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**NATURAL OPTIONS FOR THE
DEVELOPMENT OF PHARMACEUTICAL
INDUSTRIES IN NIGERIA**

by

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Mr. Vice Chancellor, Sir, it gives me great pleasure to deliver the third inaugural lecture from the Department of Pharmaceutical Chemistry. It is interesting to note that the history of Pharmaceutical Chemistry is as old as the history of Pharmacy itself. William Shakespeare may have been talking of Pharmacy when he wrote thus “a rose by any other name would smell as sweet”. Apothecary, pharmacist, chemist, or pharmaceutical chemist-what is in a name?

The apothecary emerged as a distinct profession, divorced from medicine, in 1231, through a decree issued by Emperor Frederick von Hohenstaufen of Sicily and this led to the famous Basle Apothecary's Oath (Mez-Mangold, 1989), the content of which is food for thought, even in Nigeria of today.

We, Thuring der Marschalch, Burgomaster, and the Council and the Guild Masters, have come to a unanimous agreement, having consulted the wishes and counsel of our Lord the Bishop and other honourable persons, that no physician who cares or has cared for the sick shall ever own an apothecary's business in Basle, nor shall he ever become an apothecary; and in Basle no one who tests the urine of the sick, or who is a physician shall own an apothecary's business; and if any physician who at present has an apothecary's business does not completely relinquish ownership of this business in the space of time allowed him, after that time he will have to pay, without fail, one mark of silver as often as medicine is seen in his room. And any one who has, or who superintends an apothecary's business must swear a special oath each year to the Council, that no physician owns any part or share of his business or of his medicine. And because we have learnt by experience that this is in the public interest; we desire that this arrangement shall be made permanent. We have also reached complete agreement as regards that oath, that before any man or woman shall ever again own an apothecary's business in Basle, and before anyone ever becomes an apothecary, he must convince the Council by his oath that he is worthy of the position in skill and knowledge and has practised for a sufficiently long time for people to be able to rely on him. Also any one who is or who becomes an apothecary in Basle must provide for each physician what he asks and demands, if there is anything he has not got, he must state that he has

not got it, and everything which he provides for the physician must be of such quality and of such usefulness that he knows, upon his oath, that it will be good and useful for the confection the physician is making. The physician must not come to any (private) agreement with the apothecary about what he is taking to the sick person, unless the sick person's messenger is present. Remember also to include in the oath administered to the apothecaries that they shall not allow anyone to buy poison, unless the buyer has two guarantors who will guarantee that no one shall suffer harm from it.

The later contribution of Carl Wilhelm Scheele represents a turning point in the development of pharmacy in particular and industrial chemistry in general. He started his career at the age of 14 as an apprentice pharmacist in Gotenborg and later worked as a pharmacist in Stockholm before finally settling down at Köping to manage a Pharmacy; devoting most of his income and time to chemical studies. This born chemist discovered oxygen in 1775 and this was isolated two years later by John Priestley. In addition, Scheele pioneered the technique of crystallisation, aimed at purifying the active principles of natural crude drugs and discovered glycerine, malic acid and hydrocyanic acid. If Paracelsus (Theophrastus, 1493-1541) is described as the true founder of Pharmaceutical Chemistry for introducing the notion that 'it is the task of chemistry to produce medicines for the treatment of diseases since the vital functions of life are basically chemical in nature', then Scheele's contribution guided the hands of pharmaceutical chemistry into a new era two centuries later (Mez-Mangold).

Drug is the cornerstone of medical service and this has well been appreciated even in centuries past. Indeed, drugs were as strategic to national interest as energy is in modern times. History records that during the Hellenic civilisation, Alexander the Great was advised to conquer the island of Socotra near the East African shores for the purpose of getting the drug aloe to treat his wounded soldiers (Manniche, 1989). More recently, the two world wars demonstrated a paradoxical synergy between military adventurism and drug development. As a consequence of the Japanese occupation of Java, the allied countries were deprived of access to this commercial source

