ALL IS GIVEN: FOOD, MEDICINE AND MORE

An Inaugural Lecture Delivered at Oduduwa Hall,
Obafemi Awolowo University, Ile-Ife, Nigeria
On Tuesday, 11th November, 2025

By

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Inaugural Lecture Series 409

ISSN 0189-7848

Printed by:
Obafemi Awolowo University Press Limited,
Ile-Ife, Nigeria.

Introduction

The Vice Chancellor Sir, Principal Officers of the University, distinguished colleagues, guests of the university, ladies and gentlemen, welcome to the 409th Inaugural Lecture of Obafemi Awolowo University, Ile-Ife.

It gives me great pleasure to deliver this, the 6th inaugural lecture from the Department of Biochemistry and Molecular Biology of this great university. Prof. Akintola Aboderin's lecture delivered on 17/2/1981 titled "Protein, nature's versatile devices" was the first. The second one titled "The enzyme molecule" was delivered on 14/8/1990 by Prof. Adeyinka Afolayan. My M.Sc. and Ph.D. supervisor and mentor, Prof. F. D. Onajobi delivered the third in the series titled "Fats and life" on 16/2/1999. The 4th one did not come till 10/9/2019 delivered by Prof. F. K. Agboola. It was titled "Enzymes: the molecules of life and their applications in industries, medicine and beyond." Prof. I.O. Adewale delivered the 5th lecture titled "An Odyssey into the world of enzymes" on 14/3/2023.

I am grateful for the opportunity to deliver this lecture titled "All is Given: Food, Medicine and More". This title is inspired by scripture. In the words of John the Baptist "a man has nothing except it is first given him from heaven" [John 3:27]. These words are true on many levels for all of us, and even more so for a biochemist. The things we "find out", the interactions we tease out at the molecular level, the benefits that accrue to mankind from our research endeavours etc are in a sense revealed to us, sometimes serendipitously. Two quick analogies come to mind, inspired by the book "God, Technology, and the Christian life" by Tony Reinke (2022). Think of children playing in a sandbox, or with a Lego set. While the amount of sand in the box and the number of pieces in the Lego set may be fixed, there is an infinite number of creations that could arise from them. The number and range of things created is limited only by the imagination and creativity of the children playing with them. Similarly, in spite of the Law of conservation of matter, we keep discovering many different aggregations of

molecules and compounds. Different combinations of these compounds from nature are often put to use in different ways by different people groups. It is therefore quite common to see a plant used mainly to treat fever in one place used to treat skin infections somewhere else. I fundamentally believe that God in His wisdom allows us to "discover" different things at different times for our benefit. It is both empowering and humbling at the same time.

Biochemistry studies the chemical basis of life. It is at the very core of all the life sciences. It began essentially by applying the tools of Chemistry to study the molecules involved in maintaining growth and other life processes. The modern science sits at the crossroads between being the villain and the hero of the life sciences. While life without the contributions of biochemistry is almost inconceivable, we are also at the centre of every controversial discovery in the life sciences. We are at the forefront of "playing God" as science sceptics posit. The name "Biochemistry" was coined by Carl Neuber in 1903. However, the body of work in this very living, aspect of chemistry had started much earlier with the work of Antoine Lavoisier (1775), Theodore Schwann (1836), Louis Pasteur (1856), Friedrich Miescher (1869), Eduard Buchner (1897) and others. Unsurprisingly, much of the early work focused on an attempt to understand the fundamental macromolecules; Proteins, Nucleic acids, Carbohydrates and Lipids (Singh et al., 2004). Work by Oswald Avery et. al. in the 1940s provided clear indication that deoxyribonucleic acid (DNA) was the genetic material of the cell. The structure of DNA was elucidated by Francis Crick and James Watson, and published in 1953. Their proposed structure suggested the way in which genes might be replicated. Not long after, Francis Crick linked the sequence of bases to the amino acid sequence of proteins, and that the amino acid sequence in itself determined the three-dimensional structure of these proteins. By 1960, it was established that a sequence of three DNA bases encodes an individual amino acid. Marshall Nirenberg, Severo Ochoa, and Gobind Khorana "cracked" the genetic code, the specific DNA base triplets that

specify particular amino acids in a series of experiments conducted in the 1960s.

The sequencing of significant lengths of DNA remained a difficulty until 1977 when Fred Sanger sequenced a bacteriophage genome of 5,375 nucleotides. This achievement led the way to Sanger's sequencing of the DNA of the human mitochondrial genome of more than 16,000 nucleotides in 1981. These early sequencing successes ultimately led to the idea that arose in the mid-1980s to sequence the human genome. This task was completed in 2003 (a draft sequence was published in 2001). Parallel to DNA sequencing efforts was the use of restriction enzymes, which cut DNA at specific points in the chain. Restriction enzymes made possible DNA sequencing, recombinant DNA technology, transgenic technology, and other tools, giving rise to the rapid development in the 1990s of biotechnology based on gene splicing (Biology Encyclopaedia). The era of man "playing God" had finally arrived. We could finally accomplish genetic modification of living organisms.

Our discipline has contributed to development of new drugs, therapies, and diagnostic tools to combat diseases and improve public health. We have helped to develop bioremediation strategies to clean up pollution and create sustainable energy sources like biofuels. We have helped to advance the mining of precious metals from the harsh and crude methods of the early days to more environment-friendly and sustainable methods. Every aspect of life as we live it on this planet now has major contributions from biochemistry. We have enhanced animal production by helping to unravel genes involved in maintenance of their health and contributed to understanding their physiology well enough to develop strategies to maximize human exploitation of these resources. We have contributed to enhancing crop production by creating pest-resistant and disease-resistant plants, while also improving nutritional content and ensuring food security.

However, our good intentions have not always translated to the general good. There are real and perceived problems. There is often a gap between intent and application of knowledge in science. Even well-intentioned biochemical research can have unforeseen negative impacts if ethical, legal, social and environmental implications and consequences are not thoroughly evaluated. The current debates in the public space about Genetic medicine and Genetically Modified Organisms are evidence of this. Uncontrolled or irresponsible use of biochemical technologies, such as in the development of genetically modified organisms, can have unintended negative consequences for ecosystems. We must therefore consider the ethical implications and potential impacts of our work on society and the environment. The governance and ethics frameworks for considering what is best for society must be strengthened.

How did I get here?

Right through primary school at Olowogbowo Methodist Primary and secondary school at Government College, Ikorodu, where I was in the pioneering class, I had a lot of good teachers who nudged me in the direction of life sciences. It was therefore no surprise that I ended up studying for a degree in biochemistry at the University of Lagos. My lecturers there inspired me to want to follow in their footsteps, and hopefully become a significant contributor in the field of Biochemistry. My B.Sc. final year project supervised by Prof. O.A. Magbagbeola sealed that love. She was more than a supervisor to our cohort. That project assessed the levels of various vitamins in some peppers and condiments commonly used in Nigerian cuisine. It was my introduction to the Scientific method, while also tapping into my love of food. Beyond the results of experiments reported in the project, we discovered a love of research and were inducted to the world of weekends in the laboratory.

By a series of Divinely orchestrated happenstances, I found myself in Obafemi Awolowo University, Ile-Ife for Postgraduate training in Harmattan Semester 1989/1990 Session, and ended up in the

laboratory of another woman with a titanic reputation. She had a long-standing interest in lipids generally, and in a special class of lipids, the eicosanoids. She had worked on prostaglandins and their synthesis in plants. Prostaglandins (PGs) are hormone-like mediators in many physiological and pathological processes that are present in all vertebrates, and in some terrestrial and aquatic invertebrates (Di Dato et al., 2020).

Prostaglandins and related eicosanoids were rarely found in plants. However, PGs and PG-like compounds had been identified in some plant species around 1973/74. They were first shown in onion, and later poplar, certain red, brown, and green algae, and some mosses. The direct precursors for PGs, such as arachidonic acid, di-homo-γ-linolenic acid, and eicosapentaenoic acid, are also found in various plants and algae. Their precise functions in plants are still not fully understood, but research suggests they can influence plant processes, such as flowering, fruit ripening, and mediation of stress responses. (Groenwald and Westhuizzen, 2005). A full understanding of their role is still a matter of ongoing scientific investigation.

About the time I was considering a research project for my MSc., I came to know about an *Efinrin* soup that was prepared for women to ease labour and promote after birth recovery. This fascinated me. In my mind, I somehow linked these biological actions to smooth muscle contraction. *Efinrin* was a major plant of interest in the Onajobi lab. I therefore joyfully joined Akin Famurewa, and Emmanuel Ironge Igiran who were working on different *Efinrin* projects in the Onajobi laboratory. Previously, my supervisor had demonstrated the presence of prostaglandin-like compounds in *Efinrin* (*Ocimum grattissimum*), a common medicinal plant (Onajobi 1977, Onajobi 1984).

Efinrin (Yoruba), nchanwu (Igbo), daidoya ta gida (Hausa), commonly known as scent leaf, and scientifically known as *Ocimum gratissimum* is a fragrant herb used in West African cuisine for its distinct flavour and aroma. It is used to add flavour

to various dishes, such as pepper soup, yam porridge, beans and jollof rice. The leaves can be used to make sauces and marinades for meats, fish, and poultry. Fresh leaves are chopped and added to salads for a unique aromatic flavour. Medicinally, it is believed to aid in food digestion, help with stomach aches, dysentery, and diarrhoea. Some traditional uses suggest it can help lower and normalize blood sugar levels and to aid in the detoxification, thereby contributing to liver and kidney health. It is used to treat fevers, coughs, colds and catarrh (runny nose). It is also believed that the leaves repel insects when burnt.

My project used radiolabelled Arachidonic acid, a known substrate for PG synthesis, to probe the factors affecting synthesis of prostaglandin-like compounds in *Ocimum grattissimum*. The use of this technique meant that I received training in handling radioisotopes and techniques used to measure their levels in biological material. This was to be of significant benefit to me later. It was a major factor in securing an IAEA fellowship to University of Hohenheim, Stuttgart, Germany in 2001. That fellowship allowed me to do certain aspects of my PhD project on the side, while attending to the fellowship project.

I was able to demonstrate the conversion of Arachidonic acid to prostaglandin-like compounds and confirmed it using Thin Layer Chromatography and Liquid scintillation counting. I was also able to work out the optimal conditions for the synthesis. There were two distinct PH optima, one similar to that of animal prostaglandin synthetase at between 7.5 and 8; the other at PH 6.5, suggesting differences in the mechanism of PG synthesis between plants and animals (Osoniyi, 1992; Osoniyi and Onajobi 1998).

I went off to work in industry in 1993 but returned in 1994 to join the staff and began a Ph.D. This time, my attention was on another medicinal plant, *Jatropha curcas*, known as Lapalapa or Botuje in Yorubaland. At the time, it was one of the most researched plants in the world for various reasons.

Jatropha curcas L., Barbados nut, purging nut tree, is a bush or small tree that belongs to euphorbiaceae family. The plant has been used traditionally for medicinal purposes in many cultures. It has been shown to possess wound-healing, antiparasitic, disinfectant, anti-inflammatory, antidiarrhoeal, coagulant, anti-coagulant, abortifacient, antitumor, antimetastatic and insecticidal activity. The plant has a number of active compounds including curcin, curcusone-B, curcain etc. The plant also commanded attention because of the possibility of getting high quality biodiesel from its oil-rich seeds (Laxane et al., 2013).

Jatropha Curcas studies

Blood coagulation, or clotting, is a crucial process. When a cut occurs, a cascade of reactions involving many proteins, forms a clot to stop the bleeding. However, this process must be tightly controlled. If blood clots too easily or too quickly inside the veins, it can lead to dangerous conditions like thrombosis, where clots block blood flow to vital organs. If it does not clot fast enough, a small cut can result in huge blood loss.

One of the most critical and widespread uses of medicinal plants has been as haemostatics, substances that can quickly stop bleeding from a wound. It is an age-long practice across cultures. For a city boy like me, the use of medicinal plant sap as a haemostatic was far from my experience. It therefore fascinated me when I was told. In many tropical regions, the latex, or sap of *Jatropha curcas* is a well-known traditional remedy used for this very purpose. When applied to a cut, it is known to help staunch the flow of blood. For generations, its role was simple and undisputed. I decided to take a closer look, and hopefully isolate the compounds responsible for this bioactivity. I planted seeds obtained from Aba Gbooro in our medicinal plants garden beside the department. Our first results quickly showed that the active principle(s) was extractable into organic solvents. In addition, the very same plant sap used to stop bleeding (pro-coagulant) also showed anti-coagulant properties under certain conditions. When the whole, undiluted latex was tested, it performed as expected based on

traditional use and significantly reduced the time it took for blood to clot. This confirmed its potent procoagulant (clotting) abilities. However, when the latex was diluted, it began to show the opposite effect, prolonging the clotting time. The most remarkable finding was that at high dilutions, the anticoagulant effect was so strong that the blood samples did not clot at all. This was the first documented report of the anti-coagulant properties of Jatropha (Osoniyi, Rogbesan and Onajobi, 1996). Attempting to resolve that paradox became a major part of the remaining work for the Ph.D. project. We needed to find a collaborator who would help.

I was fortunate to come in contact with Prof. A. O. Ogundaini of the Department of Pharmaceutical Chemistry, who was supervising my friend's Ph.D. thesis at the time. I liked what they were doing in their research group in IPICS and I learnt vicariously from him through my friend. Prof. Onajobi and I then discussed with him and he readily agreed. He has been a valued teacher, mentor and friend since then. I benefited from his expertise, access to solvents and reagents from his group, and mentorship from their whole friend group. Eventually, I was able to use solvent partitioning to resolve the activities. An ethyl acetate fraction of the latex, at low concentrations, was found to contain the procoagulant activity responsible for promoting clotting. A butanol fraction contained the highest anticoagulant activity, proving it was the source of the clot-preventing effect while the residual aqueous fraction had no significant effect on the overall clotting time of blood or the Prothrombin Time (PT). It did, however, slightly prolong the Activated Partial Thromboplastin Time (APTT). (Osoniyi and Onajobi, 2003).

This paradox with Jatropha curcas latex exemplifies the layers of complexity that exist in natural products. We are reminded that a single traditional remedy can possess dual, even paradoxical, functions that are only revealed under serious scientific scrutiny. This also partially explains the fact that a single plant may be used to treat different conditions in different places. Each people group evolve the processing and dosage that works in their specific

instance for their chosen purpose. The way a natural remedy is prepared and used can be as important as the remedy itself. Further attempts to isolate pure compounds responsible for the activities did not however succeed.

