Ahmadu Bello University, Zaria

FEEDING THE BRAIN: HOW YOUR DAILY FOODS SHAPE YOUR MIND

AN INAUGURAL LECTURE

Series No. 04/26

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By

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Dedication

This work is dedicated to the loving memory of my parents on who's shoulders I stood to rise to the top!

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Contents

FEEDING THE BRAIN: HOW YOUR DAILY FOODS SHAPE YOUR MIND

1.0 Background

Food is defined as any edible substance that is derived from plants, animals, or microorganisms and consumed to provide essential nutrients, energy, and nourishment to the body. It sustains life by supporting growth, repairing tissues, and enabling metabolism, primarily through carbohydrates, fats, proteins, water, vitamins, and minerals. The brain like any other organ in the body, require these ingredients for normal functioning. The brain is the organ inside the head that controls all body functions of a human being. Made up of billions of nerve cells, the brain is protected by the cranium (the bones that form the head). It is made up of three major parts: the cerebrum, the cerebellum and the brain stem. Each part of the brain controls a specific function in the body (Fig. 1).

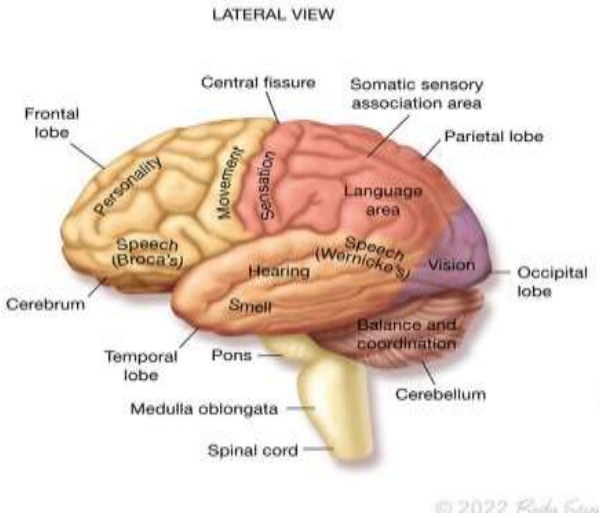

Fig. 1: Lateral View of the Brain Showing Structures and Functions

The Great Philosopher Hippocrates was quoted as saying ' *men ought to know that from the brain, and from the brain only, arise our pleasures, joys, laughter and jests, as well as our sorrow, pains, grief and tears. Through it…we think, see, hear….*' This implies that human behavior generally is coordinated by the brain. These behavioral paradigms eventually shape the human mind. According to philosophers, the mind is **an abstract concept used to characterize thoughts, feelings, subjective states, and self-awareness that presumably arise from the brain.** The mind is also defined as **the sum of the cognitive abilities that enable consciousness, perception, memory, thinking, imagination and judgment**. These processes are proven to occur in the brain as disorders of brain function impact negatively on their outcome. However it is safer to refer the sum of cognitive abilities as a domain of the mind rather than brain since brain activity is dependent also of nutrients from blood circulation. This may be the reason why 'mind' appeared in the Holy Qur'an (3 instances) but no mention of the 'brain'!

The use of psychoactive substances such as kola nut, coffee, marijuana, and other plant derived products to improve self worth, dates back to ancient times. This suggests that plants/plant parts can influence the activities of the brain in diverse ways such as relief of pain, improve mood etc. In Traditional Medicine, Herbal Medicine Practitioners employ (medicinal) plants as remedies for treatment of diseases. Traditional Medicine such as herbal medicine, indigenous therapies and others have been used by an estimated 88% of all countries globally (WHO). It has been an integral resource for health for centuries in communities around the world, and it is still a mainstay for some with inequities in access to conventional medicine. Over 40% (70%) of pharmaceutical formulations are based on natural products and landmark

drugs, including aspirin and artemisinin, originated from herbal medicine.

2.0 The Idea/Impetus

On assumption of duty in the department of pharmacology and clinical pharmacy of this great university, I met a vacuum. Two great scholars who ruled the department and faculty were Professors Gabriel G. Osuide, and Charles O. Wambebe. They were both neuropharmacologists and had employed behavioral tests to study effects of conventional drugs in chicks and mice. Within a period of four years they both had left the university and abandoned the 'research laboratory' where they worked. Professor Wambebe (Late) was appointed Pioneer Director General of the National Institute of Pharmaceutical Research and Development (NIPRD) Abuja in 1988 while Osuide became pioneer Director General of the National Agency for Food, Drug Administration and Control (NAFDAC) in 1992. While in Ahmadu Bello University Zaria, the University was refuted then to be a leading institution for neuroscience research. The department of Pharmacology hosted the headquarters of the Neuroscience Society of Nigeria (NSN). Tragically, Professor Wambebe not only left but took away with him all the staff in the department, including Technologists working in area of neuropharmacology.

I therefore inherited a 'Research Laboratory' with some equipment but little guidance and technical skills. Professor Joseph A. Anuka though a Neuroscientist, was more preoccupied with endocrine pharmacology at the time. I was fascinated however by those equipment and excited at some of the publications of Osuide and Wambebe that I saw in the laboratory. I decided to take the challenge and continue with neuropharmacology research in the department.

3.0 The Beginning

One of my earlier responsibility in the department was to accompany final year pharmacy students to the hospital to attend ward round in medical wards. Although we were limited to the medical wards, I observed many patients presenting to the hospital with stroke and others with psychiatric and neurological disorders. There appeared to be no specific treatment for stroke at the time. My earliest publication looked at '**Prevalence and Prognosis of Cerebrovascular Accident in Zaria, Kaduna State Nigeria'** (Danjuma *et al.,* 2005).

