Lecturer (1985), and Professor of Chemistry (1995).

As a University lecturer, Professor Ojinnaka contributed immensely in the education and training of many students in Chemistry, Engineering and Medicine. In fact, he successfully supervised the first PhD graduate in the Department of Pure and Industrial Chemistry, University of Port Harcourt.

Professor Ojinnaka has practically lived his life in the Laboratory searching for the active principles in one plant species or the other. A man of great curiosity about things around him, Professor Ojinnaka established himself as a leading authority in pharmacognosy and a first class scientist in natural

product chemistry. He was a guest to many international Universities. In 1981, Professor Ojinnaka was appointed Research Associate at the College of Pharmacy, University of Illinois at the Medical Center, Chicago, where he worked under Professor Norman Farnsworth; and in the 1984-85 academic session, he was awarded a Post-Doctoral Research Fellowship at Arrhenius Laboratory, University of Stockholm, Sweden.

As a staff of University of Port Harcourt, Professor Ojinnaka served University of Port Harcourt in many important capacities. Professor Ojinnaka is a member of Senate, University of Port Harcourt by virtue of his professorial rank. He was the Head, Department of Pure and Industrial Chemistry (1988-1990).

As a renowned scientist, Professor Ojinnaka attracted attention outside University of Port Harcourt. Professor Ojinnaka served as a member of National University Commission (NUC) Accreditation Team to many Nigerian universities. Professor Ojinnaka has also served as an external examiner to several universities both at the undergraduate and postgraduate levels. He was the Regional Editor, Journal of Chemical Society of Nigeria (JCSN) and Assistant Editor, Scientia Africana (1997-). He is also a Consulting Editor to several local and international scientific journals. He is a Fellow, Chemical Society of Nigeria (FCSN), member of various professional and learned societies within and outside Nigeria such as Nigeria Society of Pharmacognosy, Science Association of Nigeria, West African Science Association, American Society of Pharmacognosy and Society for Medicinal Plant

Research (Europe). Professor Ojinnaka is also cited in two International Biographies – **Marquis Who's Who in Science and Engineering** (1996, 1997) and **Who's Who in the World** (1997).

It is in his leading roles in pharmacognosy and natural product chemistry that Professor Ojinnaka is delivering the 19th Inaugural Lecture of University of Port Harcourt entitled "A Forest for Novel Drugs: Natural Product Chemistry". This is also borne out from his immense contributions to knowledge, especially in advancement of our knowledge of modern chemistry. An author of five books and many scholarly articles in international journals, Professor Ojinnaka has made world-acclaimed contributions, especially in a study captioned "Carbonyl Peak Index in the Study of Lubricant Oxidation" where he demonstrated a technique that could be used to monitor the deterioration of engine oils. He was the first to isolate, characterize and propose the name 'Myrianthic acid' for a pentacyclic triterpene acid from Myrianthus arboreus. At the 35th International Union of Pure and Applied Chemistry held in Istanbul, Turkey, in 1995, Professor Ojinnaka discussed the isolation of Napoleonaside (first isolated by him from a Nigerian plant Napoleonaea imperialis) and proved that Napoleonaside was one of the most potent naturally occurring molluscicides for the control of Schistosomiasis, a disease that is endemic in Nigeria.

Vice-Chancellor, Ladies and Gentlemen; it is therefore, my honour to present Professor Chukwunonye Moses Ojinnaka, an intellectual giant, the developer of carbonyl peak index technique and

the discoverer of Myrianthic acid, to deliver the 19th Inaugural Lecture of University of Port Harcourt, Nigeria.

Presented by
Professor Charles C. Nnolim
Professor of English
Thursday, July 30, 1998