UNIVERSITY OF ILORIN

THE TWO HUNDRED AND FIFTY-NINTH (259TH)
INAUGURAL LECTURE

"WHITE MATTER MATTERS IN THE SEARCH FOR PHYTOCHEMICAL CANDIDATES FOR DEMYELINATING DISORDERS"

By

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THURSDAY, 30TH MAY, 2024

This 259th Inaugural Lecture was delivered under the Chairmanship of:

The Vice-Chancellor

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30th May, 2024

ISBN: 978-978-8556-64-0

Published by:

The Library and Publications Committee,
University of Ilorin, Ilorin, Nigeria

Printed by
Unilorin Press, Ilorin, Nigeria

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My Lords, Spiritual and Temporal,
Distinguished Students of the College of Health Sciences,
Esteemed Invited Guests,
Gentlemen of the Press,
Great Students of the University of Ilorin,
Distinguished Ladies and Gentlemen.

Preamble

It is with all sense of humility and gratitude to God, the Omnipotent, Omnipresent and Omniscient, that I deliver the two hundred and fifty-ninth (259^{th}) inaugural lecture of the University of Ilorin. Vice-Chancellor sir, today's inaugural lecture is the third from the Department of Anatomy since the establishment of this University several decades ago.

Growing up as a child, my dream had always been to become a medical doctor. Hence, I chose MBBS and University of Ilorin for my Universities Matriculation Examination (UME) in 1993. Unfortunately, I was not offered this noble course, though I had a good score. Through appropriate guidance, I changed my course to Anatomy, a new course, which just started about two years before then, with Dr. Abayomi Odekunle (later

Professor) as the acting Head of Department. Although I undertook the B.Sc. Anatomy programme and completed it successfully on the 3rd March, 1999, it never occurred to me that I would build a career in Anatomy, as my dream of becoming a medical doctor was never aborted. I enrolled for the medical programme through Direct Entry immediately after my Youth Service, and by 3rdMarch, 2006, my childhood dream became a reality. I give God all the Glory for this.

Who would have thought a career in Anatomy should be the right path for a medical graduand! Of course I had got materials to prepare myself for the Primary Fellowship Examinations. It was King David that said in Psalms 37 verse 23: "*The steps of a good man are ordered by the LORD: and He delighted in his way*". God, Who knows all things, guided my path back to the course I started with even after working for three months at the Federal Medical Centre (FMC), Owo as a medical officer at the Surgery Unit. I am grateful to Dr. Leye Fadahunsi, a renowned (now retired) Obstetrician & Gynaecologist at FMC, Owo, who was instrumental to my employment there, and also for his understanding when I informed him of my intention to disengage and take up a lecturing offer at the University of Ilorin in August, 2008, despite the huge pay difference. I took up the appointment as a Lecturer II in August, 2008, during the leadership of Prof. I. O. Oloyede as Vice-Chancellor, and by the grace of God I rose to the rank of a Professor of Anatomy in October, 2021. I consider my involvement in Anatomy education and medical training as an appropriate choice that I made more than 15 years ago.

Human Anatomy is "beyond flesh and bone", as elucidated by Prof. O. B. Akinola who delivered the first inaugural lecture from the Department of Anatomy in January, 2022.The study of Anatomy has gone beyond being a mere structural subject. Various divisions and fields that form the components of Anatomical Sciences include cell biology, human genetics, developmental biology/anatomy/embryology, forensic anthropology, neurobiology, reproductive biology/endocrinology, and others.

Driven by the vision of this great citadel of learning, "*to be an International Centre of Excellence in learning, research, probity and service to humanity*", I conduct biomedical research that could help deepen our comprehension of clinical conditions and ultimately proffer therapeutic interventions, not only for our immediate environment, but for the global community. Hence this inaugural lecture: **"White matter matters in the search for phytochemical candidates for demyelinating disorders"**.

Introduction

Brain Anatomy

The brain is one of the most important and complex organs in the body. It controls most of the activities of the body, processing, integrating, and coordinating the information it receives from the sense organs and determining the signals or instructions sent back to the rest of the body. The brain is composed of cerebrum, cerebellum and brainstem (Figure 1).

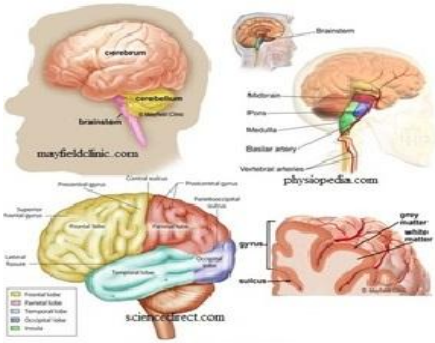

Figure 1: Anatomy of the Brain (Hines, 2018)

The **Cerebrum** is the largest component of the brain. It is divided into right and left hemispheres, with the corpus callosum, which is a collection of white matter fibres, joining the two hemispheres together. The cerebrum performs higher functions like interpreting touch, vision, hearing, speech, reasoning, emotions, learning, and fine control of movement. The outermost layer of the cerebrum is the cortex, which has a

slightly gray appearance (due to the high concentration of neuronal cell bodies), hence the term, "**gray matter**". Deep to the cortex are axons, which are long fibres that emanate from neuronal cell bodies. Axons are ensheathed by myelin, responsible for the white appearance of fibres, hence the term, "**white matter**".

Cellular Components of the Brain

The cells making up the nervous system are classified into neuronal and glial cells (Figure2). Neurons are the basic functional and structural units of the nervous system, comprising morphologically of three distinct regions, namely: the cell body, dendrites and the axon. A neuron has a single axon which extends farther than the dendritic processes and may branch considerably before terminating to form synapses with other neurons, where exchange of neural information takes place between different neurons.

Figure 2: Neuron, glia, and myclin (Mader, 2001)

There are two categories of glial cells: macroglia (e.g. astrocytes and oligodendrocytes) and microglia. In addition to the supportive roles glial cells play, their active involvement in brain physiology and the consequences of their dysfunction on the pathology of the nervous system have been emphasised (Baumann and Pham-Dinh, 2001). Oligodendrocytes are the most populous of the glial cells. Their cell bodies are found primarily in the white matter, while their cell processes extend to surround the axons, thereby forming the lipid-rich myelin sheath around the axons (Cao *et al.*, 2013).

The White Matter

Andreas Vesalius (1514-1564), regarded as the father of modern Anatomy, in one of his works in 1543 distinguished clearly between white matter and the gray matter of the cerebrum (Saunders and O'Malley, 1973). Other researchers, including Jean-Martin Charcotand Rudolph Virchow (Figure 3), continued over the years to discover the role of white matter in providing structural and functional connections between gray matter areas within the brain. Jean-Martin Charcot (1825-1893), a French neurologist and professor of anatomical pathology, in the 19th century, greatly advanced our understanding of white matter using his detailed studies of multiple sclerosis (Kumar *et al*., 2011), a clinical condition which a good proportion of this lecture focuses on.

Figure 3: (A) Andreas Vesalius; (B) Jean-Martin Charcot; (C) Rudolph Virchow (Saunders and O'Malley, 1973; Schultz, 2008; Nouri, 2011)

White matter is a vast, intertwining system of neural connections that join different lobes and regions of the brain together to form functional circuits, thus allowing the brain regions act in concert to perform their normal roles (Figure 4A). The connectivity provided by white matter occupies a central place in the elaboration of human behaviour. White matter ensures that rapid neuronal conduction takes place in the brain, directly contributing to the efficiency of information processing typical of normal cognition. The whitish appearance is a result of the myelin sheath, which was discovered by the German doctor and pathologist Rudolph Virchow, in 1854 (Boullerne, 2016).

Nerve signals are conducted through myelinated axons of the white matter via its "tracts" or pathways (i.e. **White Matter Tracts**). There are three key tracts, connecting different brain regions: Commissural fibres, Association fibres and Projection fibres.

White Matter Matters

Until it is fully developed and mature, a man's higher-level reasoning, planning and judgment are incompetent. Decision-making ability of man is directly proportional to the maturation and density of his white matter. Higher global efficiency of the white matter connectome has also been associated with better general intelligence and educational attainment in children and adolescents (Bathelt *et al.*, 2019). Hence, ***white matter matters***.

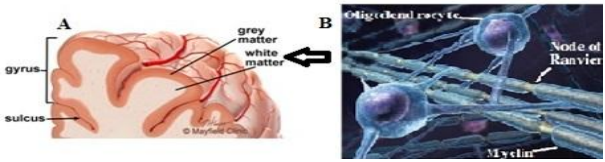

Figure 4: (A) White matter, (B) Myelination by oligodendrocytes (Mader, 2001)

Myelination

The development of the myelin sheath around CNS axons is referred to as myelination. It is essential for normal brain function, and is a cornerstone of human neurodevelopment (Figure 4B). Damage to myelin presents as derangement in sensory, motor and cognitive functions, signifying its importance in motor and cognitive functions of the brain (Jarjour *et al.*, 2012).

Remyelination

Remyelination or myelin repair can occur in cases of demyelinating conditions, which is to help restore nerve function. This is mediated by oligodendrocyte precursor cells which have responded to chemotactic cues, migrated into the lesion, proliferated, differentiated into mature oligodendrocytes, and ensheathed the demyelinated axons. However, remyelination may not effectively and efficiently restore functions in all cases of multiple sclerosis.

Disorders of White Matter

More than 100 disorders have been associated with the white matter. While some of these conditions are primarily of white matter, others are gray matter diseases which secondarily affect the white matter. White matter disorders can be categorised as genetic, **demyelinating**, infectious, inflammatory, etc. For the purpose of this lecture, my consideration would centre on **demyelinating disorders**.

Demyelinating diseases of the CNS are a group of heterogeneous neurological conditions characterised by damage to the myelin. They cause substantial disability and if not treated promptly could be associated with high mortality. Myelin-related conditions could be in form of hypomyelination, delayed myelination, or demyelination. **Demyelination** refers to the loss, removal or destruction of myelin with relative preservation of axons. It is usually due to diseases that destroy myelin sheaths or oligodendrocytes. Types of demyelinating diseases include multiple sclerosis, acute-disseminated encephalomyelitis, leukodystrophies, etc. (Wang *et al*., 2009).

Neuroprotection with Phytochemicals in Multiple Sclerosis

Mr. Vice Chancellor, today, the 30thMay, 2024 is the International Day for Multiple Sclerosis.

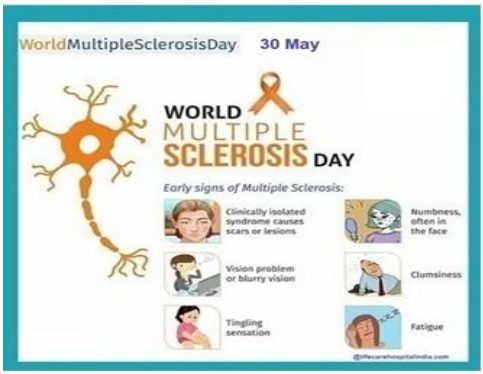

Figure 5: World Multiple Sclerosis Day 30th May (LifeCare Hospital, 2024)

This inaugural lecture is more than just a coincidence. It is to create awareness of the disorder to the Public, highlight the challenges associated with it and my contributions to scientific efforts at seeking a definitive management (Figure 5).