of *Cinchona febrifuge*, the only reputable remedy for malaria. They were forced to look for a substitute through synthesis. Using quinine, the active ingredient of *Cinchona*, first isolated in 1820, as template, a number of simpler molecules were independently studied in Germany, USA, and Soviet Union before and during the Second World War. An interesting serendipity was the capture of sontoquine from the Germans in Tunis, North Africa, which then brought 4-aminoquinolines into focus in the USA. The antimalarial drug, chloroquine, emerged from this effort but evidence later showed that it had been synthesised in Germany as far back as 1934 but was rejected in favour of sontoquine on the suspicion of toxicity. Following the end of hostilities, the superior German technology was at hand, through negotiated patents, to stimulate the chemical industry to a new height (Sweeney and Strube, 1979). It is remarkable that the search for newer antimalarials to support the USA military campaign in Asia led the US Army Medical Research and Development Command to sponsor a massive research programme that led to the development of mefloquine as a third generation antimalarial drug.

If the examples above demonstrate that indeed, necessity is the mother of invention, then given an estimated population of 124 million with a life-expectancy figure of 51 (UNICEF 2003 data) and an annual population growth rate of 2.5 (UN data for 2000-2005), Nigeria ought to have initiated a more aggressive concerted programme of developmental activities towards self sufficiency in drug supply particularly to address common tropical diseases. Consider the recent decision by the government to ban the importation of 17 selected drug items. This well meaning action is predicated on the assumption that the pharmaceutical manufacturing industry in the country can meet the needs of the country through local production. However, the reality is different as the government must have considered only the level of secondary manufacture in which case the major components (drug substances) would still have to be outsourced. Neither the objective of making drugs available at affordable cost nor that of harmonising the quality to an in-depth level would be achieved until such a time that we can source the raw materials locally.

The submission in this lecture is that nature is the primary source of drugs. Thus, minerals, plants, animals, moulds and bacteria have furnished drugs of direct clinical application. In some other cases, the primary biologically-active molecules obtained from nature have served as templates for the synthetic design of useful drugs. Chemical synthesis, as a component of drug development, can serve either of two purposes. The first is that it may be the pragmatic option for making a natural drug molecule available on a commercially viable scale. A second purpose is that it gives opportunity to explore even a natural drug molecule, make molecular modifications or designs to afford new drugs. In drug synthesis, nature provides the feedstock for the requisite raw materials and reagents. In particular, the primary chemical industry is mostly based on fossil fuels or agro-products.

Thus, given the abundance of tropical African flora exceeding 30,000 species (Dagne, 1997), solid mineral deposits and petroleum, Nigeria should be a leading drug producing country. The 2004 catalogue price of thaumatin, isolated from *Thaumatococcus daniellii* (eweran), when allowed to fruit, is 559.40 USD per gram (Sigma-Aldrich) and unfortunately, Nigeria has no share in the market in spite of its abundance in Nigeria. A remark made by the pioneer Director-General of NAFDAC, Prof. G. O. Osuide, on this campus at the 14th Marquis Memorial lecture about seven years ago, is most pertinent. *“If only Nigerians who spend their time and resources to grow and traffic in Indian hemp can be persuaded to devote the same resources to the cultivation of rose periwinkle”*. The major alkaloids of the root of this plant are ajmalicine and serpentine, both used in the treatment of circulatory disorders. In addition, the leaf produces two important anticancer drugs, vinblastine and vincristine in trace yield of about 0.0003% with the commercial price of the two alkaloids at a range of 1-3.5m USD per kg (Sayed and Verpoorte, 2005). Indeed, globally, 8 of the top 30 medicines are natural products or semisynthetics with a value of 15.9bn USD in 1999 and yet it has been suggested that perhaps only 2% of about 250,000 plant species on our planet have been thoroughly evaluated as a source of new drugs (Bartle, 2001).

