ANTIDEPRESSANT AND ANXIOLYTIC PROPERTY OF D3 ORGANIC® SUPPLEMENT IN ALBINO MICE

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(PHYSIOLOGY AND PHARMACOLOGY TECHNIQUES)

DEPARTMENT OF SCIENCE LABORATORY TECHNOLOGY

FACULTY OF LIFE SCIENCES

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CERTIFICATION

This is to certify that this work "Antidepressant and Anxiolytic Property of D3 Organic® Supplement In Albino Mice" was carried out by Chidera Princessa OKUTE (Miss) of the

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DEDICATION

This work is dedicated to God Almighty, the giver of knowledge, understanding and good health for his never ending grace, mercies and protection towards me throughout my undergraduate studies, and to my parents Apst. Dr. Okute David Ogbuzor and Evang. (Mrs.) Blessing Okute for their unconditional love and support throughout the period of my study.

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ABSTRACT

Nature has provided humans with medicine, shelter, food, clothing, fragrances, and transportation throughout history. The D3 organic® supplement's antidepressant and anxiolytic properties are assessed. Antidepressants and anxiolytics were tested in the forced swim, tail suspension, and elevated plus maze. Twenty-five 20–30 gram mice were divided into five groups of five. Group 1 received 10 ml/kg distilled water, Groups 2, 3, and 4 received 50, 100, and 200 mg/kg D3 organic® supplement extract, and Group 5 received 20 mg/kg oral fluoxetine. After receiving D3 and fluoxetine, mice were placed in an unbreakable transparent cylinder filled with water at 25°C for one hour. Animal immobility was measured after 5 minutes of swimming. Twenty 20–30 gram mice were randomly assigned to five four-animal groups. Group 1 received distilled water (10 ml/kg), groups 2–4 D3 organic® supplement extract (50, 100, and 200 mg/kg), and group 5 diazepam. The animals spent five minutes in the central maze an hour after receiving D3 organic® supplement extracts and diazepam. The number of entries and open arms time were recorded. In the forced swimming and tail suspension test, D3 organic® supplement extract (100 and 200 mg/kg) and fluoxetine (20 mg/kg) reduced immobility time compared to the control ($p<0.05$). Diazepam (10 mg/kg) and D3 organic® supplement extract (100 and 200 mg/kg) increased time spent and percentage time spent in the open arm compared to the control ($p<0.05$). D3 Organic® Supplement has anxiolytic and antidepressant properties.

CHAPTER ONE

INTRODUCTION

1.1. BACKGROUND OF THE STUDY

Throughout history, humans have depended on nature to fulfil their fundamental needs, including medicine, shelter, food, clothing, fragrances, and transportation (Dar *et al*., 2017). Among nature's resources, medicinal plants have played a crucial role in traditional healthcare systems, especially in developing countries, where they often serve as the primary treatment option due to their accessibility and affordability (Hosseinzadeh *et al*., 2015). Medicinal plants are defined as plant species containing bioactive compounds with therapeutic potential (Riaz *et al*., 2023). These compounds, located in various parts of the plant, such as roots, leaves, seeds, flowers, fruits, bark, or the entire plant, have been utilised, either directly or indirectly, for treating diseases (Riaz *et al*., 2023). Despite significant advancements in synthetic drug development, a considerable proportion of modern pharmaceuticals still derive from plant sources (Chaachouay andamp; Zidane, 2024). Experts estimate that medicinal plants account for over 25% of prescription drugs in developed nations (Chaachouay andamp; Zidane, 2024). According to the World Health Organisation (2023), in many African countries, up to 80% of the rural population relies on herbal medicine as their primary source of healthcare. Consequently, medicinal plants are of significant importance for the health of the global population.

According to the World Health Organisation (WHO, 2023), traditional medicine encompasses the entirety of knowledge, practices, and beliefs employed in maintaining health and treating illness, rooted in indigenous cultural traditions. In Africa and various regions worldwide, herbal remedies are essential for managing both physical and mental health conditions, particularly in

rural communities where access to modern medical services is limited. Estimates suggest that up to 80% of the global population depends on traditional medicine, including herbal therapies, for primary healthcare. In rapidly developing nations such as China and India, plant-derived medicines constitute nearly 80% of health treatments, whereas this figure drops to about 25% in developed countries like the United States (Parvin *et al*., 2023). This worldwide reliance underscores the ongoing significance of medicinal plants, particularly in addressing common ailments such as anxiety and depression (Kenda *et al*., 2022).

In recent years, there has been a growing interest in herbal remedies across the globe, not just in developing regions but also among industrialised nations. This increased attention is, in part, a response to the limitations and side effects associated with synthetic drugs, prompting many individuals to seek safer, plant-based alternatives (Ansari *et al*., 2025). Additionally, the rising demand for natural products has highlighted the necessity of preserving and studying medicinal plant species, particularly those sourced from the wild, where collection rates are increasing by 8% to 15% annually in areas such as Europe, Asia, and North America (Kenda *et al*., 2022).

Medicinal plants are significant not only for human health but also for ecosystem health, as they can indicate the overall wellbeing of an ecosystem (Caballero-Serrano *et al*., 2019). Their utilisation can be traced back to ancient civilisations, including those in China, Egypt, Greece, India, and Persia, where plant-based treatments laid the groundwork for early medicinal practices (Jamshidi-Kia *et al*., 2018). Historical examples of plant-derived drugs include aspirin (derived from willow bark), morphine (extracted from the opium poppy), digoxin (sourced from foxglove), quinine (from cinchona bark), and pilocarpine (from jaborandi). These instances underscore the ongoing relevance of phytotherapy—the practice of using plant-based

medicines—in contemporary drug development (Chaachouay and Zidane, 2024). Despite the central role of chemically synthesised drugs in modern medical practice, concerns regarding their potential side effects and long-term consequences have led to an increased demand for herbal alternatives (Karimi *et al*., 2015). As public interest and confidence in medicinal plants continue to rise, so does the necessity for scientific validation of their therapeutic effects (Wang *et al*., 2023). Presently, many traditional drugs derived from plants form the basis for modern treatments in clinical, chemical, and pharmaceutical research.

The "D3 Organic®" herbal mixture, developed by Nature's Renaissance International (NRI), is marketed as a multi-purpose immune-enhancing supplement, claiming to address ailments such as malaria, typhoid, respiratory disorders, and reproductive health issues. Its formulation comprises Desmodium gangeticum, Eclipta alba, Garcinia kola, Tetracarpidium conophorum, Ocimum sanctum, and Curcuma longa, which are botanicals traditionally acknowledged for their antioxidant, anti-inflammatory, and antimicrobial properties. However, despite these ethnomedicinal claims, there is currently no scientifically established evidence supporting any anti-stress effects of the product. Moreover, the broad therapeutic claims remain largely unverified by controlled clinical studies, indicating a need for empirical validation. In the absence of such evidence, and considering the extensive range of unverified benefits, caution is warranted in its use, particularly for individuals with pre-existing health conditions or those undergoing concurrent pharmacological treatments.

Given this context, the exploration of specific plant-derived compounds for their potential therapeutic effects is of growing importance (Kouba *et al.*, 2022). This study aims to enhance that initiative by assessing the antidepressant and anxiolytic effects of D3 Organic®**,** a

compound believed to be of natural origin. By investigating its efficacy, this research aims to support the broader movement toward integrating safe, plant-based remedies into modern mental health treatments.

1.2. AIM OF THE STUDY

To evaluate the potential antidepressant and anxiolytic properties of D3 organic.

1.3 SPECIFIC RESEARCH OBJECTIVES

I. To evaluate the antidepressant effects of the D3 organic supplement using standard behavioural models, such as the forced swimming test and tail suspension test, in laboratory animals.

