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Original Article

Qualitative Phytochemical Analysis, Acute Toxicity, and Antidepressant Efficacy of *Datura stramonium* (Solanaceae) whole Seeds using Swiss Albino Mice

Peter Onezeyi Obaro*, and Osasere Enohor Obaro-Onezeyi

Department of Science Laboratory Technology, Faculty of Life Science, University of Benin, Benin, Nigeria

* ***Corresponding author:*** Peter Onezeyi Obaro, Department of Science Laboratory Technology, Faculty of Life Science, University of Benin, Benin, Nigeria. Email: peter.obaro-onezeyi@uniben.edu

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ABSTRACT

Introduction: Depression is a condition that often consists of such main symptoms as lack of interest, worry, insomnia problems, appetite loss, low energy levels, and suicidal thoughts. The purpose of this experiment was to determine the qualitative phytochemical analysis, acute toxicity, and antidepressant efficacy of *Datura stramonium* (Solanaceae) whole seeds on Swiss albino mice using forced swim (FST) and tail suspension (TST) tests.

Materials and Methods: The seeds of *Datura Stramonium* were harvested, air dried, ground, and extracted using N-hexane. In the anti-depressant investigation, 60 mice (8 weeks old) were used for the two models. Each model contained 30 mice (15 males and 15 females) weighing 25-30 g. The extract and standard drug were administered orally to mice for seven days. Group 1 received Normal saline (2 mg/ml), group 2 received Imipramine (15mg/kg), Groups 3, 4, and 5 received N-hexane Extract *Datura stramonium* Seed (NEDSS) (10, 20, and 40 mg/kg), respectively, for the two models. The period of mobility in the TST and FST was determined 24 hours following the last dose.

Results: The antidepressant studies revealed that the NEDSS-treated groups had significant ($P<0.01$) increases in mobility, compared to the control group. Moreover, Group 5 obtained the best effect (40 mg/kg of NEDSS).

Conclusion: An increase in the dose of NEDSS revealed subsequent increases in anti-depression actions. Furthermore, 40 mg/kg of NEDSS proved to be the most potent in the two models of depression. However, further research should be carried out to determine its mechanism of action using laboratory animals.

1. Introduction

Throughout history, plants have been used extensively to cure illnesses and injuries in people all over the world. The growing popularity of natural products has increased demand for medicinal plants in both developed and developing nations. A crucial component of both the conventional and modern medical systems is herbal medicine[1].

Jimson weed or Datura, also known as *Datura stramonium*, is a plant in the Solanaceae family[2]. It is a branching, pubescent plant that measures 60–120 cm or more. The leaves measuring 8–17×4–13 cm are oval, sinuate dentate, and minutely puberulose. The flowers are trumpet-shaped, 6 to 9 cm long, and white to creamy to violet[3], found primarily in temperate and subtropical regions[4].

There are numerous potential medicinal uses for *D. stramonium*. Despite the plant's narcotic properties, it has specific impacts on human health, making it extremely useful as medicine[5]. This is due to the fact that it possesses antimicrobial, anti-diabetic, anti-asthmatic, anti-inflammatory, antioxidant, analgesic, insecticidal, cytotoxic, wound healing, and neurological properties[6, 7]. The *Datura* plant also has larvicidal properties against the red flour beetle (*Tribolium castaneum*), as well as mosquito-repelling properties[8]. Additionally, the seed has been used to treat animal bites (e.g., snakebites) for pain

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relief. The well-known species of this family, *D. stramonium*, is used both as an herbal remedy and for mystic and religious purposes[9]. Additionally, *D. stramonium* seed is smoked to produce a hallucinogenic effect[9].

No anti-depressant studies have been carried out on the whole seed of this plant in spite of its use by traditional practitioners in Iguobazuwa Village in Ovia-North-East local government area in Benin City, Edo state, Nigeria.

Accordingly, this study aimed to determine the qualitative phytochemical analysis, acute toxicity, and antidepressant efficacy of *Datura stramonium* (Solanaceae) whole seeds on Swiss albino mice using forced swim (FST) and tail suspension (TST) tests.

