THE ANTIDEPRESSANT EFFECT OF THE HYDRO-METHANOL LEAF EXTRACT OF *Icacina trichantha* OLIV. IN MICE

BY

Nmakanma Princess OPUTE (Miss)

LSC2007343

PHYSIOLOGY/PHARMACOLOGY TECHNIQUES

DEPARTMENT OF SCIENCE LABORATORY TECHNOLOGY

FACULTY OF LIFE SCIENCES

UNIVERSITY OF BENIN

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A PROJECT SUBMITTED TO THE DEPARTMENT OF SCIENCE LABORATORY TECHNOLOGY, FACULTY OF LIFE SCIENCES IN PARTIAL FULFILLMENT FOR THE AWARD OF BACHELOR OF SCIENCE, B.Sc. (HONS) SCIENCE LABORATORY TECHNOLOGY (PHYSIOLOGY/PHARMACOLOGY TECHNIQUES), UNIVERSITY OF BENIN, BENIN CITY.

OCTOBER, 2025.

CERTIFICATION

This is to certify that this project work, titled "THE ANTIDEPRESSANT EFFECT OF THE HYDRO-METHANOL LEAF EXTRACT OF *Icacina trichantha* OLIV. IN MICE" was carried out by Nmakanma Princess OPUTE with matriculation number LSC2007343 of the Department of Science Laboratory Technology (Physiology and Pharmacology Techniques), Faculty of Life Sciences, University of Benin, Benin City, Edo State.

_____ _____

Mrs. E. Okpakpor Date
(Project supervisor)

_____ _____

Dr. P.O. Alonge Date
(Project coordinator)

_____ _____

Prof. J.O. Osarumwense Date
(Head of department)

_____ _____

External Examiner Date

DEDICATION

This work is dedicated to Almighty God and my family for their support during the course of this seminar work.

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Abstract

Depression is a mental health disorder characterized by a persistent feeling of sadness, loss of interest or pleasure, and lack of motivation. Antidepressant drugs are not rare to find and they are not addictive however, some people may experience discontinuation (withdrawal-like) symptoms if they stop taking antidepressants suddenly especially SSRIs and SNRIs emphasizing the need for safer alternatives. *Icacina trichantha* Oliv. It is a medicinal plant that belongs to the family Icacinaceae, used traditionally in the treatment of depression. However, there is limited scientific evidence supporting such claims. This study evaluates the antidepressant potential of *I. trichantha* in mice. Fresh leaves were collected, air-dried, pulverized, and extracted using a 1:1 water and methanol solvent to obtain H-MLE of *I. trichantha* after concentrating to dryness. Phytochemical screening was carried out using Sofowara 1993 and Harborne 1973. For antidepressant activity, 25 mice were randomly allotted into 5 groups of n = 5. Group I received 10 ml/kg deionized water, groups II – IV received graded doses of the plant extract 100, 200, and 400 mg/kg, and group 5 received 25 mg/kg imipramine for both FST and TST. Phytochemical screening revealed the presence of flavonoids, alkaloids, tannins, terpenoids, phenolics, saponins, and carbohydrates. Results obtained revealed that H-MLE had a significant increase at 400 mg/kg when compared to control ($P < 0.05$) for both TST and FST. This study supports its use in the treatment of depression in traditional medicine which could be due to the presence of secondary metabolites.

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Depression is a globally prevalent neuropsychiatric disorder characterized by persistent low mood, anhedonia, fatigue, and impaired cognitive and social functioning. It arises from the complex interplay of genetic, neurobiological, environmental, and psychosocial factors. Biological evidence suggests the involvement of dysregulated hypothalamic pituitary adrenal (HPA) axis activity, increased inflammatory markers, and reduced neuroplasticity influence mood regulation and behavior (Sullivan *et al.,* 2022).

The global burden of depression is profound. According to the World Health Organization, depression affects more than 280 million people worldwide, and it is projected to become the leading cause of disability by 2030. Its impact is especially critical in low and middle-income countries where access to mental health care is limited, resulting in a wide treatment gap (Sullivan *et al.,* 2022). Adolescents and young adults are among the most vulnerable, with rising cases attributed to social pressures, trauma, and a lack of early intervention.

1.2 The Central Nervous System

The human body functions as an interconnected system with the Central Nervous System (CNS) serving as the master controller. The CNS, made up of the brain and spinal cord, processes external and internal sensory input, makes decisions, and sends out responses that regulate every voluntary and involuntary action in the body (Schwaber *et al.,* 2020). This coordination enables everything from muscle movement to cognitive processes such as learning, memory, and emotion. The complexity of the CNS lies in its unique neuroanatomy and neurophysiology, which makes it central to understanding human biology, behavior, and pathology. In modern medicine and neuroscience, increasing attention has been given to

CNS-related disorders such as neurodegeneration, spinal cord injuries, and cerebrovascular diseases (Assis and Costa, 2019).

The Central Nervous System (CNS) is defined as the portion of the nervous system that includes the brain and spinal cord, responsible for interpreting sensory data and initiating motor commands. It is distinguished from the Peripheral Nervous System (PNS), which comprises nerves outside the CNS that relay signals between the body and the brain (Purves *et al.,* 2018). Functionally, the CNS acts as the integration and command center of the body, coordinating both voluntary activities (like walking or speaking) and involuntary functions (like heartbeat and respiration). Furthermore, the CNS enables all cognitive, motor, sensory, and regulatory functions. It processes input from sensory receptors and generates appropriate output that governs behavior and physiological responses. It is also the seat of consciousness and higher cognitive functions such as decision-making and emotional regulation (Sanes *et al.,* 2019).

The structural components of the CNS include the brain and the spinal cord. The brain is the most complex organ in the body, weighing approximately 1.4 kg in adults. It is divided into the cerebrum, the cerebellum, and the brainstem (Wang *et al.,* 2021). The spinal cord extends from the brainstem to the lumbar region. It functions as a conduit for signals traveling to and from the brain and also manages reflexes independently (Ghosh *et al.,* 2018). The CNS has three major functional roles which are to receive sensory input from receptors and relay it to appropriate brain centers, initiate and regulate voluntary and involuntary movements, and maintain internal balance (homeostasis) by controlling cardiovascular, respiratory, and endocrine functions (Sanes *et al.,* 2019).

Diseases and disorders that affect the CNS include, stroke, alzheimer's disease, parkinson's disease, multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), meningitis, epilepsy, encephalitis, spinal cord injury (SCI), brain tumor, and depression.

