

Inaugural Lectures Series 48

MAN, PLANTS AND MEDICINE IN AFRICA: SOME FUNDAMENTAL PERSPECTIVES

by **Abayomi Sofowora**

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No 48

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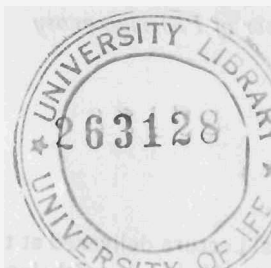
by

Abayomi Sofowora

Professor of Pharmacognosy

**An Inaugural Lecture delivered at the
University of Ife, on Wednesday, 7th January, 1981**

Inaugural Lectures Series 48



INTRODUCTION

Mr. Vice-Chancellor sir, distinguished guests, colleagues, ladies and gentlemen. It is an honour for me to have been asked to give this inaugural lecture, the first one this calendar year, and I know that an inaugural lecture is obligatory for a professor with tenure at the University of Ife. This is not the first inaugural lecture in Pharmacy in this University and I am also not the first professor of Pharmacognosy in Nigeria. Indeed, at one time, there were two professors of Pharmacognosy in this Faculty of Pharmacy and by this I refer to that world renowned Professor Egil Ramstad and Professor Moimer Kucera. Both eminent scientists left the University of Ife without inaugurating the chair of Pharmacognosy. Each of them, however, made contributions to the development of Pharmacognosy in general and to our knowledge of Nigerian medicinal plants in particular. Professor Kucera published a series of articles in various scientific journals under the general title of "Contributions to the knowledge of Nigerian medicinal plants". I shall be mentioning some of his works later on. The first Nigerian professor of Pharmacognosy, Professor William Osisioigu of the University of Nigeria, Nsukka, did not give an inaugural lecture before he was appointed Commissioner for water resources in the last military government. For this reason, this lecture thus becomes the first inaugural lecture in Pharmacognosy to be given in Nigeria.

WHAT IS PHARMACOGNOSY?

The word 'Pharmacognosy' is coined from two Greek words: 'pharmakon' meaning *drug* and 'gignosco' meaning *to acquire a knowledge of*. In fact, it is that aspect of Pharmacy which deals with the study of natural sources of drugs. These

are mainly of plant origin, but drugs of animal origin and microbial origin should rightly come within this definition.

Pharmacognosy is closely related to both botany and plant chemistry, and its history entitles it to be regarded as the parent of both. Even as late as the beginning of the present century, pharmacognosy had developed mainly on the botanical side, being particularly concerned with the description and identification of plant drugs both in the whole state and in powder, with their history, commerce, collection, preparation and storage. Such branches of pharmacognosy are still of fundamental importance but the rapid development of plant chemistry and pharmacology in recent years has led to an increased interest in the phytochemical aspects of pharmacognosy. In particular, the elucidation of the biogenetic pathways for the formation of medicinally active secondary metabolites of plants has afforded a new phytochemical foundation on which pharmacognosy is now largely based. Pharmacognosy also includes the study of other materials used in pharmacy such as flavouring and suspending agents, disintegrants, filtering and support media etc. Other fields which are naturally associated with the subject are poisonous plants, hallucinogenic plants, raw materials for the production of oral contraceptives, allergens, herbicides and insecticides. In order to cope with the variety of topics under its purview, pharmacognosy makes use of a great variety of supporting sciences from which it draws for its own purposes. Like most applied sciences, pharmacognosy unites a variety of disciplines, yet it is different from any of them.

Pharmacognosists specialize in definite areas, although they must be familiar with all areas in a general sense. The fields of specialization which pharmacognosists may choose include plant taxonomy, anatomy, morphology, physiology, genetics, biochemistry, phytochemistry, drug-plant cultivation, microbiology and several others.

THE POVERTY AND HEALTH OF MAN IN AFRICA

The countries of Africa belong to a group of those referred to as the third world or developing countries. The developing

countries are characterised by extremely limited resources, poor communication, vast distances, individual and community poverty etc. These factors act upon one another and leave the developing countries in a perpetual state of poverty. Because of lack of what could be described as very simple health-care measures, man in Africa dies daily of preventable and curable diseases, often associated with malnutrition. The *per capita* income for man in many African countries is less than US \$94 a year. This figure is staggering especially when one considers that *per capita* income in the USA is \$4,980 and in France \$3,400 *per annum* according to 1972 figures. Yet, despite these differences in incomes, the population of the less developed regions of the world (including Africa) continues to rise sharply.

The life expectancy of man in Africa at birth is estimated to be about 45 years compared with about 70 years for man in Europe or in North America. The death rate in Africa is twice that of Europe while infant mortality is nearly seven times higher in Africa than in Europe (WHO, 1979). These unfavourably high levels of mortality are caused by a number of inter-related factors including:- infection and the consequences of ill-timed, closely spaced, and too frequent pregnancies as well as the lack of health care and other social services (Djukanovic and Mach, 1975). indeed in most developing countries of the world, is also very much below the level considered necessary for the prevention and control of communicable diseases and for the promotion and maintenance of good health. For example, only 20% to 25% of rural dwellers in developing countries have access to clean water. The water supply to urban areas in these countries are grossly insufficient and the same goes for the waste disposal facilities. In Nigeria, an estimated 29 million out of a population of over 80 million have access to safe drinking water.

As if the situation is not complex enough for any Government or community to try to help the health situation of Man in Africa, the problem is further complicated by the fact that some of the people of Africa live a nomadic life. Some 50 to

100 million nomads have been estimated to be present in the World and 90% of these live in Africa and Asia. Nomads have their own needs and problems peculiar to their life style. Because of their constant movement and dispersion, special consideration must be given to provide help to this portion of the population in terms of health matters.

In tropical Africa, 1 million children die annually from malaria and in West Africa alone, half a million children die each year from measles. Diseases such as cholera, infectious hepatitis, yellow fever, tuberculosis and poliomyelitis which are largely under control in developed countries still cause great harm in developing countries. Also, 25% to 30% of the population in Africa is estimated to suffer from significant undernutrition.