Multiple sclerosis is a chronic autoimmune disease of the CNS, characterised by inflammation, demyelination, and axonal damage, leading to a range of neurological symptoms and disability. It is estimated to affect 2.9 million people worldwide, with a higher prevalence in temperate regions such as Europe and North America (Dobson *et al*., 2019). A 50% increase in global prevalence was recorded over a period of about 15 years (Figure6; Table 1). Multiple sclerosis occurs mostly in young adults between ages 20 and 40, with a major impact on affected individuals as they start their families and careers. Females are more affected than males. The disease is progressive, and symptoms may worsen over time, leading to a significant burden on patients, caregivers, and healthcare systems. Sixty percent (60%) of patients are likely to be fully paralysed 20 years after the onset of the disease.

There are different forms of multiple sclerosis, each having its own unique presentation. The most common type is relapsing-remitting MS; others are: primary progressive MS, secondary progressive MS and progressive relapsing MS.

Figure 6: Global prevalence of multiple sclerosis (Multiple Sclerosis International Federation, 2023)

Reliable data on the incidence and prevalence of MS in Nigeria are limited, but some studies put the incidence and prevalence at 0.2 and 5.6 (respectively) per 100,000 population per year (Akinyemi *et al*., 2019; and Ogwumike *et al*., 2020). As noted during the 2022 World MS Day, Nigeria has an estimated 10,048 people living with the disease (*Business Day Newspaper*, 1st June, 2022). However, experts expressed concern about rising cases of MS.

Table 1: Prevalence of multiple sclerosis per 100,000 population by world region in 2013 and 2020 (Walton *et al.*, 2020)

	Number of countries included	**2013 prevalence per 100,000 population (95% CI)**	**2020 prevalence per 100,000 population (95% CI)**	**Increase; absolute (%)**
Global	81	29.26 (29.21, 29.30)	43.95 (43.90, 44.01)	14.69 (50%)
African	6	5.52 (5.41, 5.62)	8.76 (8.64, 8.89)	3.24 (59%)
Americas	15	62.89 (62.72, 63.05)	117.49 (117.27, 117.71)	54.6 (87%)
East Mediterranean	14	23.91 (23.77, 24.04)	33.00 (32.85, 33.15)	9.09 (38%)
European	35	108.25 (108.01, 108.49)	142.81 (142.53, 143.08)	34.56 (32%)
South East Asia	4	5.44 (5.41, 5.48)	8.62 (8.58, 8.66)	3.18 (58%)
Western Pacific	7	3.64 (3.61, 3.67)	4.79 (4.75, 4.82)	1.15 (32%)

Pathophysiology of Multiple Sclerosis

The pathophysiology of MS is characterised by inflammation, demyelination, axonal loss, and glial activation. Demyelination leads to the disruption of nerve conduction and the formation of lesions in the CNS, which can cause a wide range of neurological symptoms, such as weakness, sensory disturbances, and cognitive impairment. Glial activation occurs in response to the destruction of myelin and axons, resulting in proliferation of astrocytes and microglia.

Aetiopathogenesis of Multiple Sclerosis

The exact cause of MS is not fully understood, but it is believed to involve a complex interplay between genetic, environmental, and immunological factors. The disease is

thought to be triggered by environmental factors that lead to an immune response targeting the CNS (Figure 7). Environmental factors include viral infections, vitamin D deficiency and tobacco. **Omotoso** *et al.*, (2015) demonstrated in rodents that prenatal exposure to nicotine predisposed the offspring to dysmyelination, with significant neurochemical and morphological alterations (Figure 8). Other risk factors include neurodegeneration, age, geographical location, childhood obesity, and others.

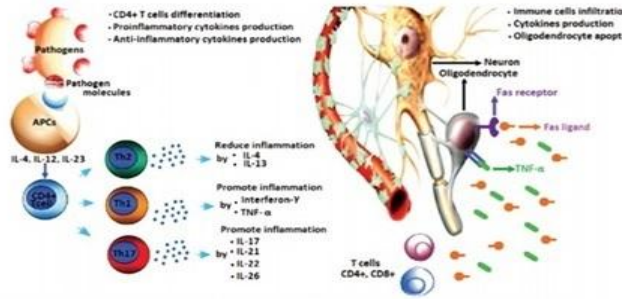

Figure 7: Immune cells and their cytokines involved in the pathogenesis of multiple sclerosis (Ghasemi *et al.*, 2017)

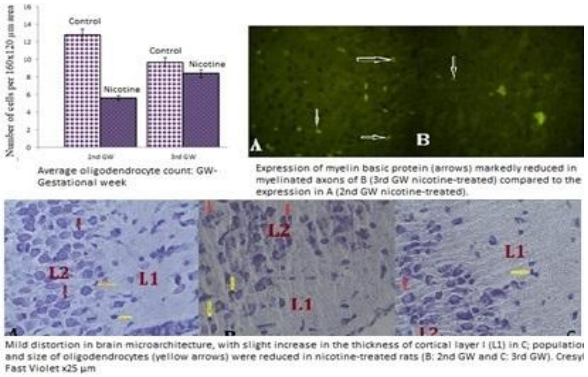

Figure 8: Effects of nicotine on oligodendrocytes, myelin basic protein and prefrontal cortex microarchitecture (**Omotoso** *et al.*, 2015)

Clinical Features of Multiple Sclerosis

Motor symptoms are common in MS; these include body weakness, stiffness of muscles, lack of coordination or balance. Sensory symptoms include numbness, tingling and paresthesia. Visual symptoms such as optic neuritis, diplopia and nystagmus are also common. Cognition is affected in up to 65% of MS patients, causing problems with attention, memory, and processing speed. Sufferers usually have emotional disturbance such as depression, anxiety and mood swings, which could be related to the physical and cognitive challenges of living with MS, as well as the disease itself. Being a progressive disorder, the disease progression and degree of disability has been measured using the Expanded Disability Status Scale, from 0 (no disability) up to 10 (death due to MS) (Figure 9).Some of these features have been demonstrated in our studies using rodent models of MS, as will be mentioned shortly.

Figure 9: Expanded Disability Status Scale (Spiteri, 2018)

Management of Multiple Sclerosis

Management of MS in Africa generally has suffered many setbacks, due to various challenges such as poor public awareness, sociocultural factors, limited access to care, diagnostic challenges, limited availability of treatments, paucity of specialists (i.e. Neurologists) and limited research in MS (Aderinto *et al.*, 2023).

There is currently no cure for MS, but a range of disease-modifying therapies are available to slow disease progression, reduce relapse rates, and manage symptoms. In

recent years, there has been increasing interest in novel treatment approaches, such as stem cell transplantation, immune tolerance induction, and neuroprotective agents.

These are motivating factors that spurred me to embark on my journey "***in the search for phytochemical candidates for demyelinating disorders***", particularly, MS, thereby offering hope of an improved disease outcome and quality of life for MS patients.

My Contributions to Multiple Sclerosis Research

My participation at the 25th Joint Biennial Conference of the International Society for Neurochemistry (ISN) in Cairns, Queensland, Australia in 2015 stirred up my interest in glial biology, with particular interest in demyelinating conditions. In 2016, I received a visiting research award from ISN to visit Texas A&M University, College Station, USA, for research training and acquisition of new technical and conceptual expertise in research area of potential therapeutic interventions for demyelinating diseases such as multiple sclerosis, under Dr. Jianrong Li (now Prof Li) (Figures 10 & 11).

Figure 10: Dr. Omotoso in Prof. Li's Lab

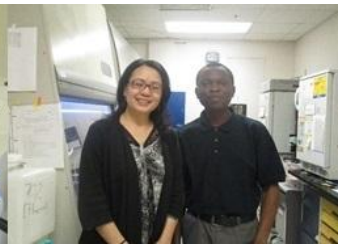

Figure 11: Prof. Li and Dr. Omotoso

Our studies have contributed significantly to the understanding of the mechanisms of oligodendrocyte development and injury, and discovered new clues for potential prevention and treatment of human white matter diseases.

Modeling Multiple Sclerosis in Rodents

There are different models available to study MS. The most commonly studied animal models are: experimental autoimmune encephalomyelitis, viral-induced models and toxin-

induced models; while others are transgenic models and use of *in vitro* models. The toxin-induced models can be used to study metabolic processes involved in myelin destruction and repair, *in vivo* imaging of demyelinated lesions, determination of the neuroprotective effect of remyelination, and to test therapies aimed at promoting remyelination.

Cuprizone, a copper-chelating agent, is the most frequently used model of toxic demyelination. Our laboratory has been able to develop cuprizone-induced demyelination by maintaining experimental rats and mice on 5 or 6 weeks cuprizone diet. The cuprizone model accurately captures a number of key aspects of the progressive MS illness course. Two key elements of the MS pathophysiology can be studied using the cuprizone model (Matsushima and Morell, 2001): (i) the mechanisms causing innate immune cell-driven myelin and axonal degeneration, and (ii) remyelination of the demyelinated axons (Figure 12).

Cuprizone targets mature oligodendrocytes and spares other brain cells (Lucchinetti *et al*., 2000). Oxidative stress has been implicated in the pathophysiology of cuprizone model of MS (**Omotoso** *et al*., 2018a). Characteristic histomorphological and pathological manifestation of cuprizone-induced demyelination typically mimics the acute and chronic courses of multiple sclerosis (Zirngibl *et al*., 2022) (Figure 13).

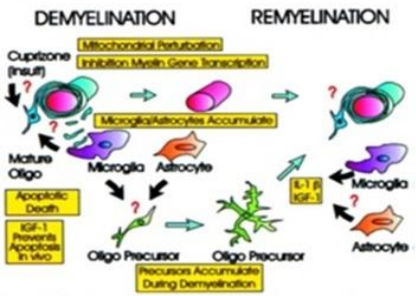

Figure 12: Interplay between oligodendrocytes, microglia and astrocytes during cuprizone insult (Matsushima and Morell, 2001)

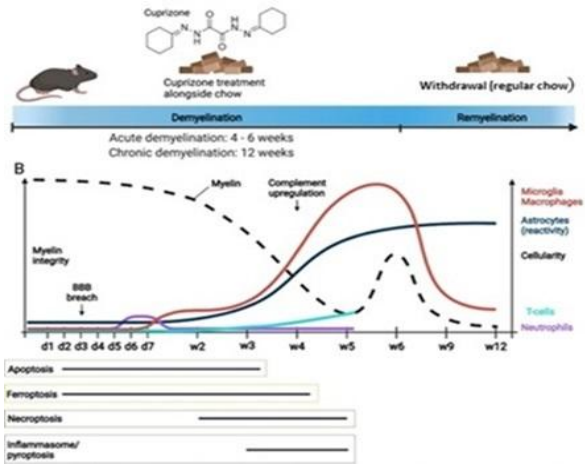

Figure 13: Course of oligodendrocyte death and myclin loss in cuprizone model (Zirngibl *et al.*, 2022)

Behavioural Characterisation of Cuprizone-induced Neurotoxicity

Cuprizone intoxication is associated with different behavioural pattern and motor dysfunctions. To evaluate these characteristics in the laboratory, we subjected experimental rodents (rats or mice) to different forms of behavioural paradigms.

Cuprizone Induced Deficits in Memory Indices

Two neurobehavioural paradigms - Morris water maze and Y- maze were used to quantify long- and short-term memory in rodents. Analysis of MWM revealed that cuprizone treatment led to a significantly higher escape latency period when compared to the control (Figure 15), showing that cuprizone caused a decline in the long-term memory index (**Omotoso** *et al*., 2018 a and b). Observation from spontaneous alternation test conducted using the Y-maze test for short-term memory showed that cuprizone-treated mice had a lower percentage correct alternation (**Omotoso** *et al*., 2019).