1.3 Depression and The Central Nervous System

Studies show that individuals with chronic depression often exhibit a smaller hippocampus, a region critical for memory and emotion regulation. The prefrontal cortex, responsible for decision-making and emotion control, shows reduced activity and connectivity in depressed patients. Serotonin, norepinephrine, and dopamine (key neurotransmitters produced and used within the CNS) are often dysregulated in depression (Schmaal *et al.,* 2017). Some recent research suggests that pro-inflammatory cytokines cross the blood-brain barrier and disrupt brain function, contributing to depressive symptoms. Depression is associated with a range of neurophysiological and anatomical changes in the brain, particularly involving the, prefrontal cortex (emotion regulation and decision-making), hippocampus (memory and stress response), amygdala (fear and emotional processing), and anterior cingulate cortex (cognitive control). These regions show abnormalities in volume, blood flow, and connectivity in individuals with depression (Schmaal *et al.,* 2017). Recent studies propose that neuroinflammation plays a significant role in the onset and persistence of depression. Elevated levels of pro-inflammatory cytokines (e.g IL-6, TNF-α) have been reported in depressed individuals, suggesting that systemic inflammation might cross the blood-brain barrier (BBB) and alter neural activity (Miller and Raison, 2016). Brain-Derived Neurotrophic Factor (BDNF) levels are found to be reduced in individuals with depression, especially in the hippocampus. BDNF supports the growth, differentiation, and survival of neurons, so its dysregulation contributes to impaired neuroplasticity in depression (Duman and Aghajanian, 2016).

1.4 Top 10 Countries by Depression Prevalence

The top 10 countries with the highest depression burden are largely conflict-affected or economically transitioning regions, where trauma, poverty, and weak mental health infrastructure drive elevated rates. High-income nations also feature due to modern stressors

and healthcare pressures. Based on the Global Burden of Disease (GBD) study (2019), here are the highest-ranking countries: Uganda has a high depression burden. It reflects a young population repeatedly exposed to trauma (war, poverty, HIV/AIDS) combined with limited access to mental health care. Adolescents and people living with HIV in Uganda show high rates of depressive symptoms, aligning with GBD estimates that rank Uganda among the highest globally (Abbo 2018). Palestinians face one of the world's heaviest depression burdens due to decades of occupation, recurrent conflict, displacement, and disrupted health systems. Studies in Gaza and the West Bank show very high prevalence of depression and PTSD — making mental health a humanitarian priority (Eloul *et al.,* 2017). The Central African Republic (CAR) ranks among the world's highest in depression burden. Prolonged armed conflict, mass displacement, and almost nonexistent mental-health services leave millions vulnerable. Surveys and NGO reports confirm widespread psychological distress (Ventevogel *et al.,* 2018). Yemen's civil war has collapsed its health system. WHO reports and local studies document epidemic levels of depression and PTSD in adults and children. GBD data places Yemen among the highest globally (Al-Amal *et al.,* 2020). Angola, after decades of civil war, still struggles with poverty and weak health systems. GBD data places it high on the list. Post-conflict studies note untreated depression as a key barrier to social reintegration (Ndala *et al.,* 2017). Despite its wealth, the United States ranks high in depression prevalence. National surveys show dramatic rises, especially among adolescents and young adults, driven by social isolation, economic stress, and healthcare access gaps (Mitchell *et al.,* 2022). Though starting from a lower baseline, Qatar shows one of the fastest increases in depression burden. Rapid urbanization, social change, and improved detection have uncovered growing unmet needs (Bener *et al.,* 2016). India and China have the highest absolute numbers of people living with depression, due to population size (Reddy *et al.,* 2016). Studies emphasize the working-age burden, showing huge economic and social

impacts (Huang *et al.,* 2019). South Africa's burden varies by province and group, with youth and urban poor most affected. Local studies report double-digit prevalences in adolescents and HIV-positive cohorts (Bantjes *et al.,* 2019). While Iraq's national depression prevalence appears moderate, conflict-affected provinces and displaced populations report much higher rates of depression and PTSD, proving the limits of national averages (Jaber *et al.,* 2017). Nigeria's GBD prevalence is low (~272 per 100,000), but local clinic and school studies show a different reality. In Lagos, 15% of primary care patients screened positive for major depression (Abiola *et al.,* 2016). Adolescents report depressive symptoms up to 17% in some schools (Adewuya *et al.,* 2018). Among people with chronic conditions (HIV, stroke), rates reach 30–50% (Olley *et al.,* 2017) (Ogun *et al.,* 2015).

1.5 What Causes Depression

Depression is a multifactorial disorder, meaning it arises from a combination of genetic (hereditary), biological (neurochemical and hormonal issues like low serotonin, dopamine, and norepinephrine levels, HPA axis dysregulation (resulting in excess cortisol), Decreased Brain-derived neurotrophic factor (affecting synaptic plasticity), environmental (childhood trauma and abuse, parental neglect or absence, chronic stress or financial hardship, loss of a loved one, loneliness or social isolation), psychosocial and lifestyle factors. It is not a contagious disease, so it cannot be transmitted like infections, but a family history of depression can increase risk due to genetic predisposition and shared environments (Wray *et al.,* 2018). Depression is not contagious like the flu or a virus. It cannot be contacted by another person. However, people in close relationships may mimic depressive behaviors (e.g spouse, sibling, or child of someone depressed), shared stressful environments (e.g poverty, abuse, trauma) increase collective risk. This is called emotional contagion, but it is not biological transmission (Kramer *et al.,* 2014).

1.6 Clinical Manifestations of Depression

Clinical manifestations refer to how depression presents in observable symptoms and subjective experiences across emotional, cognitive, physical, and behavioral domains. These manifestations vary in severity and duration, typically lasting at least two weeks for a clinical diagnosis according to DSM-5. These include, emotional manifestations (persistent low mood or sadness, feelings of emptiness or hopelessness, emotional numbness or irritability), Cognitive Manifestations (negative thoughts about self, world, or future, difficulty concentrating or making decisions, suicidal ideation or thoughts of death), Somatic (Physical) Manifestations (chronic fatigue or low energy, insomnia or hypersomnia appetite and weight changes, aches and pains without clear cause), Social withdrawal and isolation (neglect of hygiene and responsibilities, psychomotor changes, avoidance of activities once enjoyed).

1.7 Signs of Depression

Physical signs of depression include, noticeable slowness in movement or restlessness, weight loss or gain not due to dieting, lethargy, and lack of physical energy. Behavioral signs like social withdrawal or avoidance of group settings, reduced speech, minimal eye contact, loss of interest in personal grooming or appearance, tearfulness, or unexplained crying episodes. Communication and Social Signs like repeated expressions of guilt or being a burden, pessimistic speech, suicidal talk, or writing goodbye messages.