Inorganic mineral deposits

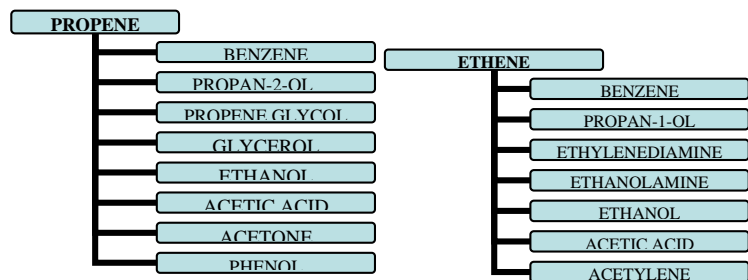
According to the data from the Bureau of Public Enterprises, Nigeria is reputed to have more than 440 commercially viable solid minerals ranging from precious metals and various stones to industrial minerals. Of pharmaceutical interest are salt deposits; iron ores such as haematite; calcium deposits in form of chalk and gypsum; the variety of silicates such as talc, bentonite and kaolin. Based on the rock salt deposit in Benue State and salt springs at Awe (Plateau State), Abakaliki and Uburu, the national reserve of salt is estimated at 1.5 million tonnes. It is incredible that bulk salt is still imported for local processing into table salt not to talk of pharmaceutical grade of sodium chloride for preparing infusions. The deposit of talc is estimated to be above 40 million tonnes and the only catalytic plant belongs to the Raw Materials Research and Development Council which produces only 3,000 tonnes of talc annually. The kaolin deposit in Nigeria is estimated at over 3 billion tonnes and it practically occurs in every state. Gypsum as an input for the production of cement enjoys some relative exploitation but it is doubtful if the local material is processed any further to produce the plaster of Paris (POP). The iron ore deposit in Kogi, Enugu and Niger States as well as Federal Capital Territory amount to 3 billion tonnes by estimation. Mining is currently at Itakpe (Kogi State). The main focus is the production of steel hence the establishment of steel complexes at Aladja and Ajaokuta. Further value can be added to this abundant resource through conversion of elementary iron to pharmaceutical grade of ferrous sulphate and ferrous gluconate both of which are used as haematinics.

It is obvious that the hopes expressed (Fashina, 1998) on this campus on the prospects of utilisation of inorganic deposits in the pharmaceutical sector, 27 years ago, are yet to be fulfilled.

Organic minerals

The birth of organic chemical industry was based on the careful distillation of coal tar into a number of fractions from which about 250 different compounds such as benzene, derivatives of benzene (toluene, xylenes, phenol, cresols, xylenols, cresols, aniline), naphthalene, thiophene and pyridine have been isolated (Beyer and Walter, 1997; Reisch, 1998). Apart from direct applications, the huge demand for benzene and its simple derivatives is largely due to the fact that they can be chemically converted to unlimited number of molecules including those of pharmaceutical importance. The shift from this solid mineral to petroleum as a source of fuel, in the modern period, also meant a shift to petrochemicals as feedstock for the chemical and pharmaceutical industries. Perhaps the future generations of Nigerians would need to fall back on the under-exploited 3 billion tonnes of coal reserve for their economic survival (BPE figures).

Crude oil is a rich source of various chemical substances which include alkanes, cycloalkanes and aromatic hydrocarbons such as benzene, toluene, xylene, and naphthalene. The Nigerian crude oil, classified as cycloalkane-based, is richer in cycloalkanes and aromatic hydrocarbons. In addition, mineral oil contains organic sulphur compounds (0-10%) such as thiols, sulphides, disulphides and thiophenes as well as nitrogen compounds such as pyridine and quinoline derivatives. A further host of compounds such as alkenes are obtainable from oil and gas by specific refining processes (Beyer and Walter, 1997).



Many of these petroleum products are industrial feedstock for the production of pharmaceutical excipients such as paraffins and solvents, packaging materials such as plastics, and starting materials for active drug molecules. It was not until 1978 that the idea of using refinery by-products as feedstock to produce petrochemical products in Nigeria was conceptualised. The Nigerian National Petroleum Company (NNPC) adopted a phased approach in the establishment of upstream petrochemical plants in view of the capital intensive nature of the industry. In March 1988, petrochemical plants were commissioned at Kaduna and Warri refineries respectively to produce linear alkyl benzene and propylene with carbon. The Eleme Petrochemicals Complex belonged to the second phase of the development programme of the petrochemical industry in Nigeria and it was commissioned to produce polymer resins. The third phase intended for the production of xylenes is still at conceptual stage. Also still in the pipe-line is the methanol project. The olefin petrochemical base-stock is very versatile and its current status is a far cry from optimal utilisation. The on-going economic reform must encourage investment in production of drug substances from available options. And if I may quote Dr. Alukaino Osakwe-Akofs (1985), then of the Petrochemical Division, NNPC,

“ after investing so much in providing the basic petrochemical raw material, no government will involve itself in setting up plants to produce butobarbitone from diethylmalonate or pyridoxine from ethylacetoacetate or proguanil from p-chloroaniline or ethambutol from nitropropane”.