The lot of man in Africa has been improving in terms of available health facilities. However, the amount of these facilities available to the population is still very far from the United Nations recommended figures. For example, from 1961 to 1972, there was an increase in the doctor population ratio from 1 in 25,100 to 1 in 17,500 in Africa. Also from a ratio of one nurse per 6,000 population in 1961, a better ratio of one nurse per 4,400 was available to man in Africa in 1972 (Akinkugbe, 1979). In Nigeria, there was a 1 doctor per 24,000 population in 1970 and 1 to 11,000 in 1978, one nurse per 4,900 in 1970 and 1 nurse to 3,600 in 1978. One pharmacist to 74,000 in 1970 and in 1978, there was 1 pharmacist to 32,000 population in Nigeria. By 1977, there was one hospital bed per population of 1,350 in Nigeria although there was only 1 hospital bed per 2,150 in 1970 (FMH, 1980). These figures are alarming especially for Nigeria where we have had an oil boom. The situation calls for drastic measures.

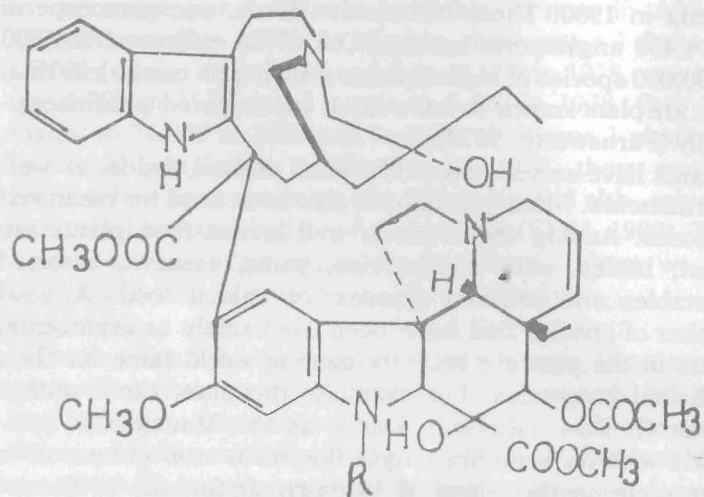
I have given these figures not to frighten you, but to remind some of us that not every Nigerian, and certainly not every man in Africa, has access to the kind of health-care facility that is available to professors and students on this campus. In our quest for knowledge and high academic ideals, it is easy to forget the masses who live outside the four walls of this

ivory tower. In this inaugural lecture, whilst we consider man in Africa in terms of the relative health-care facility available to him, I would like to propose how we can make medicine more accessible and acceptable to man in Nigeria.

PLANTS IN AFRICA AS SOURCES OF DRUGS

The endowment of good rainfall and sunshine has enabled a great variety of flowering plants to thrive in Africa. The total number of higher plant species in tropical Africa was estimated at 30,000 by Good in 1974. When the species found in mediterranean North Africa as well as those of Southern Africa are added to this, the total figure of plant species in Africa would probably come to 55,000. This already includes about 10,000 for the island of Madagascar which has a rich and highly endemic flora (Brenan, 1980). Dr. Lowe of the University of Ibadan made a total count of available plant species in Nigeria in 1980. These include 154 ferns, one gymnosperm and 4,459 angiosperm species. Out of an estimated 250,000 to 500,000 species of higher plants growing on earth, less than 15% are plant known to have been investigated pharmacologically (Farnsworth, 1977).

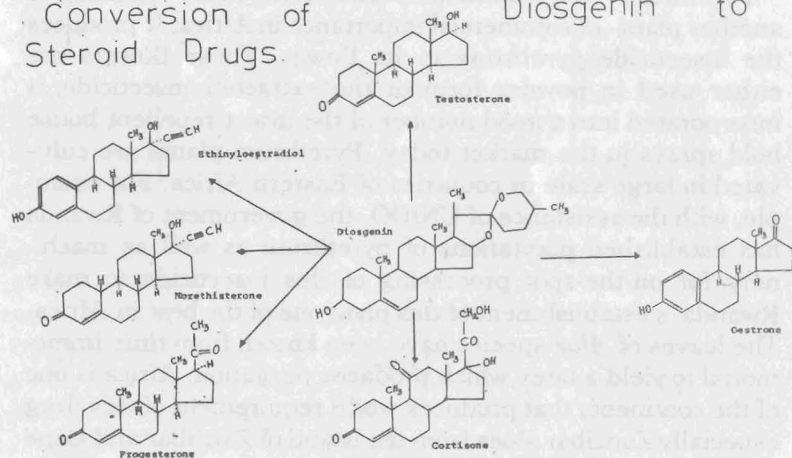
Plants have served man and animal as food, fodder as well as ornaments. Many plants have also been used for medicinal purposes. Among the common well known food plants are wheat, barley, oats, maize, rice, yams, cassava, assorted vegetables and selected grasses for animal food. A good number of species that have been used solely as ornamental plants in the past are recently gaining world fame for their medicinal properties. For example, the plant *Catharanthus roseus* G. Don. otherwise known as the Madagascan periwinkle with its beautiful purple flowers is now grown on a large scale on the island of Madagascar for sale to Europe and USA where large scale extraction of *vincristine* and *vinblastine* takes place.