1.8 Different Tests for Depression

Psychometric Tests for Depression: These are structured questionnaires and interviews used to assess severity and diagnose Major Depressive Disorder (MDD), Biological and Hematological Tests. Emerging evidence shows that inflammatory markers and blood parameters can support understanding of depression's severity, treatment response, and subtype. C‑Reactive Protein (CRP) to check for elevated CRP (>3 mg/L) seen in ~20–30% of depressed patients; associated with symptom severity and poorer outcomes, pro-

inflammatory Cytokines (IL‑6 and TNF‑α) IL‑6: Correlated with reduced motivation and anhedonia; key predictor in inflammatory profiles. TNF‑α is associated with fatigue and cognitive slowing; it varies across patient groups. Hematological Cell Ratios, elevated neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and red cell distribution width (RDW) are positively associated with depression scores in clinical cohorts. Other Diagnostic and Research Tools, Electroencephalography (EEG), Biomarker Panels, and Neuroendocrine Measures.

1.9 Therapeutic Management of Depression

Pharmacotherapy (First-line Medication) includes SSRIs/SNRIs/TCAs/atypical antidepressants widely used. Choice depends on symptom profile, side effects, and comorbidity. For treatment-resistant cases, options like tricyclic antidepressants (TCAs) or monoamine oxidase inhibitors (MAOIs) may be considered Psychotherapy is another way of managing depression. Cognitive Behavioral Therapy (CBT) is effective across diverse severity levels, works equally well for men and women. Interpersonal Therapy (IPT), Behavioral Activation, and Mindfulness-Based Cognitive Therapy (MBCT) is also strongly supported.

1.10 Rehabilitation Strategies for Depression

This refers to planned methods or approaches used to help individuals recover and gain optimal function after experiencing depression. The first strategy is occupational therapy (OT). It is a type of healthcare intervention that helps people of all /ages develop, recover, or maintain the skills they need for daily living and meaningful activities. This therapy intervention can significantly improve engagement in daily activities, social participation, symptom management, and overall well-being (Nasiri *et al.,*). Another strategy is exercise and physical activity. Regular exercise programs, particularly those integrated into occupational therapy, have been shown to enhance mood, reduce depressive symptoms, and

support community integration. Psychosocial rehabilitation focuses on enhancing mental, emotional, and social functioning by helping individuals rebuild structure, relationships, coping skills, and a sense of purpose. Work-based rehabilitation, enables individuals with depression to return or maintain employment through targeted supports and workplace adaptations.

1.11 Control of Depression

Pharmacotherapy is a first-line treatment and it includes selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs). For treatment-resistant cases, options like tricyclic antidepressants (TCAs) or monoamine oxidase inhibitors (MAOIs) may be considered. For psychotherapy, cognitive-behavioral therapy (CBT) and interpersonal therapy (IPT) are recommended, with the choice depending on patient preference and availability. Neurostimulation: Electroconvulsive therapy (ECT) is suggested for severe or treatment-resistant depression. Maintenance Treatment: Continued treatment is advised to prevent relapse, with duration tailored to individual risk factors. Integrated or collaborative care models involve a team-based approach to managing depression, particularly in primary care environments where mental health resources may be limited.

Acute Phase Treatment The goal during this phase is to achieve remission of depressive symptoms. Continuation Phase, after achieving remission, continue treatment to prevent relapse. Maintenance Phase for individuals with recurrent depression, long-term maintenance treatment may be necessary for continued use of antidepressants and/or psychotherapy. Periodic evaluations to adjust treatment as needed.

1.12 Drugs Used To Treat Depression

Selective Serotonin Reuptake Inhibitors (SSRIs) examples are Fluoxetine, Sertraline, Escitalopram. They inhibit the serotonin transporter (SERT), increasing serotonin in the synaptic cleft → enhanced postsynaptic signaling → downstream effects on neuroplasticity

(BDNF increase, HPA-axis modulation). First-line agents with relatively favorable side-effect profiles.

Serotonin–Norepinephrine Reuptake Inhibitors (SNRIs). Examples are Duloxetine, Venlafaxine. They block reuptake of serotonin and norepinephrine via SERT and NET → increased synaptic monoamines, particularly effective in treating concomitant pain or fatigue symptoms.

Tricyclic Antidepressants (TCAs). Examples are Amitriptyline, Nortriptyline, and Imipramine. They non-selectively block SERT and NET; also antagonize muscarinic, histaminergic, and α-adrenergic receptors → increased monoamines but higher side effects risk. Not first-line, reserved for resistant depression.

Monoamine Oxidase Inhibitors (MAOIs). Examples are Phenelzine, Tranylcypromine. They irreversibly inhibit monoamine oxidase A and B → increased synaptic serotonin, norepinephrine, and dopamine. Effective in atypical depression but limited by dietary drug interactions.

Atypical Antidepressants / NDRIs an example is Bupropion. It blocks norepinephrine and dopamine reuptake; minimal serotonergic activity → useful in cases with fatigue, plus smoking cessation benefit.

NMDA Receptor Antagonists (Ketamine and Esketamine). Examples are IV Ketamine, Intranasal Esketamine (Spravato). They antagonize NMDA receptors on GABAergic interneurons → glutamate surge, enhanced AMPA receptor activation, increased BDNF and mTOR signaling → rapid synaptogenesis and mood improvement; metabolite (2R,6R)-HNK potentiates AMPA without dissociative effects. They are approved for treatment-resistant depression; onset within hours.

1.13 Laboratory Models Used To Study Depression

These models aim to replicate specific symptoms or neurophysiological features of human depression. Their utility lies in face validity (symptom similarity), construct validity (underlying mechanisms), and predictive validity (response to treatment).

Learned Helplessness (LH), the subjects (rats/mice) are exposed to inescapable stress (e.g foot shocks). Later, even escapable situations fail to elicit escape behaviors, a model for despair and loss of control. The biological involvement alters the HPA - axis, induces hippocampal synaptic loss, mimicking stress-related neurobiology in human MDD.

Chronic Unpredictable Mild Stress (CUMS/CMS), is subjected to varied mild stressors (e.g food/water deprivation, cold, cage tilt) over several weeks. Mimics chronic stress causing sustained anhedonia to check for reduced sucrose preference (anhedonia), impaired motivation.

Forced Swim Test (FST), the mice/rats are placed in water; immobility is interpreted as "behavioral despair." Antidepressants reduce immobility time therefore, Immobility duration vs active swimming/climbing to infer motivational state is recorded.

Tail Suspension Test (TST), the mice are suspended by their tail, immobility time reflects despair reduced by antidepressants. This test measures response to acute stress, not chronic depression.

Sucrose Preference Test (SPT), measures anhedonia decreased preference for sucrose solution versus water suggesting a depressive phenotype.