II. To assess the anxiolytic properties of D3 and its impact on anxiety-related behaviours, e.g., elevated plus maze.

CHAPTER TWO

LITERATURE REVIEW

2.1. *Desmodium gangeticum*

2.1.1. Description of *Desmodium gangeticum*

With over 350 species, the genus Desmodium is a significant component of the Fabaceae family and is primarily found in tropical and subtropical regions of the world. This group's members are mostly herbs, shrubs, or sub-shrubs, but they are rarely trees. They can be identified by their combination of trifoliate leaves (some species are reduced to unifoliate or a mixture of both types), stipels, hooked hairs, and lomentaeous fruit, which means each seed is dispersed individually enclosed in its segment. Few of these have huge or colorful blooms, and the majority are unnoticeable legumes (Sahu *et al.,* 2023). *D. gangeticum* is one of the more than 20 species in this genus that have long been utilized in traditional medicine, either alone or in combination with other medications in Ayurvedic, Siddha, and Unani systems of medicine. "Salparni" is the popular name for it. It is a component of Ayurvedic remedies like "Dashmoolarishta" and "Dashmoolakwaath," which are advised for postpartum care in order to prevent further difficulties (Sahu *et al.*, 2023). Desmodin, hordenine, and gangetin have anti-amnesic, immunomodulatory, anti-diabetic, antioxidant, cardioprotective, hepatoprotective, and anti-inflammatory properties..

2.1.2. Distribution of *Desmodium gangeticum*

*Desmodiumgangeticum*is native to Africa, India, Sri Lanka, Southern China, throughout continental Southeast Asia, Malesia (Peninsular Malaysia, Sumatra, Borneo, Java, Sulawesi,

Moluccas, Philippines, New Guinea) and Australia. Introduced and naturalized in Jamaica, Madagascar, and the Pacific Islands (Green Institute, 2022).

2.1.3. Ethno-medicinal properties of *Desmodium gangeticum*

In many different parts of the world, *D. gangeticum* has long been utilized extensively either as a single drug or in combination with other drugs (Vasani *et al*. 2022). In India, a root preparation of Shalaparni is used to treat snake bites (Upasani *et al*., 2017). In the Dudhi area of District Sonebhadra, Uttar Pradesh, India, root paste is also customarily administered orally as a remedy for snake and scorpion bites (Rathia *et al*., 2015). One spoonful of its root decoction is used to treat rheumatism in the Eastern Ghats of Andhra Pradesh, India (Rathia *et al*., 2015). According to Kumar *et al*. (2018), E. Coli was found to be eliminated in the aqueous leaf extract of *D. gangeticum* used by the natives of Odisha, India. Furthermore, the Chandra Prabha Wildlife Sanctuary in the Chandauli District of Uttar Pradesh used a decoction made from the plant's stem and leaf as a diuretic, antitoxic, and remedy for vomiting and diarrhea (Kumar *et al*., 2015). In Raipur District, it is used to treat fever, vomiting, and Vata-Dosha (Dewangan and Acharya, 2017).

Fever and kidney diseases are treated with plant roots, bark, and leaves in tribal parts of Adilabad District, Telangana Region (Gurrapu and Mamidala, 2017). Its root decoction, which is found in the eastern Ghats of Andhra Pradesh, India, is traditionally used to treat respiratory conditions with a half-cup dose once a day for two to three months (Gurrapu and Mamidala, 2017). Tribes in the state of Chhattisgarh use a paste made from its stem bark to goiter once a day for three to four days (Vasani *et al*., 2022). Tribal people in the Jhalod taluka of the Dahod district of Gujarat, India, use a tonic called "Salampak" made from *D. gangeticum* to treat gynecological conditions

(Vasani *et al*., 2022). In the Bulamogi district of Uganda, root is used for premature ejaculation. Moreover, in the Deo-lapar forest range of Maharastra, the root is also utilized to treat colds and coughs (Kumar *et al*., 2015). The Khasia group in Bangladesh's Moulibazar district uses *D. gangeticum* ethnomedically for menstruation and stomach aches (Vasani *et al*., 2022). The roots of *D*. *gangeticum* are chewed by the tribal people of Bulamogi community, Uganda to cure premature ejaculation. In Maharshtra, root powder with honey is applied frequently to treat mouth ulcers (Mohan *et al*., 2021). Assamese people topically apply the paste of leaves to cure the eczema and 2ml of water decoction is prescribed thrice daily after meal by tribal people of Waynad of Kerala, India, to treat type 2 diabetes mellitus (Verma, 2023).

Plate 1: Image showing the *Desmodium gangeticum* plant (Green Institute, 2022)

2.2 *Eclipta alba*

2.2.1 Description of *Eclipta alba*

Ecliptaalba (L.) is an annual multibranched herbaceous plant that reaches up to the height of 30–50cm, which may be erected or prostrated (Akram *et al.*, 2022). The plant has white hair on both of its leaf surfaces. The red stem contains simple, sessile, lanceolate leaves that are 90 cm tall, 4–10 cm long, 0.8–2 cm wide, and frequently slender (Akram *et al*., 2022). With contrast, the leaves are linked to the stem with the absence of petioles. The lower nodes have roots. The single, white, 6–8 mm-diameter flowering heads have narrowly winged blooms. The plant has a well developedroot system with grey cylindrical roots present (Akram *et al.*, 2022). The plant is covered with flowers throughout the year, and has its fruiting period from September to October.

2.2.2. Distribution of *Eclipta alba*

Originating in Asia, *Eclipta alba* (Bhringraj) is now widely found in warm temperate, tropical, and subtropical regions (Kumari *et al*., 2021). It is found sparingly in Africa, Europe, Oceania, and other places, but abundantly in China, Brazil, India, and the United States. Numerous Asian countries, including Afghanistan, Bangladesh, Bhutan, Indonesia, Iraq, Japan, Korea, Malaysia, Pakistan, Philippines, Saudi Arabia, Sri Lanka, and Thailand, are home to it. In warmer regions of America, Africa, Asia, and Australia, four species have been identified thus far. The entire plant, including its roots, seeds, and seed oil, is utilized medicinally (Kumari *et al*., 2021). Bhringraj is produced organically in India without the use of chemicals.

2.2.3 Ethnomedicinal properties of *Eclipta alba*

The plant Eclipta alba is used to cure skin concerns, gastrointestinal issues, and respiratory ailments in several parts of India (Goyal *et al*., 2024). The plant's leaves are used to treat a variety of conditions, including hair loss, dry hair, gingivitis, diabetes, baldness, headaches, elephantiasis, and hair dye. The stem of the plant is also used as a blood tonic, anemia, chickenpox, and any other blood-related issues. Additionally, the plant's roots are very effective in treating constipation and irregular bowel movements (Goyal *et al*., 2024). Burns, sores, asthma, cuts and wounds, ulcers, fever, normal weakness, jaundice, liver-related, snake bite, edema, swelling, high blood pressure, diabetes, indigestion, hepatitis, spleen enlargement, anticatarrhal, febrifuge fetal development, and childbirth facilitation are among the symptoms that the entire plant is used to prevent (Bajpai *et al*., 2025). According to Goyal *et al*. (2024), the aerial section of Eclipta alba is used as a liver cleanser, hair tonic, allergic, inflammatory, burn, skin condition, anemia, headache, mental disorder, astringent, antiseptic, and anticancer.

Plate 2: Image showing the *Eclipta alba* plant (Bajpai *et al*., 2025).

2.3 *Garcinia kola*

2.3.1. Description of *Garcinia kola*

Garciniakola (bitter kola) is a dicotyledonous plant belonging to the family of plants called Guttiferae. It is a medium sized evergreen tree, about 15-17m tall and with a fairly narrow crown (Ekene and Erhirhie, 2014). The leaves are simple, 6-14cm long and 2-6cm across, shiny on both surfaces and spotted with resin glands. The small flowers are covered with short, red hairs (Ekene and Erhirhie, 2014). The fruit is a drupe of 5-10cm in diameter and weighs 30-50g. It is usually smooth and contains a yellow-red pulp. The fruit changes color during maturation from green to orange, and each fruit contains 1-4 seeds (Ekene and Erhirhie, 2014). Found in lowland tropical woods, the dioecious tree can reach a height of 40 meters.

2.3.2. Distribution of *Garcinia kola*

G. kola is a multipurpose agroforestry perennial tree species that grows in forests all over Central and West Africa (Ekene and Erhirhie, 2014). In Sierra Leone, Ghana, Cameroon, Gabon, and other West African nations, G. kola is also found in the woodland zone (Maňourová *et al.*, 2023). In Nigeria, it is prevalent in Edo State and the South Western States.

