Trop J Nat Prod Res, March 2021; 5(3):587-590 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

# Antidepressant Activity of Methanol whole Plant Extract of *Tapinanthus dodoneifolius* (DC) Danser in Swiss Mice

Nura Bello*, Mohammed G Magaji, Mohammed I Maje, Aishatu Shehu

*Department of Pharmacology and Therapeutics, Ahmadu Bello University, Nigeria*

ARTICLE INFO

*Article history:*
Received 17 September 2020
Revised 19 February 2021
Accepted 03 March 2021
Published online 01 April 2021



ABSTRACT

Depression remains one of the major contributors to global burden of disease despite multiple approaches to its treatment. Plants derived medicines serve a great role in confronting the challenges related to the treatment of various ailments. The study evaluated an antidepressant potential of the whole plant methanol extract of *Tapinanthus dodoneifolius*. Preliminary phytochemical screening was carried out using a standard method. Oral median lethal dose ($LD_{50}$) was determined using the guideline by Organization for Economic Co-operation and Development (OECD). The antidepressant effect of the extract was assessed using the Tail Suspension Test (TST) and Forced Swim test (FST) in mice. Also, effect of the plant extract on ambulation was studied using Open Field Test (OFT). Immobility duration within four (4) minutes in TST and FST as well as locomotory activity in open field was determined for each animal. Preliminary Phytochemical screening of the methanol extract of *T. dodoneifolius* indicated positive for saponins, cardiac glycosides, tannins, steroids, triterpenoids and flavonoids. Median lethal dose ($LD_{50}$) of the extract was found to be above 5000 mg/kg. The extract significantly ($p < 0.05$) shorten the immobility time in the TST at the tested dose of 375 mg/kg while only the highest dose of the extract (1500 mg/kg) significantly ($p < 0.05$) reduced immobility time in the FST. The extract did not significantly affect ambulation in the OFT. The study revealed that the methanol extract of the whole plant of *Tapinanthus dodoneifolius* produces an antidepressant activity.

***Keywords:*** *Tapinanthus dodoneifolius*, Depression, Antidepressants, Tail suspension test, Forced swim test, Open field test.

## Introduction

Depression is the most common mental disability which affects more than 264 million people globally of various ages.[1] It is associated with several disabilities like impaired quality of life and escalated health care expenses making it a very serious psychiatric disorder.[2] Depression often results in many debilitating disease conditions such as; malignancies severe infectious diseases and neuropsychiatric disorders.[3] The pathology of depression has been studied widely with the monoamine-related abnormality in the central nervous system being the most well reported.[4] Many antidepressant drugs developed and in use such as; the monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), serotonin and noradrenaline reuptake inhibitors (SNRIs), noradrenaline reuptake inhibitors (NRIs), and selective serotonin reuptake inhibitors (SSRIs) use monoamines as target.[5] However, these available antidepressants are faced with delayed onset of action, limited efficacy as well as serious adverse reactions.[6] Studies have revealed that the effectiveness of these antidepressants is only in about 50% of cases. Consequently, only about 40% of patients treated achieve remission even after multiple trials.[7] Over the past decades, a lot of people are progressively resorting to the use of traditional medicine with the expectation of solace, cost-effectiveness, enhanced efficacy, availability, and probably better safety profile.[8] The plant, *Tapinanthus dodoneifolius* is used traditionally for neurological and psychiatric illnesses.[9] It has also been proclaimed to produce other various forms of pharmacological effects including antimicrobial, anxiolytic, analgesic, as well as gastrointestinal effects.[10-13] It is being locally used in management of depression by traditional healers in northern Nigeria.[14] The study evaluated the antidepressant activity of *Tapinanthus dodoneifolius*

*Corresponding author. E mail: nb32321@gmail.com
Tel: 08030553212

Citation: Bello N, Magaji MG, Maje IM, Shehu A. Antidepressant Activity of Methanol whole Plant Extract of *Tapinanthus dodoneifolius* (Dc) Danser in Swiss Mice. Trop J Nat Prod Res. 2021; 5(3):587-590. doi.org/10.26538/tjnpr/v5i3.28

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria.