My Introduction to Cancer Biology

I applied for, and secured a postdoctoral position in the University of Fort Hare in South Africa. I was to work in natural products chemistry, beginning from January 2007. While getting ready to resume there, another opportunity came up. I secured a three-month Advanced Laboratory Training Fellowship to the University of Cape Town sponsored by the United Nations Conference on Trade and Development (UNCTAD). It held from October 16, 2006 - January 16, 2007. There were nine of us from different countries in Africa. I was one of two assigned to the lab of the Program director, Prof. Iqbal Parker in the Division of Medical Biochemistry. It was a cancer biology laboratory. His group included Dr. Denver Hendricks, Dr. Virna Leaner and a few others. I told them of my plan to proceed to Fort Hare in January when the program finished. I wrote to my prospective host in Fort Hare, notifying him of these developments and to secure his permission to resume in mid-January.

By December, I was offered another Postdoc position in UCT, in the cancer biology group. It was a better offer than the earlier one, and with people I had come to enjoy working with and know well. My direct supervisor was Denver Hendricks. It was a steep learning curve for me, learning the rudiments of cancer biology, the biological techniques and assays needed to confirm activity and to work out mechanisms of action for the compounds and synthetic analogues made by our collaborators across South Africa. I was also given the opportunity to teach a few lectures and introduced to the problem Based Learning approach to teaching. It was a busy, but very productive two years that followed.

Cancer is a generic term for a large group of diseases that can affect any part of the body. The defining feature of cancer is the

rapid formation of abnormal cells that grow beyond their usual boundaries, and which can then invade adjoining parts of the body and spread to other organs or metastasize. This rampant proliferation of cells puts a large demand on resources available to support life. Widespread metastases are the primary cause of death from cancer. According to the IARC Global cancer observatory 2022 data, nearly one in six deaths were caused by cancer. The number of new cases in Africa is 1,185,216, resulting in 763,843 deaths (Ferlay et al., 2024). The most common, in terms of new cases were: breast, lung, colon and rectum, prostate, skin (non-melanoma), and stomach cancer.

Around one-third of deaths from cancer are due to tobacco use, high body mass index, alcohol consumption, low fruit and vegetable intake, and lack of physical activity. In addition, air pollution is an important risk factor for lung cancer. Cancer-causing infections, such as human papillomavirus (HPV) and hepatitis, are responsible for approximately 30% of cancer cases in low- and lower-middle-income countries. Many cancers can be cured if detected early and treated effectively. Therein lies the problem. It is neither detected early enough nor treated effectively for various reasons. It is still a scary condition.

Every cancer type requires a specific treatment regimen. A correct cancer diagnosis is essential for appropriate and effective treatment. Treatment typically includes surgery, radiotherapy, and/or systemic therapy (chemotherapy, hormonal treatments, targeted biological therapies). Proper selection of a treatment regimen takes into consideration both the cancer and the individual being treated. Completion of the treatment protocol in a defined period of time is important to achieve the predicted therapeutic result. Determining the goals of treatment is an important first step. The primary goal is generally to cure cancer or to considerably prolong life. Improving the patient's quality of life is also an important goal. This can be achieved by support for the patient’s physical, psychosocial and spiritual well-being and palliative care in terminal stages of cancer.

Some of the most common cancer types, such as breast cancer, cervical cancer, oral cancer, and colorectal cancer, have high cure probabilities when detected early and treated according to best practices. There is, however, a significant variation in treatment availability between countries of different income levels, Comprehensive treatment is reportedly available in more than 90% of high-income countries but less than 15% of low-income countries. There is therefore a need to keep working on finding newer, better and more affordable drugs and treatments.

The major research interest of the Hendricks group was oesophageal cancer, a concern in South Africa at the time. In South Africa oesophageal cancer is the fifth most common cancer, with studies in Soweto revealing that residents there had a 5-fold higher risk of developing the cancer than the world average. Although a wide range of factors have been linked to the onset of the disease, incidences of oesophageal cancer in South Africa have been associated traditionally with low socioeconomic status, poor nutrition, the consumption of maize contaminated with a *Fusarium* fungus, and the use of alcohol and tobacco (Hendricks and Parker, 2002; Mqoqi et al., 2003). The lab was part of an oesophageal cancer research consortium and had a few grants running to study it. This was the environment in which I found myself. Collaborators of the lab in the department of chemistry at UCT, Rhodes University, University of the Western Cape and a few other universities, all united in the quest to find better anti-cancer agents were engaged in extracting bioactive compounds from various sources and isolating novel compounds and synthesizing better analogues as directed by the results of the biological testing of those compounds on cancer cell lines that was done in our laboratory. A lot of the biological testing of these compounds was carried out by me while I was there. Many significant findings arose from these collaborations. In one study, we synthesised four 2-substituted 1,4 naphthoquinones, related to the marine natural product 2-deoxylapachol. That compound had previously been tested against squamous cell oesophageal cancer. We assessed cytotoxicity, using the MTT assay to quantify cell viability and

determine the half-maximal inhibitory concentration (IC_{50}), the concentration of an extract required to kill 50% of the cells. All four synthetic compounds were cytotoxic to WHCO1 oesophageal cancer cells. Compounds 1- 4 (Fig.1) exhibited good activity (IC_{50} 5.1, 6.4, 4.1 and 1.5 µM respectively) against the WHCO1 oesophageal cancer cell line when compared to the cytotoxicity of 2-deoxylapachol (IC_{50} 14.8 µM) and the commonly used chemotherapeutic agent for SCOC, cisplatin (IC_{50} 13 µM) against the same cell line (Sunassee et al., 2007).

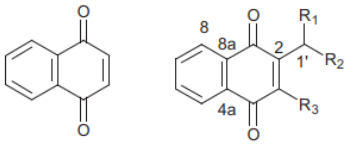

Fig. 1. Lapachol analogues evaluated against Oesophageal cancer cell line. (Sunassee et al., 2007)

1. R_1 = OH, R_2 = CH=C(CH_3)2, R_3 = H
2. R_1 = OH, R_2 = CH_3, R_3 = H
3. R_1 = OH, R_2 = CH=CH_2, R_3 = H
4. R_1 = OH, R_2 = Ph, R_3 = H
5. R1 = R3 = H, R2 = CH=C(CH_3)2 – (2- deoxylapachol)

In a similar study, we investigated extracts of the endemic South African intertidal limpet *Trimusculus costatus* obtained along the rocky shore near Cintsa on the Southeast coast of South Africa. An acetone extract of specimens collected during the autumn of 2007 was subjected to initial polymeric reversed-phase separation followed by flash chromatography using a diol solid support. Finally, an exhaustive combination of normal-phase and diol HPLC afforded two labdane diterpenes and three new metabolites (Fig.2) which were screened against the WHCO1 human oesophageal cancer cell line. Three of the compounds (**1, 2 &3**) exhibited moderate activity, IC_{50} 25, 24, and 84 µM, respectively when compared to the commonly used chemotherapeutic agent, cisplatin (IC_{50} 13 µM). Compound **4** however, exhibited reasonable activity (IC_{50} 3 µM) against this cell line (van Wyk et al., 2008).

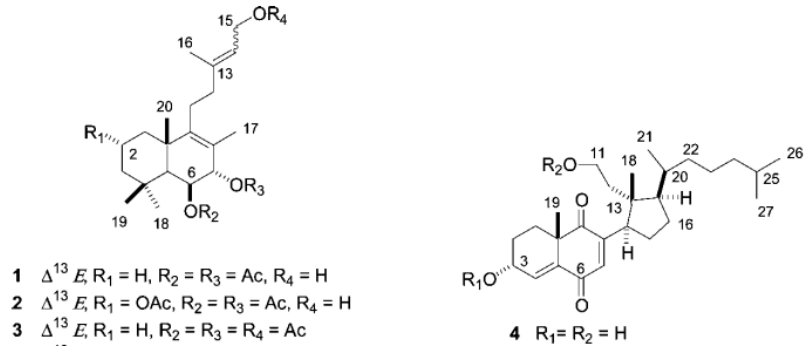

Fig. **2**. Labdane terpenes and their analogues evaluated against Oesophageal cancer cell line. (van Wyk et al., 2008)

In a more comprehensive Structure-Activity Relationship study (Sunassee et al., 2013), we revisited the previously mentioned Naphthoquinones. Lapachol, α- and β-lapachone and a series of 25 related synthetic 1,4-naphthoquinones were synthesized (Fig.3) and screened against the oesophageal cancer cell line (WHCO1). Most of the compounds exhibited enhanced cytotoxicity (IC_{50} 1.6–11.7 μM) compared to the current drug of choice cisplatin (IC_{50} = 16.5 μM). This study also established that the two new synthetic halogenated compounds 12a and 16a (IC_{50} = 3.0 and 7.3 μM) and the previously reported compound 11a (IC_{50} = 3.9 μM), were non-toxic to NIH3T3 normal fibroblast cells (Table 1). Cell death of oesophageal cancer cells by processes involving PARP cleavage caused by 11a was shown to be associated with elevated c-Jun levels, suggesting a role for this pathway in the mechanism of action of this cohort of naphthoquinone analogues.

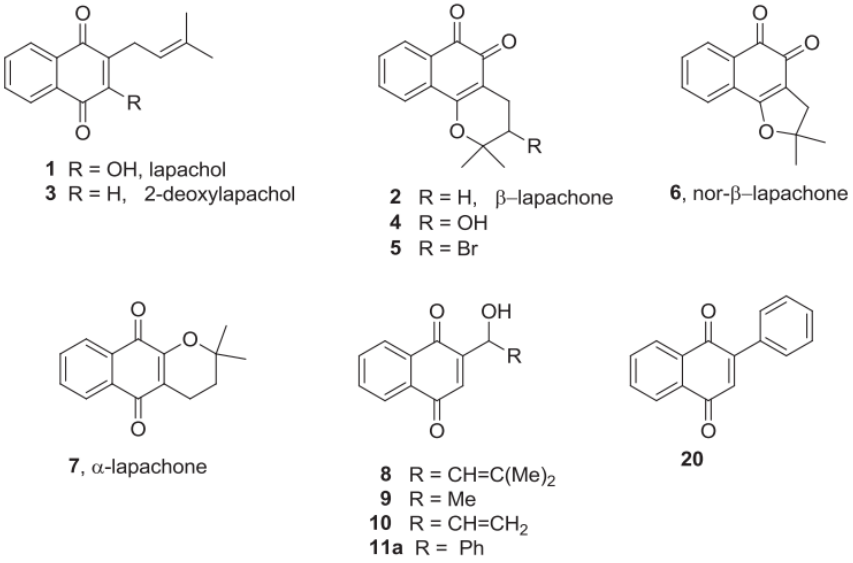

Fig. 3. Ortho and para-naphthoquinones evaluated against Oesophageal cancer cell line. (Sunassee et al., 2013)

Table 1. Summary of the IC50 values of compounds tested against WHCO1 oesophageal cancer cell line

Compounds	IC_{50} (μM)	95% C.I.[a]
Lapachol (**1**)	24.1	13.4–43.4
β-Lapachone (**2**)	1.6	1.3–1.9
3	15.0	13.2–16.8
4	6.5	6.0–6.9
5	1.8	1.3–2.3
6	2.4	2.2–2.6
7	28.7	20.1–39.8
8	5.2	4.9–5.4
9	6.4	6.0–6.8
10	4.3	3.1–5.5
11a	3.9[c]	3.7–4.1[c]
R-**11a**	4.3	4.1–4.5
S-**11a**	3.8	3.4–4.3
11b	63.4	54.6–73.6
11c	21.6	19.6–23.6
12a	3.0	2.8–3.3
12b	72.9	59.7–89.0
13a	3.4	3.2–3.6
13b	50.4	43.4–58.4
14a	5.1	4.8–5.4
14b	74.9	69.3–80.9
15a	5.5	5.0–6.0
15b	94.8	86.3–104.4
16a	7.3	6.8–7.8
16b	94.8	75.9–118.6
17a	2.4	1.3–3.4
17b	NA[b]	–
18a	10.9	9.8–12.0
18b	96.9	92.3–101.7
19a	4.8	2.4–7.2
19b	83.7	78.2–89.4
20	11.7	10.6–12.8

[a] Confidence interval.
[b] Not active.
[c] Previously reported as IC_{50} = 1.5 μM (95% C.I. of 1.1–1.9) [26].

The mechanism of action of these compounds was determined using a Western blot analysis. Poly adenosine-diphosphate ribose polymerase (PARP) cleavage which is indicative of apoptosis, and expression levels of c-Jun were determined. The WHCO1 oesophageal cancer cells were treated with varying concentrations of each compound and protein was extracted at the relevant time points. PARP is a known caspase-3 substrate and cleavage of

PARP into 116 kDa and 85 kDa fragments is indicative of apoptosis, as shown by WHCO1 cells treated with doxorubicin (dox) as a positive control (Fig. 4A). PARP cleavage was clearly observed in cells treated with 11a, R-11a and S-11a at a concentration of 20 mM, whilst only slight PARP cleavage was observed with lower concentrations (<20 mM) at all time points. A concentration-dependent increase in c-Jun levels was observed after all treatment time points, with the highest expression observed after 24 h followed by a decline in expression at 48 h (Fig.4B and C). These results suggest the activation of the JNK/c-Jun signalling pathway and the associated cleavage of PARP in WHCO1 cells, in a similar manner to the marine natural product KLM 155 previously reported by the laboratory (Whibley et al., 2007). This is the first example of JNK/c-Jun activation in oesophageal cancer cells by naphthoquinone compounds.

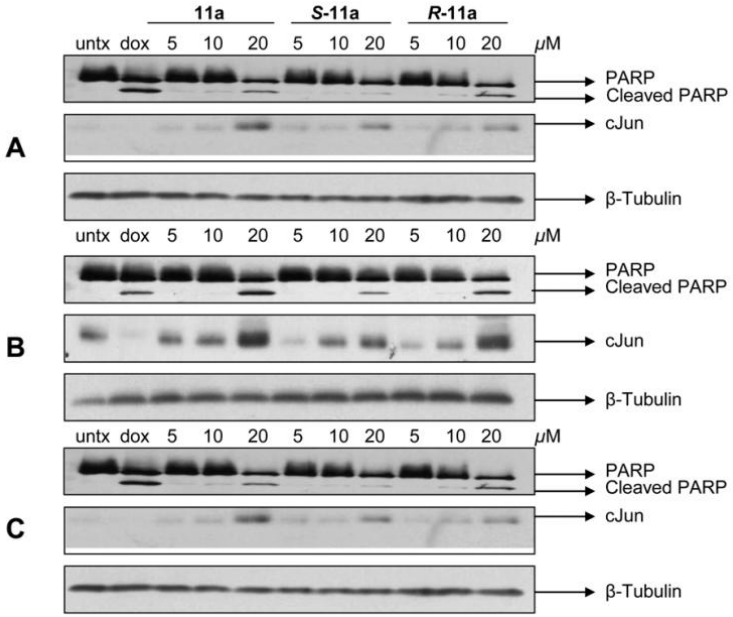

Fig. 4. Western blot analysis of WHCO1 oesophageal cancer cells treated with varying concentrations of racemic 11a, S-11a and R-11a at A) 6h B) 24h and C) 48h. Cells treated with 0.5μM doxorubicin were included as a positive control for PARP cleavage.