2.3.3. Ethomedicinal property of *Garcinia kola*

G. kola has been shown to have several ethnomedicinal properties (Ekene and Erhirhie, 2014). Due to its alleged aphrodisiac qualities, it is often referred to as male kola. It is also popularly referred to as "Orogbo" in Yoruba, "Aku ilu" in Igbo, and "Namijin goro" in Hausa (Ekene and Erhirhie, 2014). In Southern Nigeria, *G. kola* is widely chewed for the pleasure of it and is

offered to guests as a show of amity and welcome, particularly to the Igbo tribe in Eastern Nigeria (Unya, 2021). In West Africa, the plant's root is used to make popular bitter chewing sticks. The indigenous people of Eastern Nigeria use the stem bark as a purgative in their traditional treatments (Unya, 2021). Additionally, the latex is externally applied to newly opened wounds to help with wound healing by preventing infections (Tauchen *et al.*, 2023). Nigerians also use it frequently to induce sleeplessness and increase neurotic alertness. Hence, the usage of *G. kola* in medicine is highly prized (Tauchen *et al.*, 2023).

This plant has been called a "wonder plant" as all of its parts have been discovered to have therapeutic value. According to Gogo *et al*. (2025), the seeds are chewed as an aphrodisiac or used to treat a variety of illnesses, including bronchitis, laryngitis, diarrhea, pneumonia, cough, dysentery, chest colds, and liver diseases. The seed is used to treat gastritis, headaches, and stomachaches in addition to preventing and relieving colic. In addition, it has also been used as a purgative and to cure jaundice and high fever. Furthermore, the roots and bark are used as a remedy for male sexual dysfunction in Sierra Leone while in Nigeria, the bark is added to palm wine to increase its strength (Gogo *et al.*, 2025). Moreover, Nigerian traditional healers, fever, inflammation, and dysmenorrhea with a decoction of *G. kola* stem bark. Although it may sound superstitious, bitter kola possesses anti-poison and detoxifying properties. It can also ward off evil spirits and men (Ekene and Erhirhie, 2014).

Plate 3: Image showing the *Garcinia kola* plant (Ekene and Erhirhie, 2014)

2.4 *Tetracarpidiumconophorum*

2.4.1. Description of *Tetracarpidiumconophorum*

The *Tetracarpidium conophorum*, commonly referred to as the African Walnut, belongs to the Euphorbiaceae family and has a lengthy history as a sporadic natural fruit (Oke *et al.,* 2020). It is a small tropical flowering plant that grows to a length of about 6 to 18 meters once it matures. According to Nwachoko and Jack (2015), its stem can grow up to 16 cm in length and is dark grey when it is old, but green and glabrous when it is young. The petiole may reach a length of 5 cm, the leaf may be between 10 cm and 5 cm broad, and the root is fasciculate. Additionally, the leaf is oval, simple, crenate, and has a serrated edge. They have alternating leaf arrangements, are rounded at the base, and abruptly taper (Oke *et al.,* 2020). According to Oyekale *et al*. (2015), the majority of the time, the walnut stems wind around various trees for support, especially the kola nut and cocoa trees. The climber produces capsules that are greenish when young and greenish/yellow when fully grown; inside are four to five seeds with white portions and a darker shell (Oyekale *et al.*, 2015). A source of tasty nuts, African walnuts are typically consumed raw after boiling. The plant climbs to the summits to receive sunlight, and it may bind trees together so that, should one of them perish, it will remain in place until it decomposes (Chikezie and Yvonne, 2018).

2.4.2. Distribution of *Tetracarpidiumconophorum*

Tetracarpidiumconophorum is a notable indigenous plant that thrives in the tropical regions of western and central Africa (Oke *et al*., 2020). It is commonly found in a variety of countries, including Togo, Sierra Leone, Nigeria, Cameroon, the Republic of the Congo, and the Democratic Republic of Congo. In Nigeria, it can be found specifically in Akwa Ibom, Cross

River, Lagos, Kogi, Osun, and Oyo states. The Nigerian cities of Uyo, Akamkpa, Akpabuyo, Lagos, Akure, Kogi, Ajaawa, Ogbomosho, Ibadan, Ife, Ekiti, and Ijeshaland are all included in its range. According to Oke *et al*. (2020), African walnut is called as Asala in Yoruba territory, Ekporo by Efik and Ibibios of Cross River and Akwa Ibom, Ukpa in Ibo, Okwe in Edo, and Gwandi, Bairi in Hausa. In the southern region of Nigeria as well as in all states that produce cocoa, it is abundant (Okechukwu, 2017).

2.4.3. Ethomedicinal property of *Tetracarpidiumconophorum*

Every portion of *T. conophorum*, including the stem bark, leaves, seeds, and roots, has been utilized ethnomedically. Locals utilize the bark as a gentle laxative (Obeta *et al.*, 2021). The seed kernel is regarded as an aphrodisiac and tonic and, when consumed raw, tastes bitter like kola nuts, and has also been known to cure fibroid (Ayeni andNuhu , 2018). Drinking water right after consuming the edible nut is customarily bitter, which may be because the plant contains components that contain alkaloids (Obeta *et al.*, 2021). The boiling seeds are also used to increase sperm count in men, and the *T. conophorum* has been used to alleviate stomach issues and lower blood pressure (Salehimanesh *et al.*, 2025) The bark of the plant is often chewed to treat toothaches, and are used as a laxative in a tea. The fruits can be eaten and used for a number of things, such as masticatory, thrush, anti-helminth, syphilis, and as a snake bite remedy (Salehimanesh *et al.*, 2025). Their properties include moisturizing the intestines, strengthening the knees and back, and tonifying the kidneys. Although they are not recommended for treating acute asthma, they are thought to prevent asthma and are taken in between episodes. Additionally, older adults use them to treat flatulence and constipation (Ogundolie *et al*., 2017). Juice from the leaves is used to increase women's fertility and control menstrual flow. In some regions of West Africa, the leaves and young shoots are sometimes consumed with cooked rice. Wood varnish,

stand oil, and vulcanized oil for rubber and leather substitutes have all been made with nut oil (Ayeni and Nuhu, 2018). Husky extracts were used to make brown dyes, while leaf extracts were used to lessen hiccups (Ayeni andNuhu , 2018).

Plate 4: Image showing the *Tetracarpidiumconophorum* plant (Obeta *et al.*, 2021)

2.5 *Ocimum sancta*

2.5.1. Description of *Ocimum sancta*

Ocimum sancta, commonly known as Tulsi, is a small, erect shrub that spreads its branches widely. It usually grows to a height of 30 to 60 cm when completely grown. The leaves of the plant have a straightforward shape and a nice scent (Majumdar*et al*., 2023). Each leaf is oval with a rounded tip, has dentate or toothed margins, and they are distributed along the branches in an opposing pattern (Kulkarni and Adavirao, 2018). The leaves are up to 5 cm long on average. The *O. sancta* plant bears long racemes of flowers that are tightly clustered in whorl arrangements. These flowers' purple color adds a vibrant touch to the shrub, and like radishes, *O. sancta* seeds are small and have a yellowish hue (Majumdar *et al*., 2023).

2.5.2. Distribution of *Ocimum sancta*

Mostly found in tropical and warm climates, O. sancta is grown in temples, gardens, and even the Himalayas up to 1800 meters in elevation (Majumdar *et al*., 2023). It grows well in damp soil and is also grown in many parts of Asia and Africa. The kind of soil and fluctuations in rainfall affect the plant's size, shape, and medicinal qualities. Around 150 varieties of plants in the Ocimum genus are found in tropical parts of Asia, and their primary reason for cultivation is its ethnomedicinal qualities (Kulkarni and Adavirao, 2018).

