Project Title: Development, production, quality evaluation, and clinical trials of FIIRO-developed anti-dementia sprinkles from local raw materials

Background to the research: Dementia, a global epidemic, affects millions with progressive cognitive decline that impairs independent functioning, with Alzheimer's disease being the most common form, accounting for about 70% of cases. It involves a range of symptoms impacting memory, thinking, reasoning, personality, mood, and behaviour, often accompanied by behavioral and psychological issues like agitation, depression, and hallucinations. These symptoms lead to significant distress for patients and caregivers, often requiring long-term hospitalization. While historically more prevalent in wealthier nations, recent data shows the majority of dementia cases now occur in low- and middle-income countries. In Africa, dementia incidence peaks earlier, between ages 65–74, compared to 80–89 in other regions, with limited effective long-term treatments available, such as galantamine and donepezil.

Extensive work has been done at the laboratory stage to formulate a stable and acceptable product. Some parameters including in vitro antioxidant activities and cholinesterases and monoamine oxidase inhibition assays were done to confirm possible efficacy. Against this background, further work is required to scale up for pilot production and commercialization of this innovation for both nutritional benefits and health of Nigerians in relation to the sustainable development goals (SDG 3) on Good Health and Well-being for all by the year 2030 and the renewed Hope Agenda of the current administration.

Justification: Over 55 million people worldwide live with dementia, projected to reach 139 million by 2050, with 60% of cases in low- and middle-income countries, expected to rise to 71%. Dementia is the seventh leading cause of death globally and a major cause of dependency and impairment. In Africa, dementia prevalence varies widely from 2.3% to 20.0%, with Nigeria reporting a 4.9% prevalence and a 400% increase in incidence among those over 60 in the past 20 years. No medications currently stop dementia's long-term progression, and available treatments often have severe side effects. In Nigeria, plants like turmeric, ginger, West African black pepper, cattle stick, and drumstick are traditionally used for memory enhancement, though their efficacy is not well-documented. Nigeria's significant production of turmeric and use of these plants as spices and medicines makes them readily available for potential therapeutic exploration.

Project Objective: The project aims to commercialize FIIRO's validated anti-dementia sprinkles from local raw materials. Objectives:

1. Optimize/standardize formulation for sensory appeal, bioactive potency, nutrition, reproducibility, scalability.

2. Develop/validate pilot-scale processes for consistency, cost-effectiveness, GMP compliance.

3. Conduct microbiological, sensory, chemical, shelf-life assessments per international standards.

4. Perform ethically approved clinical studies confirming efficacy, safety, health claims.

5. Design market-ready packaging; analyze consumer markets for positioning, pricing, distribution.

Literature review: Alzheimer's disease is a progressive and relentless neurodegenerative condition that damages large portions of the cerebral cortex and hippocampus (Masters et al., 2015). Approximately 60 to 80 percent of all cases of dementia are caused by this subtype, making it the most common form of neurodegenerative dementia (Duong, Patel, & Chang, 2017). The frontal and temporal lobes of the brain are typically where abnormalities are first noticed before these abnormalities then slowly spread to other sections of the neocortex, though rates of progression vary greatly from person to person (Duong, Patel, & Chang, 2017). Both the aggregation of the microtubule protein tau in neurofibrillary tangles in neurons and the buildup of insoluble forms of amyloidβ (Aβ) in plaques in extracellular spaces and blood vessel walls are some of the pathologies associated with Alzheimer's disease (Tuzimski & Petruczynik, 2022a).

Although there has been a great number of work done to understand the aetiology and pathogenesis of the disease, there are currently no medications that can effectively stop the disease's progression for an extended period of time. As a result, the only options for treating Alzheimer's disease are symptomatic and palliative medications (Tuzimski & Petruczynik, 2022). There are currently only few medications that have been licensed to treat Alzheimer's disease, including galantamine, donepezil, tacrine, rivastigmine and huperzine A. Through the elevation of brain-based neurotransmitter molecules, these medications temporarily alleviate symptoms of Alzheimer's disease (Masondo, Stafford, Aremu, & Makunga, 2019). The biggest drawback of these medications however is their limited durational effect, which lasts for about 12 to 24 months at most. Long-term cognitive or functional capacity deterioration is not slowed by the authorized medications and side effects from currently available medications are sometimes more severe than the condition itself (Tuzimski & Petruczynik, 2022). However there are several herbs that have been traditionally used in Nigeria to treat dementia. These plants work by inhibiting the cholineesterases' activity, which helps to maintain the levels of the neurotransmitters acetylcholine and butyrylcholine and slows the accumulation of β-amyloid

peptides. In addition, they serve as antioxidants against oxidative stress and lessen neuroinflammation (Tuzimski & Petruczynik, 2022).