2. Materials and Methods

2.1. Ethical approval

Ethical approval for this study was sought and received from the institutional Ethical Review Committee of Life Sciences, University of Benin, Benin City, Edo State, Nigeria. Proper procedures were observed to ensure negligible discomfort or pain in rats used in this research. The ethical approval number is LS19116. This research was carried out in accordance with the internationally accepted principles for laboratory animal use and care by the Organization of Economic Co-operation Development (OECD) Guidelines of the care and use of animals for investigation[10].

2.2. Collection of plant sample, identification, and authentication

Disease-free plant samples (by physical examination) of *D. stramonium* were collected in September 2023 from Iguobazuwa Village in Ovia-North-East local government area in Benin City, Edo state, Nigeria. The plant was authenticated in the Department of Plant Biology and Biotechnology, Faculty of Life Sciences, University of Benin, Benin City, where a herbarium specimen number (*UBH-D321)* of the plant was deposited. After collection, the whole seeds were initially dried for two weeks in the open air at ambient temperature before being dried for an hour in a 400°F oven. Using an electric mill, the dried whole seeds were ground to a fine powder and placed in airtight containers for later use as reported by Oshomoh and Obaro[11].

2.3. Preparation of extract

N-hexane solvent was used to extract one kilogram of the powder. 2.5 liters of N-hexane were macerated well with a weighted powered sample for 72 hours while it was continuously shaken and stirred. Filtration was done using a cheese cloth, a conical flask, and a funnel to separate the residue from the filtrate. The filtrate was concentrated to paste level using a crucible and water bath at 40^0 C to actualize the concentrate which was later dried to powder in an oven at 40^0C to obtain a crude extract of 35.8 g which was preserved in a sample bottle inside the refrigerator[12]. The percentage yield was estimated using the dried powder that was used[13].

2.4. Calculation of stock Solution and Dose

To create a stock solution out of which dilutions might be made, a specific weight of the extract was diluted in distilled water and calculated doses administered to the animals during the various experimental procedures[14].

2.5. Drugs/Solvents and chemicals

Drugs and reagents were of pharmaceutical standards. Imipramines (Glaxosmith Kline Lagos State, Nigeria Plc), Absolute N- Hexane solvent, chloroform (supplied by Fharmatrends, Edo State, Nigeria Ltd), and Sodium Chloride were all of the analytical standards.

2.6. Experimental animals

A total of 60 mice (8 weeks old) were used for the 2 models. Each model contained 30 mice (15 males and 15 females) weighing 25-30 g and was purchased from the Department of Pharmacology and Toxicology, University of Benin, Benin City, Nigeria. The mice were housed in the animal house of the Phytomedicine unit of the Department of Plant Biology and Biotechnology, University of Benin. Moreover, they were kept in cages made of plastic under natural illumination and temperature settings. They were also nourished with standard feed (Top Feeds, Nigeria Plc) and water *ad libitum*. Prior to the experimental study, the mice were acclimatized for two weeks[15].

2.7. Experimental Design

2.7.1. Acute Toxicity Study

An acute toxicity study was conducted using the methods of OECD guidelines (2008). In total, six mice (3 males and 3 females) received 1000 mg/kg of the extract orally and were monitored for 72 hours for any potential toxicity, mortality, or morbidity symptoms[16].

2.7.2 Qualitative Phytochemical Screening

The N-hexane extract of *Datura stramonium* seed *(NEDSS)* was tested for carbohydrates, glycosides, saponins, flavonoids, alkaloids, tannins, eugenols, steroids, terpenoids, and phenolic compounds using standard phytochemical procedures[17].

2.7.2.1. Test for Carbohydrates (Molisch's Assessment)

To obtain 3 ml of the plant samples, a few droplets of alpha-naphthol (1-naphthol) in methanol were added. This was followed by 2 droplets of concentrated H_2SO_4 added through the test tube's side. Violet rings formed at

junctions of the two liquids were required for positive tests (darker violet rings signified a higher presence of carbohydrates).