The missing link is competent, patriotic and visionary entrepreneurship in the chemical and pharmaceutical sector, as end-user. This is necessary in order to motivate production of requisite synthetic starting materials and reagents from petrochemical base stock and thereby add value to this natural resource.

The role of the University system

At this juncture, it is pertinent to ask the question: What is the expected role of the university or the field of pharmaceutical

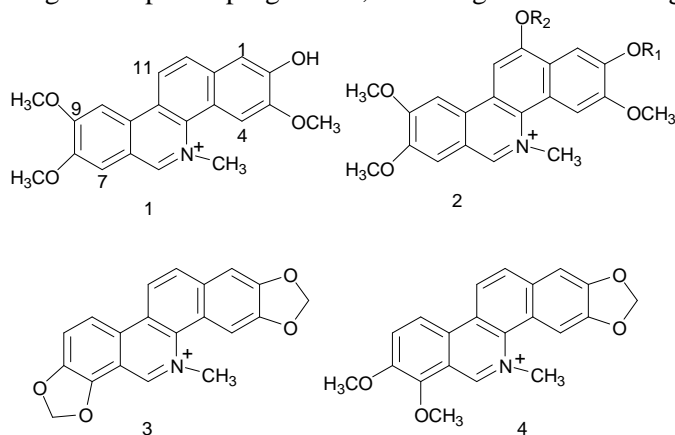
chemistry in the exploitation of Nigerian natural resources towards meeting the pharmaceutical product need of the nation? The mandate of the university system has long been extended beyond the traditional duties of teaching, research and service. For the sake of its own survival and meaningful contribution to national development, the university is expected to create new jobs through commercialisation of innovations, inventions and discoveries. There is no doubt that the Nigerian university system has been generally low-scoring on this dimension. However, the potentiality has been the theme of a number of previous OAU symposia and inaugural lectures including those which focussed on drugs from the Faculty of Pharmacy such as the most recent inaugural lecture given by A. O. Ogundaini (Ogundaini, 2005). I shall endeavour to illustrate, further, the potentiality of realising the ultimate goal of exploiting our abundant natural resources with a few examples of research work I have been involved in.

Fagara

A publication that drew attention of the scientific world to this university reported the antisickling property of 'orin-ata', the root of the plant more popularly known by its former generic name, *Fagara* (*Zanthoxylum zanthoxyloides*) (Sofowora and Isaac, 1971). The antisickling principles were subsequently identified as simple benzoic acid derivatives (Sofowora et al, 1975). On the other hand, quaternary benzo[c]phenanthridines had been reported from the genus as far back as 1958 but these alkaloids were not known to possess antitumour properties until 1971. The isolation of a potent antileukaemic alkaloid, fagaronine (1), from orin-ata by American scientists stimulated interest in this group of alkaloids. Only three of such compounds (fagaronine, nitidine and avicine) with characteristic ring substitution pattern are known from nature and they are apparently restricted to the genus *Zanthoxylum* (family Rutaceae) (Olugbade, 1983). The challenge facing medicinal chemists was how to synthesise this group of alkaloids in order to get sufficient sample size for detailed biological testing and also to afford more analogues towards optimisation of the ring system for antileukaemic activity. Indeed, a number of synthetic routes were reported and eighteen