2.5.3. Ethomedicinal property of *Ocimum sancta*

The *O. sancta* (Tulsi) is known to have several ethnomedicinal properties (Verma, 2016). It has anti-inflammatory qualities, hence, applying it externally to a region that is swollen helps to lessen pain and swelling. Numerous skin conditions such as itching, skin rashes, and bug bites

can be cured with the plant (Verma, 2016). The bark of this plant can be used to treat leucoderma and ringworm infections. Additionally, fresh Tulsi leaf juice is used in the treatment of head and neck conditions including headaches. The leaves of tulsi are a nerving tonic, and its extract is used to lessen acne, pimples, and scars. Furthermore, crushed tulsi leaves have proven to be effective in treating bronchitis, fever, cough, and other lung conditions (Verma, 2016). Tulsi cleanses blood and is used as a heart tonic. Tulsi seeds effectively induce impulsive ejaculation and have a modest aphrodisiac effect.

Plate 5: Image showing the *Ocimum sancta* plant (Verma, 2016).

2.6 *Curcuma longa*

2.6.1. Description of *Curcuma longa*

The curcuma longa plant belongs to the Zingiberaceae family of plants (Fuloria *et al*., 2022). Despite lacking stems and rhizomes across its entire body, this perennial herbaceous plant can reach a height of two meters. Rather, it has upright, leaf-covered branches that can support up to twelve leaves. The *C. longa* plant has oblong or lanceolate leaves that can reach a length of one meter (Karlowicz-Bodalska *et al*., 2017). They are dark green on top and lighter green under siege. The bud that encircles the flower is green with hints of purplish, and the plant's sterile inflorescence has pale yellow and reddish tones (Fuloria *et al*., 2022). Two distinct studies, one by Fuloria *et al*. and the other by Jyotirmayee and Mahalik, published these results (Karlowicz-Bodalska *et al*., 2017). *C. longa's* growth structure is an underground rhizome. The main focus of this plant's cultivation is its rhizome, which is identified by its hard, segmented outer covering. The length and width of the rhizome can range from 2.5 to 7.0 centimeters and 2.5 centimeters, respectively (Jyotirmayee and Mahalik, 2022). It smells incredibly nice, while having an awful flavor. With temperatures between 20 and 30 degrees Celsius and sufficient precipitation, these plants thrive in both tropical and subtropical regions (Jyotirmayee and Mahalik, 2022).

2.6.2. Distribution of *Curcuma longa*

The plant known as *Curcuma longa* can be found growing in both tropical and subtropical regions all over the world. In most cases, these plants are cultivated in the nations of Asia, most frequently in the countries of India and China (Fuloria *et al*., 2022). It has a wide range of distribution across many countries, including Andaman Island, Assam, Borneo, Bangladesh, Belize, China South-Central, China Southeast, Cambodia, and Caroline Island. It is also found in

places such as Cook Island, Costa Rica, Cuba, Comoros, Congo, Nigeria, Dominican Republic, East Himalaya, Easter Island, Fiji, Gilbert Island, Guinea-Bissau, Gulf of Guinea Island, Haiti, Hawaii, Ivory Coast, Jawa, Leeward Island, Lesser Sunda Island, Haiti, Hawaii, Ivory Coast, Jawa, Leeward Island, Lesser Sunda Island, and Malaya (Iweala *etal.,* 2023).

2.6.3. Ethnomedicinal Properties of *Curcuma longa*

In Asian nations such as Bangladesh, Malaysia, India, Nepal, and Thailand, curcuma species are used to treat pneumonia, bronchial problems, leucorrhea, diarrhea, dysentery, infectious wounds or abscesses, and insect bites (Jacob, 2016). Turmeric is used in both traditional and modern Indian medicine to treat rheumatism, cough, jaundice, and other conditions (Iweala *et al.*, 2023). Vaughn *et al*. (2016) described the usage of curcumin to treat inflammation and obesity, highlighting its maximum ethnomedical efficacy in India. In Pakistan, wounds and acne are treated with powdered *C. longa* extract (Ayati *et al.*, 2019). In the Philippines, arthritis is also treated using the juice made from powdered C. longa. *C. longa* leaves are used to alleviate arthritis and give facial massages to the Kurdish minority in Iraq. Simultaneously, the rhizome decoction has been reported to have anticancer properties (Iweala *et al.*, 2023). It was also reported that parts of *C. longa* were used to treat gastrointestinal illnesses in Korea (Iweala *et al.*, 2023). Among its many medicinal uses in Colombia, the herb is used to cure thrombosis, diabetes, obesity, and indigestion (Bussmann *et al*., 2018). Curcumin, which is made from the rhizomes of C. longa, has been used for over 2500 years by a variety of societies, most notably the Asian population, as an ancient cure for a wide range of illnesses (Iweala *et al.*, 2023).

Plate 6: Image showing the *Curcuma longa* plant (Iweala *etal.,* 2023).

2.7. DEPRESSION

Depression is a common mental health condition that is characterized by the loss of interest in once-pleasurable activities, persistent sadness, widespread guilt or feelings of worthlessness, sleep or eating disturbances, low energy, and difficulty concentrating (Chand and Arif, 2023). An individual's capacity to carry out everyday duties and responsibilities may be severely hampered by these symptoms, which may develop into chronic or recurrent conditions (Vélez-Santamaría *et al*., 2023). An estimated 850,000 people die each year from suicide as a result of severe depression (World Health Organization, 2025a). In terms of years lived with disability (YLDs), it is the most common cause of impairment; in 2000, it ranked fourth globally in terms of disease burden (disability-adjusted life years, or DALYs) (WHO, 2022). It was anticipated to rank as the second most common cause of DALYs for all age groups and genders by 2020 (WHO, 2022).

Depression is currently the second most common cause of DALYs in people between the ages of 15 and 44, affecting both men and women (Chen *et al.*, 2025). This brain malfunction is mostly influenced by genetic, environmental, psychological, and physiological variables and can affect anyone of any age, gender, or background. Depression is more common in women and usually appears between the ages of 15 and 30. Postpartum depression can also strike women after giving birth, and seasonal affective disorder can strike some people, particularly during the winter. Fortunately, there are effective therapies available, like psychotherapy and antidepressant drugs, and a combination approach yields the best results (Chen *et al*., 2025).

An estimated 121 million individuals worldwide suffer from depression, which continues to be one of the major causes of disability (World Health Organization, 2025b). Less than 25% of

people with depression have access to appropriate therapies, despite the fact that primary care facilities can accurately diagnose and treat the condition. 60–80% of people respond well to short, structured psychotherapies and antidepressant medications, which can be given in primary care (World Health Organization, 2025b). Nevertheless, less than 25% of people with depression (and in certain places, less than 10%) obtain the proper care. Inadequate funding, a lack of qualified medical professionals, and the stigma associated with mental health conditions like depression are obstacles to successful treatment (World Health Organization, 2025b).

Depression manifests as a variety of symptoms, such as a loss of interest in once-enjoyable activities, impatience or frustration over trivial matters, and chronic melancholy or unhappiness (Sawchuk, 2022). Reduced libido, insomnia or excessive sleep, appetite changes (from decreased appetite and weight loss to increased desires and weight gain), restlessness or agitation, impatience, and trouble thinking, speaking, or moving are some other symptoms (Higuera, 2023). Along with feelings of exhaustion, worthlessness, or guilt, other common symptoms include indecision, distractibility, and difficulty focusing (Higuera, 2023). In extreme situations, people may have bodily problems such unexplained headaches or back discomfort, as well as thoughts of suicide, death, or self-harm (Harmer *et al*., 2024). Individual differences in depression manifestation are caused by a variety of factors, including age, gender, cultural background, and genetic predisposition (Harmer *et al*., 2024).

2.7.1 ANTIDEPRESSANT DRUGS

2.7.1.1 Monoamine Oxidase Inhibitors (MAOIs) and Tricyclic Antidepressants (TCAs)

Monoamine oxidase inhibitors, or MAOIs, raise neurotransmitter levels by blocking the breakdown of dopamine (DA), serotonin (5-HT), and norepinephrine (NE) (Laban and Saadabadi, 2023). Newer MAOIs are made to target either MAO-A or MAO-B and are usually reversible for MAO-A, whereas conventional MAOIs, like tranylcypromine, act on both MAO-A and MAO-B enzymes and do not quickly stop acting. Moclobemide is the only reversible MAO-A inhibitor that is commercially available in Turkey, while several others are presently being studied (Laban and Saadabadi, 2023).