2.7.2.2. Reducing Sugar Test (Fehling's Assessment)

Equivalent measurements of Fehling's solution A and B were boiled for one minute and 1 ml of the plant extract after which it boiled for five minutes. A positive test required a brick-red precipitate (a darker precipitate indicated higher reducing sugar present).

2.7.2.3. Test for Cardiac Glycosides

To obtain 1 ml of the extract, 1 ml of glacial acetic acid using one drop of ferric chloride solution was dissolved. 1 ml of concentrated H_2SO_4 was used as the under-layer. The presence of glycoside requires a ring with brown color, and darker rings showed more presence of cardiac glycosides[18].

2.7.2.4. Test for Saponins

To obtain 0.5 g of the plant extracts, water was introduced, placed inside a test tube, shaken, and examined for signs of frothing. As a benchmark, saponins rein Weiss (provided by Merck) were utilized.

2.7.2.5. Test for Flavonoids

To attain 2 g of the plant extract, 10 ml of distilled water was added, boiled, and filtered. Two distinct sections, A and B, each containing 5 ml of the filtrate, were separated.

To obtain portion A, a few drops of a 10% lead acetate solution were added. Positive outcomes were indicated by a yellowish precipitate. To get portion B, a few drops of diluted HCl were introduced to the solution along with 5 ml of 20% NaOH. A positive test was indicated when a colorless solution formed.

2.7.2.6. Test for Phenolic Compounds

5 ml of ethanol at a 90% concentration was added to 1 ml of plant extracts. Additionally, 1 drop of 10% $FeCl_3$ was applied. A positive test will have a faint yellow coloring.

2.7.2.7. Test for Tannins

10 ml of water from a distilled source was applied to 2 ml of the extract, and the mixture was heated for 5 minutes before being filtered into two equal parts.

Ferric chloride ($FeCl_3$) solution was then introduced to 2 drops of the filtrate because hydrolyzable tannin must form a bluish precipitate. After boiling 2 ml of diluted HCl for 5 minutes, 5 droplets of the filtrate were mixed with. Condensed tannin can only exist as a crimson precipitate.

2.7.2.8. Test for Eugenols

5 ml of a KOH solution at 5% was added to plant extract of 2 ml. Separation and filtering were done on the aqueous layer. To the filtrate, a few drops of diluted HCl were added. A positive test was indicated by a pale-yellow precipitate.

2.7.2.9. Test for Steroids

0.5 g of plant extract in 2 ml of diluted H_2SO_4 was applied to acetic anhydride 2 ml. The presence of terpenoids was indicated by a shift in color from violet to blue or green.

2.7.2.10. Test for Terpenoids (Salkowski test)

2 ml of chloroform and 3 ml of concentration H_2SO_4 were gently put down to the side of the test tube's inner wall to form a layer and applied to each extract (5 ml). Terpenoids must be present for the interphase to be reddish-brown in color.

2.7.2.11. Test for Alkaloids

Alkaloids were detected using Dragendoff's and Wagner's reagent, as well as picric acid. The extract was divided into three test tubes with the letters A, B, and C, each receiving around 1 ml. To obtain portion A, Dragendoff's solution, which included salts of potassium bismuth and iodide, was added in an amount of 2 ml. A reddish-brown precipitate indicates a favorable examination**.** To attain portion B, Wagner's reagent (2 ml) was applied. A positive test result was shown by the reddish-brown precipitate. To get portion C, Picric acid (2 ml) was introduced. A positive test result is a yellow precipitate.

