EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 8
121-125
Year: 2020

ANTIDEPRESSANT-LIKE EFFECTS OF THE HYDROALCOHOLIC EXTRACTS OF LEAVES FROM *MORINDA LUCIDA* IN MICE

Bakou Niangoran François[1]*, Coulibaly Siendou[1], Bleu Gomé M.[1], Ba A.[2] and Atayi E.[3]

[1]Unit of Animal Physiology, Jean Lorougnon GUEDE University, Daloa, (Côte d'Ivoire).
[2]Laboratory of Neuroscience, UFR Biosciences, Felix HOUPHOUET-BOIGNY University, Abidjan, (Côte d'Ivoire).
[3]Neurology Service, Functional Exploration Unit of the Nervous System, C.H.U. from Cocody-Abidjan, (Côte d'Ivoire).

***Corresponding Author: Dr. Bakou Niangoran François**
Unit of Animal Physiology, Jean Lorougnon GUEDE University, Daloa, (Côte d'Ivoire).

Article Received on 10/06/2020 **Article Revised on 30/06/2020** **Article Accepted on 20/07/2020**

ABSTRACT

Objective: The aim of the present study is to evaluate the antidepressant-like effect of hydro ethanolic extract of leaves from *Morinda lucida* in mice. **Material and Methods**: Mice were randomly divided into five groups ($n = 5$/group): control group (distilled water), standard group where Amitriptyline (20mg/kg b.w., IP) was used as standard drug and three test groups where three doses of the hydro ethanolic extract of *Morinda lucida* (100, 200, and 400 mg/kg) was used for two weeks treatment. To assess the antidepressant-like effect of hydro ethanolic extract of leaves from *Morinda lucida* forced swimming test (FST), tail suspension test (TST) and measurement of locomotor activity test (OFT) have been done in mice. **Results:** The results showed that a strong and dose-dependent antidepressant effects in different mice models. The main findings of the hydro ethanolic extract of *Morinda lucida* significantly reduced the duration of immobility times in the forced swimming test ($p < 0.001$). Likewise, the extract significantly decreased the immobility time in the tail suspension test ($p < 0.001$). **Conclusion**: The results of the present work suggest that a hydro alcoholic extract of the hydro ethanolic extract of *Morinda lucida* leaves may possess an antidepressant effect.

KEYWORDS: *Morinda lucida, antidepressant, activity, mice.*

1 INTRODUCTION

Depression is a widespread chronic psychiatric complaint which interferes with social life and work performance. Today, millions of people of all ages suffer from this disease.[1] According to figures from the World Health Organization, by the year 2020, depression is estimated to be the second known cause of world disability[2], and through 2030, it will probably make the greatest contribution to the burden of disease.[3] In last few decades, several drugs have been discovered to treat depression such as tricyclic antidepressants, monoamine oxidase inhibitors[4] and selective serotonin reuptake inhibitors (SSRI). But unfortunately, all of the drugs have serious side effects including insomnia, anxiety, weight gain etc. It is well known that nature is the best and safe source for all medicine. So it becomes worth to search for a new antidepressant drug from natural source with less side effects and complications.[5] Plant of *Morinda lucida* (Benth), a member of Rubiaceae family, is among important medicinal plants in Ivorian traditional medicine. It is widely distributed in West Africa and is used in African folk medicine to treat several diseases.[6] The leaves are bitter and are used by the natives to treat malaria, yellow fever, jaundice, hepatitis, eczema, edema, cough, hypertension, diabetes, and sexual weakness.[7,8,9] In some cases, the plant is employed in the treatment of cerebral congestion, dysentery, stomach ache, ulcers, leprosy, and gonorrheal.[10] Literature survey revealed a variety of pharmacological actions such as analgesic, anti-inflammatory, antipyretic activities for these plants.[11] No scientific report regarding the in vivo antidepressant activity of hydro ethanolic extract of leaves from *Morinda lucida* has been published. That's why, the present study was undertaken to assess the possible antidepressant effects following single administration of hydro ethanolic extract of leaves from *Morinda lucida* in mice. For this purpose, we used the forced swim test (FST), open field tests (OFT) and the tail suspension test (TST).