From the study, prognosis seemed to be poor and I decided to venture into discovery and development of new agents that could be useful in treatment of disorders of the brain including stroke. Although ethnopharmacology had been officially established in Nigeria since 1961, it was not until 1990s and 2000s that significant progress had been made in scientific validation and standardization of of traditional herbal remedies. I decided to key into this area and screen medicinal plants with folkloric claims of treating neurological and psychiatric disorders. Medicinal plants, mostly consumed as foods locally, were screened for the following commonly encountered disorders of the brain:

3.1 Nociception/Pain Perception

Pain and mental health share a deep, bidirectional relationship. Persistent pain increases the risk of developing mental health conditions like depression, anxiety, and post-traumatic stress disorder. Conversely, psychological distress can heighten the body's sensitivity to pain, creating a self-perpetuating cycle. Enduring relentless pain leads to profound emotional distress, social isolation, loss of independence, and diminished quality of life. Up to 60% of people with chronic pain experience depression or anxiety. Psychological distress triggers the

nervous system, making the brain more perceptive and sensitive to physical discomfort. An untreated mental health condition can make a physical injury or chronic condition feel much worse.

The bidirectional relationship in pain outcome in an African population and other relationships affecting pain response have been elaborately studied in Zaria (Umar *et al.*, 2024a; Umar *et al.*, 2024b; Umar *et al.*, 2021; Umar *et al.*, 2020).

3.2 Anxiety Disorders

Anxiety belongs to the group of mental disorders that are characterized by a sudden feeling of intense fear, panic, shortness of breath, chest pain, insomnia, fatigue, sweating. The disorder occurs because of hyper responsiveness of *amygdala* and the *limbic system* connected to the prefrontal cortex in the brain. Anxiety is mediated in the central nervous system (CNS) via γ-aminobutyric acid (GABA), norepinephrine (NE), 5-hydroxytryptamine (5HT), Dopamine or peptide receptors (Martinez *et al.,* 2007; Keeton *et al.,* 2009).

There are several different kinds of anxiety disorders such as generalized anxiety disorder (characterized by excessive worry), panic disorder (characterized by panic attack), social anxiety disorder (characterized by excessive fear and worry in social situations), separation anxiety disorder (characterized by excessive fear or anxiety about separation from those individuals to whom the person has a strong emotional bond), post-traumatic stress disorder (develop following an exposure to an extremely threatening or horrific event or series of events) and others (WHO).

A study on the prevalence of academic stress, anxiety and depression among medical and health sciences students of Ahmadu Bello University Zaria (Farrau *et al*., 2024) revealed a remarkably high rate (68.1%) of anxiety among these students with 33% experiencing moderate to severe form. Contributing factors according to the study are heavy workload, examination pressure and other related academic activities.

3.3 Depression

Depression is different from usual mood fluctuations and short-lived emotional responses to challenges in everyday life. During a depressive episode, the person experiences depressed mood (feeling sad, irritable, emptiness) and a loss of pleasure or interest in activities for most of the day, nearly every day, for at least two weeks. Several other symptoms are also present, which may include poor concentration, feeling of excessive guilt or low self-worth, hopelessness about the future, thoughts about dying or suicide, disrupted sleep, changes in appetite or weight, and feeling especially tired or low in energy. People with depression are at an increased risk of suicide.

People with bipolar disorder experience alternating depressive episodes with periods of manic symptoms. During the depressive episode, the person experiences depressed mood or a loss of pleasure or interest in activities for most of the day, nearly every day. Manic symptoms may include euphoria or irritability, increased activity or energy, and other symptoms such as increased talkativeness, racing thoughts, increase in self-esteem, decrease in need for sleep, distractibility, and impulsive reckless behavior. People with manic disorder are at increased risk for suicide.

Farrau *et al*., (2024) showed that depression impacts 47.3% of medical sciences students of Ahmadu Bello University Zaria.

3.4 Schizophrenia

People with schizophrenia have a life expectancy 10-20 years below that of the general population. Schizophrenia is characterized by significant impairment in perceptions and changes in behavior. Symptoms may include persistent delusions, hallucinations, disorganized thinking, highly disorganized behavior or extreme agitation. People with schizophrenia may experience persistent difficulties with their cognitive functioning.

3.5 Epilepsy

Epilepsy is a chronic non communicable disease of the brain that affects around 50 million people worldwide. It is characterized by recurrent seizures, which are brief episodes of involuntary movement that may involve a part of the body (partial) or the entire body (generalized) and are sometimes accompanied by loss of consciousness and control of bowel or bladder function.

Seizure episodes are as a result of excessive electrical discharges in a group of brain cells. Different parts of the brain can be the site of such discharges. Seizures can vary from the briefest lapses of attention or muscle jerks to severe and prolonged convulsions. Seizures can also vary in frequency, from less than one per year to several in a day.

Epilepsy is defined as having two or more unprovoked seizures. One seizure does not signify epilepsy as up to 10% of people worldwide have one seizure during their lifetime. Fear,

misunderstanding, discrimination and social stigma have surrounded epilepsy for centuries. This stigma continues in many countries today and can impact on quality of life for people with the disease and their families.

Symptoms of epilepsy include loss of awareness or consciousness, and disturbances of movement, sensation (including vision, hearing and taste), mood or other cognitive functions. People with epilepsy tend to have more physical problems (such as fractures and bruising from injuries related to seizures), as well as higher rates of psychological conditions, including anxiety and depression. The risk of premature death in people with epilepsy is up to three times higher than in the general population, with the highest rates of premature mortality found in low and middle income countries and in rural areas.

Epilepsy and mental health share a complex, bidirectional relationship. People with epilepsy are 2 to 5 times more likely to develop psychiatric disorders than the general population, with about 1 in 3 patients receiving a lifetime psychiatric diagnosis. Depression, anxiety, and stress are the most common mental health challenges faced by these individuals

3.6 Autism Spectrum Disorders

Autism spectrum disorder (ASD) is a lifelong neurological difference in brain development that affects how individuals perceive the world, socialize and communicate. It is characterized by persistent challenges and the presence of restricted or repetitive patterns of behavior, interests or activities. Core symptoms and signs include difficulty with back-and-forth conversation, struggles with reading non verbal cues (like eye contact or body language), and trouble developing and maintaining relationships. Also engaging in

repetitive movements (hand flapping, rocking), strictly adhering to rigid routines, having intense, highly focused interests and experiencing heightened or lowered sensitivity to sensory inputs (sound, lights, textures).