## Materials and Methods

*Drugs and chemicals*

Fluoxetine capsule 20 mg (V.S International PVT. Ltd. Dabhel, India), Distilled water (A.B.U Zaria), Methanol (Fluka-Aldrich).

*Laboratory animals*

Swiss mice (23-28 g) of both sexes were purchased from the Animal House Facility, Department of Pharmacology and Therapeutics, Ahmadu Bello University Zaria. The animals were placed into cages made of polypropylene and sustained under normal environmental conditions of ventilation and hygiene. They were fed with laboratory rodent pellet and free drinking water. The protocols adopted in the experiments for the study were approved by the Ahmadu Bello University Committee on Animal Use and Care (ABUCAUC/2020/010).

*Collection and identification of plant*

The whole plant was collected together with parts of the host plant from a secondary forest area within Sabon-Gari Local Government of Kaduna State in March, 2019 and was taken to the herbarium unit, Botany Department of Ahmadu Bello University Zaria, for identification. The voucher specimen number, 0350, was assigned to

the plant while for the host plant, 02846 was assigned by comparing with an existing herbarium specimen.

*Plant preparation and extraction*
The whole plant was shade-dried for 2 weeks to a constant weight. One thousand grams (1000 g) of the dried plant material was reduced to fine powder using wooden mortar and pestle. It was subjected to Soxhlet extraction with three litres (3L) of 70% methanol for 24 hours. The extract was placed on a water bath at 45$^{o}$C to remove excess solvent and obtain the concentrate subsequently labelled as the methanol extract of *Tapinanthus dodoneifolius* (TD extract).

*Preliminary phytochemical screening*
Preliminary phytochemical tests were conducted on TD extract according to a previously described method.[15] The tests were confirmed on Thin Layer Chromatography plates developed in n-butanol + acetic acid + water 4:1:5 (BAW) solvent system and sprayed with Aluminium chloride, Ferric chloride, Bontrager's reagent, Dragendoff's reagent and Liebermann-Burchard's reagent to confirm the existence of flavonoids, phenols, alkaloids, and steroid/triterpenoids respectively.[16]

*Acute toxicity test*
The median lethal dose – 50% ($LD_{50}$) of the extract was estimated using the guideline by Organization for Economic Co-operation and Development (OECD) 425.[17] A limit dose of 5000 mg/kg TD extract was administered orally to a single mouse, observed for four hours to detect any sign and symptom of toxicity or death. Subsequently, two more mice were dosed with the same 5000 mg/kg of TD extract and observed for another 24 hours to detect any sign and symptom of toxicity or death.

*Animal groupings and treatment*
In each study, forty (40) mice were divided into five (5) sets each comprising about eight (8) animals. First group was treated with Distilled water; 1 ml/kg, the second, third and fourth groups were treated with the extract (TD) at doses of 1500 mg/kg, 750 mg/kg and 375 mg/kg respectively while the last group was treated with fluoxetine 20 mg/kg.

*Antidepressant study*
*Tail Suspension Test (TST):* The total duration of immobility succeeding tail suspension was estimated according to a method described previously.[18] One hour after treatment, each mouse was hanged on the edge of a bar, placed 50 cm high above the floor by the use of an adhesive tape stuck at estimated 1 cm from the tip of the mouse tail. The animal is allowed to hang for 6 minutes under camera recording. Immobility was recorded each time the animal despair from moving any part of its body and suspend indifferently.

*Forced swimming test (FST):*
The procedure was carried out in accordance to the method described previously.[19] One hour after treatment, each mouse was placed in a cylindrical container made of Plexiglas (10 cm: diameter by 25 cm: height) filled to a height of 10 cm with water at 25 °C. The animal was allowed to swim for six (6) minutes under camera recording. The animal's immobility time was recorded within four (4) minutes after the initial two (2) minutes of intense striving to escape. A mouse was considered to be immobile when it remains afloat on the water in an erect posture and only makes minor movement to avoid drowning.