Cuprizone is Anxiogenic and Impairs Locomotion and Exploratory Drive

The open field test was used to score exploratory drive and anxiety. Cuprizone toxicity caused significant reduction in rearing frequency; number of lines crossed, centre square entry and duration, while it significantly increased stretch attend posture frequency, and freezing duration, suggesting that cuprizone caused anxiety-related behaviour and poor motor functions (**Omotoso** *et al*., 2018c and d; 2019; 2020a and b).

Cuprizone Induced Disturbance of Neurochemical Redox in the Brain

Cuprizone caused a significant reduction in anti-oxidative enzymes activity due to excessive production of reactive oxygen and nitrogen species, and increased lipid peroxidation. This suggests the role cuprizone plays in inducing oxidative stress (**Omotoso** *et al*., 2019; 2020a) (Figure 15).

Neurohistomorphological Characterisation following Cuprizone Demyelination

Our studies revealed that cuprizone extensively compromised the integrity of neurons in different brain regions of rodents. Neurons showed early signs of pyknosis, extreme central chromatolysis, intercellular fragmentation, axonal degeneration and cytoplasmic condensation (**Omotoso** *et al*., 2018e). Cuprizone compromised cellular morphology through oxidative damage to the cells (**Omotoso** *et al*., 2018a; **Omotoso** *et al*., 2019). Examination of myelin integrity revealed significant decrease in myelin density in the *corpus callosum*, and down regulation of the expression of myelin basic protein (Jaji-Sulaimon and **Omotoso**, 2021). Assessment of glial morphology using molecular markers to express astrocytes and microglia revealed glial activation characterised by morphological changes (**Omotoso** *et al*., 2019; Figure 16). The perturbation of biochemical redox correlates with morphological modification of the brain and the decline in memory indices of the cuprizone-treated rodents (Figure15).

Exploring Ethnomedicine for Neuroprotection in Multiple Sclerosis

Our laboratory is currently exploring various natural products and their phytochemicals to assess their neuroprotective roles in the management of neurodevelopmental and neurodegenerative disorders (including Alzheimer's disease, Parkinson's disease and multiple sclerosis), and we have achieved some positive outcomes. In our search for phytochemical candidates for Multiple Sclerosis, the plants we have investigated include *Garcinia kola*, *Moringa oleifera*, *Nigella sativa* and Sesame (Figure 14).

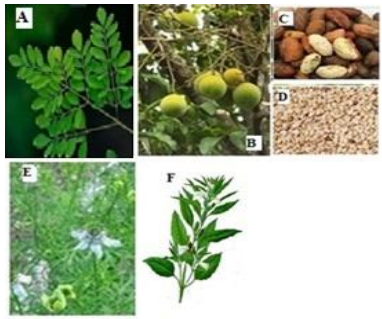

Figure 14: *Moringa oleifera* tree (A); *Garcinia kola* tree (B) and seed (C); *Nigella sativa* plant (E); Sesame plant (F) and seed (D) (Anzano *et al*., 2021)

Moringa oleifera (MO) is a small-sized tree widely cultivated in most parts of the world for its nutritional and medicinal benefits (Figure 14A). We reported that the anti-inflammatory and anti-oxidative properties of MO contributed to their neuroprotective role in neurotoxicity, including cuprizone-induced neurotoxicity (Gbadamosi *et al*., 2016; **Omotoso** *et al*., 2018b; Akinlolu *et al*., 2020; Alabelewe *et al*., 2024).

Some of the phytochemical candidates present in *Moringa oleifera* which we have explored include quercetin, novel fractions of the aqueous leaf extract (MoF6), and the oil. *Moringa oleifera* mitigated cuprizone-induced memory decline

and anxiety, restored long-term memory deficit (Figure 15) and improved exploratory drive and emotional balance (**Omotoso** *et al*., 2018a and c).

Moringa oleifera significantly raised the levels of antioxidant enzymes thereby mopping up the excessive production of both reactive oxygen and nitrogen species associated with cuprizone neurotoxicity. It restored neuromorphologic integrity, resolved extensive central chromatolytic and pyknotic changes in the pyramidal cells of the hippocampus and prefrontal cortex (Figure 16) (Gbadamosi *et al*., 2016; **Omotoso** *et al*., 2018f).

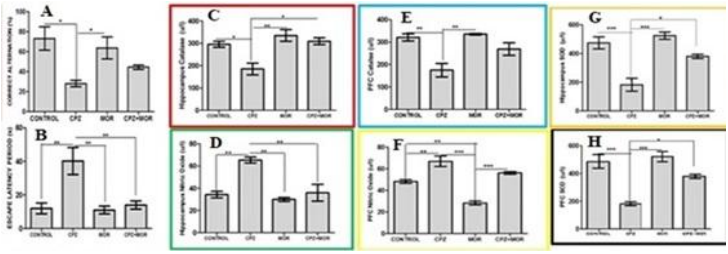

Figure 15: Cuprizone (CPZ)-induced memory Impairment (A & B) and oxidative damage (C-H) ameliorated by Moringa oleifera (MOR) intervention. SOD-superoxide dismutase; PFC-prefrontal cortex (**Omotoso** *et al.*, 2018a and c)

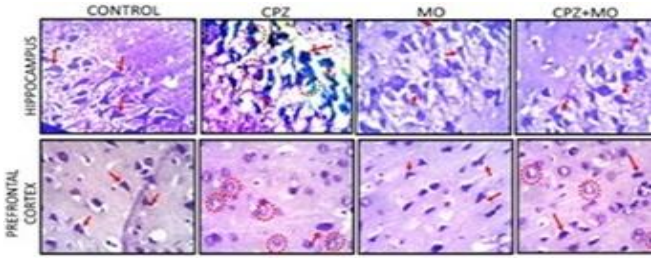

Figure 16: Representative photomicrographs showing the pyramidal cells of CA3 of hippocampus and external pyramidal layer of prefrontal cortex. CPZ = cuprizone and MO = *Moringa oleifera* (**Omotoso** *et al.*, 2018f)

In 2017, I received the Tertiary Education Trust Fund/Institution-Based Research (TETFund/IBR) grant to carry out a study on "***Assessment of the Therapeutic Potentials of Kolaviron in Experimental Model of Multiple Sclerosis***". **Kolaviron** is a natural bioflavonoid isolated from ***Garcinia kola,*** also called bitter kola (Figures 14B & C). Our studies have explored its anti-oxidative and anti-inflammatory activities, and documented the neuroprotective roles of kolaviron in neurotoxicity and in some neurologic disease models (**Omotoso** *et al*., 2017a, 2018b, 2019, 2020 a, b and c; Mutholib *et al*., 2022, Mutholib and **Omotoso**, 2024).

The activities of kolaviron from our studies are comparable to those of *Moringa oleifera* earlier highlighted. In summary, it mitigates cuprizone-induced memory loss, prevents anxiety-related behaviours, sustains exploratory drive, counterbalances cuprizone-induced disturbance of neurochemical redox and minimises neuromorphological changes in various regions of the brain (Figures 17& 18).To the best of our knowledge, our study was the first to show line of evidence to support the ability of kolaviron to mitigate degenerative changes associated with cuprizone-induced neurotoxicity in mice (**Omotoso** *et al*., 2018d,2019 and 2020b).

In 2019, I received financial support from International Society for Neurochemistry to equip my laboratory with some research supplies towards promoting our research on Kolaviron and *Moringa oleifera* in the search for phytochemical candidates that can enhance remyelination in demyelinating disorders. Our Laboratory was also supported by funds obtained from the TETFund/IBR Grant.

We have explored two other plant products, *Nigella sativa* oil and Sesame seed oil, and we found a good outlook. These two are neuroprotective, protecting the brain against oxidative stress and neuroinflammation (Kolo and **Omotoso**, 2023).

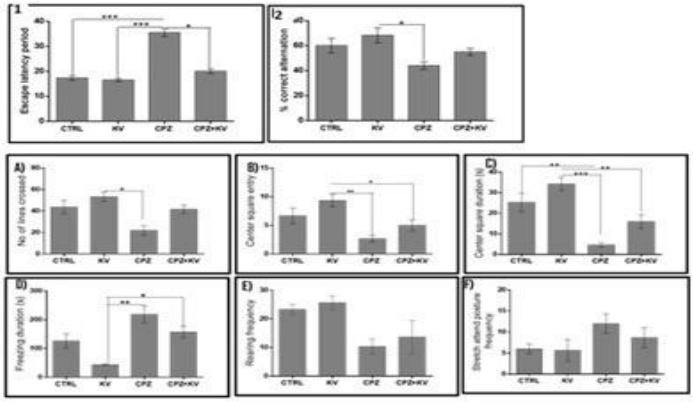

Figure 17: Neurobehavioural outcomes of mice in the Morris water maze (Fig. 17.1) and Y-maze (Fig. 17.2). Figure 17 A to F are performances of mice in the open field test. K.V-kolaviron; CPZ-cuprizone (**Omotoso** *et al.*, 2019)

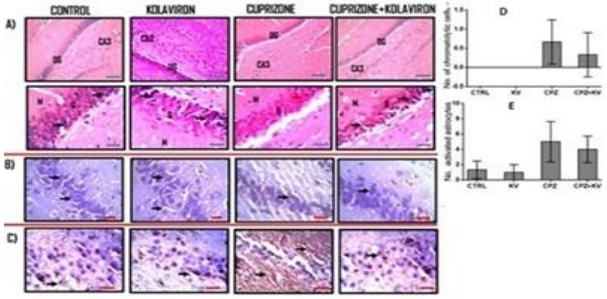

Figure 18: Representative photomicrographs of the histomorphological manifestation of the dentate gyrus of mice (A); hippocampal CA3 characteristic chromatolytic cells (B); and anti-GFAP expression of astrocytes (C); Chromatolytic cell count (D); and activated astrocytes count (E) in the hippocampus (Omotoso *et al*., 2019)

Mr. Vice-Chancellor, before concluding this lecture, permit me to mention a few other aspects of the anatomical sciences in which I have been able, by God's grace, to make some contributions.

My Contributions to Environmental Health

Toxic Environmental Substances:

(A) The Threat of Tobacco Exposure

As a young academic, I began my research exploration with a desire to know how the body reacts to environmental insults. I examined the effects of exposure to passive smoke (from cigarette) on various parts of the body. This formed part of my Master's dissertation under the supervision of late Prof E.A. Caxton-Martins.

Vice-Chancellor, sir, tomorrow, 31st May, 2024 is the "World No Tobacco Day". This global campaign is aimed at raising awareness on the harmful effects of tobacco use (Figure 19). The World Health Organisation (WHO) rightly themed the 2022 campaign, "*Tobacco: Threat to our Environment*". This year, the theme is **"Protecting Children from Tobacco Industry Interference".**

Figure 19 (A and B): Protecting the children from exposure to tobacco smoke and against Industry interference (Palit, 2024)

The latest global estimate of tobacco users is 1.25 billion people (WHO, 2024), and 80% of this population are in low- and middle-income countries. Tobacco causes more than 8 million deaths yearly, out of which 1.3 million are non-smokers exposed to second-hand smoke (WHO, 2023), making it a leading cause of preventable death and disease worldwide. Although a declining rate of smoking has been recorded (Figure 20), one out of ten of the Nigerian population smokes tobacco daily (Adeloye *et al*., 2019).