Mr Vice chancellor Sir, return to Ile-Ife after the postdoc was rather traumatic. One ran into a technical hitch with every new project designed in cancer drug discovery occasioned by lack of resources. I had to go back to the drawing board.

Nutraceuticals; Food as medicine and medicine from foods.

I had transferred my first M.Sc. student to a colleague when I was starting my postdoc. He had just started benchwork when I was leaving. It was sad to find him still on the programme when I returned. He was bright and hard-working so I could not explain the delay. My first priority was to see him complete his work and defend his thesis. In this was also my redemption. I got straight back into research mode with him. The project was simple and straightforward. We were interested in functional foods and nutraceuticals.

A nutraceutical is any substance that may be considered a food or part of a food and provides health or medical benefits, including prevention and treatment of disease. It may include nutrients, dietary supplements, herbal products, processed foods, cereal, soups (Fig. 5). Nutraceuticals are formed from active compounds obtained from plant foods or from foods of animal origin, which are concentrated and provided in the appropriate pharmaceutical form, and also have a pharmacological effect and nutritional value (DeFelice, 1995).

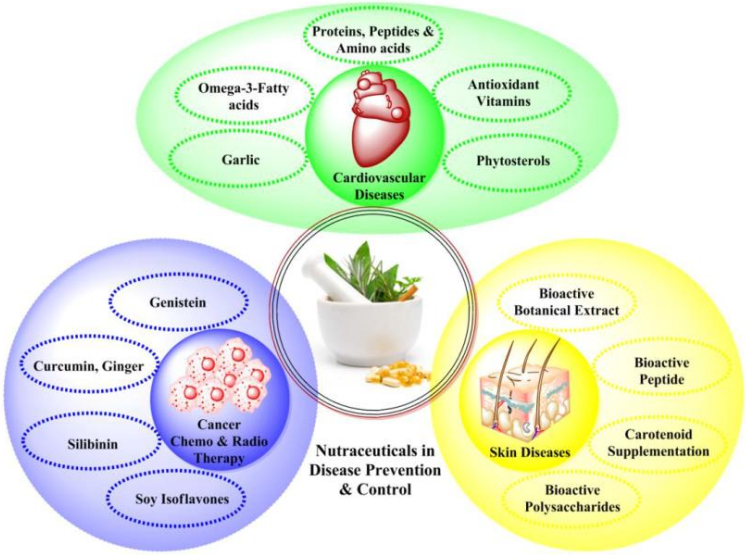

Fig.5. Nutraceuticals and Dietary supplements in various diseases. (Puri et al., 2022)

Our foods and spices are indeed medicinal treasure troves. Understanding their potential to protect, and promote health has been one of our research interests. Omede Ameh, my first M.Sc. student, was the first of a few postgraduate students under my supervision that examined the problem of hyperlipidemia, and how to ameliorate it with food. His thesis was titled "Evaluation of the Lipid-Lowering Effect of *Moringa oleifera* (Lam) Leaf Extracts on Triton WR 1339 – induced Hyperlipidaemia in the Rat". Triton WR 1339 also known as Tyloxapol is a non-ionic surfactant, or non-ionic liquid polymer, primarily used in scientific research and animal models to aid in the removal of bronchopulmonary secretions and to induce hyperlipidemia and atherosclerosis. It blocks the activity of lipolytic enzymes, preventing the breakdown of triglycerides, which leads to an increase in blood lipids. Ethyl acetate extracts of moringa mitigated all the effects of dyslipidemia occasioned by intraperitoneal administration of the detergent in a dose-dependent manner (Omede, 2010). Beyond confirming the health benefits of Moringa, this model became one of our primary tools for probing the efficacy of other plants and condiments

reputed to have lipid-lowering properties. The methodology has since been adopted in similar studies (Omede, 2016; Omede et al, 2018).

Another study in the lab established antioxidant and anti-hyperlipidemic properties of the humble *iru or dawadawa*, a fermented condiment prepared from the seeds of *Parkia biglobosa* (Ayo-Lawal et al., 2014), and *ogiri*, another fermented condiment prepared from the seeds of *Citrullus vulgaris* (Ayo-Lawal et al., 2015).

Globally fermented foods form an integral part of the staple diet of people. *Iru* and *Ogiri* (known by various names in the local dialect) are nutritious natural fermented condiments that feature frequently in the cuisine of many West African communities. In addition to their role in the cuisine, there are various claims about their efficacy in treating various conditions (Ayo-Lawal et al., 2016). In our studies, normal rat chow was modified by including either *Iru* or *Ogiri* up to 20%. These were fed to rats over a period of 42 days, at the end of which hyperlipidemia was induced by intraperitoneal administration of tyloxapol. The antihyperlipidaemic potential of these condiments in tyloxapol-induced hyperlipidaemic rats with reference to that of fluvastatin, a standard antilipidemic statin drug was determined. The antioxidant potential of the condiments was also examined using different relevant in vitro assays. In the Fermented Citrullus vulgaris (FCV) or *Ogiri* study for example, administration of tyloxapol induced a significant ($p < 0.05$) increase in total-cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and triglyceride (TG). These lipid increases were significantly mitigated in groups initially pre-fed with supplemented FCV feed. Plasma TC decreased by 69.38% ($p < 0.05$); TG by 80.58% ($p < 0.05$); LDL-C by 7.80% ($p < 0.05$) and high-density lipoprotein cholesterol (HDL-C) levels increased by 78.61% ($p < 0.05$). FCV showed appreciable antioxidant activities in vitro in a dose dependent manner. Histomorphological examination of the liver suggested that the FCV possessed hepatoprotective potential. These results

suggest that FCV consumption may be a possible dietary measure for the control of hyperlipidemia. Similar results were obtained for fermented *Parkia biglobosa* (*Iru*).

Essentially the same methodology was used to probe the hypolipidemic effects of some other foods. In the "fattening room practice" of the Efiks and some other tribes of the South-south region, in preparation for the wedding ceremony, young women were kept in seclusion for a period of time to prepare them for womanhood and marriage. During this period, they are groomed extensively, fed a rich diet and receive education on homemaking. Many of them get really fat, but they are the very picture of health. During the period, they eat a lot of soup containing cocoyam leaves, along with various special spices including *Aridan* (*Tetrapleura tetraptera*). This informed our decision to explore the lipid-lowering properties of a formulated diet containing the two (Odejide, 2016). As we had suspected, the combination exerted a protective effect against tyloxapol-induced dyslipidemia. Similarly, we also found that *Solanum nigrum*, commonly known as Efo odu among Yorubas has lipid-lowering properties (Adeoba, 2011).

Beyond lipid-lowering properties, we investigated other bioactivities in some other vegetables consumed as food. One of the other vegetables we studied was *Crassocephalum crepidioides*. This is Efo ebolo, commonly known as fireweed ragleaf. It typically grows as a weed. In many African countries, its leaves and stems are a valued vegetable, commonly used to enrich soups and stews. It has also been used for generations to treat a variety of ailments including skin conditions like wounds, boils, and burns, soothing digestive issues such as indigestion and stomach ulcers, and managing symptoms of fever and inflammation. In Opeyemi Oyedele's PhD project co-supervised by Prof. Onajobi and I, we conducted a series of studies on this plant. Secondary metabolites from dried and ground *C. crepidioides* leaves were extracted with 70% methanol, and the concentrated crude extract was subsequently subjected to solvent partitioning with Hexane, Ethyl

acetate, and Butanol. Varying concentrations (5–20 mg/mL) of the extract and fractions were tested *in vitro* on blood coagulation profile; clotting time (CT), prothrombin time (PT), and activated partial thromboplastin time (aPTT) of apparently healthy human volunteers. Phytochemical characterization of the Hexane fraction was also carried out by gas chromatography-mass spectrometry (GC-MS). We found that *C. crepidioides* leaf methanol extract and fractions significantly ($P<0.05$) prolonged the clotting time, prothrombin and activated partial thromboplastin times in the blood. The highest prolongation effect was recorded with the Hexane fraction at concentration of 10mg/mL (Fig. 6A & 6B). GC-MS analysis of the Hexane fraction indicated the presence of phytochemicals such as unsaturated fatty acids and esters, phenolic compounds, flavonoids, and coumarin-related compounds known to exhibit antiaggregant, antiplatelet and antimicrobial activities. These results showed that *C. crepidioides* possesses bioactive components with anticoagulant properties which may be exploited in the treatment of blood coagulation disorders (Ayodele et al, 2019).

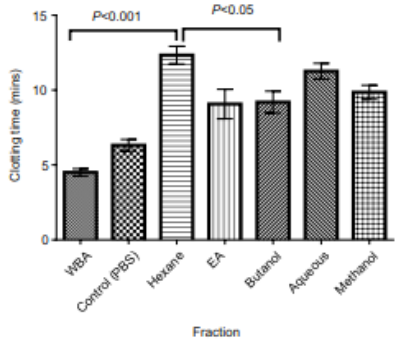

Fig. 6A. Mean clotting time of normal human blood treated with the leaf extract and fractions at 10 mg/mL.
Data are mean ± SEM (n=15). All fractions and extract were suspended in PBS.
Abbreviations: EA, Ethyl acetate; WBA, whole blood alone, Control, test control consisting of whole blood and PBS (vehicle).

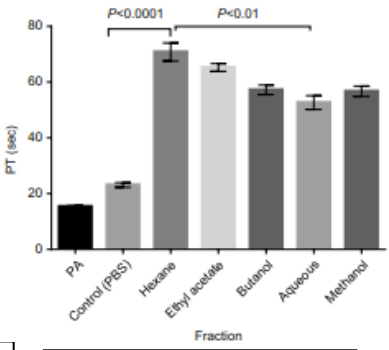

Fig. 6B. Prothrombin time of normal human plasma treated with all fractions at 10 mg/mL.
Data are Mean ± SEM values (n=15).
Abbreviations: PA, Plasma alone; Control, test control consisting of Plasma and PBS (vehicle).

Table 2. Some phytochemical components of the Hexane fraction of C. crepidioides leaf extract identified by GC – MS with possible anticoagulant activity

S/N	Retention time (mins)	Name of compound (Library ID)	Molecular formula	Peak Area (%)	Reported Biological Activity
1	13.640	Thujone	$C_{10}H_{16}O$	0.56	Antiplatelet, Antibacterial, Antifungal, Antinociceptive, Insecticidal, Anthelmintic Antioxidant.[26,27]
2	14.180	Eugenol	$C_{10}H_{12}O_2$	4.43	Antiaggregant.[28] Anti-inflammatory, Antiseptic.[29]
3	10.286	Benzofuran	C_8H_6O	1.43	Antidepressant, Anticancer, antiviral, antifungal, antioxidant, anti-psychotic, anti-inflammatory.[30]
4	19.795	Benzofuranone	C_8H_6O	2.99	Antioxidant, Anticancer.[27]
5	22.151	1,9 octadecadiene	$C_{18}H_{34}$	0.78	Not stated
6	29.404	9,12,15-Octadecatrienoic acid (α-linolenic acid)	$C_{18}H_{30}O_2$	4.52	Antiaggregant, Anti-Inflammatory, Hypolipidemic, Anti-leukotriene, Antiprostatic, Immunostimulant, Vasodilator, 5-alpha reductase inhibitor.[27]
7	5.449	Benzene acetaldehyde	C_8H_8O	1.11	Antioxidant Antibacterial, Anaesthetic.

With these results from in-vitro experiments, we further decided to see if the plant could produce similar effects in a living organism in a diabetes model. Diabetes mellitus and its complications is a potentially morbid condition characterized by hyperglycaemia, which is often accompanied by dyslipidemia. About 80% of people with diabetes mellitus die from thrombosis arising from enhanced activation of platelets and clotting factors. In the diabetic state, there is an impairment of the thrombo-haemorrhagic balance that exists in the blood flow of a healthy individual. This makes diabetic patients susceptible to thromboembolic complications, atherosclerosis, and increased plaque rupture (Gosh, 2002; Stratmann and Tschoepe, 2009). These, in turn, may lead to aggravation of the diseased state. Erythrocyte (RBC) aggregation and decreased deformability predominate among the hematological abnormalities reported in diabetes. The structures and architecture of platelets, erythrocytes, and fibrin networks have been reported to be of importance in the pathogenesis of cardiovascular complications in diabetes mellitus (Rooy and Pretorius, 2014).

First, we induced diabetes in rats using streptozotocin (STZ). Then, we treated these diabetic rats orally for two weeks with different concentrations (50, 100, and 200 mg/kg) of hexane and aqueous

fractions of *C. crepidioides*. As expected, the STZ-induced diabetic rats had dangerously high blood glucose levels. The results of the treatment were remarkable. *C. crepidioides* fractions significantly reduced plasma glucose levels by 51.3% to 62.2%. Histological examination of the pancreas, the organ responsible for producing insulin, also showed that the plant extract repaired the damage caused by the STZ. This suggests the plant may help regenerate or protect these vital insulin-producing cells of the pancreas. In addition, the extracts significantly lowered triglycerides in both blood plasma and the liver, reduced total cholesterol and LDL-cholesterol concentrations, and markedly increased HDL-cholesterol levels in both the plasma and the liver, helping to restore a healthier lipid balance. Because the plant fractions so effectively improved the overall cholesterol profile, they also significantly lowered atherogenic risk indices, suggesting a protective effect against cardiovascular disease. The study also confirmed the initial *in vitro* findings on the plant's anticoagulant properties in this diabetic rat model. The fractions significantly prolonged both the bleeding time (how long it takes for a small cut to stop bleeding) and the clotting time. They significantly reduced platelet counts, consistent with an anti-clotting effect (Ayodele et al., 2020a; 2023).

Analysis of the hexane fraction, which was particularly effective in this rat study by GC-MS, revealed several bioactive compounds known for their bioactivities (Ayodele et al., 2020b). Among the compounds identified in this fraction were n-Hexadecanoic acid and α-Linolenic acid. Both are fatty acids known for their ability to lower cholesterol. This provides a direct chemical explanation for the improved lipid profiles seen in the treated rats. Eugenol and Thujone were also present. These are known to interfere with blood clotting and prevent platelets from clumping together, which supports the observed anticoagulant effects. The presence of Benzofuranone was particularly interesting. This compound is chemically related to coumarins, a class of chemicals that includes warfarin, one of the most widely used anticoagulant drugs in modern medicine. This suggests that the anticoagulant property of

this plant extract might be similar to that of warfarin. These findings provide a clear scientific rationale for the traditional medicinal uses of ebolo. More importantly, they highlight the potential of *Crassocephalum crepidioides* as a valuable natural source for developing new and effective treatments for managing diabetes and its life-threatening complications.