3.7 Infectious Diseases (Meningitis)

Bacterial meningitis is the most common serious infection of the central nervous system (*pia mater* and *arachnoid* inflammation of brain *parenchyma* called encephalitis) and spinal cord (myelitis). Bacterial endotoxins in the blood infect the *pia mater*, *arachnoid* and *subarachnoid* space to cerebrospinal fluid (CSF) causing meningeal irritation, headache, fever and meningism. Bacterial meningitis is associated with unacceptable high rate of morbidity and mortality in sub Saharan Africa.

4.0 Behavioral Test Models

In the search for novel agents in psychopharmacology, behavioral test models are often employed. These tests maybe specific for a particular disease state or general. Most compounds that exhibit central nervous system depressant activities in animals are potential agents as anxiolytics, antidepressants, antipsychotics or anti-epileptics.

The following are some of the commonest behavioral tests used in our laboratory:

1. **Hole-board Test**: This is employed to evaluate certain components of behavior of mice, such as curiosity or exploration (Boissier *et al*., 1964; Boissier and Simon, 1964). Poking the nose into a hole is a typical behavior of the mice indicating a certain degree of curiosity. An increase in head dipping by an experimental animal

following the administration of a plant extract is an indication of anxiolytic action (Takeda *et al*., 1998) whereas a decrease in head dipping signifies sedative action (File and Wardil, 1975; File and Pellow, 1985).

2. **Beam Walking Assay**: This is another behavioral test carried out to induce minimal anxiety in a rodent. This test is also employed to determine the central nervous system depressant action as well as muscle relaxant properties of new compounds. In this test, decrease in motor coordination after the administration of compound suggests sedative property (Stanley *et al*., 2005). The parameters evaluated are the time taken to reach a goal box and the number of foot slips involving one or both hind limbs.
3. **Inhibition of Amphetamine Stereotypy in Mice:** Amphetamine is an indirect acting sympathomimetic agent which release catecholamines from its neuronal storage pools. In mice the drug induces a characteristic stereotypic behaviour characterized by continous sniffing, licking or gnawing, jumping and circling. Inhibition of amphetamine induced stereotypies in mice can be regarded as a simple method to detect neuroleptic activity (Vogel and Vogel, 1997).
4. **Diazepam-induced Sleeping Time:** This test evaluates sedative action of new compounds with loss of righting reflex as the index of sleep (Miya *et al.*, 1973).
5. **Phenobarbitone/Pentobarbitone Induced Sleeping Time:** These tests also screen compounds with sedative activity.
6. **Forced Swim Test:** The use of this to test for antidepressant activity was described by Porsolt *et al* (1977 & 1978). It was suggested that mice forced to swim in a restricted space from which they cannot escape are induced to a characteristic behaviour of

immobility. This immobility reflects a state of despair which can be reduced by several agents that are therapeutically active in human depression. This model is suitable also for evaluating drugs against schizophrenia, since depression is a component of the disease – negative symptom (Noda *et al.,* 1995).

7. **Tail Suspension Test:** The principle behind this test (Steru *et al.*, 1985) is similar to the forced swim test and employs behavioral despair as index of depression.
8. **Open Field Test:** This test is employed to screen for both sedative and anxiolytic activities of a new agent as well as effect on locomotor activity of a laboratory animal (Acher, 1973). Rodents when placed in a new environment may experience signs of anxiety such as decreased mobility, exploration, grooming and rearing with concurrent increase in micturition and defecation (Acher, 1973).

It is important to note that many of the apparatuses used were improvised based on description from journal publications. They were pretested and validated and data generated were accepted and published in reputable journals. Reviewers of my publication 'Residual Aqueous Fraction of Stem Bark Extract of *Xeromphis nilotica* and Behavioral Effects in Mice' which appeared in *International Journal of Applied Research in Natural Products* (2009) had to request for a picture of the beam walk apparatus during the review process. We were very successful at improvising these apparatuses and decided to organize a pre-conference workshop and share our experience on how to improvise during the NSN conference in 2016. Over 50 students subscribed for the workshop from all over the country and who later went back to their institutions and replicated same. To this end, I must appreciate Professor Abdullahi Yaro Hamza,

currently at Bayero University Kano, who made that dream a reality by providing the much needed funds at the time!

5.0 Behavioral Animal Models

Animal models are of equal significance as equipment or apparatus in experimental pharmacology. An animal model is a non-human species used in medical research because it can mimic aspects of a disease found in humans. Animal models are used to obtain information about a disease and its prevention, diagnosis and treatment. By using animals, researchers can carry out experiments that would be impractical or ethically prohibited in humans. Mice and rats make up about 95% of laboratory animals with mice commonly used in behavioral research. Mice are commonly selected for a number of reasons such as:

- Small size (facilitating housing and maintenance);
- Short reproductive cycle and lifespan
- Generally mild tempered and docile
- Wealth of information regarding their anatomy, genetics, biology and physiology;
- Possibility of producing genetically manipulated mice and mice with spontaneous mutations

In recent times in our community, the use of insects notably *Drosophila melanogaster* as an animal model for biomedical research is on the increase. *Drosophila melanogaster* (fruit fly) possess advantages over rodents as follows:

- The fly has a very rapid life cycle (a single fertile mating pair can produce hundreds of genetically identical offspring within 10 to 12 days at 25^0C);

- The fly may be considered multiple model organisms each with its own specific advantages defined by developmental stage (embryo, larva, pupa, adult);
- The adult fly has structures that perform the equivalent functions of the mammalian heart, lung, kidney, gut and reproductive tract;
- The flies are easy to keep and handle (corn flour, glucose, yeast and agar);
- The fly genome has been completely sequenced and annotated (encodes a little more than 14,000 genes on four chromosomes);
- It has been estimated that nearly 75% of disease related genes in humans have functional orthologs in the fly;
- Experimental manipulation and observation of cells are relatively easy