VINBLASTINE — R = — CH₃
 VINCRISTINE — R = CHO

Vincristine is considered to be the drug of choice for the treatment of leukaemia today. World sales of these two antileukaemia alkaloids in the industrialised countries of the world is now estimated at well over U.S. \$30 million annually. This plant is still used in Nigeria only for ornamental purposes. Other countries of Africa have also developed large scale plantations of plants that can be used as medicines as such or that can be used as starting material for the chemical synthesis of other important drugs. For example, the increase in use of oral contraceptives, sex hormones, cortisones and similar drugs of the steroid group has raised the world demand for natural sources of diosgenin or hecogenin and similar compounds which are used as starting material for the synthesis of oral contraceptives. For example, in 1974,

Conversion of Steroid Drugs. Diosgenin to



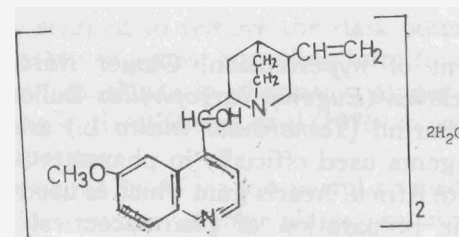
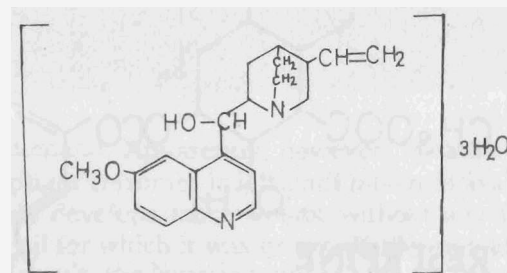
1 million kilogramme of steroid raw material was utilised (about 90% of this came from natural sources), and it is estimated that 1,700 tons of sapogenins will be required by

1985. This figure should go up to 5,300 tons by 1995, if the world steroid demand is to be met (Applezweig, 1976).

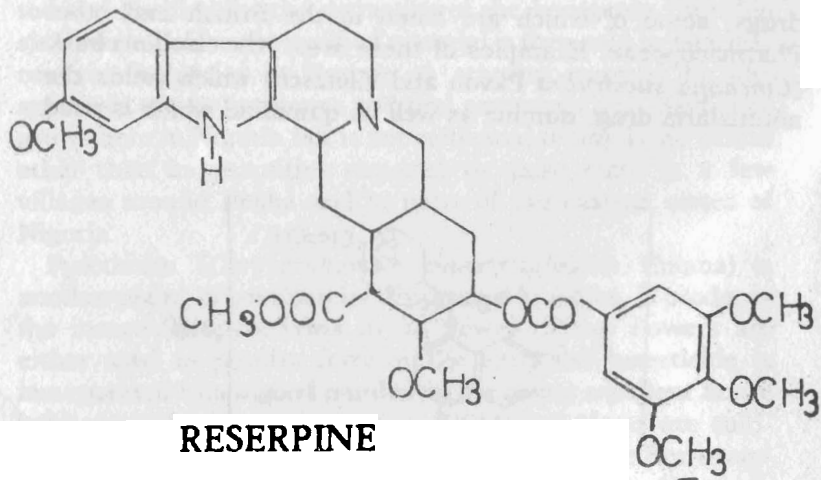
Sisal (*Agave sisalana* Perrine) which thrives very well in tropical Africa is one of the plants that produces sapogenin (hecogenin) in commercially exploitable quantities in its leaves. The government of Tanzania has developed large scale plantations of sisal in the Tanga region of the northern province of Tanzania where the sisal is grown, its juice extracted and purified for the extraction of the hecogenin from the sisal waste before the purified material is then sold to pharmaceutical industries in Europe as starting material for the synthesis of sex hormones and oral contraceptives. Sisal also grows here in Nigeria but is not cultivated to any large extent other than in quantities required to make mats in a few villages around Ilesha and in parts of the eastern states of Nigeria.

Pyrethrum (*Chrysanthemum cinerariaefolium* Visiana) is another plant of commercial importance in Africa. It produces the insecticide *pyrethrine* in its flower. These flowers are either used in powder form or the extracted insecticide is incorporated into a good number of the insect repellent household sprays in the market today. Pyrethrum plants are cultivated in large scale in countries of Eastern Africa. For example, with the assistance of UNIDO, the government of Rwanda has established plantations of pyrethrum as well as machinery for on-the-spot processing of this insecticide to make Rwanda's establishment of this plant one of the best in Africa. The leaves of *Aloe* species have been known from time immemorial to yield a latex which produces purgation. Africa is one of the continents that produces world requirement of this drug especially Zanzibar aloes from the island of Zanzibar and Cape aloes (from South Africa). Recently, the demand for aloe in Africa grew much higher when Professor El-Zawahry of Egypt reported that the yellow flowered *Aloe vera* L. proved helpful in the management of a number of skin problems including chronic leg ulcers and radiodermatitis. Extracts from *A. vera* also dry oily skins, help in the management of alopecia, acne vulgaris as well as scaly scalps (El-Zawahry,

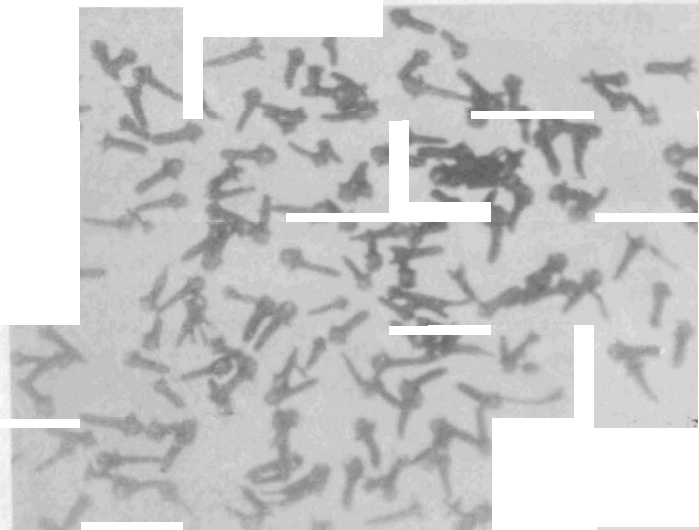
1979). This plant extract has since been formulated into lotions for treating certain acute eczemas and as a cream to ameliorate certain cases of psoriasis and *lichen planus*. The action of the plant drug has been likened to that of crotisone which is used in modern therapy of some of these skin problems. Plantations of *Aloe vera* have now been established in Egypt where the extract is incorporated into skin creams and sold freely under the trade name - "Aloderm". Catharanthus, Pyrethrum and Sisal are only examples of plants in Africa that have become important commodities to the pharmaceutical industry recently. Africa is known as a source of a number of other plant drugs, some of which are listed in the British and other Pharmacopoeae. Examples of these are: the cinchona bark (*Cinchona succirubra* Pavon and Klotzsch) which yields the antimalaria drug, quinine as well as quinidine which is used



for cardiac arrhythmia; or Alexandrian senna [*Cassia senna* L.] which is used either as such or in form of the tabletted leaf called 'Senokot' to produce purgation. The African rauwolfia, (*Rauwolfia vomitoria* (Afs.) called "asofeyeje" in Yoruba, has long been considered a suitable substitute for the Indian variety [*R. serpentina* Benth. ex Kurz]. The African rauwolfia produces *reserpine* which is used as a sedative as well as in