A return to fermented Citrullus vulgaris and Parkia biglobosa seeds.

Ayo-Lawal, R.A. returned to my laboratory for PhD studies and we decided to have a closer look at our super-condiments, *iru* and *Ogiri* (Plate 1). The studies were part-funded by a fellowship from TWAS which enabled her to do a research visit to one of our collaborators in South Africa where she carried out the parts of the work that we could not do here. This time, the focus was an evaluation of antimitotic, antiproliferative, and anticancer activity of extracts from these fermented foods. Some fermented foods and beverages had been reported to be useful in cancer prevention and treatment including kefir (Otes & Cagindi.,2003; Wang et al., 2009), sauerkraut a fermented vegetable food of Germany (Kris-Etherton et al., 2002), kimchi (Park et al., 2014) and many others. The fermentation process, driven by microorganisms, can transform the chemical constituents of raw materials, enhancing their nutritional value and creating novel bioactive compounds with medicinal properties.

Our studies aimed to provide the first scientific evaluation of the potential of these condiments to combat cancer, specifically by investigating their effects on cancer cell viability, proliferation, and programmed cell death. The investigations employed a range of *in vitro* models and assays to comprehensively assess the anti-cancer potential of the fermented condiments; *iru* and *ogiri*, and their aqueous (reflecting the readily edible state) and methanolic extracts.

Plate 1. Raw (a) and Fermented (b) *Citrullus vulgaris* and *Parkia biglobosa*

Allium cepa (onion) root meristematic cells were used to evaluate anti-mitotic and genotoxic effects, while *Saccharomyces cerevisiae* (yeast) cells were used to assess anti-proliferative activity. In addition, effect on human cancer cell lines; breast adenocarcinoma (MCF-7), cervical cancer (HeLa) and hepatocellular carcinoma (Hep-G2) were assessed using fibroblast cells (KMST-6) as a non-cancer control to assess selective toxicity. Clonogenic (colony formation) assays were used to measure the ability of cancer cells to reproduce and form colonies after treatment, indicating long-term, irrecoverable cytotoxic effects. Cell death analysis was carried out by morphological evaluation, flow cytometry and DNA Fragmentation.

Extracts from *iru* induced time- and dose-dependent cytotoxicity in all tested cancer cell lines- breast, cervical and liver. Notably, higher concentrations were required to inhibit the growth of

normal KMST-6 cells, indicating a selective action against cancer cells. This is shown in Table 3.

Table 3. Activity of Fermented *Parkia biglobosa* against selected cancer cell lines

Extract	Cell Line	IC_{50} at 24h (mg/mL)	IC_{50} at 48h (mg/mL)
Aqueous	MCF-7	1.51	0.98
Aqueous	KMST-6	1.90	1.37
Aqueous	Hep-G2	1.3	1.2
Aqueous	HeLa	0.6	0.4
Methanolic	MCF-7	1.91	1.28
Methanolic	KMST-6	1.67	1.71

Furthermore, treatment with the aqueous extract caused cancer cells to lose their original structure, detach from the culture plate, and float in the medium, with evidence of dead cells observed. The clonogenic assay showed that the aqueous extract significantly reduced the ability of both Hep-G2 and HeLa cells to reproduce and form colonies, indicating a lasting cytotoxic effect. For instance, untreated HeLa cells formed 832.66±23 colonies, while treated cells formed only 115.33±6. Flow cytometric analysis showed that the aqueous extract induced significant, concentration-dependent apoptosis in Hep-G2 cells (73.03±0.73% apoptotic cells at the IC_{50} concentration). The effect on HeLa cells was less pronounced in this assay (35.10±3.28% apoptotic cells). Agarose gel electrophoresis confirmed apoptosis by showing DNA fragmentation bands (around 200-250 base pairs) in both Hep-G2 and HeLa cells after treatment, suggesting this is a key cell death pathway. (Fig. 7).

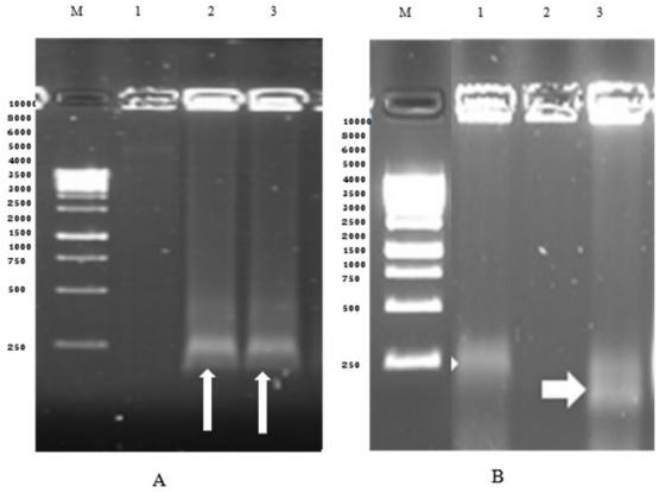

Fig. 7. Qualitative analysis of DNA fragmentation by agarose gel electrophoresis in treated and untreated Hep G2 (A) and HeLa (B) cells.

Hep-G2 (M – DNA marker, 1 –Untreated sample (control), 2,3, - Aqueous FPB extract- treated sample.

HeLa (M – DNA marker, 2 – Untreated sample (control), 1,3, - Aqueous FPB extract-treated sample.

Similar to the *iru*, extracts from *ogiri* displayed potent anti-cancer effects across multiple models, acting through cytotoxic, anti-mitotic, and anti-proliferative mechanisms. An interesting finding with the *ogiri* was that while the toxicity of extracts increased over time in cancer cells, the normal KMST-6 cells appeared to recover, with IC_{50} values increasing at 48 hours (Table 4). Both aqueous and methanolic extracts of *ogiri* significantly reduced the mitotic index (MI), a measure of cell division, in *A. cepa* root cells in a dose-dependent manner. At high concentrations (10 and 20 mg/mL), cell division was completely halted with several chromosomal aberrations induced.

Table 4. Activity of Fermented *Citrullus vulgaris* against selected cancer cell lines

Extract	Cell Line	IC_{50} at 24h (mg/mL)	IC_{50} at 48h (mg/mL)
Aqueous	KMST-6	1.610	1.749
Aqueous	HeLa	1.020	0.707
Aqueous	Hep-G2	1.507	1.276
Methanolic	KMST-6	1.463	1.854
Methanolic	HeLa	0.648	0.642
Methanolic	Hep-G2	0.733	0.538

The collective findings from these studies robustly demonstrate that traditional West African fermented condiments, fermented *Parkia biglobosa* (iru) and fermented *Citrullus vulgaris* (ogiri), possess significant anti-cancer properties in vitro. Both condiments exhibit dose- and time-dependent cytotoxicity against breast, cervical, and liver cancer cell lines while showing lower toxicity to normal cells. The anti-cancer activity is not limited to a single pathway or mechanism. The extracts effectively induce apoptosis or programmed cell death, prevent cell reproduction (clonogenic inhibition), halt cell division (anti-mitotic effects), and cause genetic damage (genotoxicity). These studies establish a strong foundation for the potential of *iru* and *ogiri* as sources of nutraceuticals with anti-cancer properties. There is need for further research to isolate, identify, and characterize the specific active compounds and to validate these findings in in vivo models.

The Periwinkle projects

Mr Vice chancellor Sir, Periwinkles are almost a staple in the cuisine of the people of the south-south region of Nigeria. They are a source of additional protein and flavour in soups and sauces. They are marine molluscs, the two most commonly eaten species being, *Tympanatonus fuscatus* and *Pachymelania aurita*. They are also found along the coasts of West Africa, Angola, and Gabon. Notably, *T. fuscatus* is utilized in the traditional folk medicine of Nigeria's South-south region for the treatment of ulcers and wounds. Their use in traditional folk medicine is not surprising, as

their bigger "cousin", the Giant African Land Snail (*Archachatina marginate*) is well known in the ethnomedicine of West Africa.

The phylum Mollusca is a diverse group of invertebrate organisms that play a variety of crucial ecological roles in marine ecosystems, including oceans, seas, and estuaries. Having adapted to survive in complex and often high-stress marine environments characterized by wide variations in pressure, temperature, and nutrient availability; molluscs have evolved unique biosynthetic pathways to produce a range of secondary metabolites. These compounds are essential for chemical defense against predators and pathogens, communication, and competition. These bioactive secondary metabolites can be categorized by their origin:

1. De Novo Biosynthesis: Compounds synthesized entirely by the mollusc itself.
2. Bioaccumulation: Compounds acquired directly from their diet, particularly from algae, and stored in their tissues.
3. Sequestration and Modification: Compounds bioaccumulated from their diet and then chemically modified to enhance their potency or serve a different biological function.

Marine molluscs are highly valued as a functional food due to their dense nutritional profile. The three major classes; Bivalves, Gastropods, and Cephalopods are common seafood items that offer a wide array of compounds with health benefits. These include:

a) Proteins and Peptides: They are rich in high-quality proteins (collagen, gelatin, albumins) and bioactive peptides that possess antioxidant, antihypertensive, and anticoagulant properties, supporting cardiovascular health and tissue repair.
b) Lipids: The lipid content is a key nutritional feature, dominated by phospholipids. Molluscs are an excellent source of omega-3 Polyunsaturated fatty acids (PUFAs), particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are renowned for their cardiovascular and neurodevelopmental benefits. They also contain marine sterols with anti-inflammatory and antioxidant properties.

c) Polysaccharides: Mollusc shells are a primary source of chitin and chitosan, which exhibit antitumor, bactericidal, and fungicidal properties. Other polysaccharides, like glycosaminoglycans from the bivalve *Perna canaliculus*, have demonstrated anti-inflammatory and anti-arthritic effects.
d) Polyphenolic Compounds and Pigments: Molluscs bioaccumulate polyphenols from their diet (e.g., algae), including carotenoids like astaxanthin and zeaxanthin, which are potent antioxidants.
e) Vitamins and Minerals: They are excellent sources of essential minerals, including zinc, iron, calcium, selenium, and iodine, as well as fat- and water-soluble vitamins such as B12, B6, riboflavin, Vitamin D, and Vitamin A.

Bioactive compounds isolated from marine molluscs have shown significant potential in modern medicine, building on their historical use in traditional remedies. Numerous compounds with specific therapeutic properties have been isolated from these animals including the antimicrobial peptides, myticin and mytilin from mussels that create pores in microbial cell membranes; conotoxins from cone snails that target key enzymes essential for microbial survival and replication; mytimycin C which generates reactive oxygen species (ROS) that damage microbial cells. There are also compounds with anticancer properties like dolastatins isolated from the sea hare *Dollabella auricularia*, which interfere with mitotic cell division; kahalalide F from the sea slug *Elysia rufescens*, which induces a form of cell death called oncosis in cancer cells; and other compounds like spisulosine from the clam *Spisula polynyma*), zalypsis from the nudibranch *Joruna funebris*, and aplyronine A from the sea hare *Aplysia kurodai* which are potent cytotoxic agents. There are also natural antioxidants from molluscs, including polyphenols, peptides, and PUFAs which combat oxidative stress by scavenging free radicals. Examples include astaxanthin from octopus and cuttlefish (Eghianruwa et al., 2019a; Ngandjui et al., 2024).

The general consensus among researchers in the field is that traditional knowledge of coastal and indigenous communities who have used molluscs for food and medicine for centuries could provide invaluable leads for targeted scientific investigation. This was the basis of our investigations. This particular charge was led by Queensley Eghianruwa for her Ph.D. project which I co-supervised with Kenyan collaborators at PAUSTI in JKUAT, followed a little later by Paul Abraham and Grace Oparinde for their M.Sc. projects here in Obafemi Awolowo University. The projects were funded by JICA and the AU through PAUSTI.

The studies aimed to evaluate the antioxidant, anti-inflammatory, analgesic, antimicrobial, and antiproliferative potential of various extracts from these organisms. Samples were procured from Oron Beach Market in Akwa Ibom State, Nigeria. Aqueous (phosphate-buffered saline) and Alcohol (acetone-methanol) crude extracts were prepared from the samples: TFAC- *T. fuscatus* alcohol extract, PAAC- *P. aurita* alcohol extract, TFAQ- *T. fuscatus* aqueous extract and PAAQ- *P. aurita* aqueous extract. The crude extracts were further fractionated by molecular sieve chromatography and ultrafiltration to isolate peptide fractions of varying molecular weights. The extracts and their peptide fractions from both mollusc species were tested for a wide range of significant biological activities across multiple *in vitro* and *in vivo* models.

Antimitotic Activity was probed using the *Allium cepa* (onion root tip) assay. Both aqueous and alcohol extracts of *T. fuscatus* and *P. aurita* demonstrated dose-dependent antimitotic activity as evidenced by a significant decrease in the mitotic index of actively dividing root cells. The extracts also induced various chromosomal abnormalities, including anaphasic bridges, c-metaphase, micronuclei formation, and vagrant chromosomes, indicating interference with the cell cycle (Eghianruwa et al., 2019b).

Antiproliferative activity was probed with assays against several human cancer cell lines including human prostate (DU145), breast

(HCC1395), and laryngeal (Hep-2) carcinoma, as well as a normal monkey kidney cell line (VeroE6) to determine selectivity. The alcohol extract of *T. fuscatus* (TFAC) was identified as the most potent and selective agent against the tested cancer cell lines (Table 5). Gene expression studies on Hep-2 laryngeal carcinoma cells revealed that TFAC's mechanism involves inducing apoptosis. It significantly upregulated the expression of key pro-apoptotic genes; P53, Caspase-3 and Caspase-8. The increases were 6.1, 48.3 and 5.1-fold respectively. This suggests that TFAC triggers programmed cell death through P53 and caspase-dependent pathways. The other extracts, while showing some antiproliferative activity, did not significantly alter the expression of these specific genes (Eghianruwa et al., 2019b).