synthetic analogues were tested. All the available synthetic routes were too long and too low-yielding. Thanks to the staff development programme of this university, by way of probationary study leave, of which I was a beneficiary after the initial encouragement and financial support from my late uncle, Chief O. B. Akin-Olugbade. I was baptised into the chemistry of this group of alkaloids during my period of study as a PhD student at the University of Manchester under the supervision of Roger D. Waigh. We accomplished a simple, versatile, five-step synthesis of the ring system (Olugbade et al, 1990; Euerby et al, 1991). Three of the new analogues (generally of structure 2) obtained after final quaternisation demonstrated antileukaemic activity in animal models (Olugbade and Waigh, 1996). While we waited and hoped for higher stakes with the target compounds, every new compound synthesised as intermediate in unsuccessful routes was offered to companies, which were readily at hand, for mass screening in their Research and Development Programmes at token charges and the fund realised from this practice was made available as supplementary fund to fund activities of the research group at the discretion of the supervisor thus providing an opportunity to learn some lesson about the role of the industry in funding academic work. Further hopes were raised in this group of alkaloids when in the mid-eighties the search for the anti-HIV drug intensified. As if in anticipation of the emergence of the disease, nitidine and fagaronine had been established to inhibit reverse transcriptase as far back as 1976, albeit in RNA tumour virus (Sethi, 1976). Indeed, these natural alkaloids demonstrated activity against HIV-1 reverse transcriptase (Tan et al, 1991). Also, two of the 12-oxygenated analogues, introduced through our earlier effort, hydroxidine and methoxidine and a new addition to the series, ethoxidine were later examined for antiretroviral activities with the latter two exhibiting activity against reverse transcriptase (Kerry et al 1998). While the interest in 5,6,8,9-tetra-oxygenated benzo[c]phenanthridines as potential anticancer or antiviral agents waned when further studies indicated toxicity, Roger Waigh has further advanced the cause of these efforts and asserted that these analogues as typified by ethoxidine, are topoisomerase I suppressors and not topoisomerase poison like fagaronine, the lead natural compound (BPC 2001). Meanwhile, the isomeric 7,8-oxygenated analogues, such as sanguinarine (3) and chelerythrine (4)

(found in Papaveraceae) are known to be devoid of antitumour or antiretroviral activity but instead are potent anti-inflammatory and anti-microbial agents with low toxicity and have survived as components of oral dental preparations. The dichotomy of activity between the two groups' centres on the electrophilicity of the iminium ion which is greatly enhanced by oxygenation at position 9 and enables intercalation with nucleic acid template primers presumed to be the initial step in the binding process. I have deliberately dwelt on this aspect of my academic exposure because of two reasons. Firstly, as Roger Waigh chose the forum of the British Pharmaceutical Conference of 2001, held at Glasgow, to raise further hope in the work, I recall that 20 years earlier I had the privilege of presenting our preliminary results at the Brighton BPC, sponsored as a young author (Olugbade and Waigh, 1981). And incidentally, at the 2002 Manchester BPC, he was awarded the Harrison Memorial medal for a distinguished career in advancing the science and practice of Pharmacy. The Harrison biennial medal award was instituted by the British Pharmaceutical Society in memory of the distinguished Pharmaceutical Chemist, Col. E.F. Harrison, who was appointed the Director of the Chemical warfare in 1918. The overall experience poses a serious challenge to our local professional and scientific associations to support research efforts by motivating students, young and established researchers alike. The second point is that the project serves to illustrate the long tortuous journey that may be involved in a drug development programme, with no guarantee of a big hit.

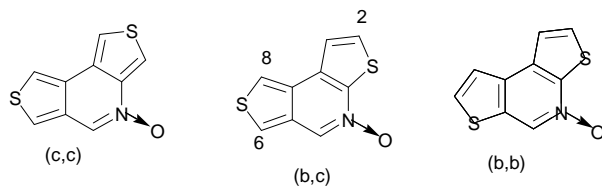


Further interest in Fagara which resumed at Ife, in collaboration with S. K. Adesina, was with respect to the phytochemical investigation of one of the eleven co-generic species found in the country. Thus, with part support from the University Research Committee grant, we identified 30 different compounds including amides, coumarins, lignans and derivatives of chelerythrine from the root bark of *Z. lemarie* (Adesina et al 1997a). A follow up study with the pericarp led to the isolation of two new aromatic amides and other known compounds (Adesina et al, 1997b). Amides had, hitherto, been identified as the principles responsible for the pungent or peppery taste of the members of the genus. Although these phytochemical studies were not supported with bioassay evaluations, it is noteworthy that lignans are widely distributed in the *Zanthoxylum* genus and represent another group of lead antitumour natural compounds. Sesamin, a ubiquitous lignan, was only recently reported to inhibit human leukaemia cells *in-vitro* (Ju et al, 2001). And in particular, teniposide, currently used in the treatment of acute lymphatic leukaemia and brain tumours in children (Phillipson, 1999) is a semi-synthetic product derived through the development of podophyllotoxin, a natural lignan from *Podophyllum* genus. My other adventure into the chemistry of the Rutaceae was in association with C. A. Adebajo and others leading to the report of novel coumarins from the common curry plant, *Murraya koenigii* (Adebajo et al, 1997). There is certainly a lot more than meets the eye about this condiment plant. We look forward to the full story from A. Adebajo in the near future.