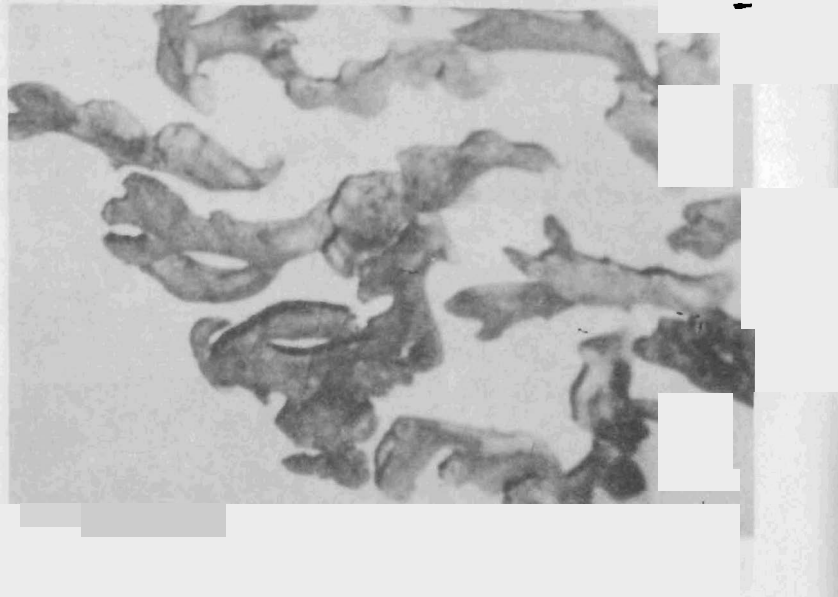


the treatment of hypertension. Ginger rhizome [*Zingiber officinale*], cloves (*Eugenia caryophyllus*, Bullock and Harrison) and tamarind [*Tamarindus indica* L.] are examples of flavouring agents used officially in pharmacy and which are collected from Africa. Acacia gum which is used as a dispersal agent in the preparation of pharmaceutical emulsions or mixtures for internal administration is collected from trees growing wild in Sudan. Although each one of the plants mentioned above is available in various parts of Nigeria, only ginger is cultivated (around Sokoto State) in response to



the world demand. Apparently, however, because the collection of the ginger rhizomes is left until labour is available, the rhizome only develops more weight without any increase in the volatile oil for which it was grown (Kulkarni and Ramstad, 1972). As a result, the Nigerian ginger with its low oil content, is not as highly esteemed as the Jamaican ginger of world commerce which is collected at the time of peak oil content and carefully scraped to remove the dark outer skin and to present the ginger in a most appealing form for sale. In addition to its traditional use in pharmacy, ginger was recently shown from the work of Kucera et al (1975) to possess schistosomicidal properties.

Not all the plants in Africa are useful or medicinal. Some are toxic. Quite a number of toxic plants produce fruits which appeal to children, who then become most susceptible to poisoning by unwary ingestion of the various phytotoxins. Further, due to the rapid migration from rural to urban areas



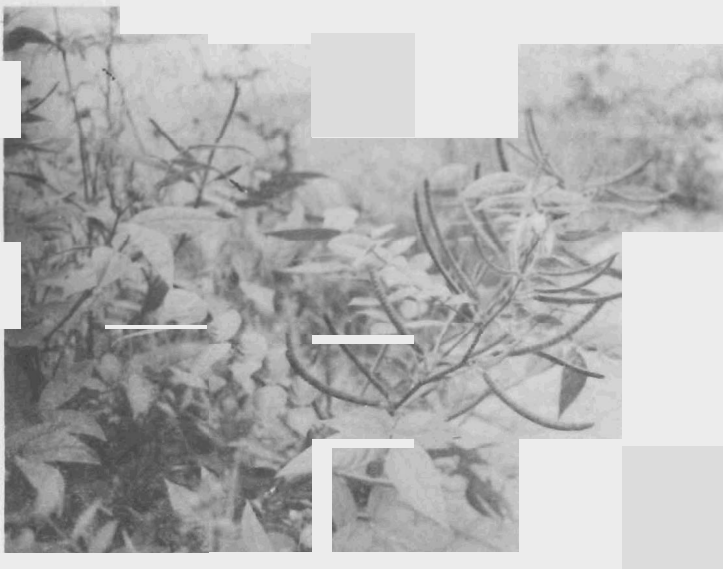
for dilation of the pupil of the eye or Liquorice [*Glycyrrhiza glabra* L.] for sweetening pharmaceuticals were well known to the average school leaver in Britain.

We have started a course in Nigerian medicinal plants as an elective course available to all undergraduates in this University. The pharmacy students have over the years found this course so interesting and useful that, as a body, they have formally requested that this course be made compulsory for pharmacy students. Every year, when I teach this course, I have been appalled by the fact that our final year students when they entered for this course knew little or nothing about common medicinal plants like *Azadirachta indica* A. Juss ("Dongo Yaro" in Yoruba) or *Ocimum gratissimum* L. ("Efirin" in Yoruba) or *Cassia occidentalis* L. ("Rere" in Yoruba).