*Open field test (OFT):*
The procedure was carried out by a method previously described.[20] Each mouse was dropped at the centre of an open field apparatus (70 cm: length × breadth and 35 cm: height) made of three dark walls and one transparent front wall. The base of the apparatus was divided into sixteen (16) visible squares. Each animal was allowed in the arena for five (5) minutes under video camera recording. The number of lines crossed by a mouse with all its four limbs was counted and recorded. Each time a mouse is removed, 10% ethanol was used to clean the base before placing another mouse into the experiment to remove all faecal pellets and wipe up all spots of urination.

*Statistical analysis*
Values are presented in form of mean ± Standard Error of Mean and were analyzed in SPSS® by One Way Analysis of Variance (ANOVA). Bonferroni post hoc test for multiple comparison was carried out to detect point of significance. A significant difference was recorded at $p < 0.05$.

## Results and Discussion

*Tapinanthus dodoneifolius* is a popular medicinal plant reported to be used locally for various purposes and to treat many ailments including depression and some other neurological and psychiatric illnesses.[21, 22] Local use of the plant in depression has been reported in ethno-medical surveys by researchers in Cameroon and Nigeria respectively.[9, 13] The oral acute toxicity profile of the extract revealed median lethal dose ($LD_{50}$) greater than 5000 mg/kg body weight. No sign and symptom of toxicity or death was recorded in the acute toxicity study indicating the relatively non-toxic nature of the extract via the oral route of administration. [23] This finding agrees with an earlier research that asserted non-toxic property of other similar species like *T. bangwensis* and *D. falcata* also via oral route of administration.[24] The extract produced a significant ($p < 0.05$) reduction in immobility period in tail suspension test (TST) comparable to Fluoxetine (20 mg/kg) in comparison to the negative control group (Table 2). However, the extract only at the dose of 1500 mg/kg produced a significantly ($p < 0.05$) reduction in immobility period in comparison to the negative control group in forced swim test (FST) (Table 3). The tail suspension test (TST) and Forced swimming test (FST) are behavioural models of distress in animals established according to the expectation that when the animals are subjected to unescapable stress, they strive and attempt to escape, but they ultimately lose hope and display immobility which was assumed to be a reflection of a despair behavioural congruent to the one seen in depression.[25] A lot of antidepressants have to be taken for several days to elicit clinical significance in individuals but that has been achieved with TST and FST from both acute and chronic administrations.[26] while the forced swimming and the tail suspension tests are similar in terms of construct and predictive validity, they differ in terms of sensitivity as well as mechanistic performance where the forced swim is associated with additional distress which the animals suffer due to hypothermia as a result of submerging in the water. Therefore, the TST is more responsive to subtle neurochemical and neurobehavioral distortion than FST.[27] This explains the better immobily time reduction at even the lower dose in the TST in contrast to the FST. The forced swim test is a popular behavioral model in rodents which prognosticate the clinical efficacy of various classes of antidepressants and predict the mechanism by which they act. Many antidepressant drugs such as tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRI), and NMDA receptor antagonists restore the immobility state and enhance the performance of behavior indicating struggle to escape.[28] The mechanism of action of drugs in forced swimming is predicted based on climbing and swimming behaviour where, drugs that enhance adrenaline action such as imipramine affects climbing while drugs that enhance serotonin action such as fluoxetine affect swimming. Moreover, drugs affecting dopamine were recently shown to enhance climbing.[29] These observations, however, sometimes produce a false positive or negetive results.[30] Similarly, OFT was conducted to rule out possibility of antidepressant effect due to psychostimulation. Psychostimulants have been demonstrated to affect immobility in FST and TST similar to antidepressants, but conversely stimulate motor activities in contrast to antidepressants.[31] TD extract and fluoxetine did not affect locomotion as there was an insignificant change in number of lines crossed within five (5) minutes compared to the negative control group (Table 4). This indicates that the antidepressant activity is most probably distinct and not related to the stimulation of general motor activity as observed with psychostimulants which may result to a false positive action in both FST and TST. The Preliminary phytochemical analysis of the