With a wide range of pharmacological effects, tricyclic antidepressants (TCAs) are a class of medications (Moraczewski and Aedma, 2023). According to Willner *et al*. (2024), they include anticholinergic-antimuscarinic properties, alpha-1 adrenergic antagonism, antihistamine (H1) activity, serotonin reuptake inhibition, and norepinephrine reuptake inhibition.

At large doses, TCAs can also block sodium channels, which can result in severe cardiac arrhythmias and convulsions. TCAs primarily function by inhibiting the reabsorption of norepinephrine and serotonin (Willner *et al.*, 2024). The NE reuptake pump is where desipramine and maprotiline are most effective, whereas the 5-HT reuptake pump is where clomipramine is most potent (Sánchez-Salcedo *et al.*, 2021). The adverse effects of TCAs are linked to their interaction with alpha-1, M1, and H1 adrenergic receptors. However, different TCAs exhibit variable levels of this inhibition in terms of both specificity and degree (Sánchez-Salcedo *et al*., 2021).

2.7.1.2. Selective Serotonin Reuptake Inhibitors (SSRIs)

Selective serotonin reuptake inhibitors (SSRIs) work by inhibiting the serotonin transporter, which elevates serotonin levels rapidly, particularly in certain regions of nerve cells that produce serotonin (Chu and Wadhwa, 2023). Long-term SSRI use raises serotonin levels, which may cause some serotonin receptors in the brain to become desensitized. Serotonin's inhibitory effect over neuronal impulse flow decreases as these auto receptors become desensitized, increasing serotonergic neurotransmission. Postsynaptic serotonin receptors eventually become desensitized as a result of increased serotonin release from axon terminals (Chu and Wadhwa, 2023). Both the development of tolerance to the acute adverse effects of SSRI usage and their therapeutic efficacy may depend on this desensitization process. Potent but delayed disinhibition of 5-HT neurotransmission across multiple serotonergic pathways in the central nervous system (CNS) characterizes the pharmacological profile of SSRIs. Notably, the antidepressant effects of SSRIs are thought to be mediated via disinhibition along the pathway from the midbrain raphe to the prefrontal cortex (Chu and Wadhwa, 2023).

However, there are a number of unpleasant side effects linked to SSRIs. Anxiety, sleep disorders, sexual dysfunction, and digestive problems are a few examples. Interactions with particular serotonergic receptors, especially the 5-HT2 and 5-HT3 receptors, are frequently blamed for the adverse effects (Miranda, 2024). For example, it is believed that the reciprocal interaction between serotonin and dopamine—increased serotonin inhibits sexual performance while dopamine promotes it—is the cause of sexual dysfunction, which may show up as lower libido or decreased arousal (Miranda, 2024). By blocking serotonergic pathways that influence mesolimbic dopamine systems, SSRIs may upset this equilibrium and cause sexual dysfunction.

On the other hand, drugs that increase dopamine, like stimulants or bupropion, can frequently lessen libido loss brought on by SSRIs (Atmaca, 2020).

The serotonergic pathway that descends from the brain stem to the spinal cord is implicated in problems related to ejaculation and orgasm (Calabrò *et al.*, 2019). It is thought that increased serotonin flow along this route prevents sexual function. The fact that 5-HT2 antagonists can occasionally reverse SSRI-induced sexual dysfunction while antidepressants with 5-HT2 antagonistic properties typically do not cause these side effects provides evidence for serotonin's detrimental effect on sexual functioning via 5-HT2 receptors (Chu and Wadhwa, 2023). Additionally, SSRIs may cause anxiety or even sporadic panic attacks, possibly via activating 5-HT2 receptors in circuits that project to the limbic cortex and hippocampus. The stimulation of 5-HT2 receptors in the brain stem's sleep centers, especially those that project to cholinergic neurons in the lateral tegmentum, may also be linked to SSRI-induced insomnia (Calabrò *et al*., 2019). The activation of 5-HT3 receptors in the gastrointestinal tract and central pathways, such as the brain stem vomiting center, is probably responsible for the gastrointestinal adverse effects of SSRIs. Additionally, the decreased appetite, nausea, and possible weight loss seen in certain SSRI users may be explained by disinhibition of the serotonergic route from the brain stem to the hypothalamus, which controls appetite and eating behaviors (Mouawad *et al.*, 2025).

2.8. ANXIETY

Anxiety disorders rank as the most common types of mental health issues, impacting a large number of individuals (Penninx *et al*., 2021). These conditions involve various issues where intense or unhealthy anxiety is the main problem affecting mood and emotional control. Anxiety is often seen as an unusual version of regular fear, showing up through mood changes, problems

with thinking, changes in behavior, and physical reactions. The different types of anxiety disorders include panic disorder (which may or may not relate to agoraphobia), agoraphobia (which may or may not relate to panic disorder), generalized anxiety disorder (GAD), specific phobias, social phobia, obsessive-compulsive disorder (OCD), acute stress disorder, and post-traumatic stress disorder (PTSD). Moreover, signs of anxiety can also appear in adjustment disorders and conditions caused by medical issues or substances (Penninx *et al*., 2021).

Anxiety disorders are diagnosed based on the presence of persistent concern and anxiety for at least six months, as well as difficulties managing these emotions (Holland, 2023). Anxiety must be accompanied by at least three of the following symptoms for at least six months in order to be diagnosed: restlessness, being easily startled, fatigue, difficulty concentrating, irritability, tense muscles, difficulty sleeping, and increased irritability (Holland, 2023). A personal sensation of distress, which frequently includes difficulties sleeping, concentrating, and interacting socially or professionally, is a common symptom of several anxiety disorders. Despite many similarities, these illnesses differ significantly in terms of symptoms, development, and treatment. Many people seek medical attention for physical problems, which can conceal their actual anxiety concerns. This is particularly true for panic disorder, which is marked by brief bouts of intense terror and a sense of approaching disaster (Penninx *et al*., 2021). Physical symptoms of this illness include breathing difficulties, disorientation, and chest pain. When agoraphobia exacerbates panic disorder, people may avoid situations where it would be difficult to flee, which can make functioning even more difficult. The Greek word "agoraphobia" originally meant "a fear of open markets," but today it refers to a severe fear of circumstances that make escape difficult, such being in crowds, traveling by vehicle, bus, or airplane, or being alone outside the house (Penninx *et al*., 2021).

Agoraphobia usually appears after the onset of panic disorder and is best understood as a behavioral consequence of frequent panic attacks, together with the anxiety, obsession, and avoidance behaviors that follow (Balaram and Marwaha, 2023). Rarely does generalized anxiety disorder (GAD) occur on its own; instead, it typically coexists with other mental diseases. People with generalized anxiety disorder (GAD) experience ongoing worries about many parts of their lives for a minimum of six months (Mishra and Varma, 2023).

People with social phobia frequently experience the fear and anxiety that come with social interactions, which might cause them to avoid these circumstances. Insects, animals (especially snakes, rodents, or dogs), or other objects (like spiders or bees), heights, elevators, flying, driving, water, storms, or medical procedures involving blood or injections are examples of specific phobias that share similar symptoms, even if they are triggered by particular things or events (Mishra and Varma, 2023). Reactions to stressful situations include acute stress disorder and post-traumatic stress disorder. They are typified by avoidance of the incident, memories of it, and other symptoms that cause physiological arousal. the event's replayed experience and associated triggers. PTSD is a longer-lasting symptom of mental illness, while acute stress disorder is its short-term counterpart (Mann *et al.*, 2024). In obsessive-compulsive disorder (OCD), repetitive behaviors (compulsions) are an attempt to lessen anxiety caused by intrusive, unwanted thoughts (obsessions). Repeatedly checking appliances, including stoves, to prevent fires or cleaning or washing in response to contamination concerns are examples of frequent compulsions. Some people may constantly seek confirmation or double-check their work because of their persistent self-doubt (Mann *et al*., 2024).