in Nigeria, resulting from the oil boom, the schools are getting larger and the students do not get a sufficient knowledge of the plants and animals around us. As a result of this, a good number of our students in pharmacy these days come to the University with little or no knowledge of the plant drugs around us. They cannot distinguish between those plants that are toxic and those which have medicinal properties. I recall my own experience at the start of my pharmacy course in the University of Nottingham when I had to learn about a number of plant drugs like Rauwolfia and Cinchona for the first time in Britain. As it were, these drugs came from Africa and my student colleagues thought that I should have known about these drugs before coming to Britain. In the same breath, I found myself handicapped by the fact that a number of the plant drugs which we studied in pharmacy in those days, were already known to my English college mates. Drugs like Fox glove [*Digitalis purpurea* L.] for treating heart disease or Belladonna [*Atropa belladonna* L.] which produces atropine



and a number of others. The course is now designed such that at the end of the course, the student can identify some 25 common medicinal plants in Nigeria; he will be able to give the



botanical name and the vernacular names in Yoruba, Ibo and Hausa. He will be aware of the local use of the plant in traditional medicine and be able to explain the efficacy or otherwise of such uses in terms of the chemical constituents already reported for such plants. When I look back on how ridiculous I felt about learning basic information about African plant drugs for the first time when I was doing my pharmacy course, I am impelled to recommend that an introductory course on toxic and medicinal plants be included in the secondary school (as well as primary school) curriculum in Nigeria and Africa as a whole. Alternatively, the course in botany in secondary schools, should be a little more applied to medicine and agriculture.

MAKING MEDICINE MORE AVAILABLE IN AFRICA

In September 1978, at a joint meeting of the World Health Organisation and the United Nations Children's Fund at Alma-Ata in the USSR on primary health care, the following

declaration was made: "Governments have a responsibility for the health of their people which can be fulfilled only by the provision of adequate health and social measures. A main social target of governments, international organisations and the whole world community in the coming decade should be the attainment by all peoples of the world, by the year 2,000, of a level of health that will permit them to lead a socially and economically productive life. Primary health care is the key to attaining this target as part of development in the spirit of social justice". This target plan has come to be known as the Alma-Ata declaration and is now commonly referred to as: "Health for all by the year 2,000". This is a target that every government of the world has agreed to strive to achieve. In the definition and expatiation of primary health care in the proceeding of the Alma-Ata meeting, primary health care is said to rely on "health workers, including physicians, nurses, midwives, auxiliaries and community workers as applicable, as well as traditional practitioners as needed, suitably trained socially and technically to work as a health team and to respond to the expressed health needs of the community". The fact that traditional practitioners provide health care for an average of 75% of the population in the developing world (including Nigeria) necessitated the consideration given to this class of health practitioners at such an international meeting. Indeed, WHO, UNIDO, UNICEF, OAU and many other international organisations now have big programmes for the development of traditional medicine.

A WHO consultation group to which I was invited described African traditional medicine as "the sum total of all knowledge and practices, whether explicable or not, used in diagnosis, prevention and elimination of physical, mental or social imbalance and relying exclusively on practical experience and observation handed down from generation to generation whether verbally or in writing". You will observe from this definition that not every aspect of traditional medicine can be explained or rationalised. Indeed, this has been one of the major criticisms levelled against this form of medicine by scientists as a whole. It should be noted, however, that

acupuncture analgesia was used in Chinese medicine for years without its scientific basis being understood. Only recently was it shown that endorphins are released by the acupuncture needles inserted to specific parts of the body prior to surgery. The aspect of traditional medicine which is explicable involves essentially the use of medicinal plants and research on these holds promise in providing new drugs.

While drugs alone are not sufficient to provide adequate health care, they do play an important role in protecting, maintaining and restoring the health of people. In an effort to provide cheaper drugs especially by producing them from plants, pharmacognosists all over the world have engaged in researches aimed at finding new drugs from plants or richer sources of already known drugs from plants. Such research and development programmes on plants have to be multidisciplinary with a pharmacognosist collaborating with related specialists in science. Research trend on medicinal plants before 1968 in Africa was not multidisciplinary in many cases, and it was not particularly application oriented. For example, chemists were more interested in isolating and characterising organic compounds from plants without bothering to test whether such compounds had biological activity or not. However, there was a turning point at the 1968 1st OAU STRIC (Scientific Technical and Research Commission of the Organisation of African Unity) symposium on Traditional Pharmacopoeia and African Medicinal Plants. The meeting was held in Dakar, Senegal. Under the dynamic leadership of the late Mr. A.O. Odelola, the then executive secretary of the OAU/STRIC, the symposium resolved that henceforth, research on African medicinal plants should be aimed at providing scientific evidence for the efficacy claimed for medicinal plants.

Mr. Vice-Chancellor, sir distinguished ladies and gentlemen, during the period 1972 to 1979, I was Head of the Drug Research Unit of this University and I think it is only fit and proper that I should devote a small portion of this inaugural lecture to that Unit. Someone once said that "big buildings and small people never make great Universities. People and

imagination are the major resources." I think this is also true of academic departments and units. When the then Vice-Chancellor, Professor H.A. Oluwasanmi appointed me as acting Head of the newly established Drug Research Unit (DRU) in 1972, I saw it as a great challenge and it became compulsory that I had to sink or swim. I did swim, because that Unit became one of the few recognised within and outside Africa for its contributions to the development of African medicinal plants. During that period of about seven years, the Unit produced four proceedings of conferences which have since become reference works in the study of African medicinal plants. About 2,000 recipes of traditional medicine were documented and deposited in the rare book section of our library and, believe me, there is enough material there for scientific investigation for the next fifty years or more. The compilation of those recipes was aided by the donation of ancient records of some recipes by Papa Chief Obafemi Awolowo (who is here present), Chief M.A. George, Chief A.O. Oluwole and Professor A.A. Adegbola to name a few. Our consultant herbalist - Mr. Elewude also made home-to-home visits to collect authentic traditional recipes for the compilation. That exercise is still continuing so as to ensure that this information is recorded, if only as a cultural heritage for the future.

In that period of seven years, research grants came into the Unit from within and outside the University (especially the OAU/STRIC) and University of Ife's DRU was visited by scientists from afar for short and long periods of research.