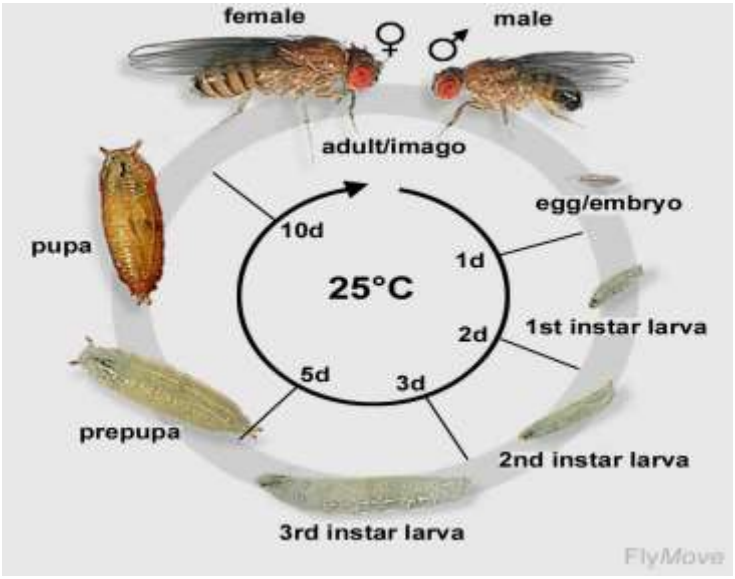

Fig. 2: Life Cycle of *Drosophila melanogaster*

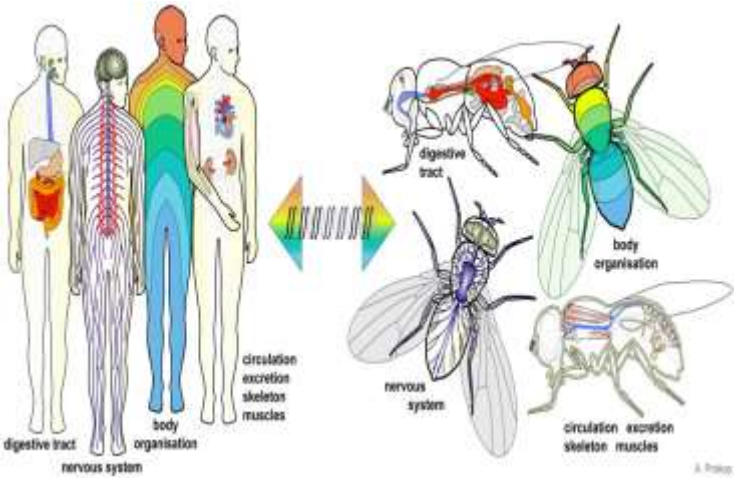

Fig. 3: Structural and Functional Analogy of *Drosophila melanogaster* and Humans

To the best of my knowledge, I was the first person to introduce fruit fly to ABU research community and perhaps beyond, through:

i) Departmental staff seminar with the title 'Paradigm Shift in Neuroscience Research: Insects as Models of Diseases' presented on the 5th of March 2015 in the Department of Pharmacology and Therapeutics;

ii) Pre-conference workshop (hands on) Drosophila ecology, handling, behavior and disease models during the 14th Neuroscience Society of Nigeria Annual Conference held in Ahmadu Bello University Zaria from 3rd to 4th August 2016;

In 2013, I secured a travel grant from International Brain Research Organization (IBRO) to attend the 2nd IBRO School on 'Insect Neuroscience and Drosophila Neurogenetics' organized by a higher education charity organization, Teaching and Research in Natural Sciences for Development in Africa (TReND). The three weeks intensive course was held in Uganda and we were taught how to use Drosophila in biomedical research. Subsequently I introduced and forwarded the course materials to Professor Dalhat Mukhtar Shehu of the Department of Biological Sciences who placed an MSc student (Rashidatu Abdulazeez) to work on ecology and diversity of wild Nigerian Drosophila.

The TReND workshop not only taught us the use of Drosophila in biomedical research but also exposed us to the power of advocacy. Within a short period of time, TReND was able to train many young researchers across Africa on the application of Drosophila in research. **I therefore co-founded an organization, Blossom Stem Initiative (Droso4Nigeria) registered with CAC, committed to knowledge sharing on the use of drosophila in research and as a tool for teaching**

high school biology. A number of workshops and outreaches were organized to train high school students and their teachers.

6.0 Foundation Research

From the early beginnings where undergraduate project students were guided on screening of plants as potential therapies for mental health conditions to the foundation research in which my postgraduate project also focused on same topic. Many plants commonly available and used as foods and medicines were screened based on their folkloric claims.

6.1 Screening of Plants for Antiepileptic Activities

Many plants have been used by the locals in treatment of epilepsy but without scientific validation. The search for an ideal antiepileptic agent continues and several plants were screened using chemical and electrical methods. The antiepileptogenic potentials of some of the plants have also been explored and many have shown good promise (Table 1).

Table 1: Medicinal Plants and Compounds Screened for Antiepileptic and or Antiepileptogenic Properties

S/No.	Plant/Compound Name	Local Name (Hausa)	Reference
1.	*Parquetina nigriscense*	Kwankwani	Mahmud *et al*., 2024
2.	*Zingiber officinales*	Citta	Yakubu *et al*., 2022
3.	*Albizia chevalieri*	Katsari	Danbala *et al*., 2019
4.	*Tapinanthus globiferus*	Kauchi	Abdullahi *et al*., 2018
5.	*Diospyros mespiliformis*	Kanya	Muhammad *et al*., 2017
6.	*Hymenocardia acida*	Jan yaro	Wada *et al*., 2017
7.	*Laggera aurita*	Taba-taba	Malami *et al*., 2016
8.	*Pseudocedrella kostchyi*	Tuna	Abubakar *et al*., 2016
9.	*Ficus platyphilla*	Gamji	Chindo *et al*., 2014
10.	*Acacia albida*	Gawo	Danjuma *et al*., 2010
11.	*Randia nilotica*	Tsibra	Danjuma *et al*., 2009
12.	Vitamin C	-	Yusuf *et al*., 2020
13.	Ellagic acid	-	Mshelia *et al*., 2022

6.2 Medicinal Plants with Antinociceptive, Analgesic and Anti-inflammatory Properties

Pain is the most common reason for Physician's consultation in various health care delivery systems in Nigeria and many other countries in the world. Majority of clinical conditions associated with humans are usually accompanied with pain: cancer, migraine, sickle cell anemia, gouty arthritis, angina pectoris, burns and surgery (post operative pain). Pain relievers (analgesics) are often used as adjuncts in the management of these conditions. However, chronic use and or uncontrolled abuse of analgesics and their combinations could lead to renal damage (Zezi e*t al*., 2011b, 2007a, 2007b, 2007c).