Thiophenes

While the international oil market places high premium on the sweet or light oil for its low sulphur content, this refinery nuisance is indeed the delight of Salo Gronowitz, who devoted most of his research career to sulphur compounds. I was introduced to his laboratory, when he was serving as the chairman of the Nobel Prize Committee in Chemistry, by J. O. Oluwadiya. As a Swedish Guest Scholar, I was privileged to join his team in addressing basic organic chemistry

problems. Organic chemistry is necessarily a component or a tool of the field of medicinal chemistry. A new heterocyclic system, dithienopyridines, had just been produced from his laboratory at the Department of Organic Chemistry 1, Chemical Center, University of Lund, through an elegant synthesis (Yang et al, 1998). Towards understanding the chemistry of the N-oxides, we studied the orientation effects of three isomeric forms in nitration reactions. The orientation preference of the parent base had been found to be based on ionic reaction between the base, in protonated form and the nitronium ion. The mechanism was supported by geometrical calculations at *ab-initio* level, for the protonated substrate, the Wheland intermediate and the transition states. With the three possible annellation isomers of the tricyclic system, the N-oxide presented a complicated but interesting case. Protonation to give the conjugate acid required a stronger acid medium and produced different orientation effects from the unprotonated species with nitronium ion, by way of ionic mechanism. Further, nitration with nitrosonium ion, presumably via an electron transfer mechanism, demonstrated a predominant third option of orientation preference. Thus, positions 2, 6, and 8 of the b,c-fused isomer, for instance, can be selectively nitrated with dinitrogen tetroxide, nitric acid, and nitric acid-sulphuric acid respectively. Although the system was not explored for biological potentials in the specific study, the value of such studies is that functional groups can be introduced to the different positions on the ring by deliberate choice of the parent heterocycle or its N-oxide and an appropriate nitrating agent (Gronowitz et al, 1992).



DITHIENOPYRIDINE N-OXIDES

Heterocycles from Chalcones

Other synthetic endeavours at Ife include the use of a class of natural substances, chalcones, as synthetic precursors by direct condensation reaction or via the isoflavones to heterocyclic systems like sulphamidopyrimidines (Usifoh et al, 1989; Olugbade et al, 1990) or pyrimidobenzimidazoles (Makanju, 2001).

On-going Research

There was personal conviction to concentrate on exploration of plant materials. The enduring support received from the International Program in Chemical Sciences (IPICS) towards local capacity building in our laboratory enabled substantial work in this area as has been emphasised by A. O. Ogundaini only two months ago in his inaugural lecture. While further acknowledgements of the support received from the (IPICS) are forthcoming from future presentations from the faculty, permit me, Mr. Vice-Chancellor, Sir, to give two other examples of work so supported within the theme of the topic of today.

Frankincense

The resin, frankincense, of international commerce comes mainly from *Boswellia sacra* Fluckiger (synonym *B. carteri*) (Saudi Arabia, Yemen, Oman, Somalia); *B. frereana* Birdwood (Somalia); *B. serrata* (India); and *B. papyrifera* (North East Africa). Its historic applications in religious practices, perfumery and medicine have survived till present day. It rose to become a precious article comparable only with gold and worthy of presentation as a gift to baby Jesus. In Aryuvedic medicine, the Indians employ the resin of *B. serrata* in the treatment of arthritis, gastrointestinal disorders, as a diuretic and treatment of asthma and other respiratory conditions. Historically, the Egyptians were prolific users of frankincense. The traditional uses in Egypt include use as fragrance, as a component of embalming mixture, and in the treatment of cough and asthma.