2 MATERIEL AND METHODS

2.1 Plant material

Fresh leaves of the plant were collected from Daloa, (Cote d'Ivoire) in October, 2019. The plant was identified and verified by botanist Professor from Jean Lorougnon GUEDE university of Daloa (Cote d'ivoire). The collected leaves were dried under a shade during two

weeks and pulverized using the crushing assistance (IKAMAG RCT®). The powder of leaves obtained, constituted our sample to be analyzed.

2.2 Extract preparation

A 100 g sample of crushed *Morinda lucida* was used for extraction. The sample was soaked overnight in 70% alcohol (30:70) and filtered using Whatman No.1 paper. The process was repeated twice by adding fresh solvent every time. The pooled extract was subjected to flash evaporation followed by lyophilization. The lyophilized sample was further analyzed to determine its antidepressant activity.

2.3 Animals

25 healthy adults males Swiss albino mice weighing (20–30 g) were obtained from the animal house of Jean Lorougnon GUEDE University, Daloa. These animals were housed under standard environmental conditions. The mice were fed with FACI® (Fabrication d'Aliments de Côte d'Ivoire) pellets, groundnuts and dried fish. They had free access to drinking water ad libitum.

2.4 Drugs and chemicals

The standard drugs Amitriptyline and saline water were collected from Square Pharmaceuticals Ltd., Cote d'Ivoire. Distilled water which was used for dilution purpose was prepared was obtained from Jean Lorougnon GUEDE university of Daloa (Cote d'ivoire).

2.5 Behavioral parameters used to test antidepressant activity

-Forced swim test

The procedures for the FST, a widely used behavioral test for the detection of antidepressant-like effects, were similar to those described earlier.[12,13] Animals were initially placed individually to swim in plastic cylinders (30 cm of diameter by 40 cm in height containing 25 cm of water at 24 ± 1°C for 15 min (pretest).[14] They were then removed and allowed to dry in a separate cage before returning to their home cages. Twenty-four hours later the animals were submitted to a 5 min session of forced swimming session (test). During this session the total amount of time in which animals remained immobile (except for small limb movements necessary for floating) were recorded by an observer that was blind to the treatments. The water was changed after each trial to avoid the influence of alarm substances.

-Tail suspension test

TST was carried out according to the method described by Porsolt *et al*.[13,14] Briefly, mice were suspended by their tails using an elastic band attached to the tails by adhesive tape, and the elastic band was hooked onto a horizontal rod. The distance between the tip of the nose of the mouse and the floor was approximately 20 cm. they were suspended for a period of 5 min, and the time spent immobile during the last 4 min of the 5 min was recorded for each individual, by an observer blinded to the genotype.

-Open field test

Locomotor activity and exploratory behavior were assessed in an open field by the method described by Souza.[15] The apparatus consisted of a wooden box (60 × 60 × 30 cm^3) with the floor divided into 16 squares (15 × 15 cm^2). The apparatus was illuminated with a 40-W lamp suspended 100 cm above. they were placed individually in one of the corner squares. The number of rearing, assisted rearing (forepaws touching the wall of the apparatus) and squares traveled were counted for 5 min.

2.6 Experimental study design

Twenty-five mice were randomly divided into five groups (5 mice/group). The control group received vehicle (distilled water 0,1mL/mouse). Amitriptyline (20mg/kg b.w., IP) was used as the positive control or standard group while the treated mice received hydro ethanolic extract *of* leaves from *Morinda lucida* (100, 200, and 400mg/kg body weight i.p). A single dose of hydro alcoholic extract of leaves from *Morinda lucida* was administered daily for 14 days. the behaviors of all groups were assessed for antidepressant activity 30 min after the last treatment dose on the 14th day. Different standardized depression models were used for behavioral tests to evaluate the antidepressant activity, such as forced swim test (FST), tail suspension test (TST) test and open field test (OFT).

2.7 Statistical analysis

The results are presented as mean ± SEM. The statistical analysis was performed using one-way analysis of variance (ANOVA) followed by Dunnett's post hoc test as appropriate using statistica 10.0 software for windows. Differences between groups were considered significant at a level of $p < 0.001$.