Many plants have been identified for their analgesic and anti-inflammatory properties but most have not been subjected to studies to ascertain their safety and efficacy. A number of such plants have been identified in our laboratory and screened (Table 2). The methods employed were hot plate (thermal) and acetic acid-induced writhing (chemical) to account for central and peripheral mechanisms respectively. Formalin-induced method will also identify compounds with anti-inflammatory potentials. The ability of the plants to mitigate neuropathic pain was evaluated for some species.

Table 2: Medicinal Plants and Compounds Screened for Antinociceptive, Analgesic and Antiinflammatory Properties

S/No.	Plant/Compound Name	Local Name	Reference
1.	*Rothmannia longiflora*	Katambiri	Danjuma e*t al.*, 2025a
2.	*Costus spectabilis*	Takalmin zomo	Shehu *et al.,* 2023
3.	*Andropogon gayanus*	Zandam	*et al*., 2020
4.	*Chlorophytum alismifolium*	Rogon makwarwa	Abubakar *et al.*, 2020;2016
5.	*Olax subscorpoidea*	Gwanon kurmi	Odoma *et al.*, 2020
6.	*Caralluma dalzieli*	Karan masallachi	Umar *et al.,* 2013
7.	*Burkea africana*	Bakuru, Kiri	Danjuma *et al.*, 2019
8.	*Cissampelos mucronata*	Damal gwaraajii	Yaro *et al*., 2008
9.	*Ziziphus mucronata*	Magaryar kura	Danjuma *et al*., 2007; 2006
10.	Resveratrol		Muhammad et al., 2022

6.3 Medicinal Plants Used to Enhance Memory and for Alzheimer's Disease

Alzheimers's disease is a neurodegerative disorder that damages and destroys brain cells, leading to severe memory loss, cognitive decline and an inability to perform daily tasks. It is the most common cause of dementia, primarily affecting adults over 65. At the early stages there is difficulty remembering recent events, frequently misplacing items, trouble finding the right words, and struggling to manage complex tasks like finances. Middle stage is characterized by getting lost in familiar places, repeating questions, personality and mood changes (e.g depression or anxiety) and needing assistance with daily grooming. Finally, there is complete loss of short term and long term memories, inability to recognize family members, difficulty in swallowing or eating, and loss of motor control.

Some commonly available plants consumed locally are known to improve these conditions and guarantee healthy ageing. Few of such plants have been evaluated for efficacy using behavioral animal models (Table 3).

Table 3: Medicinal Plants and Compounds Screened for Memory Enhancement and for Alzheimer' Disease

S/No.	Plant/Compound Name	Local Name	Reference
1.	*Parquetina nigriscense*	Kwankwami	Mahmud *et al*., 2024
2.	Resveratrol	-	Muhammad *et al*., 2022
3.	*Eragrostis tremula*	Burburwa, Komayya	Nazifi *et al*., 2022
4.	Ellagic acid	-	Mshelia *et al*., 2018
5.	*Eragrostis tremula*	Tsintsiya	Nazifi *et al*., 2019
6.	*Persea americana*	Piya, Bawon Allah	Danjuma *et al*., 2019

6.4 Medicinal Plants with Central Nervous System Depressant and other Behavioral Activities

It has been established that compounds that exhibit CNS depressant properties are good candidates for treating depression, anxiety, schizophrenia and other mental disorders, A few of such other plants have been evaluated in our laboratory (Table 4).

Table 4: Medicinal Plants Screened for Central Nervous System Depressant Activity and other Behavioral Effects

S/No.	Plant Name	Pharmacological Action	Reference
1.	*Ficus platyphylla*	Behavior	Chindo *et al*., 2014
2.	*Randia nilotica*	Anxiolysis	Danjuma *et al*., 2009
3.	*Randia nilotica*	CNS depression	Danjuma *et al*., 2008
4.	*Xeromphis nilotica*	Behavior	Danjuma *et al*., 2018
5.	*Ficus thoningii*	CNS depression	Musa *et al.*, 2006
6.	*Mitracarpus villosus*	sedative	John-Africa *et al*., 2014
7.	*Tribulis terrestris*	anti-autism	Kyari *et al.*, 2025
8.	*Acacia seyal*	Antidepressant	Magaji, 2020; Gambo *et al*., 2024
9.	*Rothmannia longiflora*	Anxiolytic	Mallam *et al.*, 2025
10.	*Tapinanthus globiferus*	Antidepressant	Abdullahi *et al*., 2021

7.0 Mechanism for Psychoactivity

Pharmacologists always strive to understand how drugs act and not what drugs do. The mechanism through which our medicinal plants/foods work has become subject of our study. It is understood that plants contain several chemical compounds known as secondary metabolites which will interact with chemical substances in our body to elicit cellular changes. In the brain, chemical substances known as neurotransmitters are targets for this interaction. Changes in neurotransmitters such as gamma amino butyric acid (GABA), glutamate, glycine, dopamine, serotonin, acetylcholine, histamine, epinephrine and norepinephrine are important in cellular communication and are responsible for maintaining a healthy mental status. It is important to note that these

compounds are end products of carbohydrate, fat and protein metabolism (food).