2.8.1. CAUSES OF ANXIETY

Anxiety can be caused by the following conditions; herbal medications, substance abuse, medications, trauma, childhood experiences, panic disorders

2.8.2. PATHOPHYSIOLOGY

The exact mechanism remains incompletely understood. Anxiety is a frequent phenomenon in children. Infants begin to exhibit stranger anxiety between the ages of seven and nine months (Van Hulle *et al*., 2017). This is believed to be the cause of anxiety symptoms and subsequent disorders. to interfere with central nervous system modulation. Both physical and emotional symptoms are a result of this dysregulation, which is caused by variable degrees of heightened sympathetic activation (Van Hulle *et al.*, 2017). This dysregulation has impacted many neurotransmitter systems, which are believed to be engaged in one or more of the regulatory processes. The noradrenergic and serotonergic neurotransmitter systems are the most commonly taken into consideration. In general, it is thought that the noradrenergic system's overactivation and the serotonergic system's underactivation are important factors (Teleanu, 2022). Physiological arousal and the emotional reaction to this stimulation are dysregulated as a result of these systems' control and regulation by other neural circuits and pathways across the brain (Teleanu, 2022).

It is commonly thought that high noradrenergic system activity and low serotonin system activity are the causes (Bamalan *et al.*, 2023). Therefore, selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) are the first-line treatments. Gamma-aminobutyric acid (GABA) system disruption has also been suggested by the fact that

benzodiazepines are effective in treating several anxiety spectrum disorders. Some emphasis has been paid to the role of corticosteroid regulation and its connection to symptoms of anxiety and dread (Bamalan *et al.*, 2023). Corticosteroids may change how the brain reacts to stimuli that cause fear as well as the activity of certain nerve pathways, which may have an effect on behavior when under stress. Cholecystokinin has long been considered a neurotransmitter that aids in emotional regulation. Any alteration in one neurotransmitter system will inevitably result in a change in another due to the neurotransmitters' excellent coordination, which also creates important feedback loops (Asim *et al.*, 2024). GABA and serotonin are inhibitory neurotransmitters that reduce the stress response.

2.8.3. ANTIANXIOLYTIC DRUGS

For thousands of years, people have utilized drugs to reduce anxiety. One of the first and still used anxiolytics is ethanol. During the first part of the 20th century, a number of different drugs were utilized, including barbiturates and carbamates (meprobamate), some of which are still in use today.

2.8.3.1. Serotonin Receptor Modulators and Reuptake Inhibitors

Serotonin has long been thought to be a neurotransmitter that aids in emotional regulation. In the literature, anxiety has been connected to at least four of the approximately 14 known mammalian serotonin receptor subtypes in various animal models (Mitroshina *et al.*, 2023). According to Mitroshina *et al*. (2023), reducing serotonin levels may have anxiolytic benefits, which led to the first theory connecting serotonin to anxiety. An autoreceptor located presynaptically on serotonin neurons, the serotonin 1A receptor subtype (5HT1A) is one of the receptor subtypes believed to

be involved in anxiety. When this receptor is engaged, serotonin synthesis and release are inhibited.

The Food and Drug Administration (FDA) licensed buspirone, a 5-HT1A receptor agonist with anxiolytic effects in animals, to treat generalized anxiety disorder in humans in 1986 (Wilson and Tripp, 2023). The 5-HT2A, 5-HT2C, and 5-HT3 receptors are additional serotonin receptors that might be involved in anxiety. The development of fluoxetine, sertraline, and other selective serotonin reuptake inhibitors (SSRIs) in the 1980s and 1990s greatly expanded the range of treatments available for depression. Recently, medications such as paroxetine and venlafaxine have gained traction in the treatment of anxiety disorders, including panic, GAD, obsessive compulsive disorder, and social phobia. GAD has been successfully treated with venlafaxine, paroxetine, and other drugs (Wilson and Tripp, 2023).

SSRIs will lead to the development of a class of medications that work through the serotoninergic system (Chu and Wadhwa, 2023). Swierkosz-Lenart *et al*. (2023) claim that the cornerstone of pharmacologic therapy for OCD is a 10- to 12-week trial in his examination of the diagnosis and treatment of the disorder. The scientists looked at buspirone's ability to improve the efficacy of the standard OCD treatment, which is an SSRI at adequate dosages. As an enhancing agent, it is identical to a placebo. Additionally, it appears that drugs that target distinct subtypes of serotonin receptors do not work to treat OCD (Swierkosz-Lenart *et al.*, 2023).

2.8.3.2. Γ-Aminobutyric Acid Receptor Modulators (Benzodiazepines and Related Drugs)

Glycine, I-glutamic acid, or γ-aminobutyric acid (GABA) are used by most synapses in the central nervous system of mammals to transmit signals (Caire *et al*., 2023). The typical

inhibitory transmission observed in the mammalian nervous system is replicated by GABA. I-glutamate is decarboxylated to create it, which is then stored in neurons, released, and its effects are stopped by reuptake. For more than 20 years, GABA has been recognized as a neurotransmitter due to these discoveries (Barakat and Aljutaily, 2025) In addition to acetylcholine, serotonin, and I-glutamate, GABA has two distinct receptor types that control both excitation and inhibition and are present in all animals. Proteins from two distinct superfamilies mediate GABA's actions on ionic transmission (ionotropic) and metabolism (metabotropic), according to molecular biology research on the phyla. the receptors that bring about these effects. The ligand-gated ion channels (ligand-gated superfamily) that mediate GABA's impact on rapid synaptic transmission include the first superfamily, known as GABAA receptors (Barakat and Aljutaily, 2025). An ion channel opens (gates) when a GABAA receptor is activated, allowing chloride to enter the cell (Allen *et al.*, 2023). This often causes the cell membrane potential to become hyperpolarized, which slows down neural activity. GABA's second subfamily (GABAB) mediates its effects more slowly. involves modifying the function of particular guanine nucleotide-binding proteins (G proteins) on intracellular effectors through a seven transmembrane spanning receptor (serpentine superfamily). By changing the quantity of second messengers, G proteins can affect signal transduction and gene expression through their impact on other effector systems. According to Allen *et al*. (2023), they can also activate ion channels that rely on the G-protein subunits' activities. GABAA receptor-mediated events have a shorter temporal scale than both stimulatory and inhibitory effects. The structural variety of GABAA receptors is extensive within the ligand-gated superfamily. Many popular and advised drugs for sleep, anxiety, seizure disorders, and cognitive enhancement target these receptors, and they may also contribute to the effects of these drugs. ethanol in the body. Benzodiazepines, barbiturates,

neurosteroids, anesthetics, and convulsants are known to have allosteric modulatory sites in the GABAA receptors in addition to binding GABA neurotransmitter locations (Ghit *et al*., 2021).

CHAPTER THREE

MATERIALS AND METHOD

3.1. Apparatus and Equipment Used

The apparatus and equipment used in this study are as follows:

Analytical weighing balance (Ohaus Corp., Pine Brook, NJ, USA, China), beaker (50 ml), conical flask (500 ml), cotton wool, hand gloves, mortar and pestle, measuring cylinder (100 ml), transparent bowl, wooden stool, masking tape, mice cage, stopwatch, needle and syringe (1 ml, 2 ml), oral gastric tube (1 ml), universal bottle (10 ml), and elevated plus maze.

3.2. Chemicals and Reagents Used

The following chemicals and reagents were used for this study:

Fluoxetine (20 mg/kg), diazepam (10 mg/kg), distilled water, and D3.

3.3. Procurement of D3®

D3 Organic® supplement (Batch No: 0001, NAFDAC REG NO: A7-4333L, PRD: 02/10/2024, BB: 02/10/2026) was obtained from Nature's Renaissance International Limited (90 Allen Avenue, Ikeja, Lagos, Nigeria) and manufactured by UTAD HERBAL RESOURCES LIMITED (Fredineri Street, Ugbor Village, Benin City, Edo State, Nigeria).

3. 4. Extraction

The D3 Organic® supplement was extracted using maceration. A 30g D3 supplement was soaked in 500 ml of distilled water and allowed to macerate for 72 hours. The mixture was filtered through muslin cloth and Whatman No. 1 filter paper and concentrated over a water bath. The extract was stored in a refrigerator at four degrees Celsius before use.