In retrospect, I have often wondered as to the reason for the success of that Unit and, each time, I came up with the same answer which is that I got the candid support of everyone that had anything to do with that Unit from the most junior laboratory attendant to the technicians, the research affiliates, the full time researchers and, of course, the management committee. One of the great assets of that Unit in its early days was the semi-autonomy granted to it by the University Senate. The Drug Research Unit was merged in 1979 with two other Units in our Faculty of Pharmacy to form the Drug Research

and Production Unit and is now under a new management. The Unit tackles research problems that are relevant to Africa in general and Nigeria in particular. Time will permit me to mention only a few of those researches in which I have collaborated with others.

One of the first investigations we carried out was to attempt to explain whether the chewing sticks used in cleaning the teeth in many African homes help in anyway to explain why Africans have a better set of teeth than their counterparts in other parts of the world. Some of the chewing sticks which we investigated included for example - the stem of *Massularia acuminata* G. Don ("Pako Ijebu" in Yoruba), the root of *Anogiessus leocarpus* Guill. and Per. ("Pako dudu" in Yoruba), the root of *Fagara zanthoxyloides* Lam. ("Orin ata" in Yoruba) etc.

SOME CHEWING STICKS COMMON IN NIGERIA

Botanical Source.	Part Used	Vernacular Names			
		Yoruba	Benin	Ibo	Hausa
<i>Zanthoxylum</i> (<i>Fagara</i>) <i>zanthoxyloides</i> (Rutaceae)	R	Ata	Ughanghan	Okor	Fasa Kwari
<i>Terminalia glaucaescens</i> (Combretaceae)	R	Idi Odan	Eghoinsebi	Edo	Baushe
<i>Anogiessus symperfi</i> (Combretaceae)	R	Ayin Pako Dudu		Atara	Marike
<i>Vernonia amygdalina</i> (Compositae)	R	Ewuro	Oriweni	Ubol	
<i>Massularia acuminata</i> (Rubiaceae)	S	Ewurodo or Pako Ijebu	Okor	Atu	
<i>Garcinia kola</i> (Guttiferae)	R	Orogbo	Edun	Adu.	

R = Root

S = Stem

Investigations carried out on the antimicrobial activity of the common chewing sticks used in Nigeria have shown that they all possess antimicrobial activity against oral microbial flora but to varying degrees when tested by the *cup plate agar* method. This would indicate therefore that these

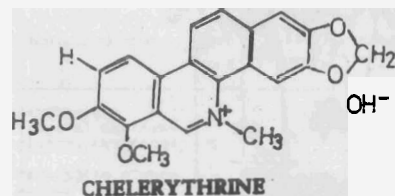
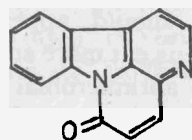
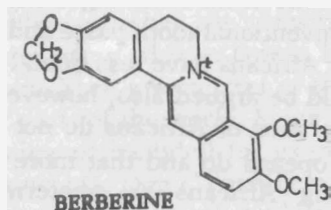
chewing sticks, in addition to providing mechanical exercise for the gums, also destroy microbes present in the mouth, a feature which is absent in many of the tooth pastes in the market. The chewing sticks also play the role of removing food particles from the teeth crevices in a way similar to what the modern toothbrush does. The extra advantages which the chewing stick has over the conventional tooth paste and brush could well explain why many Africans have less dental caries than caucasian people. It could be argued also, however, that perhaps the present old generation of Africans do not eat as many sweets as western Europeans do and that more dental caries should appear among Africans as westernisation makes us eat more sugary foods.

The antimicrobial activity of the chewing stick - *Fagara*



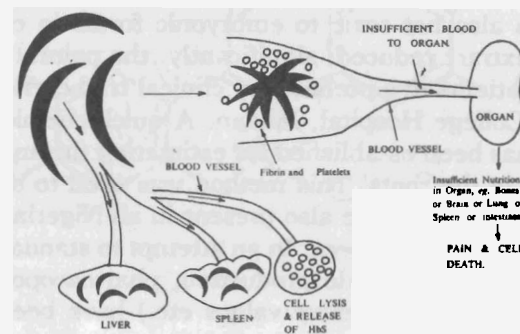
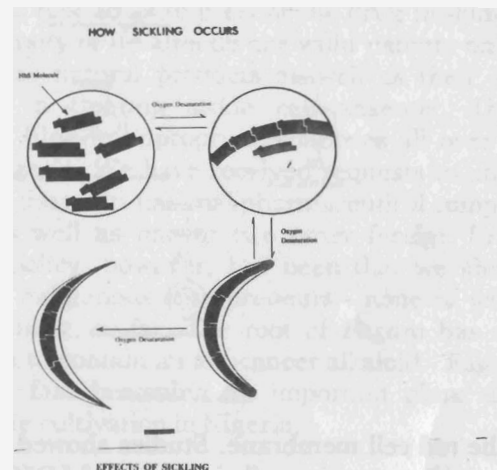
zanthoxyloides ('orin ata' in Yoruba) has been pinned down to the phenolic benzoic acid which are active at low pH of about 5 and four alkaloids among which are canthine-6-one, berberine and chelerythrine which are active at alkaline

pH-7.4. In this chewing stick root, therefore, there exists compounds which will be active during heavy tooth decay (alkaline pH) as well as after a drink of say lime juice (low pH) (Sofowora, 1980).



'Orin ata' became very famous lately in Nigeria not just because it is one of the best chewing sticks but because it also has been shown by the work of Professor Isaacs-Sodeye and myself to have antisickling activity and to hold promise for the management of sickle cell anaemia. For some time, the name *Fagara* became synonymous with Sofowora. In fact, I was mistakenly introduced at one international scientific meeting recently as Professor Sofagara! Luckily, the plant genus *Fagara* has changed its name. Evidence accruing from chemo-taxonomic studies including information just compiled into an M.Phil thesis by one of my post-graduate students has supported the idea that the genus *Fagara* should now be called *Zanthoxylum* (Moody, 1980).

The current interest in the plant *Fagara zanthoxyloides* or *Zanthoxylum zanthoxyloides* for the treatment of sickle cell anaemia came from a chance observation made when we tested the chewing stick extract for antimicrobial activity on blood agar. We observed then that the extract preserved the colour of blood within the area where that chewing stick diffused into the blood agar. Further investigation to explain this curious observation led us to the discovery that this extract has the ability to bring sickled cell back into normal shape as well as reduce the tendency of red blood cells to assume the sickle shape under reduced oxygen tension.