Table 5. Potency and selectivity of Periwinkle extracts

Extract	Cell Line	IC_{50} (µg/ml)	Selectivity Index (SI)*
TFAC	DU145	96.48 ± 1.36	4.94
	HCC1395	61.44 ± 2.45	7.78
	Hep-2	0.52 ± 0.36	921.97
PAAC	HCC1395	78.41 ± 17.89	1.82
	Hep-2	52.79 ± 6.94	2.71
TFAQ	Hep-2	9.16 ± 0.69	51.36
PAAQ	Hep-2	91.52 ± 1.35	5.147

**A Selectivity Index (SI) greater than 3 is considered highly selective.*

Our studies also confirmed that the periwinkle extracts possess significant anti-inflammatory and peripheral analgesic properties, supporting their traditional use in treating wounds. In *in vitro* tests on lipopolysaccharide (LPS)-stimulated mouse peritoneal macrophages (Eghianruwa et al, 2022), both alcohol and aqueous extracts from the two species significantly inhibited the production of key pro-inflammatory mediators, including nitric oxide (NO), tumour necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and prostaglandin E2 (PGE2).

Analgesic potential was assessed in mice using two models; the tail flick test and the formalin test. None of the mollusc extracts showed activity in the tail flick test model, indicating they do not act on central pain pathways, while the formalin test induces a biphasic pain response. The extracts had no effect on Phase 1 (direct nerve stimulation) but produced a significant, dose-dependent reduction in pain-related behaviour during Phase 2a, which is driven by inflammation. This confirms a peripheral-acting analgesic mechanism (Eghianruwa et al., 2020).

Extracts of *T. fuscatus* were more effective analgesics than those of *P. aurita*, with the aqueous extract (TFAQ) being the most potent. The extracts demonstrated a high safety margin in acute toxicity tests, with doses up to 2000 mg/kg being non-lethal. However, at the highest dose of 2000 mg/kg, the alcohol extract of *P. aurita* (PAAC) caused single-cell necrosis in the liver and patchy tubular epithelial necrosis in the kidney. (Eghianruwa et al., 2020).

Protein hydrolysates derived from the periwinkles via simulated gastrointestinal digestion (SGID) were found to possess potent angiotensin-I-converting enzyme (ACE)-inhibitory activity, primarily attributable to low molecular weight peptides. ACE is a key target for hypertension treatment. Low molecular weight ($\leq$ 3 kDa) ultrafiltered permeates of the hydrolysates exhibited the strongest ability to inhibit ACE. *T. fuscatus* permeate (TFUFP) had an IC_{50} of 54.93 ± 2.83 µg/ml, while *P. aurita* permeate (PAUFP) had an IC_{50} of 65.2 ± 6.4 µg/ml (Paul et al., 2021a). The periwinkle extracts and their peptide fractions also demonstrated potent antioxidant capabilities across multiple assays. Alcohol extracts showed DPPH radical scavenging activity comparable to vitamin C, and a dose-dependent ability to reduce ferric ions in a Ferric Reducing Antioxidant Property (FRAP) assay. In addition, low molecular weight peptide fractions demonstrated remarkable metal-chelating ability, with IC_{50} values superior to that of the standard chelator EDTA and a high hydroxyl radical scavenging and an ability to inhibit lipid peroxidation. The $\leq$ 3 kDa peptide fractions were the most effective (Paul et al., 2021b).

Antimicrobial Potential of the periwinkle crude extracts were evaluated against ten bacterial isolates and the yeast *Candida albicans*. While aqueous extracts showed no antimicrobial effect against the tested microorganisms, alcohol extracts demonstrated broad-spectrum antibacterial activity at 100 mg/ml against five isolates: *Staphylococcus aureus*, *Bacillius stearothermophilus*, *Micrococcus luteus*, *Clostridium sporogenes*, and *Klebsiella pneumoniae*. They also inhibited *C. albicans*. Further analysis using TLC bioautography revealed that peptide fractions from the alcohol extracts exhibited bactericidal activity against the five susceptible bacterial isolates and bacteriostatic activity against *C. albicans* (Eghianruwa et al., 2019c).

Several analytical techniques were used to isolate and characterize the compounds responsible for the observed bioactivities. Isolation, using molecular sieve chromatography (Sephadex G100, LH20) and ultrafiltration (3 kDa cutoff) were the primary methods used to separate proteins and peptides based on molecular weight. Chemical Profiling by Fourier Transform Infrared Spectroscopy (FT-IR) analysis of the extracts confirmed the presence of functional groups characteristic of peptides, including Amide I (C=O stretch) and Amide II (N-H bending) bands, alongside alkanes, alkenes, and aromatic groups. SDS-PAGE and Thin Layer Chromatography (TLC) were used to generate unique peptide profiles, or "fingerprints," for the fractions from each mollusc species (Eghianruwa et al., 2019d).

We extended the mollusc study to investigate the antioxidant, cytotoxic and antibiofilm activities of the crude extracts and peptide fractions of another edible marine mollusc- *Thais coronata* (L.). This was Grace Oparinde's M.Sc. project, executed in collaboration with Iruka Okeke's laboratory in University of Ibadan. We prepared an aqueous extract (phosphate buffered saline, pH 7.2, 0.1 M), an acetone/methanol extract (TCM) and an acetone/ethyl acetate extract (TCE) of *Thais coronata*. The crude extracts and their fractions were investigated for ferric ion reducing power (FRAP), hydroxyl radical scavenging activity, total

antioxidant capacity, brine shrimp lethality activity, *Allium cepa* genotoxicity (antimitotic) activity and antibiofilm activity. Similar to what was obtained for the periwinkles, **t**he results of the assays indicated high activity in the crude extracts and fractions which were significantly ($p < 0.05$) different from the standards. The lower molecular weight (MW) fraction of the crude aqueous extract (TCA ≤ 3 kDa) exhibited a higher ferric ion reducing power than the aqueous extract (TCA) and the high molecular weight fraction (TCA > 3 kDa). The lower molecular weight (MW) fractions of both TCM and TCE also exhibited higher hydroxyl radical scavenging activity than their corresponding crude extracts and the standard (mannitol) with IC_{50} values ranging between 0.07115 ± 0.0331 mg/ml and 0.005254 ± 0.00175 mg/ml. TCA ≤ 3 kDa also had a higher cytotoxic activity (IC_{50} = 18.648 µg/ml) than the crude extract and TCA > 3 kDa with IC_{50} values of 59.950 and 25.706 µg/ml respectively. The peptide fractions (TCE B and TCE C) of the crude acetone/ethyl acetate extract displayed higher antimitotic activity than other fractions. Their antimitotic activity was found to be significant at concentrations ≥ 23.4 µg/ml and 4.52 µg/ml respectively. The results of the antibiofilm assay carried out on *T. coronata* crude extracts (TCA) and its fractions showed that the aqueous extract showed antibiofilm activity only against the *Staphylococcus aureus* ATCC 29213 (16.2 %) and *E. coli* ATCC 25922 (40.9 %). For the other isolates, the aqueous extract actually improved biofilm formation. It is therefore interesting that the crude acetone/ethyl acetate extract (TCE) inhibited the activity of three out of the five reference strains tested. Neither extract showed significant antibiofilm activity against *Pseudomonas aeruginosa* ATCC 27853 and *Salmonella Typhimurium* ATCC 14028, however there was promising, if variable activity against the *E. coli* strains, including the Enteroaggregative *Escherichia coli* strains (EAEC) tested.

This study concluded that the crude extracts and peptide fractions of *Thais coronata* possess antioxidant, cytotoxic and antibiofilm properties, which could protect cells from free radical accumulation and also serve as a potential anticancer/antibiofilm

drug candidate capable of blocking specific bacterial targets (Oparinde, 2023).

Taken together, these mollusc studies demonstrate that the whole-body extracts of *Tympanatonus fuscatus*, *Pachymelania aurita* and *Thais coronata* are rich sources of bioactive peptides with multifaceted therapeutic potential. The studies provide strong scientific validation for the traditional medicinal use of *T. fuscatus* in wound and ulcer treatment, given its demonstrated anti-inflammatory, analgesic, and antimicrobial properties.

The alcohol extract of *T. fuscatus* stands out as a particularly promising candidate for further anticancer drug development due to its high potency, selectivity, and its defined mechanism of inducing apoptosis. Furthermore, the potent ACE-inhibitory and antioxidant activities of low molecular weight peptides released during digestion highlight the potential of these molluscs as functional foods for preventing or managing cardiovascular diseases.

Future research is required to isolate, purify, and elucidate the structure of the individual peptides responsible for these effects. Conducting further *in vivo* studies will be crucial steps in translating these findings into novel therapeutic agents and health-promoting food products.

Fishy Business

Fishing is almost as old as other kinds of agriculture. As human populations grow, there is pressure on wild fish populations due to over-fishing. Fish farming, or aquaculture, complements fishing of wild populations and has been the fastest growing sector of animal food production in the world since 1970. *Clarias gariepinus*, or the African sharp-tooth catfish is a species of the family Clariidae, the airbreathing catfishes. The African catfish is cultured mainly in Africa and Europe. The African catfish is considered to be one of the most important tropical catfish species for aquaculture because of a number of characteristics/factors, among which are its good

meat quality, ability to tolerate adverse environmental conditions far better than other fishes do and its high growth rate even at high stocking densities. These factors contribute to its geometric rise in preference for commercial aquaculture.

Many nutritional benefits attributed to fish are particularly obtained from its exceptionally advantageous fatty acid profile. In recent years, increasing attention has been focused on the significance of polyunsaturated fatty acids in human nutrition, particularly eicosapentanoic acid (EPA) and docosahexaenoic acid (DHA) that are practically only found in fish. This increased attention is as a result of their positive effect in ameliorating some disease conditions, especially cardiovascular diseases. The -3 polyunsaturated fatty acids (PUFAs) also play a vital role in the development and function of the nervous system (brain) and the reproductive system. Eicosapentaenoic acid and docosahexaenoic acid, along with other monounsaturated and polyunsaturated fatty acids have demonstrated benefits in the prevention and treatment of cardiovascular diseases, stroke, lupus nephropathy, hypertension, rheumatoid arthritis, breast cancer, colon cancer, prostate cancer, autoimmune diseases, preventing unhealthy weight loss in cancer patients, eye sight and the improvement of learning ability. EPA and DHA are particularly proven to be precursors of eicosanoids, which are involved in several metabolic processes of the human body (Kris-Etherton et al., 2002). At the time we got involved in our laboratory, most of the work done on the nutritional value of our fishes focused primarily on proximate analysis. While this is an important factor of nutrition, it does not directly address the health value of the fish, with respect to its fatty acid profile. We therefore did a comparative study on the African Catfish (*Clarias gariepinus*) with the aim of providing insight into how environment and diet (wild vs. cultured) affect nutritional value, specifically the lipid and fatty acid profiles (Taiwo et al., 2014).

Proximate analysis of muscle tissue showed no statistically significant differences between wild and cultured catfish,

establishing both as nutritionally valuable (Table 6). Both varieties fall into a high-protein (18-20%) and low-oil (<5% muscle fat) category, classifying them as lean fish. Fat content in the liver (7-8%) was significantly higher than in the muscle (4-5%), which is characteristic of lean fish that primarily store lipids in the liver.

Table 6. Proximate composition (%) of muscles of the cultured and wild African catfish, *Clarias gariepinus*.

Parameter	Cultured Catfish (Mean)	Wild Catfish (Mean)
Moisture	75.58%	77.83%
Ash	1.20%	1.20%
Crude Protein	19.33%	18.76%
Muscle Lipid	4.39%	4.68%
Caloric Value	1200.8 cal/g	1204.4 cal/g

While chemically similar in proximate terms, the fatty acid profiles of muscle lipids revealed significant, nutritionally relevant differences, with the wild catfish showing a healthier composition. This variation is attributed to the diverse natural diet of wild fish (plankton, plant matter) compared to the controlled feed used in aquaculture. The wild catfish demonstrated superior levels of beneficial polyunsaturated fatty acids (PUFAs), particularly omega-3s (Table 7).

Table 7. Fatty acid profiles of Lipids Extracted from the Cultured and Wild Variety of the African Catfish, *Clarias gariepinus*.

Fatty Acid Parameter (%)	Cultured Catfish	Wild Catfish	Nutritional Significance
Total SFA	38.86%	36.96%	Lower is generally preferred.
Total MUFA	42.83%	41.57%	Similar levels.
Total PUFA	18.31%	**21.47%**	Higher is better.
Total Omega-6 PUFA	**12.01%**	11.85%	Higher in cultured.
Total Omega-3 PUFA	6.30%	**9.62%**	Significantly higher in wild.
EPA + DHA	6.15%	**9.51%**	Key omega-3s, higher in wild.
Omega-3: Omega-6 Ratio	0.52	**0.81**	Higher ratio is healthier.
DHA: EPA Ratio	7.42	**16.94**	Higher ratio is beneficial for health.

In a second and related study, another member of my research group is studying genetic adaptation to environmental stress in Cichlids. Tilapias, perhaps the second most important cultured fish in Nigeria are cichlids. It is a culinary favourite with many, thus profitable for aquaculturists. The cultured tilapias grow big rather quickly. However, they do not have the hardiness of their wild-type cousins or the cat fishes. This could mean financial disaster for the fish farmer as they tend to die off rapidly when exposed to stress. Samples were collected from two locations characterized by different salinity levels, using a stratified random sampling strategy. We collected from brackish water at Badore Jetty, Lagos State, Nigeria (average salinity: 29.06 ± 0.68‰); and from a freshwater habitat at Erinle River, Osun State, Nigeria (average salinity: 0.5 ± 0.2‰).

Morphometric analysis revealed distinct species distributions influenced by the environment. There was consistent expression of the target cytokine genes across all species and environments. Among other things, our findings so far reveal significant genetic variation in immune-related genes, such as Tumor Necrosis Factor-alpha (TNF-α) and Tumor Necrosis Factor-beta (TNF-β) in the wild tilapia populations, which serves as a molecular basis for their adaptation to environmental stressors like salinity. The core of the genetic investigation revealed that Single Nucleotide Polymorphisms (SNPs) within the coding regions of TNF genes are the primary molecular basis for the observed variations in stress adaptability among tilapia populations and species. Work is ongoing to further elucidate these variations.

A critical discovery is a unique Single Nucleotide Polymorphism (SNP) in the freshwater tilapia *Coptodon zilli*. This mutation results in a truncated TNF-α protein. This significant structural alteration is proposed to be the molecular basis for the recognized high stress adaptability of *C. zilli*, suggesting that the SNP provides a physiological advantage in its native freshwater environment. This genetic diversity in the wild fish, which distinguishes them phylogenetically from more homogenous aquaculture species like

Oreochromis niloticus, presents a potential resource for improving farmed stocks (Bawa, 2022).