1.14 Significance of Tail Suspension Test (TST)

The Tail Suspension Test (TST) is a behavioral assay widely used to evaluate depression-like states in rodents, especially mice. It measures the time an animal spends immobile when suspended by the tail, and longer immobility is interpreted as behavioral despair or passive coping (Aslam 2016). The test has strong predictive validity because clinically effective antidepressants such as selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants significantly reduce immobility time in mice (Chellian *et al.,* 2016). It is considered a reliable screening tool for antidepressant-like activity because it is simple, inexpensive, and quick compared to other models such as the forced swim test (Aslam 2016). The TST is also important in genetic and neurobiological studies of depression, as mouse strains differ in baseline immobility and drug responses, making the test suitable for exploring genetic predispositions to depression (Ueno *et al.,* 2022). Additionally, the TST has been modernized with automated video-scoring systems such as DBscorer, which improve reliability and reproducibility by reducing human observer bias (Nandi *et al.,* 2021). However, limitations like immobility may reflect motor impairment, fatigue, or reduced activity rather than depression itself, and results can be influenced by strain, sex, or testing conditions. These concerns highlight that the TST should be interpreted as a model of coping strategies under stress, not as a complete model of human depression (Chellian *et al.,* 2016).

A systematic review and meta-analysis of prototypic antidepressants in the mouse TST. It showed that antidepressant drugs (e.g. imipramine, fluoxetine) consistently decreased immobility time, and the effect size correlated with dose, which supports the predictive validity of TST. It was also discovered that strain differences were not significant in many studies, possibly because too few experiments used each strain (Stukalin *et al.,* 2020). Ueno *et al* . (2022) tested whether conducting the TST simultaneously with two mice (with or without an opaque partition) versus singly affects immobility. They found that, unlike the

forced swim test, the tail suspension test did not show significant differences in immobility time under these different testing-environment setups. This supports that TST may be more robust to some environmental changes. The same study by Ueno *et al*. (2022) emphasises that test conditions (lighting, presence of partition, simultaneous vs isolated testing) are often underreported in TST studies, which complicates reproducibility across labs. (Ueno *et al.,* 2022). Stukalin . (2020) also found in their meta-analysis that scoring immobility in the last 4 minutes of a 6-minute suspension (rather than the full 6 min) may provide better sensitivity to drug effects. They recommend standardizing scoring windows to improve consistency. In the same meta-analysis, they reported a dose-response correlation: higher doses of antidepressants led to larger decreases in immobility (effect size), supporting quantitative sensitivity of TST to treatment.

1.15 Principle of Tail Suspension Test (TST)

The principle of the Tail Suspension Test is based on the observation that when mice are suspended by the tail, they initially engage in escape-oriented struggling, but after repeated failure, they eventually adopt a state of immobility, which is interpreted as behavioral despair or passive coping. This immobility is reduced by antidepressant drugs, supporting its use as a screening model for antidepressant-like activity. The core mechanism of this principle is the Behavioral despair concept – it describes that mice suspended by the tail become immobile after initial escape attempts, and that antidepressants reduce this immobility (Steru *et al.,* 1985). Interpretation of immobility reflects a passive coping strategy to inescapable stress rather than simply motor inhibition. Aslam (2016) emphasized that immobility is not absolute inactivity but the adoption of a "state of behavioral despair," which is sensitive to drugs targeting monoaminergic systems (Aslam 2016). Antidepressant sensitivity demonstrates that α-Asarone produced a biphasic effect on immobility in the TST, mediated through

serotonergic and noradrenergic systems, highlighting the predictive validity of the test for antidepressant-like drugs (Chellian *et al.,* 2016). A systematic review and meta-analysis confirmed that prototypical antidepressants (imipramine, fluoxetine) consistently reduced immobility in the TST across mouse strains, reinforcing that the principle of the test lies in detecting antidepressant efficacy through reduced immobility (Stukalin 2020). The neurotransmitter systems involved tests are sensitive to the modulation of monoamines, especially serotonin and norepinephrine. This aligns with the monoamine hypothesis of depression, where increasing synaptic levels of these neurotransmitters reduces despair-like immobility (Chellian *et al.,* 2016). The principle also relies on the fact that baseline immobility varies by mouse strain, reflecting genetic and neurobiological differences in stress coping (Eltokhi *et al.,* 2021). Thus, the principle of the TST is that immobility under acute stress represents a measurable endpoint for antidepressant efficacy and depression-like behavior in rodents.

1.16 Significance of Forced Swim Test (FST)

The forced swim test is widely used to detect antidepressant-like activity because drugs that are clinically effective in humans (e.g SSRIs, tricyclics, SNRIs) reliably reduce immobility time in rodents (Roni *et al.,* 2015). The FST is best interpreted as a measure of stress-coping strategy (active vs passive coping) rather than a full recapitulation of human depression drugs that promote active coping (swimming/climbing) are often effective antidepressants in the clinic (Kathryn *et al.,* 2017). Force swim test can be used quantitatively to help translate preclinical findings toward human dosing: population PK/PD modelling of mouse FST data for multiple antidepressants (e.g citalopram, desipramine, bupropion, etc.) showed that FST effect sizes can inform human exposure targets, although direct ED_{50} →human dose scaling may mispredict without concentration-based approaches (Eunice *et al.*, 2017). It is sensitive

to interactions and potentiation: for example, co-treatment with caffeine potentiated the antidepressant-like effects of several standard antidepressants (greater reduction in immobility than drug alone), showing the test's utility for studying drug interactions (Aleksandra, 2016). The FST's predictive validity is robust across many compounds in meta-analyses, but methodological variation (pool size/shape, scoring window, and timing of drug administration) produces between-study heterogeneity standardization improves Interpretability (Stukalin, 2020). The results depend on biological variables (strain, sex, age): some strains or sexes show different baseline immobility and different drug sensitivity, so reporting strain/sex/age and (where possible) testing multiple backgrounds strengthens conclusions. (Nikos 2015). Ethically and practically, the FST induces acute stress; recent position papers and reviews call for careful justification, refinement (minimizing distress), and transparent reporting and encourage considering alternatives when possible (Mohseni and Rafaiee 2025).

1.17 Principles of Forced Swim Test (FST)

The basic principle of the FST is that when rodents are placed in an inescapable container filled with water, they initially attempt to escape by swimming and climbing, but eventually adopt a posture of immobility, floating with minimal movements necessary to keep their heads above water. This immobility is interpreted as a passive coping strategy under stress (Roni 2015). The principle further assumes that antidepressant drugs reduce immobility time by shifting behavior toward more active coping (swimming or climbing), which reflects enhanced motivation and resilience to stress (Kathryn *et al.,* 2017). The test works because different classes of antidepressants produce distinct active responses: for example, selective serotonin reuptake inhibitors (SSRIs) increase swimming, whereas noradrenergic antidepressants increase climbing. This behavioral shift is the mechanistic basis for interpreting antidepressant activity (Nikos 2015). Importantly, the FST's principle is not to

"model depression" in its entirety, but to provide a behavioral readout of coping strategies under acute inescapable stress, which can be pharmacologically manipulated (Eunice *et al.,* 2017).