2.7.3. Anti- Depressant Studies

2.7.3.1. Tail Suspension Test (TST)

The procedure followed a similar outline to that given by Steru *et al*.[18], with few modifications. For seven days, extracts were used to pre-treat mice. Mice were individually held 50 cm above the ground, 50 cm over the table's edge, by their tails, 24 hours following the last dose, using adhesive tape that was applied about 1 cm from the end of the tail. The test was conducted with each animal visually separated from the other animals. Testing was done in a quiet, dimly lit space with minimum background noise. The remaining 4 minutes of the test were used to measure the length of immobility[18]

2.7.3.2. Forced Swim Test (FST)

The approach outlined by Porsolt *et al*.[19] was used. A glass cylinder loaded to a depth of 15 centimeters (24°C) with water and measuring 20 cm in height by 12 cm in diameter served as the FST's instrument, after a 2-minute initial period of intense exertion. After giving the medications to various groups of animals, the variations in immobility time were investigated. There was just one use of each animal[19].

2.8. Statistical analysis

Results from these experiments were provided as Mean± Standard Error of Mean (SEM). One-way analysis of ANOVA was performed to analyze the results using Graph Pad Prism 8.0 software. P-values of 0.05 or lower were used to denote significance.

3. Results

3.1. Qualitative Phytochemical Screening

Results of phytochemical tests of NEDSS showed the presence of glycosides, carbohydrates, saponins, flavonoids, phenolics, eugenols, terpenes, reducing sugar, and alkaloids. The phytochemical study also revealed that there was no steroid or tannin (Table 1).

Table 1. Qualitative phytochemical compounds of N-hexane Extract of *Datura stramonium* Seed

S/N	Phytochemicals	NEDSS
1.	Cardiac Glycoside	++
2.	Saponins	+
3.	Flavonoids	++
4.	Phenolics	++
5.	Tannins	-
6.	Eugenols	++
7.	Terpenoids	++
8	Eugenols	++
9	Steroids	-
10.	Reducing Sugar	++
11.	Alkaloids	++

Key: -: Absent, +: Present, ++: abundantly present

3.2. Acute Toxicity Study

The acute toxicity study was performed using a dosage of 400 mg/kg per oral on the treated animals, and the extract was discovered to be devoid of harmful and deadly side effects (Table 2). Therefore, the doses for antidepressant studies were selected at 10, 20, and 40 mg/kg per oral.

An acute toxicity study was carried out to determine the safety of the extract at a single dose of 400 mg/kg. Results from the acute toxicity study revealed the LD_{50} was greater than 400 mg/kg as there was no mortality recorded in the mice.

3.3. Anti-Depressant Tests

3.3.1. Tail Suspension Test

Mice treated with the three doses of the NEDSS exhibited increases in mobility times, which were significant, compared to the normal control. The mobility time for 10, 20, and 40 mg/kg of the extract (111.4 ≤ 6.4, 120.8 ≤ 1.9, and 145.0 ≤ 9.6 seconds) were significant at P≤0.001 (***), 0.0001 (****), and 0.0001(****), respectively, compared to the control (71.0 ≤ 6.4 seconds) and Imipramine 15 mg/kg (102.6 ≤ 2.5 seconds) (P≤0.01**) Figure 1.

3.3.2. Forced swim test (FST)

Mice treated with the three doses of NEDSS exhibited increases in mobility times in the FST and were significant, compared to the normal control. The mobility time for 10, 20, and 40 mg/kg of the extract (107.4±2.7, 117.4±2.5, and 131.0±3.7 seconds) were significant at P≤0.001 (***), 0.0001 (****), and 0.0001(****), respectively, compared to the control (80.0 ≤ 3.5 seconds) and Imipramine 15 mg/kg (98.6±2.7 seconds) (P≤0.01**) Figure 2.

Table 2. Acute toxicity study of N-hexane Extract *Datura stramonium* Seed on Swiss albino mice after 72 hours of administration of single-dose (400 mg/kg) of extract.