Studies on Abrus precatorius

Mr Vice chancellor Sir, another one of the Ph.D. students co-supervised by Prof. Onajobi and I championed our examination of this well-studied plant. His thesis is titled "Cytotoxic and Antiproliferative Activities of Fractions and Isolated Compounds of *Abrus Precatorius* Linn. Root against Selected Cancer Cell Lines". At the critical point of needing access to cell culture facilities and structural elucidation of the compounds isolated from the plant, he was fortunate to get an ICCBS-TWAS fellowship from World Academy of Sciences for the advancement of Science in Developing Countries (TWAS), Trieste, Italy, for a research visit to the H.E.J. Research Institute of Chemistry, ICCBS, University of Karachi, Karachi, Pakistan. This was truly divine intervention as it enabled us to tease out a lot more from the work than we would have otherwise been able.

Abrus precatorius, a member of the Fabaceae family, is a woody, climbing shrub found in tropical regions, including Nigeria. It is commonly known as rosary bean, crab eye or jequirity bean. Here in Nigeria, it is known by various local names, including: Oju ologbo (Yoruba), Otuobiribiri (Igbo-Ohafia), Anya nwamba (Igbo) and Idon zakara (Hausa). The plant has extensive use in traditional medicine. Various parts are used to treat a wide range of ailments, such as diabetes, skin infections, rheumatism, malaria, typhoid, respiratory infections, hepatitis, jaundice, ulcers, and tumours. Powdered seeds have been used as oral contraceptives, and hot water extracts of the roots are administered for malaria and convulsions.

Pulverized roots were subjected to crude extraction with 70% methanol. This crude extract was then partitioned using solvents of increasing polarity to yield n-hexane, ethyl acetate, n-butanol, and aqueous fractions. Consistently, the ethyl acetate and n-butanol fractions demonstrated high levels of biological activity across

various assays. Phytochemical screening revealed the presence of various chemical classes, including flavonoids, triterpenes (lupeol, α-amyrin), alkaloids, glycosides, and aromatic carboxylic acids. Systematic bioassay-guided fractionation of the methanol root extract led to the isolation and characterization of numerous bioactive compounds, primarily a class of rare isoflavanquinones known as abruquinones (Okoro et al., 2021). Seven of them, Abruquinone A, B, D, E, F, G, and I were previously known, but four, Abruquinones M, N, O, and P (1-4) were previously undescribed compounds (Fig.8).

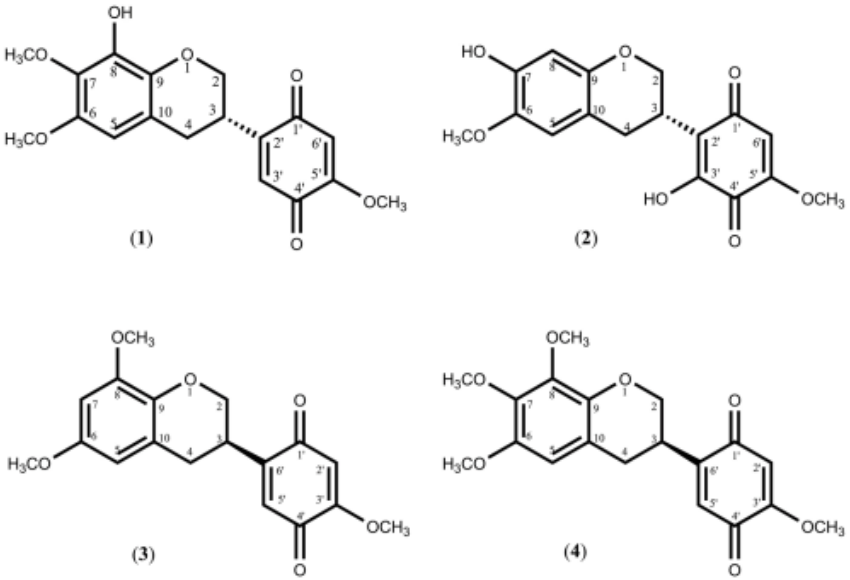

Fig.8. Structures of the novel abruquinones, M, N, O and P isolated from A. precatorius root (Okoro et al., 2021)

Antiproliferative and anticancer activities

The fractions and isolated compounds from *A. precatorius* roots demonstrated significant and selective cytotoxic activity against a range of human cancer cell lines (Okoro et al., 2019a). Considering solvent fractions, the ethyl acetate fraction: Showed the most significant antiproliferative activity against human breast adenocarcinoma (AU565) cells (IC_{50} 18.10 µg/mL) and cervical cancer (HeLa) cells (IC_{50} 11.89 µg/mL). The hexane fraction was

significantly active against HeLa cells (IC_{50} 18.24 μg/mL) while the aqueous fraction exhibited mild inhibition of AU565 cell proliferation (IC_{50} 46.46 μg/mL). Importantly, none of the fractions showed cytotoxicity against normal NIH-3T3 murine fibroblast cells, indicating a selective effect against cancer cells.
Screening against the isolated compounds was even better, showing potent activity against various cancer cell lines, with results suggesting potential for targeted therapies (Table 8).

Table 8. Anticancer and antiproliferative activities of the abruquinones

Compound	Cancer Cell Line	Type	IC_{50} (μM)
Abruquinone M	CAL-27	Oral Squamous Cell Carcinoma	6.48 ± 1.35
	Caco-2	Colorectal Adenocarcinoma	15.79 ± 5.93
	NCI-H460	Lung Carcinoma	31.33 ± 5.93
Abruquinone N	CAL-27	Oral Squamous Cell Carcinoma	5.26 ± 0.59
	Caco-2	Colorectal Adenocarcinoma	10.33 ± 0.22
Abruquinone A	Caco-2	Colorectal Adenocarcinoma	8.66 ± 0.49
	AU565	Breast Adenocarcinoma (ER+)	29.98 ± 0.02
	MDA-MB231	Breast Adenocarcinoma (Triple-Neg)	10.04 ± 0.70
Abruquinone B	CAL-27	Oral Squamous Cell Carcinoma	1.27 ± 0.07
	NCI-H460	Lung Carcinoma	0.79 ± 0.22
	AU565	Breast Adenocarcinoma (ER+)	23.13 ± 1.60
	MDA-MB231	Breast Adenocarcinoma (Triple-Neg)	9.05 ± 0.65

Antimicrobial and Antiparasitic Properties

The plant extracts and their constituents show a broad spectrum of activity against protozoan, fungal, and bacterial pathogens. Very significantly, *A. precatorius* demonstrates potent activity against

the protozoa responsible for cutaneous leishmaniasis, *Leishmania major*. The crude extract had IC_{50} 22.20 µg/mL, n-hexane fraction had IC_{50} 19.35 µg/mL, and the ethyl acetate fraction was particularly potent with IC_{50} 6.32 µg/mL.

The pure compounds Abruquinone A and B showed significant, potent activity against both *L. major* and *L. tropica*. Abruquinone A had IC_{50} 6.35 µg/mL against *L. major* and 6.29 µg/mL (*L. tropica*). Abruquinone B had IC_{50} 6.32 µg/mL against *L. major* and 6.31 µg/mL against *L. tropica* (Okoro et al., 2019b). This is the first time these compounds were ever shown to be active against cutaneous leishmaniasis.

The ethyl acetate fraction also showed moderate activity against two key pathogenic fungi involved in dermatology infections, *Microsporum canis* with 42.5% inhibition and *Fusarium solani* with 55.0% inhibition. Other fractions were inactive against the tested fungi.

With respect to antibacterial activity, the crude, n-hexane, ethyl acetate, and n-butanol fractions all showed significant (>60%) growth inhibition against *Bacillus subtilis* and *Staphylococcus aureus*. However, none were active against the tested gram-negative bacteria (*E. coli*, *P. aeruginosa*, *S. typhi*). Isolated abruquinones were tested, and showed significant inhibitory activity against a multidrug-resistant (MDR) *S. aureus* (NCTC 13277). Atomic Force Microscopy (AFM) revealed that the abruquinones induce significant morphological damage to the bacterial cell surface, including membrane segmentation, hole formation, invaginations, and cytoplasm leakage, leading to cell death (Okoro et al., 2022).

Anti-inflammatory and Immunomodulatory Effects

The compounds exhibit potent anti-inflammatory potential by modulating key components of the immune response, such as oxidative burst and cytokine production. The methanolic crude and ethyl acetate fractions potently inhibited reactive oxygen species

(ROS) production in whole blood. Abruquinone M, N, A, and B, all demonstrated significant inhibition of ROS produced from human whole blood phagocytes and isolated polymorphonuclear cells (PMNs), with IC_{50} values mostly below 10 μM. Abruquinones A and B were the most active. Solvent fractions, as well as the isolated abruquinones M, A, and B also strongly inhibited the pro-inflammatory cytokine (TNF-α). It was the same with inhibition of Nitric Oxide (NO), as fractions potently inhibited NO production with IC_{50} values of < 1 μg/mL (Okoro 2019a).

Urease, a nickel-dependent metalloenzyme found in plants, some bacteria, and fungi, catalyzes the hydrolysis of urea to form ammonia and carbon dioxide, providing these organisms with a source of nitrogen for growth. In pathogenic bacteria, urease is a virulent factor essential in the colonization of host organisms and maintenance of bacterial cells in tissues and is responsible for urolithiasis, acute pyelonephritis, ammonia encephalopathy, gastritis, as well as hepatic coma. Identifying potent urease inhibitors especially from natural product sources bearing a variety of scaffolds that decrease the ureolytic activity of ureases from different organisms has reinvigorated research interest in recent times in the quest to design new first line treatments for infections caused by urease-producing microorganisms. All tested fractions significantly inhibited urease, with the butanol fraction being the most potent (IC_{50} 12.0 ± 0.48 μg/mL). Isolated abruquinones A and B had IC_{50} of 37.7 ± 1.10 μM and IC_{50} of 35.2 ± 1.68 μM respectively. Molecular docking studies revealed that Abruquinone A and B bind tightly within the active site of the urease enzyme. The interaction is stabilized by hydrogen bonds with the residue His222 and π-cation interactions with His324, competitively inhibiting the enzyme (Okoro et al., 2022).

The collective findings from these studies strongly establish the roots of *Abrus precatorius* as a rich source of bioactive isoflavanquinones (abruquinones) with diverse and potent therapeutic properties. The consistent efficacy and selectivity

against pathological targets, with low toxicity to normal cells, underscore the potential of these compounds for further drug development. Furthermore, these studies provide a scientific rationale for the plant's traditional medicinal uses. The broad-spectrum activity—spanning anticancer, anti-inflammatory, antileishmanial, antifungal, antibacterial, and anti-urease effects suggests these compounds could address complex health challenges, including multidrug resistance and opportunistic infections in cancer patients. Future in vivo studies, is warranted to further elucidate the mechanisms of action and advance these natural products towards clinical application.

The leishmanicidal activity of our compounds from *A. precatorius* is particularly noteworthy. Leishmaniasis, one of the neglected tropical diseases, is a parasitic disease caused by genus Leishmania and transmitted via the bite of various species of sandflies. More than 20 species have been shown to be pathogenic in mammals, with affected hosts including domesticated and sylvatic animals presenting four main clinical syndromes: cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis (MCL), visceral leishmaniasis/kala azar (VL), and post kala azar dermal leishmaniasis (PKDL) (Advait et al. 2014). Cutaneous leishmania caused by *Leishmania major*, *Leishmania tropica*, *Leishmania mexicana*, and *Leishmania braziliensis* is the second most severe form of Leishmaniasis, and is prevalent in Southwest Asia, Middle East, Central Asia, Africa, Southern Europe, Central, and Southern America. It has contributed to considerable global mortality, with reported 0.7 to 1.2 million cases (75%) occurring each year (Alvar et al. 2012). Despite the rise in the prevalence of this disease, available treatment drugs are inadequate and present with deleterious side effects, and resistance, hence the need for drug repurposing and novel drugs from natural product sources.

White death and Garcinia kola

White death disease is an old nickname for tuberculosis (TB), a contagious infectious disease caused by *Mycobacterium tuberculosis* (MT), a bacterium. It was called commonly

consumption, white death or white plague due to the pale complexion of sufferers, along with a chronic, debilitating cough. Symptoms can include chronic cough, fever, night sweats, and weight loss, but it was historically widespread, causing significant death before the cause and treatments were understood. *Mycobacterium tuberculosis*, the causative organism has almost been a permanent challenge over the course of human history. There are more than 10 million new cases of TB each year as almost one third of the world's population are carriers of the TB bacillus and are at risk for developing active disease. Due to its infectious nature, complex immunological response, chronic progression and the need for long-term treatment, TB has always been a major health burden. In cases of HIV, TB takes advantage of the depressed immune system and appears as an opportunistic co-infection. Multi-drug resistant forms have emerged (Berberis et al., 2017).

The standard treatment for TB is a multi-drug, short-course chemotherapy regimen administered for a minimum of six months. The combination of Isoniazid (INH) and Rifampicin (RIF) forms the cornerstone of this therapy. While effective in curing approximately 90% of cases, this prolonged treatment is frequently associated with adverse effects, with neurotoxicity and hepatotoxicity being among the most severe. Late diagnosis and failure to adhere to treatment schedules are major drivers of treatment failure, relapse, and the emergence of multi-drug-resistant tuberculosis (MDR-TB). INH is metabolized in the liver, primarily through acetylation and hydrolysis, into toxic metabolites such as hydrazine (HZ) and monoacetyl hydrazine. RIF acts as a potent inducer of cytochrome P450 enzymes (specifically CYP2E1). This induction accelerates the metabolism of INH, leading to an increased production of its toxic metabolites. These toxic metabolites generate highly reactive oxygen species (ROS), which overwhelm the liver's natural antioxidant defenses. This state of oxidative stress leads to lipid peroxidation, damaging of cell membranes and widespread cellular injury.

One evening in early 2012 during a coffee break, Efere Obuotor, Andy Fakoya and I had a conversation around TB and its woes. We decided to design a study to test the story we had heard that *Garcinia kola* (bitter kola or orogbo), a plant widely used in African traditional medicine for treating liver disorders could help. Our study was in two parts; the first, to explore neurotoxic effects induced by the combined administration of INH and RIF on the cerebral cortex of adult Wistar rats and the second to investigate the hepatotoxicity occasioned by this therapy and to see if and how it is mitigated by garcinia cola.