methanol extract of *Tapinanthus dodoneifolius* revealed carbohydrates, cardiac glycosides saponins, flavonoids, steroids, terpenoids, alkaloids, and tannins (Table 1). Some of these arrays of phytochemicals were suspected to possess antidepressant activity according to various studies on plant metabolites ranging from polyphenols (phenolic acids, coumarins, flavonoids, and lignanes), terpenes and terpenoids, saponins and sapogenins, alkaloids, amines and carbohydrates .[32]

**Table 1:** Phytochemical Constituents of the Methanol Extract of *Tapinanthus dodoneifolius*

| S/No. | Phytochemicals | Inference |
|---|---|---|
| 1. | Carbohydrates | + |
| 2. | Saponin glycoside | + |
| 3. | Steroids | + |
| 4. | Terpenoids | + |
| 5. | Flavonoids | + |
| 6. | Alkaloids | + |
| 7. | Cardiac glycosides | + |
| 8. | Tannins | + |

+ = present, - = absent

**Table 2:** Effect of *Tapinanthus dodoneifolius* Methanol extract on Immobility Duration of mice in Tail Suspension Test

| Treatment | Dose (mg/kg) | Mean immobility Time (seconds) |
|---|---|---|
| DW | 10 mL/kg | 149.75 ± 11.79 |
| TD | 1500 | 74.50 ± 17.55** |
| TD | 750 | 82.57 ± 8.71* |
| TD | 375 | 79.75 ± 15.96* |
| FLUOXETINE | 20 | 68.75 ± 12.63** |

Immobility time presented in form of Mean ± Standard Error of Mean. (n = 8). Values were analysed by One-way Analysis of Variance (ANOVA) followed by *post hoc* (Bonferroni) test. * = $p < 0.05$ vs. Distilled water. ** = $p < 0.005$ significant difference in comparison to negative control (DW) group. DW = Distilled Water; TD = *Tapinanthus dodoneifolius* methanol whole plant Extract

**Table 3:** Effect of *Tapinanthus dodoneifolius* Methanol Extract on Mice Duration of Immobility in Forced Swim Test

| Treatment | Dose (mg/kg) | Mean immobility Time (seconds) |
|---|---|---|
| DW | 10 mL/kg | 204.00 ± 4.20 |
| TD | 1500 | 131.40 ± 13.80* |
| TD | 750 | 162.00 ± 13.80 |
| TD | 375 | 159.00 ± 18.60 |
| FLUOXETINE | 20 | 129.00 ± 24.00* |

Immobility time presented in form of Mean ± Standard Error of Mean. (n = 8). Values were analyzed by One-way Analysis of Variance followed by *post hoc* (Bonferroni) test. * = $p < 0.05$ vs. negative control (DW) group.
DW = Distilled Water; TD = Methanol Extract of *Tapinanthus dodoneifolius*.

**Table 4:** The Effect of *Tapinanthus dodoneifolius* Methanol extract on Mice Number of Lines Crossed by Mice in Open Field Test

| Treatment | Dose (mg/kg) | Mean number of lines crossed |
|---|---|---|
| DW | 10 mL/kg | 53.13 ± 11.18 |
| TD | 1500 | 69.38 ± 8.83 |
| TD | 750 | 86.00 ± 5.86 |
| TD | 375 | 86.75 ± 9.16 |
| FLUOXETINE | 20 | 64.75 ± 10.20 |

Number of lines crossed presented in form of Mean ± Standard Error of Mean. (n = 8). Values were analysed using One-way Analysis of Variance (ANOVA)
DW = Distilled Water; TD = Methanol Extract of *Tapinanthus dodoneifolius*.