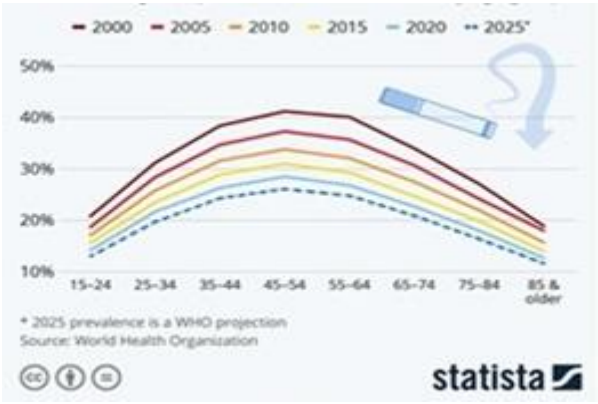

Figure 20: Estimated global prevalence of tobacco use by age group (Richter, 2021)

Despite a great deal of health education and awareness on the grave implications of cigarette smoking, many people are still caught in the web of the habit, while tobacco companies continue to make a fortune on their business and sabotage efforts at curbing the menace (WHO, 2024). Hence the need for all of us to arise and "*Protect our Children from Tobacco Industry Interference*".

In assessing the health risks of cigarette smoke in animal models, we constructed smoking chambers for the exposure (**Omotoso** *et al*., 2013a). We observed adverse consequences of cigarette smoke on different organs of the body, both structurally and functionally. These include its adverse effects on male gonads and reproduction/fertility (**Omotoso** *et al*., 2011; 2017b); degenerative changes in the liver parenchyma, disruption of the canalicular network and lipid metabolism, and other hepatocellular injuries. In **Omotoso** *et al*. (2013a and b) and **Omotoso** and Babalola (2014), we also established the detrimental effects of passive cigarette smoke on adult brains.

Nicotine and Neurodevelopmental Disorders

My Ph.D. Thesis provided scientific evidence on the adverse effects of prenatal nicotine on brain development.

Prenatal nicotine exposure is one of the main contributors to developmental neurological alterations and behavioural disorders in the offspring. It is associated with the development of learning disabilities, attention deficit hyperactivity disorders, autism, schizophrenia and other behavioural disorders in children, and this relationship is dose-dependent (Buck *et al.*, 2020).

Prenatal Nicotine before and after Neurulation is Detrimental to Neurodevelopment

Using a rat model, we determined the vulnerability of the developing brain to teratogens (in this case, nicotine). We time-mated adult female Wistar rats and gave them different doses of intraperitoneal nicotine injection at different weeks of gestation. In rats, neurulation begins at the early part of 2nd gestational week (GW).

Prenatal nicotine exposure before the start of neurulation resulted insignificantly reduced birth weights, but the body weights increased in an accelerated manner after birth (**Omotoso** *et al*., 2018g). The prefrontal cortex had significantly elevated astrocytic count, dose-dependent degeneration of neurons (Table 2); alterations in somatic size, neuronal somatic diameter, nuclear diameter, nuclear-to-soma ratio (as an index of nuclear size); the space between the nuclear envelope and the somatic membrane, occupied by the cytoplasm (which I called, the "Perinuclear-Somatic Space") was significantly increased (Table 3).

Table 2: Proportion of apparently normal neurons and degenerated neurons per Counter Window in layer V of the lateral prefrontal cortex of rats (**Omotoso** *et al*., 2018g).

Neurons	**1st Gestational Week**		
	A	**B**	**C**
Average Total Neuronal Count	48.8±3.7	67.6±10.0	46.8 ±5.0
Degenerated Neurons (%)	12.3	35.8	53.0
Normal Neurons (%)	87.7	64.2	47.0

A: Control; B: Low dose nicotine; C: High dose nicotine

Furthermore, exposure during the 2nd and 3rd weeks of gestation caused reduced oligodendroglial count; reduced neuronal cell count; significantly more in rats exposed in the 2nd GW (Table 3) (**Omotoso** *et al*., 2014a). Microarchitecture and ultrastructure of the neurons and oligodendrocytes revealed remarkable alterations especially in rats exposed in the 3rd GW (Figures 8, 21A, C and D).

Our studies established that exposure of the foetus to nicotine adversely affects the brain even before the brain begins to develop, although the most damaging effect occurs after commencement of neurodevelopment.

Table 3: Measurement of nuclear and somatic diameters of neurons in the lateral prefrontal cortex in exposure at 2nd week (A) and 3rd week (B) of gestation (**Omotoso** *et al*., 2018g).

	Groups			
Parameters	**A_1**	**A_2**	**B_1**	**B_2**
Somatic diameter (µm)	15.737 ± 0.515	14.377 ± 1.009	14.140 ± 0.682	13.897 ± 0.452
Nuclear diameter (µm)	11.823 ± 0.316†	8.529 ± 0.467†	11.045 ± 0.746	8.792 ± 0.517
Perinuclear-Somatic space (µm)	3.914 ± 0.289	5.848 ± 1.245	3.095 ± 0.278	5.105 ± 0.264
Nuclear-Somatic ratio	0.7513	0.5932	$0.7811^{\neq}$	$0.6327^{\neq}$

Statistically significant difference ($p < 0.05$) between †A_1 and A_2; $^{\neq}B_1$ and B_2. **NB**: The perinuclear-somatic space is the difference between the somatic and nuclear diameter (or the interval between the soma and the nucleus), which represents the part of the cytoplasm not occupied by nucleus. Control: 1; nicotine: 2 (subscript)

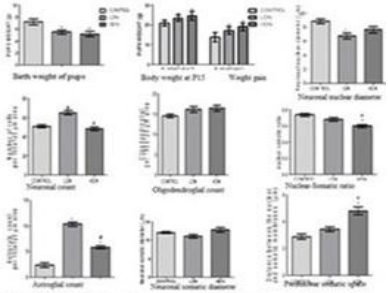

Fig. 21A: Weight changes and brain cells morphometry (LDN- low dose nicotine, HDN- high dose nicotine); *p< 0.05 (Omotoso *et al*., 2018g)

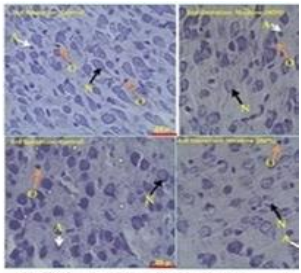

Fig. 21C: Altered microarchitecture and morphology in the lateral prefrontal cortex of treated rats. A- astrocytes; N- neur oligodendrocytes; cresyl fast violet (Omotos 2014a)

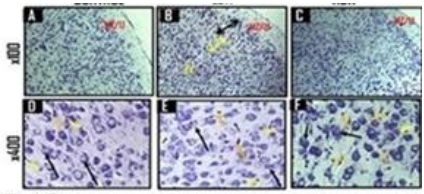

Fig. 21B: Increased neuronal density (black arrows) with prominent nuclei and nucleoli, but reduced sizes, and increased glial population (oligodendrocytes - orange arrows; astrocytes - yellow arrows) (B and E). Fewer and slightly large-sized neurons; Nissl positivity, many degenerated neurons (black arrows), reactive astrocytes (short yellow arrows) and myelinating oligodendrocytes (short orange arrows) (C and F). (Omotoso *et al*., 2018g)

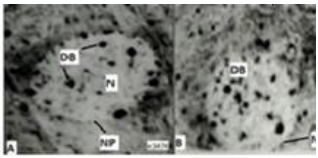

Fig. 21D: Ultrastructure of neuronal nuc of lateral prefrontal cortex of rats treat with nicotine during 2nd (A) and 3rd (gestational week; DB- dense bodies; N nuclear membrane; NP- nuclear pore (Omotoso, 2015)

(B) Exposure to other Neurotoxic Substances

Vice-Chancellor, sir, some other neurologic and neurodegenerative conditions are parts of the scope of my laboratory. For example, we were able to establish the extent of neurotoxicity associated with metals such as lead, which caused neurodegeneration, behavioural changes, cognitive deficits, oxidative stress (Amedu and **Omotoso**, 2020a and b) and cerebellar ataxia (Amedu and **Omotoso**, 2020c). We also reported toxicity associated with insecticides/pesticides (such as permethrin) in **Omotoso** *et al*., 2014b; 2020d; Zubair *et al*., 2023; Alabelewe *et al*., 2024). Phytochemicals/flavonoids employed in some of these studies, with positive outcomes included vitexin, sesame seed oil, *Moringa oleifera* oil, *Nigella sativa* oil and kolaviron.

Further Contributions to Neurodevelopmental Biology:

Early Life Experiences and Development of Neuropsychiatric Disorders

Mr. Vice-Chancellor, genetic and environmental factors affect how the brain develops. During the crucial stages of neurodevelopment, proper diet is key as well as emotional bond between a baby and the mother. This critical time in a person's life sets the stage for the development of their cognitive, motor, and socioemotional skills throughout adolescence and adulthood. Thus, exclusive breastfeeding in the first six months of a baby is usually advocated, for adequate nutrition and emotional attachment. Early life experiences affect a person's propensity for pathophysiological processes, such as behavioural abnormalities or incorrect stress reactions, and their ability to function normally physiologically later in life.

Maternal deprivation is one of the strongest stressors during neonatal development (Neves *et al.,* 2015). In carrying out maternal deprivation, we separated pups temporarily from their mothers on postnatal day 9 for a period of 24 hours (**Omotoso** *et al*., 2020c) and the study revealed that early maternal deprivation led to disruptions in the postnatal development of the brain, resulting in learning disabilities, behavioural changes, neurochemical alterations, redox imbalance and neuromorphological changes later in life (Figure 22).Interventional administration of biflavonoid kolaviron and vitamin B complex after the period of maternal deprivation, contributed significantly to reducing the adverse behavioural, histomorphological and neurochemical abnormalities later in life (**Omotoso** *et al*., 2020c, 2020e; Abdulsalam *et al*., 2022; Mutholib *et al*., 2022).

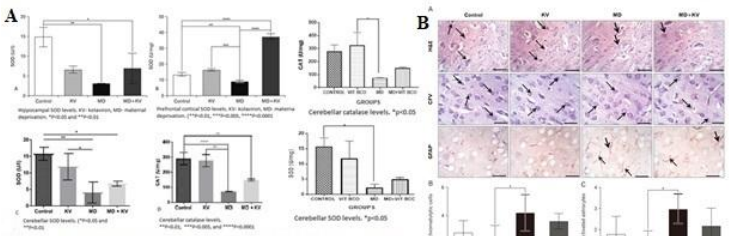

Figure 22: (**A**): Activities of oxidative enzyme markers; (**B**): Amelioration of maternal deprivation (MD) effect by kolaviron (KV) in the prefrontal cortex of rats (Omotoso et al., 2020c)

My Contributions to Cosmetic Facial Anatomy

In my earliest studies as a Lecturer, I also desired to know the prevalence of simple dominant traits in a target population, e.g. facial dimples and midline diastema, and their cultural, social and clinical implications.

Cosmetic facial procedures aim to enhance or alter the appearance of the face.

Facial Dimples

Dimples are small visible indentations on the surface of the skin and may appear on various parts of the body, such as the cheeks and chin (Figure 23).