3.5. Experimental animals

Seventy-five (75) healthy mice (20-30 g) were obtained from a commercial animal house in Ibadan, Oyo State, Nigeria. The mice were housed at the Phytomedicine Animal Unit, Department of Plant Botany and Biology (PBB), Faculty of Life Sciences, University of Benin, under standard laboratory conditions with a 12-hour light/dark cycle. The mice were acclimatised for two weeks and well fed with standard animal pellets and water. All procedures adhered to the National Institute of Health (NIH) guidelines for the care and use of laboratory animals. This study was approved by the Science Laboratory Technology Research Ethical Committee with reference number.

3.6. Experimental Design

The antidepressant activity of the D3 organic supplement was evaluated using the forced swim test (FST) and tail suspension test (TST), two widely used models to screen for antidepressant-like effects (Castagné *et al*., 2010; Uwaya *et al.*, 2025).

3.6.1. Forced Swim Test (FST):

Twenty-five mice weighing 20-30 grams were allotted into five groups with five animals in each. Group 1 received distilled water at 10 ml/kg; groups 2, 3 and 4 received 50 mg/kg, 100 mg/kg and 200 mg/kg of Nature Gift extract, respectively, while group 5 received 20 mg/kg of the standard drug, fluoxetine, orally. One hour after administration of Nature's Gift and fluoxetine, respectively, the mice were placed in an inescapable transparent cylinder (height 40 cm, diameter 20 cm) filled with water (depth 30 cm) at 25°C. The animals were allowed to swim for 5 minutes, and the time of immobility (a sign of despair-like behaviour) was recorded. A reduction in immobility time after treatment is indicative of antidepressant-like activity (Koek *et al.*, 2018; Unal and Canbeyli, 2019).

3.6.2. Tail Suspension Test (TST):

Twenty-five mice weighing 20-30 grams were allotted into five groups with five animals in each. Group 1 received distilled water (10 ml/kg); groups 2–4 received Nature Gift extract at 50, 100 and 200 mg/kg, respectively; and group 5 received the standard drug fluoxetine (20 mg/kg) orally. One hour after administration of Nature's Gift and fluoxetine, the mice were suspended from the edge of a shelf 60 cm above the tabletopby their tails using adhesive tape, and the time of immobility (immobility being indicative of a depressive state) was recorded for 5 minutes for each animal. The test was conducted in a noise-free room to minimise external stressors (Koek *et al.*, 2018; Unal and Canbeyli, 2019).

3.7. Anxiolytic Activity

The elevated plus maze (EPM) test was employed to assess the anxiolytic effects of the extract (Mechiel and De Boer, 2003).

Elevated Plus Maze (EPM): The maze consists of two open arms and two closed arms, elevated 50 cm above the floor. Twenty mice, weighing 20–30 grams, were randomly divided into five groups with four animals in each. Group 1 received distilled water (10 ml/kg); groups 2–4 received D3 extract (50, 100 and 200 mg/kg, respectively); and group 5 received the standard drug diazepam (10 mg/kg). One hour after the administration of D3 extract and diazepam, the animals were placed in the centre of the maze and allowed to explore for 5 minutes. The percentage of time spent in the open arms and the time of entries into the open arms were used as indicators of anxiety. Increased exploration of the open arms is considered a sign of anxiolytic-like behaviour (Mechiel and De Boer, 2003).

3.8 Statistical Analysis

The mean ± SEM was used to express the data. GraphPad Prism 9.0 was used for statistical analysis. Statistical significance was set at $p < 0.05$, and differences between groups were compared using Tukey's post hoc test after one-way Analysis of Variance (ANOVA) (Field,

2013).

CHAPTER FOUR

RESULTS

4.1 FORCED SWIMMING AND TAIL SUSPENSION ENDURANCE TEST

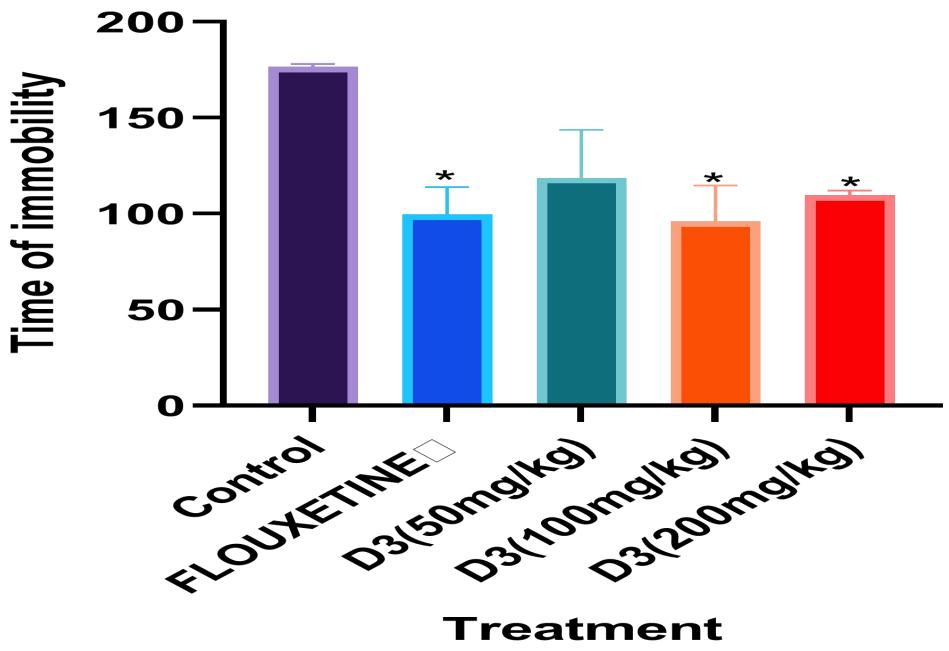

Figure 1: Effect of D3 Organic® on immobility time in the Forced Swim Test (FST).

D3 at 100mg/kg and 200 mg/kg and fluoxetine (20 mg/kg) reduced immobility time in the force swimming test when compared with control ($p < 0.05$). Values are represented as Mean ± SEM, n=5 per group.

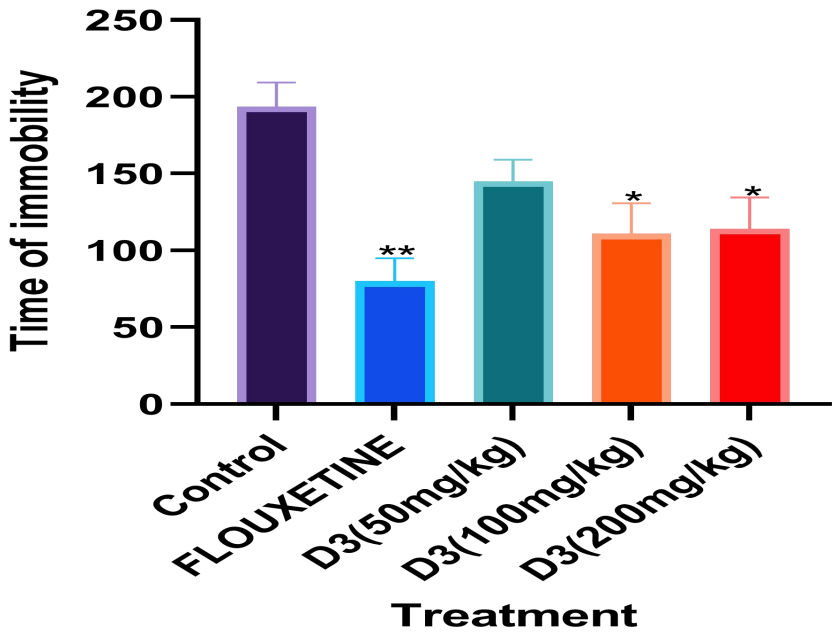

Figure 2: Effect of D3 Organic® on immobility time in the Tail Suspension Endurance Test

D3 at 100mg/kg and 200 mg/kg and fluoxetine (20 mg/kg) reduced immobility time in the tail suspension endurance test when compared with control (*$p < 0.05$; **$p<0.01$). Values are represented as Mean ± SEM, n=5 per group.