## Conclusion

The methanol whole extract of *Tapinanthus dodoneifolius* possesses moderate antidepressant activity. The study, therefore, provides justification on the benefit of the whole plant in the treatment of depression in traditional medicine.

## Conflict of interest

The authors declare no conflict of interest.

## Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

## Acknowledgements

The authors acknowledge the technical assistance of Mr. Abubakar Balarabe Chawai of the Pharmacology and Therapeutics Department, Ahmadu Bello University, Zaria.

## References

1. Global Burden of Disease 2017. Disease and Injury Incidence and Occurrence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet. 2018;
2. Al Qahtani A and Al Qahtani N. Prevention of Depression: A Review of Literature. J Depress Anxiety. 2017; 6:292.
3. Jia H, Zack MM, Thompson WW, Crosby AE, Gottesman II. Impact of depression on quality-adjusted life expectancy (QALE) directly as well as indirectly through suicide. Soc Psychiatry Psychiatr Epidemiol. 2015; 50(6):939-949.
4. Hillhouse TM and Porter JH. A brief history of the development of antidepressant drugs: from monoamines to glutamate. Exp Clin Psychopharm. 2015; 23(1):1-21.
5. Park BK, Kim YR, Kim YH, Yang C, Seo C, Jung IC, Jang I, Kim S, Lee MY. Antidepressant-Like Effects of Gyejibokryeong-hwan in a Mouse Model of Reserpine-Induced