Cheek Dimple

In 2010, using the South-western population as target, I examined the frequency of cheek dimples in five hundred (500) subjects randomly selected between age 16 to 30. The study revealed that 29.4% had cheek dimples on either or both cheeks, with most of them (65.3%) having bilateral cheek dimples. It occurred more in females (59.9%) than in males (40.1%). Unilateral cheek dimple occurred more on the right (52.9%) than the left (47.1%); 61.9% were hereditary, and 14.2% of the people without cheek dimples have parents with cheek dimples (**Omotoso**, 2010). Comparing our findings with data from other population groups in Nigeria, the frequency was higher among South-south and South-eastern population (37% and 37.7% respectively), but percentage heredity was lower (50.9% and 52.8% respectively) (Oladipo and Amangi-Peters, 2005; **Omotoso** *et al*., 2010).

Figure 23: Facial dimples (Longo, 2024)

Most respondents (64.5%) liked cheek dimples. Many that did not have cheek dimples, especially females signified their desire for it if possible. Many believe cheek dimples add to their beauty, make them attractive and admirable to others, give them a smiling facial appearance, and even make them look younger (**Omotoso** *et al*., 2014)! Although the occurrence of cheek dimples has been structurally and genetically proven, dimples can be created artificially by means of a short and simple cosmetic procedure.

Chin Dimple

Chin dimple occurs less commonly than cheek dimples (Figure23). We reported only 10.8% frequency in the South-western Yoruba-speaking population, and is common in females (6.4%) than males (4.4%) (**Omotoso** *et al*., 2010). We surveyed the co-existence of cheek and chin dimples and observed that 7.2% of the population had both cheek and chin dimples. The incidence was higher in females (4.4%) than males (2.8%). Twenty-five percent (25%) inherited the two forms of facial dimples from either one or both parents who also expressed both phenotypes (**Omotoso** *et al*., 2010).

Midline Diastema

Diastema is a distinctive gap or space between two teeth (Figure 24), called "open-teeth", "gapped teeth", or *eji* (in Yoruba), found especially between the two front teeth.

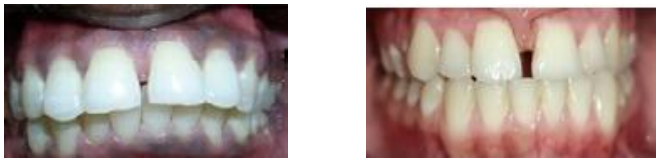

Figure 24: Maxillary midline diastema (Prasada *et al.,* 2014)

Our survey of the incidence and perception of midline diastema among the Yoruba-speaking population of South-west Nigeria revealed an incidence of 26.1%, of which 21.0% had maxillary midline diastema (between the upper incisors), 1.9% had mandibular midline diastema (between the lower incisors), and 3.2% had co-existing maxillary and mandibular midline diastema. As much as 64.9% inherited it from either one or both parents (**Omotoso** and Kadir, 2010).

Diastema is more prevalent among females (33.9%) than among males (19.5%). Maxillary midline diastema occurred more in females (65.3%), while mandibular midline diastema occurred more in males (90.9%). Only about a quarter (29.7%) of people without diastema signified their interest in artificial creation of diastema (**Omotoso** and Kadir, 2010). In some African countries, diastema symbolises fertility. In France, it symbolises luck and happiness, while most respondents (72.8%) saw it as a sign of beauty, and 29.7% of people not having diastema would love to have it created through cosmetic dentistry, showing the importance attached to it in this part of the world (**Omotoso** and Kadir, 2010).

New Approaches in Anatomy Research:

Models of Neurodegenerative Diseases

With the emergence of molecular anatomy and the development of genetic and molecular tools, new approaches to anatomy research have become possible.

One of my Ph.D. students (Ismail Gbadamosi, 2021) investigated the effects of ascorbic acid and nicotine on aluminum-induced neurotoxicity as a model for Alzheimer's disease. The methodology involved the use of molecular cloning, polymerase chain reaction, western blot, and flow cytometry to investigate the effects of different concentrations of ascorbic acid

and nicotine on transferrin expression and neuroprotection in human embryonic kidney (HEK) cells. This aspect of his work was carried out at Medical University of Vienna, Austria under the guidance of Prof Christian Nanoff.

The findings showed that the combination of ascorbic acid and nicotine effectively mitigated aluminum-induced cortico-hippocampal neuropathology and perturbed neuroenergetics. Nicotine reduced transferrin expression, thereby mitigating intracellular iron overload, while ascorbic acid acted as a scavenger of reactive oxygen species to reduce the production of singlet and triplet oxygen species generated by nicotine's action. These findings demonstrate the potential of genetic and molecular tools in uncovering new insights into disease pathology and potential therapeutic targets.

In another study undertaken by another Ph.D. student (John Adediji, 2021) and co-supervised by Dr. Olumayokun Olajide (School of Applied Sciences, University of Huddersfield, Huddersfield, United Kingdom), we explored the use of *in vitro* techniques to study cellular models of Parkinson's Disease (PD). The study determined the neuroprotective role of methyl jasmonate (a stress phytohormone used as food preservative) and identified its mechanisms of neuroprotection in immortalised microglial cells (BV-2) and neuroblastoma (SH-SY5Y) cells of PD following l-methyl-4-phenylpyridinium (MPP+)-induced neurotoxicity.

Some of my Contributions to the Department of Anatomy

Mr. Vice-Chancellor, at this point, kindly permit me to mention some of my contributions to the Department when I headed the Department in the Acting capacity from 1st August, 2019 to 31st July, 2021. With a vision to enhance students' learning process in Anatomy, we created the **Digital Anatomy Laboratory**. The Laboratory which began with three (3) sets of Computer Systems, has increased to more than forty (40), with support from TETFund Needs Assessment Funds. The systems were installed with e-Resources to support students' learning of Gross Anatomy and Histology, and are useful for the conduct of practical examinations.

I gave special attention to **Postgraduate training.** We revived regular Seminar Series, including virtual seminars. One of such virtual seminars featured an International Guest Speaker, Prof. Paul Manger from the School of Anatomical Sciences, University of Witwatersrand, Johannesburg, South Africa.

Knowing the importance of recognising academic excellence, I initiated the **Students Honours' Roll,** to recognise all our best graduating students and first-class graduates since inception of the B.Sc. Anatomy programme. This culture is believed to serve as motivation for all our students. Coincidentally, the Department recorded for the third time (since inception of the Programme in 1991), **first class** position (the last being in 2014). And for the first time, three students bagged first class honours position in Anatomy, and this marked the beginning of multiple first class positions per session in the Department.

Contribution to Training and Supervision of Students

Ever since I was appointed Lecturer II in 2008, I have been engaged in students' teaching and supervision. I have supervised more than 100 B.Sc. Projects and successfully trained 14 M.Sc. and 4 Ph.D. students. The Ph.D. holders trained are Rukayat Jaji-Sulaimon, Nathaniel Amedu, John Adediji and Ismail Gbadamosi. During his training, Ismail received the Ernst Mach Fellowship and had his predoctoral fellowship at Medical University of Vienna, Austria. He also obtained a doctoral fellowship at the Centre of Excellence for Neural Plasticity and Brain Disorders, Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland (where he is currently).There are currently four (4) Ph.D. and one (1) MPhil/Ph.D. trainees in my laboratory.

My Contributions to Manpower Development in the Department of Anatomy

I was involved in the training of a few faculties and staff of the Department at various levels (undergraduate and graduate levels). Dr. R Jaji-Sulaimon completed her Ph.D. training in

2021 under my supervision and she is due for promotion to the rank of a Senior Lecturer this year.

Through my collaboration with Prof. M Lakshman of SVV University, Rajendranagar, Hyderabad, India; I facilitated the hosting of Dr. F.S. Lewu for her predoctoral CV Raman Fellowship for African Researchers, in India (Figures 25 and 26). Similarly, I facilitated the hosting of Dr. M.Y. Adana's postdoctoral fellowship at Prof. O. Olajide's Laboratory in University of Huddersfield in 2023 (Figures 27 and 28). Furthermore, through the support of International Society for Neurochemistry and TETFund/IBR Grants, I was able to establish a modest Cell and Molecular and Neurobehaviour Laboratories for Research and Development.

Figure 25: Dr. F. S. Lewu, at RUSKA Laboratory, SVVU

Figure 26: Prof. M. Lakshman (1st on the left). RUSKA Laboratory, SV Veterinary University, Rajendranagar, Hyderabad, India

Figure 27: Dr. M. Y. Adana at University of Huddersfield, UK

Figure 28: Prof. Olumayokun Olajide, University of Huddersfield, UK

My Contributions to the Ilorin Community

I have been involved in organising outreaches, workshops and volunteer medical programmes to different arms of the society, especially to the Ilorin community. Thus, in March 2013 and March 2014, I organised (in collaboration with Dana Foundation and Dana Alliance for Brain Initiatives, New York, U.S.A) Brain Awareness Sensitisation Campaigns within Ilorin Metropolis, Schools and the University of Ilorin.

I am an active member of the Ilorin Neuroscience Group (ING). This Group organises brain-related outreaches and advocacy periodically to advance neuroscience education and research as well as promote mental health of the Society. Members of the Group include Prof B.V. Owoyele (President), Prof. O.B. Akinola, Prof. M.S. Ajao, Prof. M.T. Yakubu, among several others.

Looking into the Future

By the special grace of God, I hope to continue my studies on demyelinating disorders amongst other research interests, and in collaboration with other scientists in translational medicine. I will continue to explore ethnomedicine to identify more refined molecules for the management of developmental and neurodegenerative conditions.

Conclusion

Human Anatomy is indeed “beyond flesh and bone”. Biomedical researchers should embrace new approaches and interdisciplinary collaboration to advance our understanding of the human body. The use of genetic and molecular tools in anatomy research has the potential to uncover new insights into the mechanisms underlying physiological processes and diseases. It is my expectation that in no distant time, some of these neurological-based conditions, which hitherto have no effective therapeutic solution would benefit immensely from our search of more accessible, more affordable and more effective phytochemical and pharmacological candidates.

Recommendations

I want to make the following recommendations which I am optimistic, will be beneficial to the government, University, society and the individual:

To the Government

1. Nigeria is in dire need of Neurologists, and efforts should be made to retain them within the country as they are being trained;
2. there is need to improve access to diagnostic tools to mitigate the challenge of disease diagnosis;
3. public enlightenment is urgently needed to educate the Society about MS; and that
4. there is need to enforce Tobacco Production laws. Government should take a cue from other countries, such as New Zealand, United Kingdom and Australia to effect this.

To the University

1. The University should continue to promote and emphasise quality of research papers for promotion. Fewer, but exceptional papers in very highly rated journals should attract special consideration;
2. motivation for research outputs should include equipping the laboratory of such researchers with research facilities, laboratory equipment, and others;
3. the University Research Laboratories must be accessible to researchers 24 hours a day, even during Unions' industrial actions; and that
4. with increasing population of students offering Human Anatomy, more computer systems, as well as an Anatomage, are required at the Digital Anatomy Laboratory to enhance their teaching, practical sessions and conduct of practical examinations.

To the Society

1. Tobacco smoking - actively or passively is deadly. We should avoid it like a 'plague'. Pregnant women or women planning to have pregnancy should avoid tobacco exposure;
2. for nursing mothers, exclusive breastfeeding for the first six months as well as mother-baby intimacy is essential for brain development of the newborn; and that
3. individuals should engage in regular medical check-up.

Acknowledgements

I give all thanks, honour and glory to God for His faithfulness and mercies towards me from birth till this moment, and for making this inaugural lecture a dream come true. Everything I am today is made possible by God through His Only Begotten Son, Jesus Christ, Who is ever willing to receive as many as would trust their lives and future into His hand. The Psalmist rightly said, **"*Commit thy way unto the LORD; trust also in Him; and He shall bring it to pass***" (Psalm 37:5 KJV).