Secondary metabolites from plants such as saponins, tannins and flavonoids (Table 5) are known to have psychoactive properties. **My PhD project is one of the earliest in the department to extract and screen saponin-rich fraction for psychoactivity (Danjuma *et al.*, 2014).**

Table 5: Phytochemical Components of *Randia nilotica S*tem Bark Extract

Compound group	Present/Absent
Alkaloids	–
Tannins	+
Saponins	+
Cardiac glycosides	+
Sterols/Terpenes	+
Anthraquinones	–
Flavonoids	+

Aside secondary metabolites, plants also contain minerals (herbominerals), amino acids and metals which contribute to their activity. The mineral content of garlic (Table 6) and it's role in management of meningitis has been studied (Tijani *et al.*, 2020) while that of *Boswellia dalzielli* (Nazifi *et al.*, 2017) and *Costus spectabilis* (Shehu *et al.*, 2021) have also been determined and shown to influence their pharmacological effects.

Table 6: Herbomineral Elements and Proximate Values of Juice Extract of *Allium sativum*

Macro/Microelement	Proximate Values (mg/600mg)
Sodium	19.00
Potassium	154.00
Calcium	184.00
Magnesium	26.00
Phosphorus	390.00
Sulphur	450.00
Manganese	0.03
Silver	0.01
Iodine	0.05
Zinc	1.18
Selenium	0.014

Ellagic acid is a naturally occurring polyphenolic antioxidant found in many fruits, vegetables and nuts. It is best known for its potential to reduce inflammation, neutralize oxidative free radicals and inhibit the growth of certain cancer cells. Research suggests it may help preserve brain function and protect against neurodegenerative conditions like alzheimers (Mshelia *et al*., 2022). Another compound with similar activity and from similar sources is **resveratrol,** believed to possess neuroprotective (Muhammad *et al.*, 2021) and anti-aging properties.

Amino acids are also found to be major constituents of most plants (Table 7) and these have been implicated in neuroprotection and neuroplasticity. Leucine is a branched-chain amino acid (BCAA) that is essential for protein synthesis and energy production where it serves as a regulator of the activity of some enzymes important for brain energy metabolism (Murín and Bernd, 2008). Whereas,lysine is a basic amino acid that has been shown to exert neuroprotective effect (Cheng *et al*., 2020), by playing an important role in

brain plasticity (Gupta *et al*., 2005). Tyrosine is the precursor to dopamine, norepinephrine, and epinephrine, which are critical for regulating mood, attention, and cognition (Molloy and Litchfield, 2020). Dopamine is crucial for motivation, reward processing, and learning (DiCarlo and Wallace, 2022).

The Gut Brain Axis (GBA) is a complex communication network linking the Gastrointestinal (GI) system and CNS through neural, hormonal, immune, and metabolic pathways (Cryan and Dinan, 2012). The influence of the GBA on mental health has become more evident, with research highlighting the role of the gut microbiota: a diverse ecosystem of microorganisms within the GI tract that produces neurotransmitters, hormones, and metabolites that play key roles in brain function (Bercik and Collins, 2014; Evrensyl and Ceylan, 2015). The *vagus* nerve, one of the primary pathways between the gut and the brain, facilitates direct communication that can modulate brain activity and influence behaviors associated with anxiety and mood (Kelly *et al.,* 2016). Dysbiosis, or an imbalance in the gut microbiota, has been closely linked to neuropsychiatric disorders such as anxiety, depression, and cognitive impairment, as the altered microbiota can disrupt normal signaling along the GBA (Maqsood and Stone, 2016; Foster and McVey Neufeld, 2013).

Table 7: Amino Acid Content of Methanol Leaf extract of *Tribulus terrestris*

Amino Acid	**g/ 100g protein**	**FAO/WHO/UN Permissible/ limit g/ 100g protein**
Leucine	6.22	6.6
Lysine	5.74	5.8
Isoleucine	3.29	2.8
Phenylalanine	3.01	6.3
Trytophan	0.40	1.1
Valine	3.67	3.5
Methionine	1.49	2.2
Proline	5.16	10.7
Arginine	2.66	2.80
Tyrosine	6.46	7.1
Histidine	1.14	1.9

Cystine	0.21	1.0
Alanine	4.37	6.1
Glutamic acid	3.67	4.7
Glycine	3.31	2.2
Threonine	2.55	3.4
Serine	3.26	7.0
Aspartic acid	6.10	7.7

8.0 Safety Considerations

Drugs are used when their benefit outweigh their risk. Plants used as foods will normally have a high margin of safety. However, some plants have been found to exhibit moderate toxicity in animals. Because they contain active biochemical compounds, they can cause side effects and be harmful to vulnerable groups. This further supports the argument that being 'natural' does not automatically mean safe. The effect of extracts of some plants to cause kidney damage (Zezi *et al.*, 2011) and blood disorders following chronic use has been established (Nazifi *et al*., 2022 & 2023; Micah *et al*., 2022; Mamman *et al*., 2024). Because a large portion of the population relies on herbal remedies and traditional medicines, monitoring safety is essential. Traditional Medical Practitioners (TMPs) have also alluded to possibility of Adverse Drug reactions (ADRs) but reporting among TMPs in Zaria was found to be critically low (Mohammed *et al*., 2019). Barriers in ADR reporting among TMPs in Zaria were found to include knowledge deficit, lack of training, and lack of previous exposure (Mohammed *et al*., 2019).

All the plants studied in our laboratory have been screened for safety following single (acute) and sometimes multiple (sub acute, chronic) administration in rodents. The high level of estimated median lethal dose (LD50) following acute oral administration for most of the plants studied in rodents,

suggests relative safety for these plant materials as widely believed in folklore (Table 8). According to the Organization of European Economic Cooperation and Development (OECD) classification of toxic compounds and which is consistent with Global Harmonized System (GHS), substances with LD50 greater than 2000 but up to 5000 mg/kg are considered category 5 (may be harmful).