1.18 Aim of Study

To evaluate the antidepressant-like effect of the hydro-methanol leaf extract of *Icacina trichantha* Oliver in mice using behavioral models.

1.19 Objectives of the Study

1. To prepare a hydro-methanol extract of *Icacina trichantha*;
2. To evaluate the acute behavioral effects of the extract using the tail suspension test (TST) and the forced swim test (FST); and
3. To compare the extract's activity with a standard antidepressant drug imipramine as a positive control.

CHAPTER 2

LITERATURE REVIEW

2.1 History of *Icacina Trichantha*

Icacina trichantha was first scientifically described by Daniel Oliver in October 1868, in Flora of Tropical Africa (Vol. 1:358). Herbarium specimens collected before this formal naming include an 1858 sample from Onitsha, Nigeria, by C. Barter, indicating recognition and collection of the plant nearly a decade earlier. It belongs to the Icacinaceae family in the Icacinales order and remains an accepted species. The species is native to West and Central Africa, particularly Benin, Nigeria, Cameroon, Ghana, and possibly DR Congo. It thrives in woodland, savanna, forest edges, and forest regrowth areas, from sea level up to ~1,000 m, in wet tropical climates with 800–1,500 mm annual rainfall. In Nigeria, it's widely recorded from screenings in Lagos, Ibadan, Onitsha, Shasha, Okomu, and Degema, indicating dense wild populations.

The genus comprises six recognized African species, with *I. trichantha* being one of the most studied. Nutritionally, its leaves are protein and fibre-rich, while its tubers are carbohydrate-dense (Alawode, 2024). Icacina trichantha, commonly known as urumbia or eriagbo in Igbo and gbegbe in Yoruba, is a drought-resistant shrub native to West and Central Africa, renowned for its edible tubers, fruits, and medicinal value. (Wahua and Awogbayila, 2024). Commonly occurs in colonial stands and can become a weed in crops like rice paddies. It is traditionally used as a famine food during droughts and as a medicinal plant in West Africa

(Wahua and Awogbayila, 2024). Indigenous communities have long used it as a famine food and emergency staple during droughts or crop failures. Tubers are processed into flour after leaching bitter/toxic compounds.

2.2 Taxonomy

Kingdom: Plantae

Phylum: Tracheophyta

Clade: Angiosperms

Subclass: Magnoliidae

Order: Icacinales

Family: Icacinaceae

Genus: Icacina

Species: *Icacina trichantha*

2.3 Botanical Description

Icacina Trichantha, is a semi-climbing woody shrub, typically 1–2 m tall. It arises from a large, tuberous root often heavy and yam-like in appearance. It is commonly known as false yam. *Icacina trichantha* is a perennial shrub or small tree typically growing up to 2-4 meters in height.

Leaves: The leaves are simple. They are arranged alternately on stems, leathery and clustered toward the ends of the branches with entire margins. They are broadly elliptic to lanceolate

(6–23 cm long, 3–12 cm wide) with a pointed tip and sometimes a rounded base. The surface is glossy and hairless on top beneath, the central veins can bear fine hairs (hispid) and they are utilized as wrappers for processed oil bean seeds.

Flowers: The plant bears unisexual flowers (male and female flowers on the same plant). They occur in axillary or terminal panicles, sometimes densely clustered. The flowers are small, about 2–4 mm in diameter. They are greenish-white to yellowish. The sepals are small, 4–5 in number, free or slightly fused at the base. The petals are also 4–5, valvate in bud, and remain small and inconspicuous. In male flowers, there are 4–5 stamens, alternating with the petals. In female flowers, the ovary is superior, 3-celled, with one ovule in each cell.

Fruits: The fruit is a drupe. They are ellipsoid to ovoid, sometimes nearly round. Usually about 2–3 cm in diameter. The surface is smooth when fresh. When unripe, they are green, but on ripening they turn bright red to orange-red. The fleshy part of the drupe is edible but not widely consumed. Each fruit contains a single large stony seed (stone) inside the fleshy mesocarp. The fruits often occur in clusters, making them conspicuous when ripe.

Tuber: The plant produces an underground tuberous root. The tuber is usually massive, sometimes weighing up to 20–30 kg or more. It is generally irregular, oblong to globose in shape. The outer surface is rough, woody, and brownish. The inside (parenchyma) is white to creamy, rich in starch. It is very bitter due to the presence of alkaloids and other phytochemicals, and therefore toxic unless properly processed.

Stem: It is a woody shrub or liana-like climber, often sprawling. The plant can reach up to 2–4 meters high, sometimes more if supported. The stem is much-branched, somewhat weak, and flexible when young. Young stems are green and smooth, while older stems become brownish and slightly roughened. The stem is fibrous inside, which helps it sprawl and climb.

Stems bear alternate large leaves with long petioles at distinct nodes. The stem is pubescent (covered with fine hairs), connecting the visible trunk to the underground storage tuber.

Roots: It develops a large tuberous root system that stores nutrients. The root tubers can be very massive, sometimes weighing 20–30 kg or more. The root tuber is irregular, oblong to globose, and extends deep into the soil. The outer surface is thick, brown, and woody. The internal tissue is white to creamy, fleshy, and rich in starch granules. The root is extremely bitter, containing alkaloids, saponins, and other secondary metabolites. Despite its bitterness and potential toxicity, it is sometimes processed into a famine food after detoxification and also used in traditional medicine for various ailments.

To identify this plant in a field, look for a 1–2 m shrub with a thick, visible root-crown and vine-like branches. Check the leaves for big, glossy on top, veined, lanceolate to elliptical, and alternately arranged. Inspect the underside, find fine hairs, and note occasional glandular trichomes. In season, spot small greenish-white flower spikes, and later vivid red, velvety drupes. Dig carefully: presence of a starch-filled tuber confirms *I. trichantha.*

Plate 1: The leaves of *Icacina trichantha* (Wahua and Awogbayila, 2024).

2.4 Phytochemicals in *Icacina Trichantha*

Research shows that *Icacina trichantha* has several classes of compounds with potential pharmacological significance. Here are some of the phytochemicals found in *Icacina trichantha.*

Alkaloids: Detected using Dragendorff's reagent in methanol tuber extracts, reddish-brown precipitate indicates their presence. Known for neuroactive, antimicrobial, and anti-inflammatory properties, supporting traditional medicinal uses (Onakpa *et al.,* 2016).