That finding has been extended to the isolation, characterisation and synthesis of the active agents. Synthetic analogs of the active compounds have been made with a view to improving the activity and reduce toxicity. The site of action of *Fagara* extracts and its active constituents is believed to be

Antisickling acids from

ZANTHOXYLUM (FAGARA) SPECIES



2-Hydroxymethyl benzoic acid



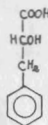
p-Hydroxy benzoic acid



Vanillic acid



m-Hydroxy benzoic acid



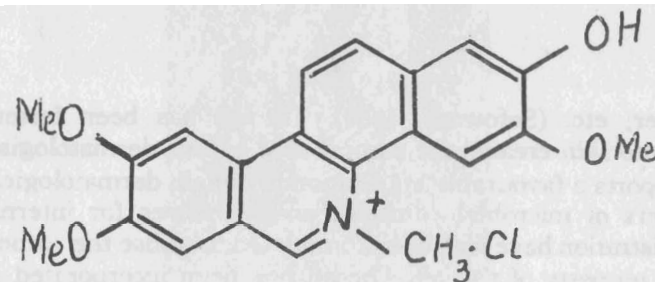
2-OH-Phenylacetic acid

PHENOLIC CARBOXYLIC ACIDS

on the red cell membrane. Studies showed that the extract of the root is not toxic orally in mice and LD50 values have been recorded for intravenous and intramuscular administration in rats. It was also not toxic to embryonic forms in chick and duck. The extract reduced, significantly, the painful crises of sickle cell patients in a preliminary clinical trial carried out in University College Hospital, Ibadan. A quick chemical assay procedure has been established for estimating the antisickling compounds in the roots. This method was used to show that the anti-sickling acids are also present in all Nigerian *Fagara* roots, but to varying degrees. In an attempt to standardise the root extract for large scale production, pharmacopoeia standards (ash values, extractive values etc.) have been set for

the three most common *Fagara* species growing in Nigeria and pharmacopoeia monographs have been prepared for these roots in readiness for this drug becoming a commercial commodity in Nigeria's crude drug market (Sofowora, 1980).

The unit of antisickling activity for any antisickling agent whether of natural or synthetic origin has now been defined by us and by following a biological assay procedure designed here, various roots of *Fagara* in Nigeria have been assayed and their biological potency determined (Adesanya, 1980). A stable tablet formulation of one of the active antisickling principles from this root has been designed as well as a tablet of the extract of the root so as to present the drug in uniform dosage. The University of Ife already has valid patents on the preparation of these natural products as well as their synthetic derivatives in treating sickle cell anaemia. These patents have been filed in appropriate countries all over the world including Nigeria. We have received requests to utilise these patents from the multi-national pharmaceutical company -Bristol Meyers as well as one or two other foreign firms. The University's policy, however, has been that we should give preference to indigenous entrepreneurs - none of whom have been forthcoming, so far. The root of *Fagara* has also been shown in USA to contain an anticancer alkaloid - Fagaronine. This root is fast becoming an important plant drug worthy of large scale cultivation in Nigeria.



Ocimum gratissimum L. ("Efinrin" in Yoruba)

This herb produces a volatile oil which has been shown to have both antimicrobial and anthelmintic properties. The yield of oil produced by plants growing in various parts of the western states of Nigeria was evaluated to select a high yielding strain. The composition of the oil has been established and its relative amount in the various morphological parts (inflorescence, leaves, stem and fruit) determined. The effect of age on the oil yield, so as to crop for a high yield of oil, is now known as well as the best agronomic practice-



fertiliser, etc. (Sofowora, 1980). The oil has been formulated into skin creams for clinical trial by our dermatologist, who reports a favourable application in certain dermatological disorders of microbial complications. Mixtures for internal administration have also been formulated to utilise the anthelmintic property of the oil. The oil has been incorporated in toothpastes on an experimental basis for oral hygiene. Insect-repellent properties of the oil have been established and it is being formulated appropriately for such an application.

Thaumatococcus danielli Benth. ("Adundunmatan" or "Ketemfe" in Yoruba).

Attempts to cultivate this plant on a large scale resulted from the finding that it contains a low-calorie high-intensity protein sweetener in the aril of the fruit. This protein is 5,000 times as sweet as sucrose on a molar basis. The leaves, which are used in wrapping food, and the leaf stalk, which is used in making mats could serve as byproducts. The seed is surrounded by a carbohydrate jelly-like material which swells to several times its own volume in water and is a likely substitute for agar and household jellies. The amino acid composition of the sweetener is known. A simple industrial procedure for the extraction of the protein has been designed by Tate and Lyle Co. The effect of shading and various fertiliser treatments on the cultivation of this plant has been investigated (Onwueme, Onochie and Sofowora, 1979). A plantation of this plant is ready for replanting on a large scale for the use of the sweetener in soft drinks and pharmaceuticals. The protein will have a particular use for sweetening foods and medicines for diabetic patients.



Time will not permit me to give other examples of research which I carried out in collaboration with other scientists in our Drug Research Unit. Suffice it to say that the group of re-