Table 8: Acute Safety Estimate Values (LD50) for Some of the Plants Screened in our Laboratory

S/N	Plant Name	LD50 (mg/kg)	Route	Animal Specie	Method
1.	*Tapinanthus globiferus* (Abdullahi *et al.*, 2018)	1300 3800 **5000**	*i.p.* *i.p.* ***p.o.***	Mice Rat Rat	Lorke “ “
2.	*Diospyros mespiliformis* (Muhammad *et al*., 2017)	774 **> 5000**	*i.p.* ***p.o***.	Rats, Mice “	Lorke “
3.	*Hymenocardia acida* (Wada *et al*., 2017)	**> 2000**	***p.o.***	Rats	OECD
4.	*Pseudocedrella kostchyi* (Abubakar *et al*., 2016)	**> 5000** > 2000 3800	***i.p.*** *p.o.* *p.o.*	Chicks Rats Mice	Lorke “ “
5.	*Mitracarpus villosus* (John-Africa *et al*., 2014)	1265 **> 5000**	*i.p.* ***p.o.***	Mice Mice	Lorke “
6.	*Rothmannia longiflora* (Danjuma e*t al.*, 2025a)	**> 5000**	***p.o.***	Mice, rats	OECD
7.	*Olax subscorpoidea* (Odoma *et al.*, 2020)	**> 5000**	***p.o.***	Mice, rats	Lorke
8.	*Eragrostis tremula* (Nazifi *et al*., 2022)	**> 5000**	***p.o.***	Rats	OECD
9.	*Persea americana* (Danjuma *et al*., 2019*)*	**> 5000**	***p.o.***	Mice	Lorke

p.o - oral; *i.p. - intraperitoneal;*

9.0 Challenges

A) Recording electroencephalographs (EEGs) in animals using a polygraph machine is a classic electrophysiological technique used to study brain waves, sleep stages, and neurological disorders (like epilepsy) in research settings. While modern laboratories often use digital amplifiers and wireless telemetry, the core principles remain the same. Traditionally, researchers used a multi-channel **polygraph** (e.g., Grass Instruments) connected to multiple amplifier channels. The polygraph translates microscopic electrical voltage differences from the brain into visible ink waves on continuously moving paper, or into digital signals on a connected computer.

Common Applications of EEG Machine include:

- **Sleep Research:** Polygraph machines are extensively used for polysomnography. They record the EEG alongside Electromyography (EMG, muscle tone) and Electrooculography (EOG, eye movement) to identify Rapid Eye Movement (REM) and non-REM sleep states.
- **Seizure Monitoring:** Identifying epileptiform activity (spikes and sharp waves) in animals predisposed to epilepsy. **The polygraph 79D was used to screen extracts of *Randia nilotica* for antiepileptic activity during my PhD project (Fig. 2).**
- **Pharmacology & Toxicology:** Testing the effects of drugs or assessing anesthesia depth during veterinary surgeries.

The department is in possession of 3 Grass Polygraph 79D apparatuses currently and are serviceable but the skills needed to continue using this technology is missing. The

only Technologist with the skills to operate the machine is now late (Mr Ibrahim Jura). This is a big challenge to investigators particularly in epileptology.

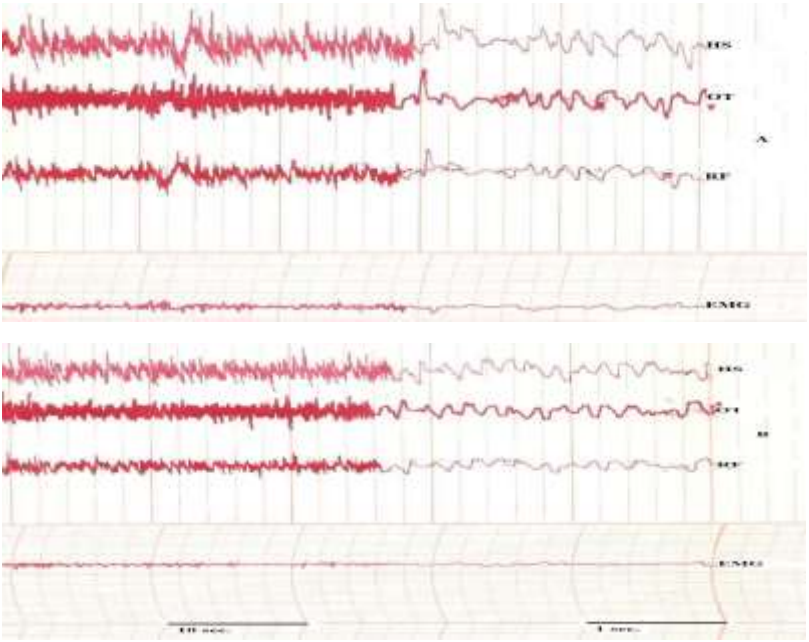

Fig. 4: Effects of Saponin Fraction of *Randia nilotica* (10 mg/kg) on Rat EEG and EMG.

Upper panels (A) are controls, lower panels (B) are extracts after 30 min. pre-treatment.

10.0 Current and Future Research Perspectives

Our current and future research focus is aimed at unraveling these mechanisms through which our plants (foods) modulate brain activity. The presence of numerous compounds with antioxidant properties (mainly phenolic compounds) is being investigated. The interaction of these compounds with

signaling molecules (e.g. cytokines) is also a subject of our study (Odoma *et al.*, 2020).

11.0 Conclusion

A sound mind, especially amidst the current tribulations, can be achieved and maintained by responsible consumption of foods that balances our microbiota.

12.0 Recommendations

i) Establishment of Ahmadu Bello University Brain Research Institute or Center where all stakeholders will come together and collaborate to advance knowledge relating to the brain. Such an Institute to be modeled towards UCLA Brain Research Institute or the Paris Brain Institute will focus on understanding nervous system functions to treat neurological and psychiatric disorders.

The scope of the center or institute will cover:

- **Basic Neuroscience:** Investigating neuronal diversity, brain mapping, neural networks, and how cellular circuits drive behavior, learning, and memory.
- **Clinical and Translational Research:** Turning laboratory discoveries into treatments for conditions like Alzheimer's, Parkinson's, epilepsy, depression, and addiction.
- **Neurodevelopment and Ageing:** Tracing how human brains develop and studying genetic variations that lead to age-related neurodegenerative diseases.