My journey through life has been by His Divine help, mercies, grace and strength. Like Prophet Isaiah said, **"*He* (that is, God) *giveth power to the faint; and to them that have no might He increaseth strength***" (Isaiah 40:9 KJV).

My sincere gratitude goes to my Employer (University of Ilorin), and for the opportunity to work in this great University. I thank the Vice-Chancellor, Prof. Wahab Olasupo Egbewole, for my appointment as a Professor, and for giving me this privilege to present this inaugural lecture.

I appreciate the Library and Publications Committee under the Chairmanship of Prof. A. A. Adeoye, for his deep reflection and intervention on this inaugural lecture. I equally appreciate the Dean of Basic Medical Sciences (Prof. M. S. Ajao), former Deans of the old Basic Medical Sciences, especially Prof. C. N. B. Tagoe (a former Adjunct Professor of Anatomy and former Vice Chancellor, University of Ghana), Prof. A. A. Akande and Prof. E. A. O. Afolayan, for their academic tutelage and administrative mentorship. I equally appreciate the Provost of College of Health Sciences (Prof. B. S. Alabi), the former Provosts (Prof. O. T. Adedoyin, Prof. W. B. R. Johnson, Prof. A. B. O. Omotoso and Prof. B. J. Bojuwoye) and all members of the College Academic Board and College Assembly.

Very many people have contributed to making me who I am today. Consequently, I am grateful to my teachers while pursuing my first degree in Anatomy. Of note is the sacrifice of Mr. B. U. Enaibe (now Prof. B. U. Enaibe), my teacher and supervisor, Dr. A. Adu (of blessed memory), and Prof. A.

Odekunle, who as the Head of Department also contributed to my admission into the Anatomy programme. Other academic mentors are Prof. A. O. Soladoye (former H.O.D., Dean and Ag. Provost), Prof. C. O. Bewaji, Prof (Mrs.) E. A. Balogun, of the then Department of Physiology and Biochemistry.

I must also not forget to appreciate all my teachers during my medical training. Although I might not be able to mention all of you by names, you are definitely a source of inspiration to my academic career. Permit me to mention a few names: Prof. M. O. Buhari (former Deputy Vice-Chancellor, Research, Technology and Innovation), Prof. I. A. Katibi, Prof. A. A. Fawole (Deputy Vice-Chancellor, RTI), Profs. F. O. Ologe, O. R. Balogun, T. M. Akande, O. O. Adesiyun, O. A. Mokuolu, and many more.

I appreciate all my teachers within the Department: Late Prof. E. A. Caxton-Martins, who supervised my postgraduate training (M.Sc. and Ph.D.) in Anatomy, but could not complete that role before the completion of my Ph.D. due to his demise); Prof. B. U Enaibe, for accepting to take up the main supervisory role of my Ph.D. Thesis; Prof. O. B. Akinola, who co-supervised my Ph.D. Thesis and played a pivotal role in my academic career and also assisted in reviewing this inaugural lecture; Prof. M. S. Ajao for his academic and administrative tutelage and mentorship. Special thanks to my H.O.D., Prof. A. Olawepo and all members of staff of the Department for their numerous support in cash and kind towards this inaugural lecture: Prof. A. O. Oyewopo; Prof A. S. Alabi (*Crown*) my brother, friend and roommate of many years, with whom I have many things in common; Dr. E. R. Kadir, for all her supports; Dr. M. Y. Adana, Dr. O. J. Olajide, Dr. A. Imam, Dr. S. M. Gwadabe, Dr. S. B. Kareem, Dr. R. Jaji-Sulaimon, Dr. F. S. Lewu, Dr. F. A. Sulaimon, Dr. A. Ibrahim, Dr. K. M. Ibiyeye, Dr. A. Alabi, and the technical staff, Mr. P. O. Awolola, Mrs. F. M. Adigun, Mr. J. T. Adetoro, Mr. Danlami Sule, Mr. M. Adewole, Mrs. O. D. Agbaje, Mrs. S. O. Quadri, and all former staff members, Dr. A. I. R. Abioye, Dr. A. A. Akinlolu, Mr. Abel Uweru and Mrs. Shade Ibrahim. I also appreciate all former H.O.Ds, including

Prof. S. B. Agaja (for his often encouragement and prompting, even after retirement) and Dr. O. R. Jimoh.

I acknowledge all professors and colleagues from other sister Departments in the Basic Medical and Basic Clinical Sciences, including Prof. B. V. Owoyele, Prof. L. A. Olayaki, Prof. L. A. Olatunji, Prof. T. M. Salman, Prof. O. E. Olorundare, Dr. M. O. Ologe, Dr. M. T. Ayinla, Dr. L. S. Ojulari, Dr. T. O. Ayinde, Dr. A. O. Oyabambi, Dr. A. L. Oyewole, Dr. H. O. Jimoh-Abdulghaffaar, Dr. A. O. Imam-Fulani, Dr. H. A. Abdulrahim and Dr. A. Z. Lawal.

I am greatly indebted to the following Professors: Jianrong Li (who invited me to her laboratory at the Texas A&M University, College Station, Texas, U.S.A. and for the research training I received); Joby Joseph (Centre for Neural and Cognitive Science, University of Hyderabad, for having me in his laboratory as a Research Scholar), M. Lakshman (RUSKA Labs, Sri Venkateswara Veterinary, University (S.V.V.U), Rajendranagar, Hyderabad); O. Olajide (University of Huddersfield, U.K), Sharon Juliano (Uniformed Services University of the Health Sciences, U.S.A. and the leader of the Teaching Tools IBRO Teaching Tools School and Workshop); Y. Raji (Physiology Dept., University of Ibadan; he donated the nicotine I used for my Ph.D. research) A. D. Zagga (Usmanu Danfodiyyo University, Sokoto), F. I. O. Duru, A. A. Oremosu, A. A. Osinubi, M. Ibeabuchi (of blessed memory), O. O. Dosumu (all from University of Lagos), G. S. Oladipo (University of Port-Harcourt), K. W. Wahab (Department of Medicine, for sparing time to review and correct this inaugural lecture), P. M. Kolo (Department of Medicine), P. O. Ajiboye (Department of Psychiatry), M. T. Yakubu, J. O. Adebayo (Department of Biochemistry), M. Ameen (Department of Chemistry, who provided most of the *Moringa oleifera* extracts we used); for all your encouragement and support in the advancement of my career in Anatomy.

I also appreciate all my elders in the Compatriots, the Convener, Prof. A. B. O. Omotoso and all members, for the love and togetherness enjoyed.

I specially acknowledge all members of staff of the University Health Services under the leadership of the Director of University Health Services, Dr. Abdulrasheed Odunola.

My past and present students and supervisees are highly recognised and appreciated: my past masters students (Kolo Rhoda, Omoboye Labake, Ayodeji Ayodele, Ayeni Busola, Babalola Abdulsalam, Abdulsalam Fatimah, Bature Abdulkabir, Mutholib Nafisat, Kalu Orji, Arietarhire Leviticus, Ukwubile Ileje, Gbadamosi Ismail, Babatunde Dare and Dada Habeeb), my past Ph.D. students (Jaji-Sulaimon Rukayat, Amedu Nathaniel, Adediji John, Gbadamosi Ismail); my current research students at different stages of completion (Mutholib Nafisat, Babatunde Dare, Babalola, Abdulsalam, Arietarhire, Leviticus, and Bature Abdulkabir). All my past and present B.Sc. project students are also very warmly acknowledged.

I appreciate the support from my professional bodies, including the Anatomical Society of Nigeria, Association of Specialist Medical Doctors in Academic, Nigerian Medical Association Kwara State Branch, International Society for Neurochemistry and International Brain Research Organisation.

I appreciate the Old Students Association of All Saints' Unity Secondary School, Usi-Ekiti, especially the 1988-1993 set. I also appreciate the support of my B.Sc. Anatomy classmates, especially Prof. A. O. Oyewopo (University of Ilorin), Prof. G. S. Oladipo (University of Port-Harcourt), Prof. A. A. Akinlolu (Federal University of Health Sciences, Otukpo). I equally appreciate the Unilorin Medical College 2005 Set, "*Blazing Forth*", colleagues in UITH and in different parts of the country and the globe.

I thank all my spiritual fathers and leaders in Kwara State, beginning with Pastor and Mrs. David Adebiyi, the State Overseer of Deeper Christian Life Ministry, Kwara State and all the Pastors, leaders and members of Deeper Life Bible Church, Ilorin Region. Special thanks to Pastor Sunday Adewara, Prof. Timothy Fayeye of the Faculty of Agriculture, Pastor G. S. Ajiboye and Pastor G. Y. Ajiboye and all coordinators, leaders, workers and members of G.R.A. and Airport Groups of Districts.

I also appreciate Prof. Israel Ogunlade and Prof. K. S. Olorunmaiye of the Faculties of Agriculture and Life Sciences (respectively), who were my Pastors during my undergraduate days.

Special thanks to Pastor and Mrs. E. Aladesusi, my spiritual parents from childhood; Pastor M.O. Salami, Registrar, Anchor University, Lagos and former Registrar, Kwara State Polytechnic, for his exceptional fatherly care and spiritual support for me and my family; Pastor Andy Edeh and the Success Point Team (Pastor Abraham Ojuolape, Pastor Tosin Apata, Dr. Idowu Adebara, Dr. Sola Osetoba, Dr. Peter Omefe, Dr. Amos Salami, Dr. Agboola, Engr. Samson Obaditan, Mr. Adeola Buluro), the Team with whom I share a lot of success; Mr. Moses Folorunsho, my friend and brother brought together by divine arrangement, and Mr. O. Moyosola.

I appreciate the traditional ruler of my home town; His Royal Majesty Oba Joachim Adeyemi Afolabi Ajibola, Agungesoye II, The Ojurin of Ijurin-Ekiti, as well as other traditional leaders. May your time bring more prosperity to our dear town in Jesus' name, Amen.

I am very grateful to all our fathers, elders and all descendants of the OMOSOLU OMOTOSO DYNASTY, Usolu Compound, Ijurin-Ekiti, Ekiti State. Most profoundly, I appreciate my late father, Chief James Olu Omotoso, for his love and fatherly role he played in making me the man that I am today by the Grace of God. My mother, Mrs. Rachel Olufunso Omotoso (who in less than a month will turn 90), I thank God for your love, care and all the sacrifice you made to enable me have a good education and be someone in life.

I appreciate our eldest sister in the Omotosos' family, Mrs. Abike Daramola, for her numerous support; I thank our father of the Omotosos' family; Prof. A. B. O. Omotoso, and his wife Mrs. Kikelomo Olufunmilayo Omotoso for their support and the numerous roles played in my life, including my entrance into this University, both as a student and a member of staff.

I acknowledge the roles played by Pastor (Dr.) Ayodeji Olusegun Omotoso and his wife, Mrs. Bamidele Mercy

Omotoso, Pastor and Mrs. Babatunde Omotoso, Dr. and Mrs. Oladipo Omotoso, Mr. and Mrs. Babatope Omotoso, Mr. & Mrs. Michael Olasupo, Mr. & Mrs. Alani Oyewole, Prof. and Mrs. John Ashidi, Dr. and Mrs. Oladele Omotoso, Mrs. Ronke Ajibola, Dr. Ayotunde Omotoso and Dr. Ayotade Ojuawo.