Depression. Biomed Res Int. 2018; Article ID 5845491, 12 pages. https//doi.org/10.1155/2018/5845491
6. Malhi GS, Outhred T, Hamilton A. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders: major depression summary. Med J Aust. 2018; 208:175-80.
7. Pahwa P and Goel RK. Antidepressant-like effect of a standardized hydroethanolic extract of *Asparagus adscendens* in mice. Indian J pharmacol. 2019; 51(2):98-108.
8. Kraus C, Kadri B, Lanzenberger R, Zarata CA, Kasper S. Prognosis and improved outcomes in major depression: a review. Transl Psychiatr. 2019; 9(1):127.
9. Liu L, Liu C, Wang Y, Wang P, Li Y, Li B. Herbal Medicine for Anxiety, Depression and Insomnia. Curr Neuropharmacol. 2015; 13(4):481-493.
10. Ndamitso MM, Monday MH, & Idris OJ, Tijani YS, Elijah UA. Analysis of Phytochemical Content and Antibacterial Activity of *Tapinanthus dodoneifolius* Extracts. Researcher. 2013; 5:54-59.
11. Harquin SF, David ET, Hervé H, Ngatanko A. Enhancing Spatial Memory: Anxiolytic and Antidepressant Effects of *Tapinanthus dodoneifolius* (DC) Danser in Mice. Neurol Res Int. 2014; 2014: 1-9.
12. Abdullahi Z, Jimoh AA, Patrick EB. Analgesic, Anti-Inflammatory and Anti-Pyretic Activities of *Tapinanthus dodoneifolius* (DC) Danser Extract Using Several Experimental Models in Rodents. J Biol Gen Res. 2016; 2(1):46-56.
13. Baso AA, and Mudi SY. Evaluation of antiulcer and phytochemical activities of leaf extracts from *Tapinanthus dodoneifolius* DC. (Loranthaceae) grown on *Tamarindus indica* tree. Bayero J Pure Appl Sci. 2018; 10(1):392.
14. Shehu A, Magaji MG, Yau J, Ahmed A. Ethno-botanical survey of medicinal plants used for the management of depression by Hausa tribes of Kaduna State, Nigeria. J Med Plants Res. 2017; 11(36):562-567.
15. Junaid RS and Patil MK. Qualitative tests for preliminary phytochemical screening: An overview. Int J Chem Stud. 2020; 8(2):603-608.
16. Rana PS, Mehta S, Saklani P. Phytochemical screening and TLC profiling of various extracts of *Reinwardtia indica*. Int J Pharmacogn Phytochem Res. 2017; 9523:527.
17. OECD. Test No. 425: Acute Oral Toxicity: Up-and-Down Procedure, OECD Guidelines for the Testing of Chemicals, Section 4, OECD Publishing, Paris. 2008.
18. Rodrigues AL, Silva GL, Matteussi AS. Involvement of monoaminergic system in the antidepressant-like effect of the hydroalcoholic extract of *Siphocampylus verticillatus*. Life Sci: 2002; 70:1347-1358.
19. Can A, Dao DT, Arad M, Terrillion CE, Piantadosi SC, Gould TD. The mouse forced swim test. J Vis Exp. 2012; (59):e3638.
20. Rex A, Voigt JP, Voits M, Fink H. Pharmacological evaluation of a modified open field test sensitive to anxiolytic drugs. Pharmacol Biochem Behav. 1998; 59:677-683.
21. Ofem OE, Eno AE, Imoru J, Nkanu E, Unoh F, Ibu JO. Effect of crude aqueous leaf extract of *Viscum album* (mistletoe) in hypertensive rats. Indian J Pharmacol. 2007; 39(1):15.
22. Builders MI, Uguru MO, Aguiyi C. Antiplasmodial potential of the African mistletoe: *Agelanthus dodoneifolius* Polh and Wiens. Indian J Pharm Sci. 2012; 74(3):223-229.
23. Hodge A and Sterner B. Toxicity Classes. In: Canadian Center for Occupational Health and Safety. 2005. http://www.ccohs.ca/oshanswers/chemicals/id50.htm accessed date; September 12, 2020
24. Jeremiah C, Katsayal UA, Nuhu A, Anafi SB, Ibrahim MA, Nuhu HD. Phytochemical Screening and Anti-Inflammatory Studies of *Tapinanthus globiferus* (A. Rich) Teigh. Leaves Three Extracts. Pharm Sci. 2019; 25(2):124-131.
25. Roni YY, Motty F, Avrham H, Ravid D. The Forced Swim Test as a Model of Depressive-like Behaviour. J Vis Exp. 2015; 97:e52587. Doi: 10.3791/52587
26. Cryan JF and Holmes A. The Ascent of Mouse: Advances in Modelling Human Depression and Anxiety. Nature reviews. Drug Discov. 2009; 4:775-790.
27. Chatterjee M, Jaiswal M, Palit G. Comparative evaluation of forced swim test and tail suspension test as models of negative symptom of schizophrenia in rodents. ISRN Psychiatr. 2012; 595141.
28. Cryan JF, Mombereau C, Vassout A. The tail suspension test as a model for assessing antidepressant activity: review of pharmacological and genetic studies in mice. Neurosci Biobehav Rev. 2005; 29(4-5):571-625.
29. Shehu A, Magaji MG, Yau J, Mahmud B, Ahmed A. Antidepressant Effect of Methanol Stem Bark Extract of *Adansonia digitata* L. (Malvaceae) in Mice. Tropical J Nat Prod Res. 2018; 2(2):87-91.
30. Alfaifi H, Abdelwahab SI, Mohan S, Elhassan Taha MM, Syame SM, Shaala LA, Alsanosy R. Catha edulis Forsk. (Khat): Evaluation of its antidepressant-like Activity. Phcog Mag 2017; 13, Suppl S2:354-8.
31. Garzón NJ, Rodríguez MM, Cortés ME. Increased PKC activity and altered GSK3β/NMDAR function drive behaviour cycling in HINT1-deficient mice: bipolarity or opposing forces. Sci Rep. 2017; **7**:43468.
32. Bahramsoltani R, Farzaei MH, Farahani MS, Rahimi R. Phytochemical constituents as future antidepressants: a comprehensive review. Rev Neurosci. 2015; 26(6):699-719.