- **AI and Data Science:** Integrating computer science and clinical data to accelerate drug discovery and precision medicine.
- **Education and Outreach:** Training future neuroscientists and engaging local communities in STEM fields.

ii) Establishment of undergraduate and postgraduate programs in neuroscience to improve our understanding of the brain and its functions. These programs can help us learn brain anatomy, neural signaling, cognitive functions, and the biological basis of behavior.

BSc, MSc and PhD in Neuroscience is increasingly gaining popularity as a career path globally.

13.0 Contributions other than Neuropharmacolgy

1. Medicinal plants as sources of food and medicines have been used in folklore by herbalists to treat other human diseases and some of these have been evaluated for efficacy and safety in our laboratory. Chronic illnesses are also important determinants of a sound mind. These disorders are accompanied by mood and behavior changes such as anxiety and depression. A number of locally available plants have also been evaluated for treatment of diseases like diabetes, asthma, cancer and diarrhoea. These include those used for diabetes (Abubakar *et al*., 2017 & 2016b; Olurishe *et al.*, 2016 & 2017), asthma (Aliyu *et al,*. 2022), as antidiarrheal (Usman *et al*., 2021), in management of cancer (Muhammad *et al*.,2018; Tiiba *et al.*, 2020a, 2020b) as well as those with uterotonic properties (Bakut *et al*., 2020; Wazis e*t al*., 2013).

2. I was privileged to be mentored in Clinical Pharmacy Education by Dr. Adedeji A. Odutola (late). Dr. Odutola was among the first Nigerian graduates of PharmD from the United States of America. I had therefore taught many courses in clinical pharmacy and supervised a number of postgraduate projects. Areas of engagement include medication management (Abdu-Aguye *et al.,* 2022, 2021a, 2021b, 2021c, 2021d), hypertension management (Jamiu *et al*., 2024), cancer chemotherapy (Saulawa *et al.*, 2022), HIV management (Bashir *et al*., 2026).

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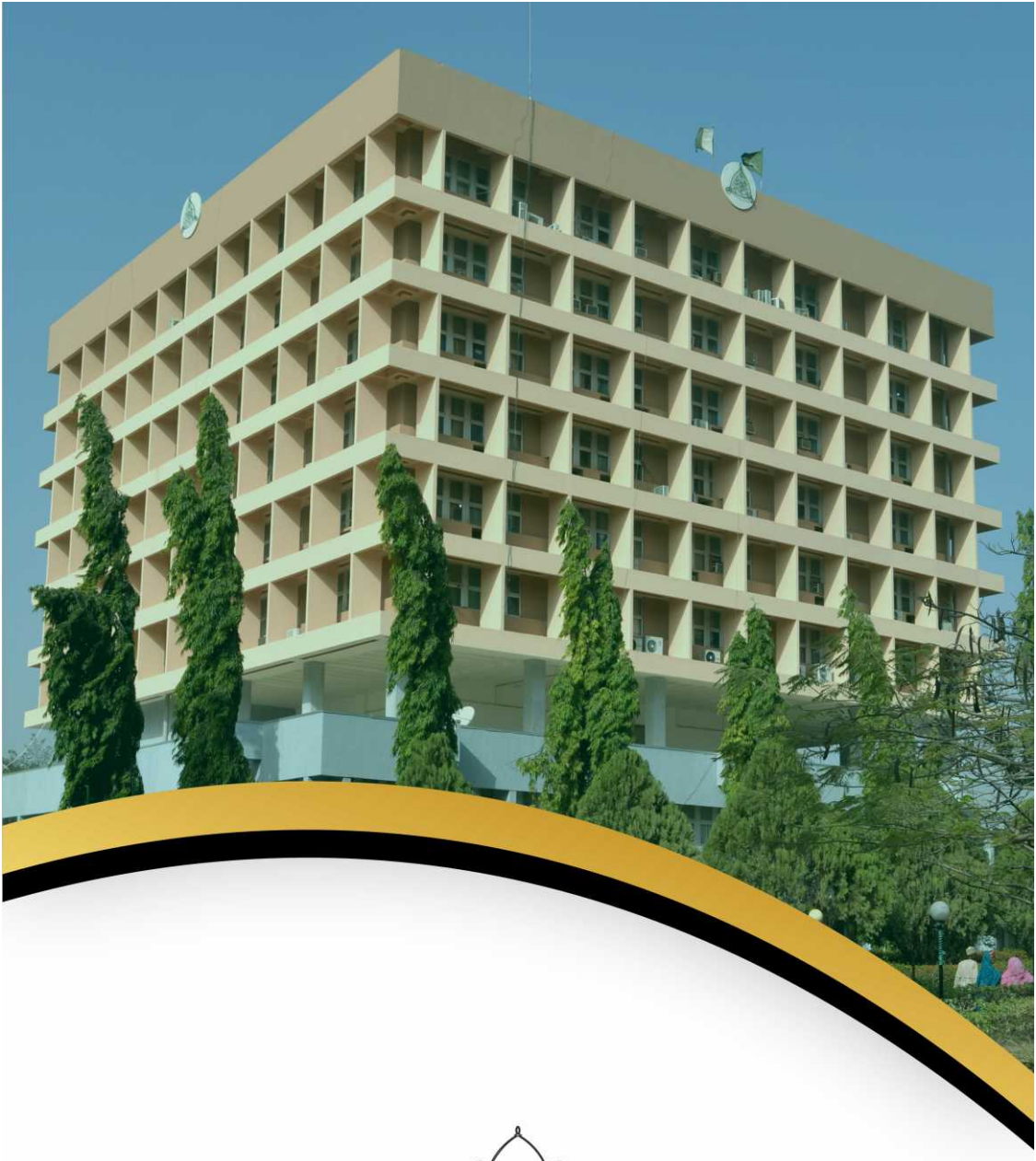

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