Special thank goes to Mrs. Olayinka Olasupo, who was saddled with the responsibility of taking me to Usi-Ekiti in January 1988 to begin my secondary education at the then All Saints' Unity Secondary School as a boarder, and for her numerous supports during my undergraduate days.

I thank my elder brother Dr. (Engr.) Oladipo Omotoso, for sponsoring my medical training in Nigeria (even though he had wanted that done in Canada). Thank you also for the moral support to achieving my academic career, although you desired I become a surgeon. Your sacrifice and understanding has made this day a reality. I also thank my elder sister; Mrs. Idowu Oyewole for all her support during my undergraduate programme.

I bless the Lord for the delightful children He has given my family. Children, thank you for making life worth living and for being a source of joy to the family. My precious children are Daniel, David, Deborah and Divine. May you continue to excel like Daniel, dominate like David, prevail like Deborah and 'be more' like the Divine, in Jesus' name.

Neither the most advanced dictionary nor any language encyclopedia has the most appropriate vocabularies, to describe the only delight specially made for me from God, and that is my wife, Olawumi. Thank you for fulfilling God's plan in my life, as the "*bone of my bones, and flesh of my flesh*" (Genesis 2:23).

Finally, I sincerely appreciate everyone who, in one way or the other, contributed to my life, even though time and space could not permit me to mention you by name.

Vice Chancellor, sir, distinguished guests, ladies and gentlemen, I thank you all for finding time to listen to my inaugural lecture. Thank you and God bless you all, amen!

References

Abdulsalam, F.A., Mutholib, N.Y., Bature, A.I., Gbadamosi, I.T. & **Omotoso, G. O.** (2022).Vitamin B complex protects against maternal deprivation-induced cerebellar damage in adolescent rats. *Nigerian Journal of Neuroscience,* 13 (3):87-93.

Adeloye, D., Auta, A., Fawibe, A., Gadanya, M., Ezeigwe, N., Mpazanje, R. G., Dewan, M. T., Omoyele, C., Alemu, W., Harhay, M. O., & Adewole, I. F. (2019). Current prevalence pattern of tobacco smoking in Nigeria: a systematic review and meta-analysis. *BMC Public Health,* 19:1719.

Aderinto, N., Muili, A. O. & Opanike, J. (2023). Navigating the journey of multiple sclerosis management in Africa, overcoming hurdles and harnessing opportunities: a review. *Annals of Medicine and Surgery*, 85(5): 1774–9.

Akinlolu, A., Ameen, M., Quadri, T., Odubela, K., **Omotoso, G.**, Yahya, R., Biliaminu, S., Adeyanju, M., Ebito, G., & Otulana, J. (2020). Extraction, isolation and evaluation of anti-toxic principles from *Moringa oleifera* (MoF6) and *Myristica fragrans* (*Trimyristin*) upregulated Acetylc holinesterase concentrations in Sodium arsenite-induced neurotoxicity in rats. *Journal of Phytomedicine and Therapeutics*, 19(2):466– 82.

Akinyemi, R. O., Afolayan, A. J., Akinwuntan, A. E., & Ogunniyi, A. (2019). Prevalence and correlates of multiple sclerosis in South-Western Nigeria. *Multiple Sclerosis and Related Disorders* 28:131-5.

Alabelewe, M. T., Odey, N. R., Sylvester, J. O., Kolo, R. M., Salaudeen, B. O., Gbadamosi, I.T., Ayodeji, A. O. & Omotoso, G. O. (2024). *Moringa oleifera* oil modulates cerebellar neuroinflammation and oxidative stress associated with permethrin neurotoxicity. *The Journal of Anatomical Sciences,* 15(1): 63-70.

Amedu, N. O. & **Omotoso, G. O.** (2020a). Evaluating the role of Vitexin on haematologic and oxidative stress markers in lead-induced toxicity in mice. *Toxicology and Environmental Health Sciences,* 12(3): 257-63.

Amedu, N. O. & Omotoso, G. O. (2020b). Lead acetate-induced neurodegenerative changes in the dorsolateral prefrontal cortex of mice: the role of Vitexin. *Environmental Analysis Health and Toxicology,* 35 (1): e2020001.

Amedu, N.O. & **Omotoso, G. O.** (2020c). Influence of Vitexin on ataxia-like condition initiated by lead exposure in mice. *Toxicology and Environmental Health Sciences,* 12(4): 305–13.

Anzano, A., Ammar, M., Papaianni, M., Grauso, L., Sabbah, M., Capparelli, R., Lanzotti, V. (2021): *Moringa oleifera* Lam.: A Phytochemical and Pharmacological Overview. *Horticulturae,* 7(10):409. https://doi.org/10.3390/horticulturae7100409

Bathelt, J., Scerif, G., Nobre, A. C., Astle, D. E. (2019): Whole-brain white matter organization, intelligence, and educational attainment. *Trends in Neuroscience and Education*, 15:38-47.

Baumann, N. & Pham-Dinh, D. (2001). Biology of oligodendrocyte and myelin in the mammalian central nervous system. *Physiological Reviews,* 81(2):871-927.

Boullerne, A. I. (2016): The history of myelin. *Experimental Neurology,* 283(Pt B):431-45.

Buck, J. M., O'Neill, H. C. & Stitzel, J. A. (2020). Developmental nicotine exposure engenders intergenerational down regulation and aberrant posttranslational modification of cardinal epigenetic factors in the frontal cortices, striata, and hippocampi of adolescent mice. *Epigenetics Chromatin,* 13(1):13.

Business Day Newspaper (1st June, 2022). Multiple sclerosis cases seen rising in Nigeria, Africa. URL: businessday.ng

Cao, J., Wang, J., Dwyer, J. B., Gautier, N. M., Wang, S., Leslie, F. M .& Li, M. D. (2013). Gestational nicotine exposure modifies myelin gene expression in the brains of adolescent rats with sex differences. *Translational Psychiatry*, 3(4): e247.

Chen, H., Iglesias, M. A., Caruso, V. & Morris, M. J. (2011). Maternal cigarette smoke exposure contributes to glucose intolerance and decreased brain insulin action in mice offspring independent of maternal diet. *PLoS One,* 6(11): e27260.

Chen, H., Saad, S., Sandow, S. L. & Bertrand, P. P. (2012). Cigarette smoking and brain regulation of energy homeostasis. *Frontiers in Pharmacology*, 3:147.

Dobsona, R. & Giovannoni, G. (2019). Multiple Sclerosis: A Review. *European Journal of Neurology*, 26 (1): 27-40.

Gbadamosi, I. T., Omotoso, G. O., Olajide, O. J., Dada-Habeeb, S. O., Arogundade, T. T., Lambe, E. & Obasi, K. K. (2016). *Moringa* protects against nicotine-induced morphological and oxidative damage in the frontal cortex of Wistar rats. *Anatomy*, 10:170-6.

Ghasemi, N., Razavi, S. & Nikzad, E.(2017). Multiple Sclerosis: pathogenesis, symptoms, diagnoses and cell-based therapy. *Cell Journal*, 19(1):1–10.

Hines, T. (2018): Anatomy of the Brain. Mayfield Clinic, Cincinnati, Ohio. https://mayfieldclinic.com/peanatbrain. htm

International Multiple Sclerosis Genetics Consortium, & Multiple Sclerosis International Federation. (2019). Multiple sclerosis genomic map implicates peripheral immune cells and microglia in susceptibility. *Science*, 365(6460), eaav7188.

Jaji-Sulaimon, R. & **Omotoso, G. O.** (2021). Effects of quercetin on glial cells and myelin integrity during cuprizone-induced cerebellar demyelination in male mice. Ph.D. Thesis.

Jarjour, A. A., Zhang, H., Bauer, N., Constant, C. & Williams, A. (2012): *In vitro* modeling of central nervous system myelination and remyelination. *Glia*, 60(1):1–12.

Kasolo, J. N., Bimenya, G. S., Ojok, L., Ochieng, J. & Ogwal-okeng, J. W. (2010): Phytochemicals and uses of *Moringa oleifera* leaves in Ugandan rural communities. *Journal of Medicinal Plants Research*, 4: 753-7.

Kolo, R. M. & Omotoso, G. O. (2023). Effects of *Nigella sativa* oil on cuprizone-induced demyelination in adult male Wistar rats. M.Sc. Dissertation.

Kumar, D. R., Aslinia, F., Yale, S. H., & Mazza, J. J. (2011). Jean-Martin Charcot: the father of neurology. *Clinical Medicine & Research*, *9*(1), 46–49.

Kundakovic, M. & Champagne F. A. (2015). Early-life experience, epigenetics, and the developing brain. *Neuropsychopharmacology*, 40:141–53.

Leelavinothan, P., Magdalena, K., Agnieszka, K., Anna, R. & Ryszard, A. (2007). Antioxidant activity of the crude extracts of drumstick tree (*Moringa oleifera lam.*) and sweet broomweed (S*coparia dulcis*) leaves. *Polish Journal of Food Nutrition Sciences*, 57: 203–208.

LifeCare Hospital, 2024: World MS Day. https://lifecare hospitalindia.com/blog/2020/05/30/world-ms-day/ (Accessed: 25/05/2024)

Lucchinetti, C., Bruck, W., Parisi, J., Scheithauer, B., Rodriguez, M. & Lassmann, H. (2000). Heterogeneity of multiple sclerosis lesions: implications for the pathogenesis of demyelination. *Annals of Neurology*, 47:707–717.

Mader, S.S. (2001): Animal Organisation and Homeostasis. In: Biology. Seventh Edition, McGraw-Hill; Columbus, pp 718-723.

Matsushima, G. K. & Morell, P. (2001). The neurotoxicant, cuprizone, as a model to study demyelination and remyelination in the central nervous system. *Brain Pathology*, 11:107–116.

Multiple Sclerosis International Federation (2023): New prevalence and incidence data now available in the Atlas of MS. https://www.msif.org/news/2023/08/21/new-prevalence-and-incidence-data-now-available-in-the-atlas-of-ms/?cn-reloaded=1 (Accessed 25/05/2024)

Mutholib, N. Y., Abdulsalam, F. A., Bature, A. I., Gbadamosi, I. T. & **Omotoso, G. O**. (2022). *Garcinia kola* biflavonoid complex mitigates cerebellar histomorphological alterations and oxidative stress in maternally deprived rats. *Nigerian Journal of Basic and Applied Medical Sciences,* 2(1):78-82.

Mutholib, N. Y. & **Omotoso, G. O**. Maternal deprivation. Ph.D. Thesis 2024.

Neves, B. H., Menezes, J., Souza, M. A. & Mello-Carpes, P. B. (2015). Physical exercise prevents short and long-term deficits on aversive and recognition memory and attenuates brain oxidative damage induced by maternal deprivation. *Physiology & Behavior,* 152:99-105.

Nouri, A. (2011): Who was Jean-Martin Charcot? URL: https://www.aaas.org/who-was-jean-martin-charcot (Accessed 25/05/2024).

Oboro, H. O., Umanah, A. U., Chukwumah, N. M. & Sede, M. (2008). Creation of artificial midline maxillary diastema: opinion of Nigerian dentists. http://iadr.confex.com/iadr/pef08techprogram/abstract_109649.htm.

Ogwumike, O. O., Abubakar, A. M., Danesi, M. A., & Ogunseyinde, A. O. (2020). Incidence of multiple sclerosis in Lagos, Nigeria: A five-year retrospective study. *African Health Sciences,* 20(3):1205-1211.