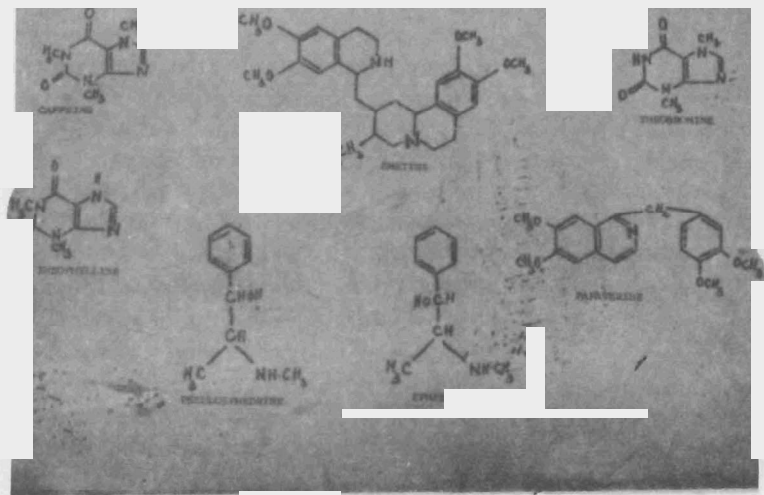
searchers at the University of Ife working on Nigerian medicinal plants have tackled the problem in a multi-disciplinary way, with expertise from various related departments in the University coming together as is the case in developed countries today. In the same breath, I want to emphasize that the development of drugs from plants is an expensive and arduous task. It is estimated that about U.S. \$3 million is spent in the development of a new drug in the USA and with the use of a good collection of scientists of various disciplines (sometimes numbering 40 on each problem) working together continuously (Farnsworth and Bingel, 1977). Also, at least, 3 to 5 years of research and development work is required before the drug can reach the market starting from when a desirable biological activity is first observed in the plant. When we consider that American pharmaceutical firms spend not less than U.S. \$1 billion annually on drug research and development of new drugs, then in Africa where research manpower is short and funds are low, the public should not expect a drug to be on the market only within months of discovery being made. The drug must pass certain toxicological tests in animals including monkeys before it can be given to man for a large scale clinical trial which these days has to be double blind - i.e. without the doctor or the patient knowing which drug is being tested. In that way, an unbiased estimate of efficacy and side effects can be made. This is necessary to ensure the safety of the public.

PROSPECTS OF PRODUCING DRUGS FROM PLANTS IN NIGERIA

Apart from Egypt, which produces a good proportion (about 90%) of the drugs that it needs in its own country, production of drugs in Africa is very little as is exemplified by Gabon, Gambia, Upper Volta and Cameroon which produce none and by Tanzania and Ghana which produce 7 to 10% of their drug needs (ECA, 1978). In 1980, it was estimated that Nigeria spent ₦200 million on drugs and only about ₦20 million (10%) of drugs were manufactured locally (FMH, 1980).

When it is considered that Nigeria imported about ₦1.5 million worth of laxatives in 1977 alone (Ekwunife, 1978), there is need for some action in the direction of producing, at least, laxatives from the many local plants that are used in traditional medicine for purgation, in this country.

A recent survey by UNCTAD (1974) has shown that 33% of total drugs produced by the industrialised nations are plant derived and that if microbes are added 60% of medicinal products are of natural origin. Indeed, higher plants have been described as the *SLEEPING GIANT* of drug development by Farnsworth and Morris (1976) who showed that, over the period 1969 to 1973, the total number of prescriptions dispensed in public pharmacies in U.S.A. had consistently contained about 25% of plant derived drugs in the form of either a crude plant material or a crude extract obtained from plant or a purified active principle obtained from plants. The proportion of plant derived drugs used in USA prescriptions amounts to an expenditure of U.S. \$4 billion annually. In that survey, 76 compounds obtained from plants appeared to be fairly common in the physician's prescriptions. One can also readily dispose of the wrong statement often advanced that plants will soon cease to be of importance to the drug industry. This is not true, because, whereas many active agents derived from plants have been synthesised in the laboratory, commercial exploitation of such synthetic processes have proved impracticable or uneconomical on industrial scale. For instance, a synthetic procedure for reserpine will produce reserpine at a cost of U.S. \$1.25/g whereas the procedure where reserpine is isolated from plants produces reserpine at a cost of U.S. \$0.75/g. It is obvious from this example that plants will continue to be a good source of drugs. This does not mean that commercial synthesis does not take place (or will be scrapped) for plant derived products. Seven drugs of natural origin used in health care delivery in USA are known to be synthesised on commercial scale. These are emetine, caffeine, theobromine, theophylline, pseudoephedrine, ephedrine and papaverine. In all, less than 3% of plant-derived drugs used in the USA today are amenable to



commercial synthetic procedures (Parnsworth, 1980). When it is considered that in a developed Country like USA, plant drugs are prescribed to the extent of 25% (excluding antibiotics) of the total prescriptions, developing countries like Nigeria should take a cue from this and produce dosage forms and galenicals from plants by establishing plantations of medicinal plants in this country.

A look at the situation in Nigeria, for example, shows that there is need to promote the use of medicinal plants for drug manufacturing. A sample survey carried out by us in 1978 showed that, in the Lagos and Ogun States of Nigeria, less than 1% of total drugs dispensed in the health centres in 1977 were of plant origin. The figure for the same period in Oyo State health centres was also less than 1% of total prescriptions. Similarly, in the retail pharmacies in Oyo State, the proportion of drugs stocked or dispensed (as shown in the sample survey) was found to be less than 2% from plant origin. These figures indicate that these states (and probably the whole country) spend far less proportionately on drugs of plant origin than does the U.S.A. It is to be suggested there-

fore that Nigeria should not only produce drugs from local plants, our physicians must be encouraged to prescribe more of such drugs for health care.

The prospects are great for finding new drugs from plants; the chances are even greater in developing countries where a lot of plants used in traditional medicine are yet to be checked. These researches, of course, must be backed by adequate funds and personnel.

In the field of research into medicinal plants, new drugs or new formulations will keep cropping up. The need for patent coverage of such findings must not be overlooked and the Federal Ministry of Science and Technology must take adequate measures to ensure that provision is made for protecting discoveries of new drugs from Nigerian plants by patent laws in Nigeria. The sickle cell patents on *Fagara* had to be filed in Britain by a British patent agent who later filed it in other countries including Nigeria.

Mr. Vice-Chancellor, distinguished Ladies and Gentlemen, I would like to end this inaugural lecture by leaving you with a quotation from late Dr. Kwame Nkurumah's speech to the Academy of Sciences in Accra on 30th November, 1963: "Unless science is used for the betterment of mankind, I am at a loss to understand the reason for it all. It does not require a clever brain to destroy life. In fact, any fool can do that; but it takes brains - and extraordinarily brilliant brains at that, to create conditions for human happiness and to make life worth living".

I thank you for your patience.

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