We were able to report in Fakoya, Osoniyi & Obuotor, 2013, that chronic administration of INH and RIF in Wistar rats induces sub-clinical neurotoxicity. Despite the absence of observable clinical symptoms like ataxia or weakness, immunohistochemical analysis of the cerebral cortex showed significant microstructural damage. This was evidenced by astrogliosis (a reactive response of astrocyte cells to brain injury, indicated by high GFAP expression) and widespread apoptosis (programmed cell death, indicated by TUNEL staining). These findings suggest that the drugs cause underlying neurological damage even when no overt symptoms are present. Ogono, took on the second half of the study for his M.Sc. project under my supervision. We found significant liver damage characterized by elevated liver enzymes, severe oxidative stress, reduced antioxidant capacity, and cellular necrosis on treatment with combines INH and RIF administration. We were also able to report that co-administration of an ethanol extract from the seeds of *Garcinia kola* along with the anti-tubercular drugs significantly mitigated the damage. Co-treatment with *G. kola* significantly reduced the plasma levels of ALT, AST, ALP, and bilirubin that were elevated by the antitubercular drugs. The extract effectively countered the oxidative stress induced by the drugs. It reversed the depletion of antioxidant enzymes (GSH, SOD, CAT, GPx) and significantly lowered the elevated MDA levels. Histomorphological analysis showed remarkable protection of the liver's structure (Ogono et al., 2014).

These studies highlight the potential of using a simple, readily accessible plant extract, or perhaps the seed itself to combat the harmful side effects of essential antitubercular drugs. By mitigating hepatotoxicity, co-administration of *G. kola* could improve patient adherence to long-term TB treatment regimens. This, in turn, would enhance treatment efficacy, reduce the risk of relapse, and help prevent the development of drug resistance.

Therapeutic potential of Tetrapleura tetraptera (Aridan) in Cadmium toxicity.

In 2023, I did a collaborative study with colleagues at Chrisland University, taking another look at *Tetrapleura tetraptera*. Our previous studies had shown us that the pod had additional bioactivities worth exploring.

Cadmium (Cd) is a non-essential transition metal that has become a widespread environmental toxicant due to industrial activities such as metal plating, and the manufacturing of batteries, pigments, and plastics. Its bioaccumulation in plants and water leads to exposure in animals and humans through oral intake and inhalation. The primary mechanisms of cadmium toxicity are the induction of oxidative stress, lipid peroxidation, DNA damage, and mitochondrial dysfunction. Cd has a long biological half-life, leading to slow elimination from the body. Its accumulation is linked to severe health issues, including neurotoxicity, organ damage, reproductive dysfunction, and abnormal cell proliferation. Research using fruit fly, *Drosophila melanogaster* has also shown that toxic effects can be transferred to subsequent generations.

Tetrapleura tetraptera is a medicinal plant of the Fabaceae family. Its fruit is recognized for being rich in multivitamins and phytochemicals, particularly polyphenols. It is traditionally used as a spice and therapeutic agent. It has demonstrated a wide range of biological activities, including antioxidant, anti-inflammatory, anti-diabetic, anti-proliferative, and hypotensive properties. Our study hypothesized that its hydro-ethanol extract could ameliorate cadmium-induced toxicity. The fruit fly, *Drosophila melanogaster*,

was selected as the in vivo model for this study due to several reasons. It shares 60% genetic homology with humans, and approximately 75% of genes responsible for human diseases are conserved in the fly. Its short life span and high fecundity make it a highly efficient model for toxicological and generational studies compared to rodents; and its use involves little to no ethical concerns, compared to rodents. The study employed a combination of *in vivo* toxicological assays and computational analysis to evaluate the effects of *Tetrapleura tetraptera* extract on $CdCl_2$-induced stress. The main findings are that $CdCl_2$ exposure significantly harms the organism by increasing markers of oxidative stress, inhibiting crucial detoxification enzymes, and reducing survival and fertility. Specifically, $CdCl_2$ increased levels of lipid peroxidation (LPO) and hydrogen peroxide (H_2O_2) while suppressing glutathione-S-transferase (GST) activity.

Crucially, co-treatment with the *T. tetraptera* extract successfully counteracted these toxic effects. The extract significantly reduced the $CdCl_2$-induced elevation of LPO and H_2O_2, restored GST activity, and increased levels of protective thiols at higher doses. Furthermore, *T. tetraptera* improved the rate of offspring emergence, mitigating the negative reproductive impact of cadmium.

Computational analysis identified numerous bioactive compounds in the *T. tetraptera* extract, including potent antioxidants like gamma-tocopherol, squalene, phytol (a precursor to Vitamins E and K) and various fatty acids and their esters (e.g., Linoleic acid ethyl ester, Ethyl oleate). Molecular docking simulations revealed that these compounds, particularly gamma-tocopherol, exhibit a high binding affinity for the GST protein potentially activating the GST enzyme, resulting in activation of the GST detoxification pathway. This enhanced activity facilitates the conjugation and neutralization of electrophilic compounds and free radicals generated by cadmium toxicity, thereby reducing oxidative damage to cellular components. Further molecular studies will be required to fully elucidate these mechanisms. The study concludes that the

hydro-ethanolic extract of *Tetrapleura tetraptera* pods effectively ameliorates cadmium chloride-induced oxidative stress in *Drosophila melanogaster*. It may also be beneficial in similar cases of heavy metal toxicity in areas suffering the hazards of mining precious ores (Oyibo et al., 2025).

Biological Approach to Weed and Pest Control: Bioherbicides and Bioinsecticides.

Modern agriculture depends a lot on chemical inputs like fertilisers, herbicides and pesticides. Accumulation of those chemicals in the environment and the food chain is an on-going concern. It is therefore necessary to develop bioherbicides, that will be biodegradable and environment-friendly. This informed a series of studies in our research group on plants that demonstrate the ability to inhibit the growth of other plants near them. Over a period of about 6 years, from 2011 – 2016. We studied extracts from *Dioscorea dumetorum* tubers (Usman et al., 2014; Ogunlola, 2014), leaf extracts of *Costus afer* (Olasebikan 2016) and leaf extracts of *Hilleria latifolia* (Popoola, 2016).

Dioscorea dumetorum, also known as bitter yam, cluster yam, trifoliate yam (èsúrú in Yoruba) is a species of yam widely consumed in Nigeria and anecdotally believed to inhibit the growth of competing plants. While many plants are known sources of medicinal agents, with 70-80% of the world's population relying on traditional plant-derived medicine, empirical evidence for *D. dumetorum*'s growth-inhibiting properties was lacking. The primary objective of our research was to scientifically investigate and quantify the allelopathic, genotoxic, and cytotoxic effects of *D. dumetorum* tuber extracts. The ultimate goal was to assess the plant's potential as a source for developing natural (bio)herbicides and anti-tumour compounds. We explored three key bioactivities related to our objectives;

1. Allelopathy, the chemical inhibition of one plant by another through the release of allelochemicals into the environment. These allelochemicals can inhibit germination or damage the growth of neighbouring plants.

2. Genotoxicity, any process that alters the structure, information content, or segregation of DNA. Genotoxicity tests are a key component in the risk assessment of chemicals like herbicides, and
3. Cytotoxicity, the quality of being toxic to living cells. Many plant-derived compounds with cytotoxic properties, such as vinblastine and vincristine from *Vinca rosea*, have been successfully developed into anti-cancer drugs.

The extracts from *D. dumetorum* demonstrated strong allelopathic properties, affecting both seedling growth and seed germination in a dose-dependent manner. Hexane extracts showed potent and irreversible inhibitory effects. At all concentrations tested. Test seedlings began withering by day 6 and were killed completely by day 11. Methanol extracts exhibited a weaker, temporary effect. Seedlings appeared wilted by day 6 but had recovered completely by day 11 at all concentrations tested, suggesting the plants were able to overcome the extract's effects. The *Allium cepa* test revealed that the extracts were genotoxic, capable of inhibiting cell division and causing direct damage to chromosomes. Microscopic analysis of the onion root tip cells exposed to the extracts revealed seven distinct types of chromosomal damage that were absent in the control group. The mitotic index (MI), an indicator of cell proliferation, was significantly reduced by the extracts, indicating an inhibition of cell division. Analysis of the treated onion roots showed classic signs of chemical-induced stress, indicated by changes observed in proline, total soluble sugar and protein content. The brine shrimp lethality assay confirmed that both extracts are cytotoxic. The hexane fraction was nearly twice as potent as the methanolic extract and a positive control.

The study provided strong empirical evidence that tuber extracts of *D. dumetorum* possess potent allelopathic, genotoxic, and cytotoxic properties, confirming the plant's anecdotal reputation for inhibiting the growth of other plants. The powerful, dose-dependent inhibition of seed germination and seedling growth makes *D. dumetorum* a viable candidate for further exploration in

the development of natural, biodegradable herbicides for weed control. The demonstrated ability of the extracts to inhibit cell division (reduced mitotic index), induce DNA damage (chromosomal aberrations), and kill cells (cytotoxicity) correlate very strongly with anti-cancer activity. This implies that *D. dumetorum* may also be a promising source for isolating novel plant-derived anti-tumour compounds.

The findings from the *D. dumetorum* project is mirrored to different extents by the *Costus afer* and *Hilleria lattifolium* studies.

It is commonly understood that weeds and pests are twin nemesis for food security. In the same season that we looked towards developing bioherbicides, we also investigated the possibility of insect pest control by manipulation of the diet. We chose the housefly as our model insect in this study anchored by Ibukun Abulude for his M.Sc. project under my supervision. Prof. O. J. Soyelu from the faculty of Agriculture was our main collaborator.
The common house fly, *Musca domestica*, is more than just a household annoyance. It is a well-known vector for a host of dangerous pathogens, capable of transmitting diseases like anthrax, cholera, and typhoid fever. The primary method for controlling these pests has been the application of synthetic insecticides. However, similar to the problem with synthetic herbicides, there are significant drawbacks, including the rise of pesticide resistance in flies and the risk of environmental pollution. We hypothesised that we could use the diet to make them weaker and weaker, and ultimately shorten their lifespan. We chose to use a high-fat diet. We started with the optimal diet for house flies, a 4:1 carbohydrate-to-protein mixture of rice and fish. We then created new diets from the base diet by adding lipid sources like lard and fish oil. The results were complex and revealing. When lipids were added but the protein source was removed, the resulting adult flies were significantly smaller and lighter. This is a clear sign of malnutrition. However, when lipids were added to the complete carbohydrate-protein diet, the flies were actually heavier than those on the standard diet. Despite their added weight, there was a

universal negative impact on longevity. The standard rice-and-fish diet produced flies with a median lifespan of 17 days. In contrast, all high-fat diets slashed this figure, reducing median longevity to between 11 and 13 days. This shows that while some high-fat diets can pack on weight, they do so at the cost of the fly's overall health and lifespan. These results were not entirely surprising. The flies do not require the same fatty acids we do for fuel; they primarily need specific sterols for functions like moulting. Thus, loading their system with the wrong kind of fat is very harmful to them, as shown by the reduction of median longevity.

While both lard and fish oil had a negative impact on the flies, we found that diets formulated with fish oil were particularly effective at reducing their adult lifespan. The most potent diet for shortening lifespan was one that combined all three ingredients, rice, fish, and fish oil. Flies on this diet had a median longevity of just 11 days. This showed that addition of fish oil to an otherwise complete diet actively harms the flies, making it a fascinating candidate for developing highly targeted baits. Our analysis revealed that the lipid-containing diets led to higher levels of oxidative stress markers, specifically catalase and malondialdehyde, resulting in cellular damage. If left unchecked, oxidative stress results in cumulative oxidative damage to DNA, RNA and proteins within the cell, resulting ultimately in ageing. This cellular damage is the explanation for why the flies on high-fat diets aged faster and died younger (Abulude et al., 2019).

The study points to the possibility of pest control using these "unsuitable" high-fat diets as baits in areas with heavy fly infestations, such as abattoirs. The strategy would involve combining the fatty diet with sugar sprays to attract adult flies. The flies would then use the bait as a food source and a place to lay their eggs. Larvae hatching from these eggs would consume the high-fat diet, leading to a new generation of weaker flies with shorter lifespans. The result would be a self-perpetuating cycle where each generation is progressively less fit, causing the local population to decline significantly without the use of harsh

chemical insecticides. It is a simple solution that can be adapted to every insect pest, dealing with pest control in an eco-friendly way.

Lassa virus studies

Adetunji Adesina did his M.Sc project titled "Phylogenetic Analysis of Lassa Virus Genetic Sequences Obtained from *Mastomys natalensis* in Edo and Ondo States, Nigeria" in 2016, and followed with a Ph.D. project titled "Molecular characterization of Lassa virus strains and rodent host species in endemic foci for Lassa fever between North-Central and Southern Nigeria" in 2021. The projects were co-supervised with Prof. Ayo Olayemi of the Natural History museum and part-funded by the Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany.

Lassa fever (ìbà ọ̀rẹ̀rẹ̀ in Yoruba) is a zoonotic rodent-borne disease resulting in massive hospitalization of people and about 18,000 deaths annually across West Africa. In Nigeria, mortality from this disease has continued to increase in recent years. Rodents are natural reservoirs of the causative Lassa virus (LASV). The Natal multimammate mouse *Mastomys natalensis*, which is ubiquitous across sub-Saharan Africa, serves as the principal host. More recently, further taxa, including the Guinea multimammate mouse *Mastomys erythroleucus*, the African wood mouse *Hylomyscus pamfi*, and Baoule's pygmy mouse *Mus baoulei* have also been implicated as carriers (Olayemi et al., 2016; Yadouleton et al., 2019). In Nigeria, there is an almost yearly ritual of outbreaks and deaths from Lassa fever. The area spanning Nigeria's Edo and Ondo states is the most endemic for Lassa fever in the country. Research conducted between 2014 and 2019 confirms this zone as a hotspot of intense viral circulation within natural rodent populations. The principal LASV reservoir, *Mastomys natalensis*, is ubiquitous across the region and displays exceptionally high levels of active infection. This species was found in all seven localities sampled and showed active LASV infections (RNA-positive) in six of them. Prevalence rates were highly variable, ranging from 3.7% in Okhuesan to an extraordinary 75.5% (37/49

individuals) in Okeluse and 46% (13/28) in Owo (Adesina et al., 2023; Oyeyiola et al., 2025). These prevalence rates are significantly higher than those described in other West African hotspots, such as Faranah, Guinea (14.5%), southern Mali (7.7%), and Bo, Sierra Leone (1%). *Mastomys erythroleucus* primarily a savanna dweller, was found to be PCR-positive for LASV in Ebudin (16.2% prevalence) and Ekpoma (20% prevalence). This is the first time LASV Lineage II has been detected in *M. erythroleucus*, demonstrating that the virus can jump between *Mastomys* hosts more easily than previously thought. Some of these findings are reported in Igbokwe et al, 2019; Olayemi et al., 2018, 2020; Soubrier et al., 2022.