Oladipo, G. S. & Amangi-Peters, D. I. (2005). Incidence of Cheek Dimples among South-South and South-Eastern Nigerians. *J. Biomed. Afric,*. 3(2):23-25.

Omotoso, G. O. (2010). Incidence of bilateral and unilateral cheek dimples amongst southwest indigenes of Nigeria. *International Journal of Biological Science,* 2(6): 95-98.

Omotoso, G. O. & Kadir, R. E. (2010). Midline diastema amongst South-Western Nigerians. The *Internet Journal of Dental Science,* 8(2):22.

Omotoso, G. O., Adeniyi, P. A. & Medubi L. J. (2010). Prevalence of facial dimples amongst South-western Nigerians: A case study of Ilorin, Kwara State of Nigeria.

International Journal of Biomedical and Health Sciences, 6(4):241-4.

Omotoso, G. O., Olagunju, A. A., Enaibe, B. U., Oyabambi, A. O. & Olawuyi, T. S. (2011). Alteration in semen characteristics and testicular histology of male Wistar rats following exposure to cigarette smoke. *West African Journal of Assisted Reproduction*, 2(1):45-49.

Omotoso, G. O., Enaibe, B. U., Akinola, O. B., Kadir, R. E., Akinlolu, A. A., Oyewopo, A. O., Olawuyi, S. T., Adebayo, J. O., Apalowo, O. S. & Sofoluwe, A. V. (2012). Lipid profile and liver histochemistry in animal models exposed to cigarette smoke. *Journal of Basic and Applied Sciences*, 8(1):20-25.

Omotoso, G. O., Kadir, R. E., Alabi, J. T., Alabi, A. S. & Oyabambi, A. O (2013a). Exposure to cigarette smoke altered the cytoarchitecture and anti-oxidant activity of the frontal cortex in Wistar rats. *International Journal of Biological and Chemical Sciences*, 7(4):1595-1601.

Omotoso, G. O., Enaibe, B. U. & Caxton-Martins, E. A. (2013b). Microarchitectural changes in the superior colliculli of male Wistar rats after cigarette and cotton wool smoke exposure. *The Tropical Journal of Health Sciences*, 20(1):37-40.

Omotoso, G. O. & Babalola, F. A. (2014). Histological changes in the cerebelli of adult Wistar rats exposed to cigarette smoke. *Nigerian Journal of Physiological Sciences*, 29 (1); 43-46.

Omotoso, G . O., Akinola, O. B., Enaibe, B. U. & Caxton-Martins, E. A (2014a). Neuromorphometric analysis of the lateral prefrontal cortex of young Wistar rats exposed to nicotine in utero. *Rawal Medical Journal*, 39(3):331-6.

Omotoso, G. O., Onanuga, I. O., Ibrahim, R. B. (2014b): Histological effects of permethrin insecticide on the testis of adult Wistar rats. *Ibnosina Journal of Medicine and Biomedical Sciences*, 6(3):125-9.

Omotoso, G. O., Ojulari, L. S. & Oyabambi, A. O. (2014c). Perception of cheek dimples amongst the Yorubas in Nigeria. *The Tropical Journal of Health Sciences*, 21(2):18-20.

Omotoso, G. O., Alabi, A. S., Femi-Akinlosotu, O., Akinola, O. B., Enaibe, B. U. & Caxton-Martins, E. A. (2015). Gestational nicotine exposure alters oligodendrocyte morphology and axonal myelination in the lateral prefrontal cortex of young Wistar rats. *Nigerian Journal of Neuroscience*, 7 (1):24-9.

Omotoso, G. O., Olajide, O. J., Gbadamosi, I. T., Suleiman, F. A. & Oladimeji, J. O. (2017a). Kolaviron ameliorates histomorphological changes associated with cuprizone-induced cerebellar damage. *The Journal of Anatomical Sciences*, 8(2):131-7.

Omotoso, G. O., Hambolu O. Z. & Alabi, A. S. (2017b). Cigarette smoke alters testicular and epididymal histology in Adult Wistar rats. *Journal of Experimental and Clinical Anatomy*, 16(1):25-8.

Omotoso, G. O., Gbadamosi, I. T., Afolabi, T. T., Abdulwahab A. B. & Akinlolu, A. A. (2018a). Ameliorative effects of *Moringa* on cuprizone-induced memory decline in rat model of multiple sclerosis. *Anatomy and Cell Biology*, 51:119-27.

Omotoso, G. O., Ukwubile, I. I., Arietarhire, l., Sulaimon, F. A. & Gbadamosi, I. T. (2018b). Kolaviron protects the brain in cuprizone-induced model of experimental multiple sclerosis via enhancement of intrinsic antioxidant mechanisms: possible therapeutic applications? *Pathophysiology*, 25(4):299-306.

Omotoso, G. O., Adunmo, G. O., Ojulari, L. S., Olawuyi, T. S., Lewu, F. S., Jaji-Sulaimon, R., Sulaimon, F. A., Gbadamosi, I. T. & Onoja, O. P. (2018c). *Moringa oleifera* attenuates biochemical and histological changes associated with the pancreas in nicotine-treated rats. *Research Journal of Health Sciences*, 6 (4); 172-81.

Omotoso, G. O., Olajide, O. J., Gbadamosi, I. T., Rasheed, M. A. & Izuogu, C. T. (2018d). Kolaviron protects the prefrontal cortex and hippocampus against histomorphological and neurobehavioral changes in cuprizone model of multiple sclerosis. *Malaysian Journal of Medical Sciences*, 25(2):50–63.

Omotoso, G. O., Kolo, R. M., Afolabi T., Jaji-Sulaimon, R. & Gbadamosi, I. T. (2018e). *Moringa oleifera* ameliorates histomorphological changes associated with cuprizone neurotoxicity in the hippocampal *Cornu Ammonis* (CA) 3 region. *Nigerian Journal of Physiological Sciences*, 33:95-9.

Omotoso, G. O., Gbadamosi, I. T., Akinlolu, A. A., Ameen, M. O. Kadir, R. E., Jaji-Sulaimon, R., Abdulwahab, A. B. & Kolo, R. M. (2018f). *Moringa oleifera* is protective against microarchitectural and neurochemical changes associated with cuprizone-induced pre-frontal cortex neurotoxicity in female Wistar rats. *Nigerian Journal of Neuroscience*, 9 (2); 47-52.

Omotoso, G. O., Kadir, R. E., Sulaimon, F. A., Jaji-Sulaimon, R. & Gbadamosi, I. T. (2018g). Prenatal exposure to gestational nicotine before neurulation is detrimental to neurodevelopment of Wistar rats' offspring. *Malaysian Journal of Medical Science, 25 (5):35–47.*

Omotoso, G. O., Olajide, O. J., Gbadamosi, I. T., Adebayo, J. O., Enaibe, B. U., Akinola, O. B., & Owoyele, B. V. (2019): Cuprizone toxicity and *Garcinia kola* biflavonoid complex activity on hippocampal morphology and neurobehaviour. *Heliyon*, 5 (7): e02102.

Omotoso, G. O., Adebayo, J. O., Olajide, O. J., Gbadamosi, I. T., Enaibe, B. U., Akinola, O. B. & Owoyele, B. V. (2020a). Ameliorative effects of kolaviron on behavioural deficits and oxidative damage in prefrontal cortex and hippocampus of cuprizone-induced demyelinated mice. *Nigerian Journal of Neuroscience*, 11(2):53-61.

Omotoso, G. O., Arietarhire, L. O., Ukwubile, I. I. & Gbadamosi, I. T. (2020b). The protective effect of kolaviron on molecular, cellular, and behavioral characterization of cerebellum in the rat model of demyelinating diseases. *Basic and Clinical Neuroscience*, 11(5):609–18.

Omotoso, G. O., Mutholib, N. Y., Abdulsalam, F. A. & Bature, A. I. (2020c). Kolaviron protects against cognitive deficits and cortico-hippoccampal perturbations associated with maternal deprivation in rats. *Anatomy and Cell Biology*, 53: 95-106.

Omotoso, G., Oloyede, O., Lawal, S., Gbadamosi, I., Mutholib, N., Abdulsalam, F., Bature, A., Babalola, A., Ayeni, B., & Amedu, N. (2020d). Permethrin exposure affects neurobehavior and cellular characterization in rats' brain. *Environmental Analysis, Health and Toxicology*, 35(4), e2020022.

Omotoso, G. O., Abdulsalam, F. A., Mutholib, N. Y., Bature, A. I. & Gbadamosi, I. T. (2020e). Cortico-hippocampal morphology and behavioural indices improved in maternal deprivation model of schizophrenia following vitamin B complex supplementation. *Neurology, Psychiatry and Brain Research*, 38:74-82.

Palit, P. (2024): World No-Tobacco Day 2024, History & Significance. https://www.oliveboard.in/blog/world-no-tobacco-day-2024/ (Accessed: 25/05/2024).

Prasada, G., Nakra, O., Gowda, M., Kumar, A. (2014): Clinical management of midline diastema (Lt Col). URL: https://api.semanticscholar.org/CorpusID:31971562(Accessed: 25/05/2024).

Richter, F. (2021): Tobacco: Global Tobacco Use Is Steadily Declining. https://www.statista.com/chart/26381/global-tobacco-use-prevalence-by-age/ (Accessed: 25/05/2024)

Saunders, J. B. D. M. & O'Malley, C. D. (1973). Illustrations from the works of Andreas Vesalius of Brussels. New York. sDover.

Schultz, M. (2008): Rudolf Virchow. *Emerging Infectious Diseases,* 14(9): 1480–1481.

Spiteri, S. E. (2018): The neural correlates of effort-related and effort-unrelated fatigue in patients with multiple sclerosis. Ph.D. Thesis. Universitat Konstanz, Konstanz. URL: http://nbn-resolving.de/urn:nbn:de:bsz: 352-2-1cw2ffkd35 oyr9

Walton, C., King, R., Rechtman, L., Baneke, P. (2020): Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. *Multiple Sclerosis Journal*, 26(14):1816-21.

Wang, Y., Wu, C., Caprariello, A.V., Somoza, E., Zhu, W., Wang, C., Miller, R. H. (2009). *In vivo* quantification of myelinchanges in the vertebrate nervous system. *The Journal of Neuroscience*, 29(46):14663-9.

World Health Organisation (2023). Tobacco. https://www.who. int/news-room/fact sheets/detail/tobacco#:~:text=The%20 tobacco%20epidemic%20is%20one,%2Dhand%20sm oke%20(4).

World Health Organisation (2024). Tobacco use declines despite tobacco industry efforts to jeopardize progress. https://www.who.int/news/item/16-01-2024-tobacco-use-declines-despite-tobacco-industry-efforts-to-jeopardize-progress

Zirngibl, M., Assinck, P., Sizov, A., Caprariello, A. V., & Plemel, J. R. (2022). Oligodendrocyte death and myelin loss in the cuprizone model: an updated overview of the intrinsic and extrinsic causes of cuprizone demyelination. *Molecular Neurodegeneration*, 17(1):1-28.

Zubair, H. O., Awujoola, M. T., Meduna, V. O., Omoboye, L. T., Ayodeji, A. O. & **Omotoso, G. O**. (2023): Sesame oil protects against permethrin-induced memory decline and oxidative stress in the hippocampus of Wistar rats. *The Journal of Anatomical Sciences*, 14(2): 63-70.