Theoretical framework: Cholinergic deficits are a hallmark of Alzheimer's disease (AD) and significantly contribute to its cognitive and behavioural symptoms. In Alzheimer's disease (AD), the cholinergic system is impaired, leading to cognitive decline. Acetylcholine (ACh), a key neurotransmitter for memory and attention, is hydrolyzed by acetylcholinesterase (AChE) and, to a lesser extent, butyrylcholinesterase (BChE). In AD, the loss of cholinergic neurons in the basal forebrain reduces ACh production, while AChE and BChE activities contribute to its rapid breakdown, exacerbating the deficit. This imbalance, where ACh is depleted faster than it is replenished, drives memory impairment and cognitive decline (Nwidu et al, 2017). Furthermore, MAO enzymes (MAO-A and MAO-B) break down monoamine neurotransmitters (e.g., dopamine, serotonin, norepinephrine), producing reactive oxygen species (ROS) as byproducts. In AD, elevated MAO activity, particularly MAO-B, exacerbates oxidative stress and neuronal damage. MAO-A and MAO-B degrade serotonin, dopamine, and norepinephrine, which are reduced in AD, contributing to cognitive and behavioral symptoms (e.g., depression, agitation). MAO inhibition preserves these neurotransmitters, improving mood and cognitive function (Adeyemi et al., 2024). Thus addressing these can help alleviate and improve or inhibit the progression of Alzheimer's disease

Research Methodology: Raw materials including turmeric and black pepper will be obtained from major farmers/wholesalers in Nigeria. They will be thoroughly washed and cleaned for analysis and product formulation/development. Bioactive compounds analysis will be done using high-performance liquid chromatography, mass spectrometry to identify and quantify bioactive compounds present in the raw materials and formulations. Design-expert software will be used for product formulations, while the safety and efficacy/mechanistic studies will be ascertained using experimental models of Alzheimer's disease (*in vitro* and *ex vivo* experiments). Thereafter, human intervention studies with alzhemier's disease patients will be done to evaluate the effects of the sprinkles on cholinergic deficits, B-secretase and other relevant biomarkers. The final stage will require the development and validation of pilot-scale production processes that ensure product consistency, cost-effectiveness, and compliance with Good Manufacturing Practices (GMP).

Expected Outcomes: Successful execution of this project will lead to the commercial availability of a scientifically validated, affordable, and culturally acceptable anti-dementia sprinkles developed from locally sourced raw materials. The project which is very much in line with SDG 3 (good health and wellbeing) will enhance public health by providing a natural, evidence-based dietary intervention for managing dementia. it is also in line with priorities 6 (Focus on Education, Health, and Social Investment as Essential Pillars of Development) and 7 (Accelerate Diversification through Industrialization, Digitization, Creative Arts, Manufacturing & Innovation) of the President Tinubu's renewed hope agenda as it will help the Nigerian economy by promoting import substitution and reducing dependence on imported functional foods. It will stimulate rural economic growth by creating sustainable market opportunities for farmers and value-chain actors, strengthen Nigeria's research–industry linkage through the commercialization of FIIRO's innovation, generate employment in food processing and distribution, and position FIIRO as a regional leader in functional food innovation against non-communicable diseases.

Innovation: Although a lot of research is being done in the area of functional foods, there are few standardized anti-dementia food products available in the market. By promoting the utilization of these plant materials in sprinkles, it may contribute to sustainable agricultural practices and local economic development.

Conclusion: This research concept proposes an innovative and interdisciplinary approach to explore the potential development of anti-dementia sprinkles. By elucidating the underlying bioactive compounds and mechanisms, this research can contribute to evidence-based dietary interventions for dementia management, improving public health outcomes and enriching the field of functional food research.