Summarily, some key findings from these studies are:

1. **Extreme Viral Prevalence in Rodent Reservoirs:** The Edo-Ondo region exhibits exceptionally high rates of active LASV infection in its primary rodent reservoir, the Natal multimammate mouse (*Mastomys natalensis*), with prevalence reaching as high as 75.5% in localities such as Okeluse. These rates are significantly higher than those reported in other West African hotspots.
2. **Expanded Host Range and Cross-Species Transmission:** The Guinea multimammate mouse (*M. erythroleucus*) is now confirmed as an active reservoir for LASV Lineage II within the Edo-Ondo axis, co-circulating with *M. natalensis*. Phylogenetic analysis indicates that the virus has jumped between these two syntopic species, with emergence in *M. erythroleucus* being more recent (c. 2005) than in *M. natalensis* (c. 1961).
3. **Rodent Abundance, Not Prevalence, Drives Human Risk:** Because LASV prevalence in rodents is consistently high year-round, the primary driver of human Lassa fever outbreaks is the seasonal peak in indoor rodent abundance. These infestation peaks are predictable but vary significantly by locality; for example, *M. natalensis* abundance peaks indoors during the dry season in the urban

town of Ekpoma but during the rainy season in the nearby rural village of Ebudin.

4. **Urban Centers as Hubs for Viral Dissemination:** Larger, more cosmopolitan towns like Ekpoma function as critical nodes in the spread of LASV. These urban centers, connected by major highways, exhibit greater genetic diversity of the virus. Communal living spaces, such as student hostels, serve as "hubs of anthropologically-aided, rodent-borne LASV variant admixture and diffusion."
5. **Evidence of Reverse Zoonosis:** Counterintuitively, time-calibrated phylogenetic analyses consistently show that LASV sequences derived from humans in key hotspots like Ekpoma are ancestral (i.e., older) to those found in local rodent populations. This finding raises the possibility of a more complex, bidirectional transmission cycle that includes reverse zoonosis (human-to-rodent transmission). This does not contradict the primary rodent-to-human route but calls for a "broader paradigm including infection in the reverse direction" to understand the full epidemiology of Lassa fever.
6. **East to West Progression**: Time-calibrated phylogenetic analysis of rodent-derived sequences indicates that LASV variants in Edo State (c. 1961) are ancestral to those in the more westerly Ondo State (c. 1977). This supports a broader east-to-west migration pattern of the virus across southern Nigeria.
7. **The threat of Host**-Switching. The continuous spillover of LASV into abundant, commensal, non-reservoir species poses a significant long-term risk of the virus adapting to a new host. Spillover to *Praomys daltoni* is a particular concern. It was the most abundant rodent captured in the Edo-Ondo study. It is a commensal species widespread across West Africa, and is phylogenetically close to the known *Mastomys* reservoirs (belonging to the same Praomyini tribe). The adoption of *P. daltoni* as a novel LASV reservoir is a potentially calamitous event that could drastically alter the epidemiology of Lassa fever.

These findings bring a better understanding of LASV ecology and transmission dynamics in Nigeria. They can help to shape a better response by the health authorities to Lassa fever outbreaks in Nigeria.

Evaluation of Spathodea campanulata Exudate for Anti-Cataract Activity

One morning in 2013, I saw the Office Assistant in the Department at the time, squeezing some liquid from a plant part into his eyes like one would use eye drops. I asked him about it, and he essentially described a "wonder drug" for treating all manner of diseases with the eye. Over a period of several weeks, I saw him use the same "eye drops" on his eyes. I saw no evidence of irritation other eye problems arising from this use. More serious conversation with him led me to consider serious empirical research on the plant. I put an M.Sc. student on this project. We benefited a lot from conversation with Prof. Toyin Onakpoya of the Department of Ophthalmology, and Prof. J. O. Faluyi of the Department of Botany, who actually collaborated with us on the project.

Cataract, characterized by the opacification of the crystalline eye lens, is the world's leading cause of blindness, with a disproportionately high incidence in developing nations. The condition disrupts the transmission of light to the retina, leading to blurred vision and eventual vision loss. While the etiology is diverse, numerous risk factors have been identified, including aging, diabetes, smoking, and excessive sunlight exposure.

A central mechanism implicated in cataractogenesis is oxidative stress. The lens is highly susceptible to damage from reactive oxygen species (ROS), which can trigger lipid peroxidation in cell membranes and cause the glycation, cross-linking, and aggregation of lens proteins. This compromises the micro-architecture of the lens, leading to osmotic imbalance, hydration, and ultimately, a loss of transparency. While the eye possesses natural enzymatic (e.g., SOD, CAT) and non-enzymatic (e.g., GSH) antioxidant

defenses, cataract develops when these protective systems are overwhelmed. Currently, the only effective treatment for cataracts is the surgical removal of the opacified lens and its replacement with an artificial one. Although the procedure is highly effective, it faces significant limitations, particularly in developing countries, due to the high cost, a scarcity of trained surgeons, and the risk of post-surgical complications. The failure of existing drugs to convincingly prevent or delay opacification is sufficient justification to explore alternative, non-surgical interventions. This was the attraction to our plant.

Spathodea campanulata, or the African tulip tree, is widely used in traditional medicine. It is called Mójútòrò by the Yoruba people, which literally translates to "something that clears the eyes". As observed, the exudate from its flower buds is commonly applied to the eyes as a local remedy, with anecdotal claims that it improves vision and prevents eye diseases. Until our study however, these claims had not been substantiated by scientific research. We therefore systematically evaluated the anti-cataract activity of *Spathodea campanulata* flower bud exudate. The primary objective was to determine if the exudate could protect against galactose-induced cataractogenesis in isolated rat lenses and to elucidate the potential biochemical mechanisms underlying its effects. Captopril, a commonly used drug in that context was used as a control.

The study employed an *in vitro* organ culture model using lenses harvested from healthy White Albino rats. Cataracts were induced by incubating the lenses for 72 hours in an artificial *aqueous humor* containing 30 mM galactose, a model that simulates the osmotic and oxidative stress associated with sugar-induced cataracts.

Morphological assessment of efficacy was done after the treatment period of 72 hours. Lenses were photographed on a grid to visually evaluate the degree of opacity and transparency. Lens homogenates were analyzed to quantify key biomarkers of oxidative stress and

antioxidant status, including: malondialdehyde (MDA), an indicator of lipid peroxidation; Total Protein (TP), to assess protein damage and leakage; Reduced Glutathione (GSH), a critical non-enzymatic antioxidant; Superoxide Dismutase (SOD), a primary antioxidant enzyme and Catalase (CAT), an enzyme that neutralizes hydrogen peroxide.

The results confirmed a potent, dose-dependent protective effect of the *S. campanulata* (SPCM) exudate against galactose-induced cataractogenesis. Photographic evaluation clearly showed the development of lens opacity in the Untreated Cataract (UC) group. In contrast, lenses in the High Dose (HD) SPCM group and the Captopril (CC) group retained a degree of transparency comparable to the Normal Control (NC) group, indicating that both treatments successfully retarded cataract formation. The Low Dose (LD) SPCM group showed a lower potency, with more opacity visible than in the HD and CC groups (Table 9).

Table 9. Effect of SPCM on rat lenses (Adapted from Adio, Faluyi and Osoniyi, 2014)

Biochemical Parameter	Untreated Cataract (UC) Effect (vs. Normal)	High Dose SPCM (HD) Effect (vs. Normal)	Captopril (CC) Effect (vs. Normal)	Interpretation
Malondialdehyde (MDA)	Increased to **300%**	Increased to **171.43%**	Increased to **142.86%**	SPCM and captopril significantly reduced lipid peroxidation and membrane damage.
Total Protein (TP)	Decreased to **85.56%**	Increased to **112.86%**	Restored to **94.06%**	SPCM and captopril mitigated protein damage and/or leakage from the lens.
Reduced Glutathione (GSH)	Decreased to **24.44%**	Restored to **57.7%**	Restored to **75.55%**	Both treatments helped preserve the lens's primary non-enzymatic antioxidant defense.

Superoxide Dismutase (SOD) Activity	Decreased to **50.49%**	Restored to **76.69%**	Restored to **64.08%**	High-dose SPCM was highly effective at preserving the activity of this crucial antioxidant enzyme, outperforming captopril.
Catalase (CAT) Activity	Decreased to **25.51%**	Restored to **80.61%**	Restored to **72.45%**	High-dose SPCM demonstrated superior protection of catalase activity compared to both the untreated group and the captopril-treated group.

The exudate was shown to work at three different levels:

1. **Retard Lens Opacification:** Visibly preventing the formation of cataracts at a level comparable to the reference drug, captopril.
2. **Combat Oxidative Stress:** Significantly reducing lipid peroxidation (MDA levels) in the lens.
3. **Preserve Antioxidant Defenses:** Preventing the depletion of reduced glutathione and restoring the activity of key antioxidant enzymes, SOD and CAT.

This study provided the first scientific validation for the traditional use of SPCM exudate in Nigerian ethno-medicine for improving vision and treating eye disorders. The findings establish the exudate as a valuable source of bioactive compounds with the potential for development into a non-surgical therapy for the prevention or treatment of cataracts (Adio, Faluyi and Osoniyi, 2014).

Complementary and weaning food – The Growstar Project.

Complementary Food (CF) is required for healthy nutrition in infants and young children (IYC) of ages 6-24 months as breast milk alone is no longer adequate in nutrients required for optimum metabolic support. Commercially produced CFs are expensive and local CFs are either poorly formulated (and) or inappropriately

processed. Therefore, the **GrowStar® – A weaning food for tropical children** project was initiated to develop cereal-legume based CF that is formulated and processed to meet the nutritional need of tropical IYC. The project resulted in nine different complementary foods, with very dynamic and novel nutritional features, collectively registered as **GrowStar® – A weaning food for tropical children**. The novelty of the research product, **GrowStar®**, attracted the award of *Utility Model Patent* (NG/PT/NC/2022/6305) dated 08/07/2022 under the Patent and Designs Act; CAP 344 Laws of the Federal Republic of Nigeria, 1990.

GrowStar – A weaning food for tropical children is a weaning food that is scientifically formulated from local grains and cereals and analytically evaluated to meet the basic nutrient needs of infants in the tropics, especially Nigeria. **GrowStar – A weaning food for tropical children** is a complementary food that is not intended to replace breast milk, but to complement it, with the target population being IYC. It contains adequate macronutrients and minerals, with very (tolerably) low antinutrients. The respective nutrient compositions of **GrowStar®** were comparable (and some cases, superior) to those of certain proprietary CFs.
GrowStar – A weaning food for tropical children, is more affordable than most branded infant formulae in the country, has a very low moisture level (below 5%) compared to related products and thus, guarantees longer shelf life and unfavorable condition for microbial invasion. Most local CFs are not as rigorously evaluated. The biological value and protein rating of **GrowStar – A weaning food for tropical children** have been analysed and verified using the Canadian protocol of evaluation and it meets recommended standard. **GrowStar – A weaning food for tropical Children** is easy to prepare and store and does not contain any mycotoxin associated with poor management of grains against other local products (Amah, 2022).

GrowStar – A Weaning Food for Tropical Children project contained an academic capacity building component that led to the

award of a Doctor of Philosophy (PhD) Degree in Biochemistry to AMAH Gogonte Hezekiah, now a Senior Lecturer at Babcock University, Ilisan-Remo, Ogun State, Nigeria.

It is hoped that **GrowStar – A weaning food for tropical Children** will contribute to winning the war against malnutrition among tropical infants within the complementary feeding window.

Miscellaneous projects

This is only a partial account of stewardship. I was fortunate to contribute to many other projects of serious significance. Those are perhaps stories for another day. These include Ojo, Osoniyi and Aboderin, 2002; and Ojo et al., 2006 which are part of a body of work attempting to accurately determine trace element status of Nigerians with sickle cell disease, and a dietary intervention in sickle cell disease. Siddhuraju et al., 2002 which looked at the effect of soaking and ionising radiation on food processing and preservation; and Iwalewa et al., 2007a; 2007b which are part of a body of work assessing some anti-malaria plants.

Other Contributions

Mr Vice Chancellor Sir, Ladies and Gentlemen, beyond research I have also had the opportunity to contribute to teaching and service at every level of the university and society at large. I have served the Faculty of Science and the University in various standing and *ad hoc* committees including, Centre for Distance Learning (2011), Directorate of Linkages and Sponsored Research (2012-2014). I have served as a member of Campus Aesthetic and Trading Regulatory Committee, CARTREC, and also as Deputy Director (2016-2018) and Acting Director of the Central Science Laboratory (2018-2020) among others.

Recommendation

Mr Vice Chancellor Sir, my research, like that of many other natural products researchers in this university has produced a lot of leads, which if followed can produce valuable products as bioherbicides, biopesticides, nutraceuticals and medicines. It is

therefore recommended that the university sets up a mechanism for investing in the raw product of research to the point of marketable product. This will be a huge source of revenue for both the university and researchers, and the society at large.

Closing

Mr Vice Chancellor sir, I believe God is not waiting to be surprised by what we might discover in our research. On the contrary, he allows us, like those proverbial children playing in their sandboxes to come up with interesting and beneficial things. It is up to us, to strengthen our ethical guardrails and regulatory frameworks, so that we will "play God" in a positive way for humanity.

In my research, I have had the privilege of discovering beautiful things concerning food, medicine and much more. It has been a pleasure to share some of that with you here today.

In the time left for us to contribute to research, teaching and service to humanity here, we are ready to ask and to receive more.

Acknowledgements and appreciation

I appreciate the contributions of all my teachers and mentors, starting from primary school to the present time. I sincerely thank the students I have had the honour of interacting with since I joined the university. I thank my colleagues for stimulating and vigorous discussions. I have been particularly blessed by the insight and generosity of my collaborators here in this university and across the world. I am also grateful for all the technical staff who have helped me over time. The data works because you worked.

I am especially grateful to my faith family – RCCG and NCGF. Thank you for being there for me and for my family all these years. I am grateful to my parents, of blessed memory, who looked beyond their own circumstances to a better future for my siblings and I. I thank God for their commitment, dedication and sacrifice. I thank God for my siblings and their spouses who have been a blessing to us. I am grateful for my other parents, Grandpa and

Grandma Ogundiran who have also supported my family in every way imaginable throughout this journey. I am equally grateful for the support of all the Ogundirans and their spouses.

I sincerely thank my wife, Olayinka Olufunke, who has sacrificed more than many can know, to strengthen us and support our family, my children, Joshua & Oluwaseun Ugba, Oluwaseyilayo, Inioluwa and Oluwafirewamiri, who knew and understood about Daddy being in the lab and working on projects long before they even started school themselves.
Finally, I give glory to God. Thank you for allowing me to be here, to partake of the wonders of your world, to dream and to play in the *sandboxes*, and to discover things of beauty and joy. Thank you for the privilege you have given me to share a bit of that joy and beauty with people in my world.

Mr Vice Chancellor Sir, Distinguished Ladies and Gentlemen, I thank you for your presence and kind attention.

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