Group(s)	Dose	Cognition	Agility	Signs of Toxicity such as Grooming, nausea, writhing,	Mortality after 72 hours of administration
Control	2 ml/kg	Normal	Normal	None	0/6
NE	400 mg/kg	Normal	Normal	None	0/6

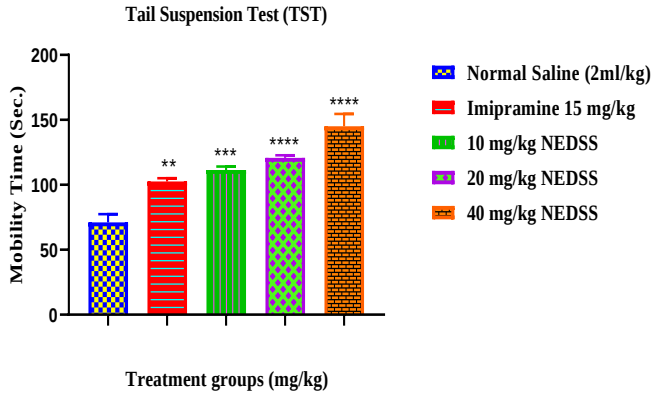

Figure 1. Effect of N-hexane Extract *Datura stramonium* Seed (10, 20, and 40 mg/kg) and Imipramine (15mg/kg) on the period of mobility in the TST. Results are expressed as mean ± S.E.M (n=6). ** =*P≤0.01;* *** =*P≤0.001 and* **** =*P≤0.0001,* compared to the control group

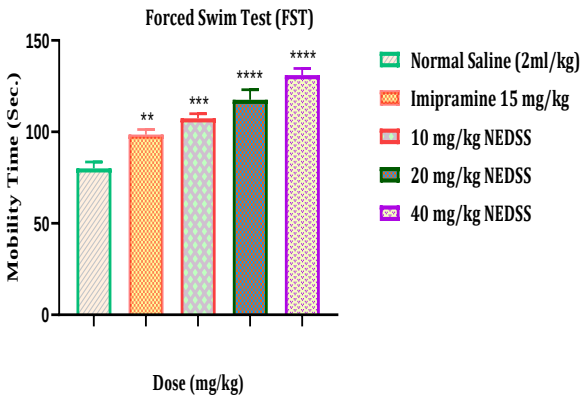

Figure 2. Effect of N-hexane Extract *Datura stramonium* Seed (10, 20, and 40 mg/kg) and Imipramine (15mg/kg) on the period of mobility in the TST. Results are expressed as mean ± S.E.M (n=6). ** =*P≤0.01;* *** =*P≤0.001, and* **** =*P≤0.0001,* compared to control group

4. Discussion

4.1. Qualitative Phytochemical Screening

Table 1 shows the various phytochemical parameters which are in support of the findings of Porter *et al*.[20] who reported similar phytochemical present in *Datura metal* Linn. in the Marathwada region, Maharashtra.

4.1.1. Cardiac glycoside

Cardiac glycoside constitutes a collection of naturally occurring chemicals that have been isolated from various plant and animal species. It is typically used to treat cancer and a variety of cardiac ailments[21].

4.1.2. Saponins

Many plants and significant plant products used by humans contain Saponins. Saponins contain hypolipidemic characteristics that can help treat dyslipidemia by lowering cholesterol levels and lower density lipoprotein. On cancer cells, saponins induce apoptosis, which has cytotoxic effects. Moreover, its chemotherapeutic effects are rooted in the processes that regulate protein expression associated with the cell cycle, the development of cancer, and metastasis[22].

4.1.3. Flavonoids

Flavonoids (or bioflavonoids), also referred to as Vitamin P and Citrin, have become a class of secondary metabolites that are typically discovered in stems, fruits, veggies, nuts, flowers, wine, honey, seeds, and tea. They are also widely present in photosynthesizing cells. Flavonoids assist in controlling cellular activity and fend against free radicals that subject your body to oxidative stress. Simply put, they make your body work more effectively while safeguarding it against common pollutants and stresses[23].

4.1.4. Phenolics

The potential health benefits of phenolic compounds, which have been shown in several studies, make them among the most researched natural substances[24]. Recent studies have demonstrated that phenolic compounds obtained from natural sources have anti-inflammatory, anti-allergic, anti-carcinogenic, anti-hypertensive, cardio protective, anti-arthritic, and antibacterial properties[24].