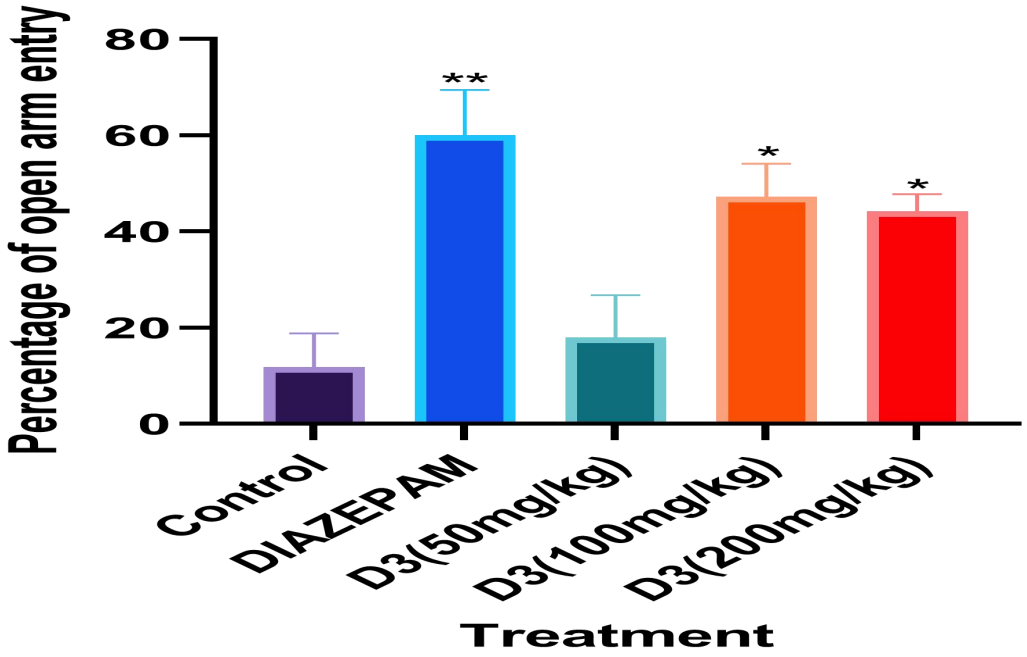

Figure 3: Effect of D3 Organic® on open-arm exploration in the Elevated Plus Maze (EPM)

D3 at 100mg/kg and 200 mg/kg and Diazepam (10 mg/kg) increased the time (%) spent in the open arm when compared with control (*$p < 0.05$; **$p<0.01$). Values are represented as Mean ± SEM, n=5 per group.

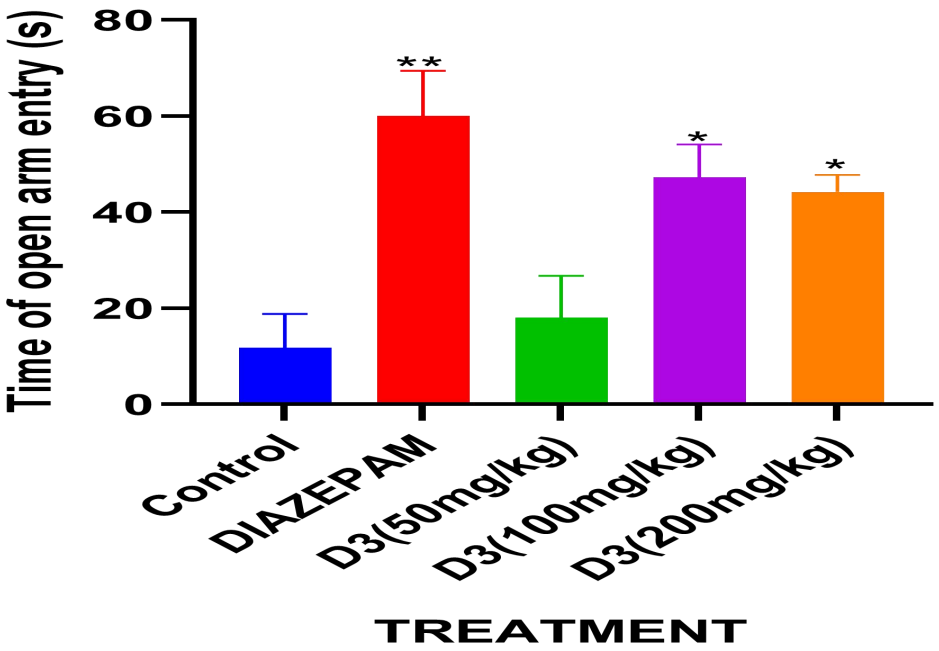

Figure 4: Effect of D3 Organic® on open-arm exploration in the Elevated Plus Maze (EPM)

D3 at 100mg/kg and 200 mg/kg and Diazepam (10 mg/kg) increased the time (s) spent in the open arm when compared with control (*$p < 0.05$; **$p<0.01$). Values are represented as Mean ± SEM, n=5 per group.

CHAPTER FIVE

DISCUSSION AND CONCLUSION

This research assessed the antidepressant efficacy of D3 Organic® through the forced swimming test (FST) and tail suspension paradigms. Researchers have defined the forced swimming endurance test as a behavioural assay that evaluates rodents' vulnerability to depressive-like states and their inclination towards behavioural despair (Uwaya *et al*., 2024). This assessment measures the animals' stress responses, particularly their reactions to the perceived threat of drowning, thus functioning as a model for helplessness and depressive behaviour in rodents ((Söderlund and Lindskog, 2018; Gencturk and Unal, 2024). The tail suspension test induces immobility in an animal confronted with an inescapable scenario, representing behavioural despair that may indicate a depression-like disorder and a stressful condition in mice (Castagné *et al*., 2010). D3 Organic®'s ability to reduce the duration of immobility in forced swimming and tail suspension tests indicates its potential antidepressant properties. The forced swimming test and tail suspension test assess a rodent's susceptibility to negative mood and reflect an animal's perception of helplessness (Uwaya *et al*., 2024). This research indicates that D3 Organic® at doses of 100 mg/kg and 200 mg/kg, along with fluoxetine at a dose of 20 mg/kg, significantly decreased immobility duration compared to the control group, as illustrated in Fig. 1.

D3 Organic® at dosages of 100 mg/kg and 200 mg/kg, along with fluoxetine at a dosage of 20 mg/kg, decreased immobility duration in the tail suspension test compared to the control, as illustrated in Fig. 2. The D3 Organic®'s capacity to diminish immobility duration in the forced swimming endurance test and tail suspension test indicates that the combination exhibits antidepressant- and antistress-like characteristics. Fluoxetine, used as a standard, belongs to the Selective Serotonin Reuptake Inhibitor (SSRI) class, commonly employed in the management of depression. It exerts its effect by inhibiting the reuptake transporter protein in the presynaptic terminal, thereby preventing the reuptake of serotonin into the presynaptic neurones (Ormel *et al.* 2019; Sohel *et al.*, 2024).

The elevated plus maze (EPM) is a commonly employed technique for evaluating anxiety-related behaviours in rodents (de Figueiredo Cerqueira *et al*., 2023). This model consists of a plus-shaped elevated maze featuring two open arms and two enclosed arms, intended to assess the inherent conflict between rodents' aversion to open areas and their exploratory behaviour (Arabo *et al*., 2014). The exploratory behaviour of an animal in the EPM is typically defined by metrics concerning the frequency of entries and the duration spent on the two arm types (Arantes *et al*., 2013). This study demonstrated that D3 Organic® at dosages of 100 mg/kg and 200 mg/kg, as well as diazepam at 10 mg/kg, significantly prolonged the duration spent in the open arm relative to the control, as illustrated in Figs. 3 and 4. Diazepam, used as the reference medication, is a rapid-acting and prolonged benzodiazepine frequently prescribed for anxiety disorders, acute seizures, severe muscle spasms, and spasticity linked to neurological conditions (Calcaterra and Barrow, 2014). D3 Organic®'s capacity to enhance open arm entries suggests it possesses anxiolytic properties.

CONCLUSION

D3 Organic® contains both antidepressant and anxiolytic properties and can be used in treating and managing conditions associated with depression and anxiety.

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