Flavonoids: Present in leaves and tubers per phytochemical screening—identified via standard colorimetric tests. Act as potent antioxidants, free-radical scavengers, and anti-inflammatory agents; responsible for the high phenolic content (93.8 mg GAE/g) and strong DPPH scavenging (IC_{50} = 0.332 mg/mL) (Onakpa *et al.,* 2016).

Tannins: Detected via ferric chloride test across extracts. Astringent, antimicrobial, and antioxidant; may contribute to detoxification during traditional food processing (Onakpa *et al.,* 2016).

Saponins: Foaming test positive in crude methanol extracts. It has surfactant, immunomodulatory, and cholesterol-lowering effects potential for hemolytic and antimicrobial activity (Onakpa *et al.,* 2016).

Glycosides: Detected in tuber and leaf extracts from various solvent fractions. Includes cardiac and other bioactive glycosides that may affect heart function, metabolism, or enzymatic processes (Onakpa *et al.,* 2016).

Phenolic Compounds (General): Confirmed by ferric chloride and DPPH assays; leaves contain high total phenolics (93.8 mg GAE/g). Strong antioxidant activity, anti-inflammatory effects, and potential anti-cancer benefits (Onakpa *et al.,* 2016).

2.5 Traditional Uses and Cultural Significance

Tubers of *Icacina trichantha* can weigh several kilograms, they are rich in starch and contain other essential calories. They are consumed fresh or dried and processed into flour, which is used in soups, porridges, and as a lustrous famine food. Traditional preparation involves prolonged soaking to remove bitter and anti-nutritional compounds (e.g. cyanide, tannins, phytates). The sweet, red fruits are eaten fresh. Seeds are processed into flour nutty, storable, and resistant to pests (Onakpa *et al.,* 2016). It can be used for treating food poisoning, constipation, malaria, rheumatism, toothache, asthma, hypertension, and as an emetic or aphrodisiac. Health traditional medicinal uses are substantiated by antioxidant, anti-inflammatory, antimicrobial, and anticough properties. Modern analysis confirms high nutritive value, especially in leaves and tubers. Leaf extracts have also shown antimicrobial effects, active against bacteria and fungi, aligning with folk usage for treating infections (Onakpa *et al.,* 2016).

2.6 Pharmacological Uses

Antiemetic and Purgative Use (Digestive and Relief): Tuber extracts contain alkaloids and saponins that stimulate gut motility and purge toxins. Saponins irritate the mucosa of the gut, leading to reflex vomiting or purging. Alkaloids modulate the enteric nervous system, reducing nausea and inducing intestinal cleansing (Onakpa *et al.,* 2016).

Antipyretic Effect (Malaria and Fever): Tuber decoctions reduce fever via flavonoids and phenolic compounds, which: Inhibit cyclooxygenase (COX) and prostaglandin synthesis,

thereby lowering body temperature. Enhance antioxidant enzyme activity, reducing oxidative stress caused by Plasmodium infections (Alawode *et al.,* 2018).

Antimicrobial Activity (Infections): Both leaf and tuber contain phenolics, flavonoids, and diterpenoids with antibacterial and antifungal effects: disrupt bacterial cell membranes and inhibit microbial enzymes. Flavonoids interfere with microbial DNA and RNA replication. Effective against pathogens like E. coli, Staph. Aureus, and Candida albicans. (Olubomehin *et al.,* 2024)

Anti-inflammatory Effect (Swelling and Pain): Methanol and chloroform extracts of the tuber inhibit inflammation by: Suppressing pro-inflammatory cytokines (e.g*et al.,* TNF-α, IL-1β). Inhibiting COX-2 enzymes, reduces the production of prostaglandins. Comparable in potency to indomethacin in reducing paw edema and ear swelling in animal models. (Alawode *et al.,* 2018)

Hepatoprotective/Antioxidant (Liver and DNA Protection): Leaf extract protects liver tissues from toxic damage restores liver enzyme balance, reduces DNA fragmentation and micronuclei formation, protecting against genotoxic agents. (Onakpa *et al.,* 2016).

Antidiabetic Action (Blood Sugar Control): Leaf extracts reduce blood glucose via enhancing insulin secretion or improving insulin sensitivity. Slowing glucose absorption from the intestines. Protecting pancreatic β-cells through antioxidant effects (Alawode *et al.,* 2018).

Anticancer and Cytotoxic Effects: Tuber-derived 17‑norpimarane diterpenoids show cytotoxicity by: Inducing apoptosis (programmed cell death) in cancer cells. Inhibiting cell proliferation in melanoma, breast, and ovarian cancer lines. Disrupting mitochondrial activity and oxidative stress in tumor cells (Zhao *et al.,* 2016).

CHAPTER THREE

MATERIALS AND METHODOLOGY

3.1 Plant Collection and Identification

Fresh leaves of *Icacina trichantha* Oliver were collected from the capital in Ovia North East Local Government Area, Benin City, Edo State, Nigeria. The plant was identified by Prof. E.I. Aigbokhan and voucher number UBH-1185 was issued by Dr. H.A. Akinnibosun; both of the department of Plant Biology and Biotechnology, Faculty of Life Sciences, University of Benin, Benin City, Nigeria. The leaves were cleaned, dried, pulverized into powder, and stored in an airtight container till further use.

3.2 Experimental Animals

A total of 50 albino mice, weighing between 15-25g were used for the study from the animal house of the department of pharmacology, Faculty of Pharmacy, University of Benin. The animals were acclimatized for two weeks before the experiment. The animals were housed in standard plastic cages, maintained under controlled environmental conditions, and had access to water and feed (Livestock feeds Ltd Ibadan Nigeria) and were exposed to natural lighting and room temperature. This study was approved by the Faculty of Science Laboratory Research Ethical Committee with reference number UNIBEN/FSLT/00042.

3.3 Extraction Process

The collected leaves were washed thoroughly with clean water to remove dust then air-dried at a controlled temperature. Once completely dry, the leaves were ground using a mechanical grinder. 100g of the powdered leaf was extracted using a hydro-methanol mixture in a ratio of 50:50 methanol to deionized water. Using a cylinder, measure 600ml of methanol then make up to the mark to 1200 ml with deionized water. The mixture was soaked in a maceration bottle on the 10th of June, by 3pm for 72 hours to ensure maximum extraction of phytochemicals. During this process, we shook the bottle vigorously to break down the cell walls of the plant and enhance solvent penetration. The extract was filtered after 72 hours using a sieve. The filtrate was obtained and the chaff discarded. The filtrate was placed in a hot air oven using a stainless sterile plate and left to dry at 53°C to obtain a solid extract. The extract was removed from the stainless plate into a universal bottle (Okoruwa et al., 2016).