A Ph.D. research in the Department, investigating a Hausa herbal recipe comprising the barks of two plant species initially identified by their vernacular names, revealed the identity of one of them as *B. dalzielii*, a species abundant in West Africa. Various parts of the plant are used in folklore medicine in Ghana. In spite of abundant report on the chemistry of the other species, the chemistry of *B. dalzielii* was hitherto unknown. We identified the antibacterial and anti-oxidant principle of the stem bark to be the ubiquitous phenol, protocatechuic acid. The non-volatile fraction of its resin showed potent anti-inflammatory properties and consistent with this result, 3 α -acetoxyurs-12-en-11-keto-23-oic acid (AKBA) was isolated. AKBA had been previously reported from the Indian species, *B. serrata* and it had been extensively investigated along with other natural analogues (collectively referred to as boswellic acids) as a very potent anti-inflammatory agent. Boswellic acids inhibit pro-inflammatory mediators in the body by a dual mode. They specifically inhibit formation of leukotrienes via a non-redox selective inhibition of the enzyme 5-lipoxygenase (Safayhi et al, 1992; Ammon, 1996)) and also inhibit tissue degradation by inhibiting the human leukocyte elastase (HLE) (Safayhi et al, 1997). Indeed, a number of standardised products of boswellic acids from *B. serrata* have been licensed for sale in the treatment of a wide spectrum of inflammatory conditions in the USA. We proceeded to examine the volatile oil of *B. dalzielii* for antimicrobial and anti-inflammatory properties as well as chemical composition by gas chromatography-mass spectrometry. It is gratifying to note that the Ph.D. student (Alemika, 2001) won the National Universities Doctoral Thesis award in Pharmaceutical sciences for 2002. Incidentally, the premier award in 1998 was won by another student in the IPICS-NIG. 01 programme, Miss Iruka Okeke (supervised by A. Lamikanra). Beyond this, studies are in progress towards exploitation of this plant species. The expensive cyclo-oxygenase 2 (COX-2) inhibitors such as celecoxib (celebrex^R) were introduced to reduce the risk of serious upper gastro intestinal bleeding and ulceration associated with older and cheaper drugs such as aspirin or indomethacin which inhibit both COX-1 and COX-2 enzyme systems. However, the improved tolerance results in a penalty of increased risk of thrombosis especially in patients with ischaemic heart diseases. The current practice is to place such high

risk patients concurrently on low dose aspirin. Unfortunately, aspirin is contra-indicated for use in asthmatic patients as non-selective COX inhibitors like aspirin generally exacerbate asthmatic symptoms. Targeting a different enzyme system such as 5-lipoxygenase, inhibited selectively by the boswellic acids with the advantage of HLE inhibition, therefore offers great potentials in resolving the dilemma and improving the versatility of the clinical applications in chronic inflammatory diseases.

A literature report on the concentration-dependent contradictory pharmacology of 3-oxo-tirucallic acid which co-occurs with the desirable tirucallic acid and ursenoic acid derivatives in *B. serrata* underscores the need for standardisation of herbal products for composition of main active components (Boden et al 2001). In addition, AKBA has been reported to form artifacts during the process of extraction and workup (Schweizer, 2000). Establishing products for even the limit of undesirable components and contaminants is a standard requirement for pharmaceutical products, not excluding herbal products, seeking registration. Work is in progress in our laboratories towards the development of *B. dalzielii* for pharmaceutical application.

African turlip

There are various approaches to the selection of plant species for study as potential drug sources. Certainly, the most popular approach is through ethnomedicine and one of the most fascinating approaches is through field study of wildlife now termed zoocognosy (Huffman, 2001). An adventure through our heritage of the biological garden and the entire estate often reveals plant species that are extensively debarked, apparently by collectors who use them in traditional herbal medicine. A plant discovered in one of such field trips receiving attention in our laboratory is *Spathodea campanulata* P. Beauv. Various parts of the plant, commonly known as African turlip, are used in ethnomedicine in Nigeria, Ghana and elsewhere in the tropics. In addition, it is widely used as a decorative plant and incidentally is one of the major ornamental plants in the environment of this monument (Oduduwa Hall). Previous literature reports had been

limited to lipophilic fractions with specific ursenoic triterpenes isolated as the antimalarial principles (Amusan et al, 1996). On the other hand, the polar fractions received little phytochemical attention in spite of interesting biological reports on the stem bark, for instance. Our interest, through undergraduate and postgraduate (M.Sc., Ph.D.) projects, has been to explore the polar fractions of various parts of the plant. Results already obtained include isolation of verminoside, an acylated iridoid from the stem bark as the major anti-oxidant principle of the plant part (Elusiyan and Olugbade, 2003). The interest on natural anti-oxidants is associated with the implication of oxidative stress in the pathophysiology of a large number of diseases particularly cancer, atherosclerosis, asthma, arthritis, inflammation and neurodegenerative diseases. In addition, the isolation of this iridoid appears to justify the application of the plant part in the treatment of dysentery as verminoside, previously isolated from a few other sources including *Kigelia pinnata*, had been reported to have potent activity against *Entamoeba histolytica* (Azam, 2002). It is interesting to note that *K. pinnata* is similarly employed in ethnomedicine.