4.1.5. Tannins

Special classes of phenolic metabolites are tannins. They are useful in the management of type 2 diabetes[25]. Tannins' astringent qualities make them important in medicine. They encourage the creation of new tissues and quick wound healing and inflammation of the mucosa. Tannins are used to treat gum inflammation, varicose ulcers, hemorrhoids, mild burns, as well as frostbite[25].

4.1.6. Eugenols

Numerous plant species' essential oils include eugenols. Chemically, this is an allyl chain-substituted guaiacol and it pertains to a class of naturally produced phenolic mono-terpenoids[26]. The chemical eugenols, a part of the phenylpropanoids class, are surprisingly adaptable and have been used in a wide range of goods, including those in the food, perfume, flavoring, cosmetic, and pharmaceutical field[26].

4.1.7. Terpenoids

Terpenoids, which make up a group of significant plant secondary metabolites and are among the most prevalent substances in natural products, have a variety of structural types[27]. Terpenoids are widely utilized as raw chemicals in the culinary, cosmetic, and pharmaceutical industries. Terpenoids both prevent and cure cardiovascular problems and have hypoglycemic effects. Terpenoids have also been identified to have a wide range of potential uses in the past, including insect resistance, immune modulation, anti-oxidation, anti-aging, and neuro-protective effects[27].

4.1.8. Alkaloids

Alkaloids include neuro-active substances (e.g., caffeine and nicotine), as well as life-saving drugs like vincristine and vinblastine, which are used to treat tumors, as well as oral intoxication, and emetine, which is used to fight them[28]. Due to their toxicity, alkaloids are effective in fighting diseases, as well as predators, and can serve as a plant's defense mechanism. Key elements of effective plant protection are rapid awareness of threats and adverse climate changes, coupled with effective and focused signal transduction for initiating alkaloid accumulation. Generally speaking, the severity of a toxin's effects depends on the dose, the duration of exposure, and the person's responsiveness, area of reaction, and stage of growth. Depending on the pharmacological or ecological setting, toxicity effects occasionally can be both detrimental and advantageous. Studying alkaloid metabolism and buildup involves a variety of methods[29]. Monitoring gene expression, enzyme activity, precursor and alkaloid concentrations during simulated pathogen and herbivore attacks or upon physical or chemical stimulus that simulates their presence is an effective strategy. For alkaloids of interest to be produced more effectively, new biological compounds to be discovered, and to be applied sustainably against goals of interest like plant eaters, pathogens, cancerous cells, or undesirable physiological states, a better comprehension of alkaloid biosynthetic pathways and methods of action is necessary[29].

Numerous phytochemicals, including terpenoids, saponins, polyphenols, eugenols, cardiac glycoside, flavonoids, alkaloids, and essential oils have been found to have effects that are similar to those of antidepressants, according to the studies by Jennifer *et al*.[29].

4.2. Acute toxicity

Acute toxicity describes the negative consequences that accompany the oral or topical delivery of a single dosage of a chemical. Numerous dosages administered over 24-72 hours or a 4-hour inhalation exposure obtained from the result of this study showed that at 400 mg/kg, there was no death recorded indicating that the lethal dose (LD_{50}) was greater than 400 mg/kg[28].

This outcome lends credence to Bouzidi *et al*.[28] conclusions. He stated that following acute I.P. treatment of the whole alkaloids from the seed of *Datura stramonium* (400 mg/kg), neither sexes of any experimental group saw any notable changes in general appearance nor any deaths.

4.3. Antidepressants

Depression is indeed a condition that often consists of such main symptoms as a lack of interest, worry, insomnia problems, appetite loss, low energy levels, and suicidal thoughts, which may be frequent[30]. In today's environment, stress is the primary, ongoing trigger of depression. It appears as the physical, mental, and/or emotional responses that the body makes in response to a stimulus[30].