3.4 Experimental Design

After 14 days of acclimatization to laboratory conditions, the albino mice were divided into 5 groups including:

Group 1 served as the control and was administered deionized water.

Group 2 was administered a dose of 100mg/kg hydro-methanol extract of *Icacina trichantha*

Group 3 was administered a dose of 200mg/kg hydro-methanol extract of *Icacina trichantha*

Group 4 was administered a dose of 400mg/kg hydro-methanol extract *Icacina trichantha*

Group 5: was administered a standard drug Imipramine 25 mg/kg

All administrations were via the oral route with the aid of an orogastric tube.

3.5 Phytochemical Screening

Simple chemical tests were carried out on the crude powdered sample and the methanol extract according to standard procedures to identify the phytochemical constituents (Stahl, 1973; Sofowora, 1982; Harborne, 1998; Evans, 2002).

Approximately 5 g of the crude powdered sample was boiled with 75 mL of distilled water for 30 minutes. The solution was filtered hot and allowed to cool. The filtrate obtained was used to carry out the following tests.

General Tests for Alkaloids

Two drops of Dragendorff's reagent were added to 2 mL of the filtrate.

Two drops of Wagner's reagent were added to 2 mL of the filtrate.

Two drops of Hager's reagent were added to 2 mL of the filtrate.

Two drops of Mayer's reagent were added to 2 mL of the filtrate.

Tests for Carbohydrates

Molisch's Test: To 2 mL of filtrate was added 2 drops of 1% alcoholic naphthol followed by 2 mL of concentrated sulphuric acid at a slanting position.

Tests for Reducing Sugars

Fehling's Test: To 2 mL of filtrate was added 2 drops of Benedict's reagent (a mixture of equal volumes of Fehling's solution A and B). The resulting solution was heated over a boiling water bath for 3 minutes.

Tollen's Test: Dilute ammonium hydroxide solution was added dropwise to silver nitrate solution containing a few drops of 10% sodium hydroxide until the precipitate of silver oxide

almost completely dissolved. A few drops of the filtrate were then added to the mixture above.

Keller Kiliani's Test for Deoxysugars: To 2 mL of filtrate was added a few drops of dilute acetic acid containing a trace of 5% ferric chloride were added. The resulting mixture was transferred to the surface of concentrated sulphuric acid.

Test for Saponins

Frothing Test: The filtrate (1 mL) was diluted with 10 mL of distilled water and shaken vigorously for one minute.

Fehling's Test: To 10 mL of the filtrate was added 5 mL of dilute H_2SO_4 was added. The mixture was boiled for 15 min, filtered, and cooled. 2.5 mL of the filtrate was made alkaline with 20% NaOH solution and boiled with 0.1 mL each of Fehling's solutions A and B for 2 minutes.

Lieberman Burchard's Test for Steroidal saponins or Phytosterols: A mixture of 1 mL chloroform and a few drops of acetic anhydride was added to 2 mL of the filtrate. To the final mixture was added 2 drops of concentrated sulphuric acid.

Test for Tannins

Gelatin Test: To 2 mL of the filtrate was added 2 mL of 1% gelatin solution in 10% NaCl.

Test for Terpenoids

Salkowski Test: The filtrate (5 mL) was mixed with 2 mL of chloroform and concentrated H_2SO_4 was carefully added (dropwise) to form a layer.

Test for Phenolic compounds

Ferric chloride Test: To 2 mL of filtrate was added 5 mL of distilled water followed by 2 drops of 5% ferric chloride solution. A blank test was done by adding 2 drops of 5% ferric chloride solution to 5 mL of distilled water.

Folin Ciocalteu's Test: To 5 mL of filtrate was added 0.5 mL 10 % Folin-Ciocalteu's phenol reagent followed by 5 mL of 7% Na2CO3.

Test for Flavonoids

Alkaline reagent Test: To 2 mL of filtrate was added a few drops of 20% sodium hydroxide solution followed by a few drops of dilute hydrochloric acid solution.

Lead acetate Test: A few drops of lead acetate solution were added to 2 mL of the filtrate.

Aluminium chloride Test: The filtrate (3 mL) was shaken with 0.1 mL each of 1% AlCl3 solution and 1 M CH3COOK solution. The mixture was allowed to stand for 30 min.

Test for Anthraquinone Derivatives

Bontreger's Test: The filtrate (2 mL) was shaken with 2 mL of petroleum ether. The ether layer was washed with 2 mL of distilled water and then shaken with dilute ammonia solution.

Test for Proteins

Xanthoproteic Test: A few drops of concentrated nitric acid were added to 2 mL of the filtrate.

Ninhydrin Test: Two drops of Ninhydrin solution were added to 2 mL of the filtrate.

3.6 Tail Suspension Test (TST)

The Tail Suspension Test was used to assess antidepressant-like behavior in mice. Each mouse was suspended by the tail using adhesive tape, approximately 1 cm from the tip, and secured to a horizontal bar at a height of 50 cm from the ground. The test duration was 6

minutes. The duration of immobility was recorded using a timer. A decrease in immobility time is interpreted as an antidepressant-like effect.

3.7 Forced Swim Test (FST)

The Forced Swim Test evaluates behavioral despair and is based on the principle that mice placed in an inescapable cylinder of water will eventually exhibit immobility. Each mouse was placed individually into a transparent cylindrical container (25 cm high × 10 cm diameter) filled with 15 cm deep water. The test duration was 6 minutes. Immobility time (absence of active escape behaviors such as climbing or swimming) was recorded during the last 4 minutes. After the test, mice were dried with a soft towel and placed under a heat lamp to prevent hypothermia. A significant reduction in immobility time suggests an antidepressant-like activity.

CHAPTER 4

RESULTS

Table 1: Qualitative Phytochemical Constituents of hydro-methanol extract of *I. trichantha*

TEST	INFERENCE
Flavonoid	+
Phenolics	+
Saponins	+
Terpernoids	+
Tannins	+
Alkaloids	+
Carbohydrates	+
Reducing Sugars	+
Assay Sugars	+
Proteins	–

- absent, + present

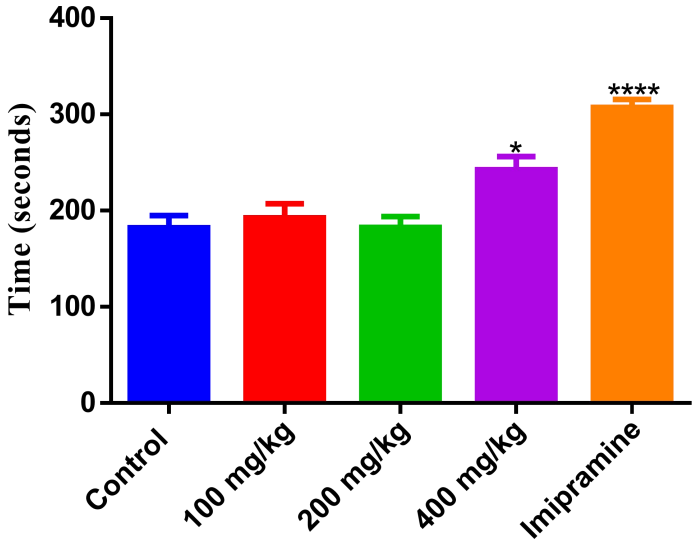

Figure 4.1: Effects of the hydro-methanol leaf extract of *I. trichantha* on the tail suspension test in mice.