THE FUTURE AND CONCLUSION

In spite of the changing paradigm in pharmaceutical education/service to emphasise patient care, the uniqueness of pharmacy as a profession or service derives from expertise in the science and technology of drugs. Thus, discovery and development of new drugs would remain a serious challenge to be addressed for the survival of our civilisation, notwithstanding the developments in genetic engineering and the associated promise of “human spare parts” for medical application. As a matter of fact, biotechnology is already in application in the pharmaceutical sector but mainly as a means of scaling up the production of potent active natural substances that can hardly be otherwise obtained at an industrial scale. If, as pharmacists, we must continue to claim expertise in drugs in the near future our graduates must be prepared for these developments in terms of curriculum strengthening. Perhaps there is no better opportunity than this to pay tribute to the Carnegie Corporation of New York for a grant to develop a Therapeutic Drug

Monitoring Laboratory as an intervention to strengthen our curriculum and also to provide specific services that are expected to impact on the larger community. In particular, pharmacopoeial and extra-pharmacopoeial evaluation of selected multisourced drug products for minor impurities and polymorphic requirements as well as chromatographic profiling of herbal products under development are part of projects in queue. I have no doubt that my colleagues in the department will dwell more about the full scope of service enabled by this facility in future inaugural lectures.

By my choice of on-going research projects for illustration I believe I have left no one in doubt that this is certainly not a valedictory lecture. On the other hand, I have underscored the enormous potential available to Nigeria in terms of natural and human resources. The Nigerian drug requirement situation, as I see it now, is not far from the lamentation of the ancient mariner “water, water every where but none fit to drink”. However, in order to avoid “bringing coal to our Newcastle”, we must urgently recognise the need to add value to the natural resources both for home consumption and for better return in terms of foreign exchange. All other desired socio-economic goals such as job employment, funding of social services and general improvement in the standard of living would inevitably result. At the institutional level we must learn to harness our resources and be more positive and more optimistic. The Central Science laboratory, housing Gas and liquid chromatographic systems, the NMR spectrometer, etc as well as the Centre for Energy Research and Development housing the Gas chromatograph-mass spectrometer would facilitate the chemical studies of medicinal plants on ground if adequately funded. As a further commitment to leave tangible legacy behind, we have initiated a project to compile and publish selected NMR spectra obtained from our instrument as teaching and reference spectra for the present and future students in the chemical sciences. This is expected to follow up on the previous initiative championed by A. A. Olaniyi as a response to the dearth of affordable standard textbooks at a time that it was not economically expedient. The earlier effort led to the publication of “Essential Inorganic and Organic Pharmaceutical Chemistry” in 1993 with A. O. Ogundaini and S. K. Ayim (later, Vice Chancellor of the University of Science and Technology, Kumasi) as co-authors.

In acknowledging the contribution of the Forest Research Institute, Ibadan and the Department of Botany, OAU to the phytochemical investigations, especially for resolving knotty plant identification problems, I wish to seize this opportunity to stress that a full drug research and development programme is necessarily a multidisciplinary affair. And so is the interdisciplinary nature of science today that Richard Stevenson (2003) recorded the observation that two medical doctors won the year's chemistry Nobel Prize (Peter Agre and Roderick MacKinnon, for research discoveries about channels in cell membranes) while the Nobel Prize for medicine was shared by a chemist (Paul Lauterbur) and a physicist (Peter Mansfield) for developing proton NMR into magnetic resonance imaging (MRI) scanners. The picture is even more interesting when we note that while Peter Agre had graduated in chemistry before studying medicine, McKinnon had earlier read biochemistry. As a national education policy we cannot, therefore, afford to neglect the basic sciences while the professional programmes cannot afford to relegate the basic science components of the curricula.

Mr Vice Chancellor, Sir, as the saying goes, the struggle continues. I thank you all for listening.

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