The use of antidepressants in treating depressive conditions, several mood disorders, certain chronic pain disorders, and some addictions is widespread. Antidepressants frequently cause dry throat, excess weight, headaches, vomiting, sexual problems, and emotional blunting as adverse effects[30]. In 2020, Jane *et al*. assessed the antidepressant drugs, and numerous models were created. The two most frequently employed models for antidepressant tests, however, are the TST and the FST . For all kinds of antidepressants, these models are extremely sensitive and specific [29].

4.3.1. Study on Tail Suspension Test

The design of a unique antidepressant drug testing method involves suspending a mouse by its tail from such a lever while simultaneously recording the animal's movements. The six-minute test can be broken down between intervals of agitation, as well as immobility. Mianserin, amphetamine, nomifensine, atropine, desipramine, and amitriptyline viloxazine are some of the psychiatric medications that have been investigated[31]. As with psycho-stimulants and atropine, antidepressant medications shorten periods of inactivity. The test can distinguish between doses of locomotor stimulants and antidepressants if it is combined with the assessment of locomotor activity under various circumstances. Diazepam lengthens the period of inactivity. The principal benefits of this method are the utilization of an easy, impartial test scenario, the agreement between the findings and Porsolt's verified "behavioral despair" test, and susceptibility to a variety of medication dosages[30].

According to the TST Results (Figure 1), the mobility time increased. Mobility time displays a condition of fighting to survive that may be caused by a variety of antidepressants that are therapeutically effective in the treatment of depression in people. The mobility shown by experimental animals in this paradigm suggests a behavioral despondency that indicates a non-depressive condition.

4.3.2. Forced Swim Test

In adapted FST, where mice were made to swim in a constrained area, they quickly gave up swimming and stopped motionless. While immobility in the FST is decreased by all antidepressants, pharmacologically selective antidepressants elicit two distinct active behavioral patterns. Antidepressants that selectively limit norepinephrine absorption decrease inertness and promote climbing while having little effect on swimming. In contrast, serotonin reuptake medications likewise lessen inactivity but promote swimming rather than climbing[30].

According to the results of this study, mice's TST and FST responses to the NEDSS significantly reduced depression. In addition to significantly influencing swimming time, the three doses of NEDSS were able to improve mobility and climb time.[15] The 40 mg/kg large dosage of the extract had effects that were comparable to those of the medication imipramine. The precise processes by which the NEDSS generated an antidepressant-like effect are not fully understood. However, findings from this experiment show that the pattern of behaviors induced by the extract in the FST are comparable to those of Imipramine, indicating that this plant extract likely functions by enhancing norepinephrine neurotransmission because it is associated with ascending behavior inside the modified FST[15].

The plant extract has demonstrated effects comparable to Imipramine by increasing mobility in modified TST and FST, although it is not necessary for it to include tricyclic components to exhibit sedative action. It is likely that it contains an organic substance that is not tricyclic but has potential antidepressant and CNS-stimulating effects. As a result, we assert that this plant extract has potential antidepressant efficacy that is not caused by its motor-stimulating properties [15].

5. Conclusion

An increase in the dose of NEDSS revealed subsequent increases in anti-depression actions. 40 mg/kg of NEDSS proved to be the most potent in the two models of depression. However, further research should be carried out to determine its mechanism of action using laboratory animals.

Declarations

Competing interests

Authors declare that they have no contending interests.

Authors' contributions

Examine development and planning was done by Dr. Obaro P. O. Data collection, analysis, and interpretation of

results were carried out by Dr. Obaro P. O. and Dr. (Mrs.) Obaro-Onezeyi O.E. Draft manuscript and preparation were done by Dr. Obaro P. O. and Dr. (Mrs.) Obaro-Onezeyi O.E. The final draft of the manuscript was approved by the authors after they had evaluated the manuscript.

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Availability of data and materials

The manuscript contains all datasets generated and/or analyzed in the current study.

Ethical considerations

The authors have examined the work for plagiarism, data falsification, multiple publications, and redundancy. The ethics committee of the Faculty of Life Sciences, University of Benin, with registration number LS19116, also authorized the study.

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