There is a significant increase at 400mg/kg when compared to the control ($P < 0.05$). Data are represented as mean ± SEM, n = 5.

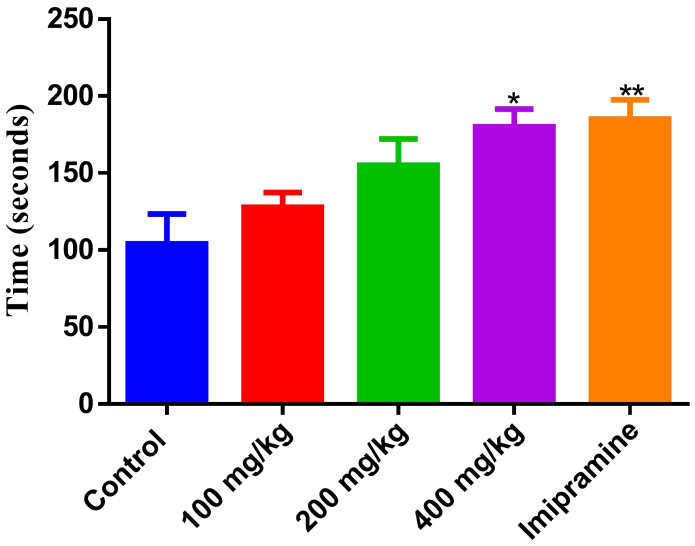

Figure 4.2: Effect of hydro-methanol leaf extract of *I. trichantha* on forced swim test in mice.

There is a significant increase at 400mg/kg when compared to the control ($P < 0.05$). Data are represented as mean ± SEM, n = 5.

CHAPTER FIVE

5.1 Discussion

Depression is one of the most prevalent psychiatric disorders globally, characterized by persistent low mood, anhedonia, cognitive impairments, and disturbances in neuroendocrine and neurochemical systems. Despite the availability of conventional antidepressant drugs such as selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants, their limitations include delayed onset of action, side effects, and incomplete remission rates (Zhao *et al.,* 2024). Consequently, there has been a growing interest in exploring medicinal plants as alternative or complementary therapies, owing to their diverse phytochemical profiles and potential to target multiple neurobiological pathways implicated in depression (Alizadeh *et al.,* 2024).

The present study demonstrated that the hydromethanol leaf extract of *Icacina trichantha* significantly reduced immobility time in both the Forced Swim Test (FST) and Tail Suspension Test (TST). These models are widely accepted for screening antidepressant agents, and decreased immobility time is interpreted as an antidepressant-like effect (Commons *et al.,* 2017). The positive results obtained from both models therefore suggest that *I. trichantha* possesses bioactive constituents capable of modulating pathways relevant to the pathophysiology of depression.

Phytochemical studies on *I. trichantha* have revealed the presence of flavonoids, alkaloids, tannins, saponins, terpenoids, carbohydrates, and phenolic compounds (Alawode *et al.,* 2024). These compounds are known to exert central nervous system (CNS) effects and may explain the observed behavioral outcomes. Flavonoids, for instance, are reported to modulate monoaminergic neurotransmission, enhance synaptic plasticity, and upregulate brain-derived

neurotrophic factor (BDNF), thereby improving mood and cognitive function (Alizadeh *et al.,* 2024). Alkaloids are also well documented for their ability to inhibit monoamine oxidase (MAO) or block monoamine reuptake, which increases synaptic concentrations of serotonin, norepinephrine, and dopamine, neurotransmitters central to the regulation of mood (Zhao *et al.,* 2024). Similarly, saponins and phenolic compounds have been linked to antioxidant and anti-inflammatory properties, which may attenuate oxidative stress and neuroinflammation, both of which are implicated in depressive disorders (Che, 2016).

The observed antidepressant-like activity of *I. trichantha* extract may therefore be attributed to a synergistic interaction of these phytochemicals. The modulation of monoaminergic systems is a plausible mechanism, given the similarity of the extract's effects in FST and TST to those of clinically effective antidepressants (Commons *et al.,* 2017). Additionally, flavonoids and phenolics in the extract may have promoted neuroprotection and neuroplasticity through BDNF upregulation and antioxidative actions, while its saponins and terpenoids may have contributed to anti-inflammatory effects, thus normalizing cytokine imbalances associated with depression (Zhao *et al.,* 2024).

Taken together, the results of this study show that the hydromethanol leaf extract of *I. trichantha* exhibits significant antidepressant activity in mice. While the precise mechanisms remain unknown, the evidence strongly shows the involvement of monoaminergic modulation, neurotrophic enhancement, anti-inflammatory activity, and antioxidative effects mediated by its phytochemical constituents. Flavonoids, alkaloids, and saponins present in the plant are known to enhance serotonergic, dopaminergic, and noradrenergic transmission, thereby contributing to antidepressant-like effects (Ibrahim *et al.,* 2020; Petroni *et al.,* 2021). Additionally, polyphenolic compounds such as flavonoids have been reported to upregulate brain-derived neurotrophic factor (BDNF), which plays a crucial role in neurogenesis and mood regulation (Molendijk and de Kloet, 2019). The anti-inflammatory properties of

triterpenoids and alkaloids may further mitigate the role of pro-inflammatory cytokines that are strongly implicated in the pathophysiology of depression (Miller and Raison, 2016). Likewise, the antioxidant activity of phenolic compounds reduces oxidative stress, a condition frequently associated with depressive disorders (Maes *et al.,* 2018). Future studies should include neurochemical assays to determine the extract's effects on monoamine levels, as well as molecular studies on BDNF expression, oxidative stress markers, and inflammatory cytokines to better clarify its mechanisms of action.

5.2 Conclusion

This study concludes that the hydro-methanol leaf extract of *Icacina trichantha* possesses flavonoids, alkaloids, tannins, saponins, terpenoids, carbohydrates, and phenolic compounds. The extract also possesses antidepressant activity at 400 mg/kg.

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