3 RESULTS

The hydro alcohol extract of *Morinda lucida* showed antidepressant-like effects in animal models, namely forced swimming, measurement of locomotor activity and tail suspension tests. The hydro ethanolic extract of leaves from *Morinda lucida* (100, 200 and 400 mg/kg body weight) significantly reduced the duration of immobility time in the forced swimming test after 14d daily treatment (Table 1). Dunnett's post hoc analysis demonstrated that the test treatments significantly decreased the immobility time in comparison to the control group ($p < 0.001$). Likewise, the hydro ethanolic extract of leaves from *Morinda lucida* reduced the duration of immobility time in the tail suspension test (Table 2). Post hoc analysis confirmed that the extract significantly decreased the immobility time in comparison to the control group ($p < 0.001$).

As shown in table 3 the hydro ethanolic extract of leaves from *Morinda lucida* (100 and 400 mg/kg) was shown the satisfactory locomotion effect. At the doses of 200 and 400 mg/kg was significantly augmented the good rearing effect of this test table 3. Moreover, Post hoc

analysis also verified that the extract significantly increased the locomotion and rearing effects in comparison to the control group ($p < 0.001$).

Table 1: Antidepressant effects of hydro ethanolic extract of leaves from *Morinda lucida* in forced swimming test.

Treatment	Doses (mg/kg)	Immobility time (s)
Distilled water	0,1ml/mouse	224,5±3,38
Amitriptyline	20	109,8±1,59*
Morinda lucida	100	157,3±2,65*
Morinda lucida	200	136,4±2,73*
Morinda lucida	400	115,5±2,42*

(n = 5); *P<0.001 (ANOVA; Dunnet post hoc)

Table 2: Antidepressant effects of hydro ethanolic extract of leaves from *Morinda lucida* in tail suspension test.

Treatment	Doses (mg/kg)	Immobility time (s)
Distilled water	0,1ml/mouse	201,5±2,18
Amitriptyline	20	98,8±1,49*
Morinda lucida	100	137,3±2,15*
Morinda lucida	200	126,4±2,53*
Morinda lucida	400	110,5±2,48*

(n = 5); *P<0.001 (ANOVA; Dunnet post hoc)

Table 3: Antidepressant effects of hydro ethanolic extract of leaves from *Morinda lucida* in measurement of locomotor activity.

Treatment	Doses (mg/kg)	Rearing	Number of square traversed
Distilled water	0,1ml/mouse	23±1,15	107,5±2,15
Amitriptyline	20	36±2,05*	210,8±2,15*
Morinda lucida	100	27±2,25	102±1,20*
Morinda lucida	200	37±2,55*	127±1,35
Morinda lucida	400	47±2,45*	156±1,55*

4 DISCUSSION

The aim of this study was assessed the antidepressant-like effect of hydro ethanolic extract of leaves from *Morinda lucida* using animal behavioral models. A major problem in the screening for new antidepressant effect is the establishment of a valid animal model able to sufficiently and accurately identified diverse depressant treatments, without making errors of omission.[16] In that case, the forced swimming and tail suspension tests are widely accepted behavioral models for the assessment of antidepressant activity. The characteristic behavior evaluated in these tests, termed immobility, has been considered to reflect behavioral despair similar to that seen in human depression, and it is well known that antidepressant drugs are able to reduce the immobility time in rodents.[17] It is interesting to note that the immobility shown by mice when subjected to unavoidable stress such as forced swimming test is thought to reflect a state of despair or lowered mood, which is thought to reflect depressive disorders in humans. In addition, the immobility time is reduced by treatment with antidepressant drugs.[18] There is a significant correlation between the clinical efficacy of antidepressant drugs and their potency in the FST, this was not found in any other model.[18,19] Interestingly, our data indicate that higher doses of plant extracts were more effective than smaller doses both in forced swimming and tail suspension tests.

In our present study, antidepressant-like effect of hydro ethanolic extract of leaves from *Morinda lucida* in all the classic models of depressants, where it was found to possess antidepressant-like activity comparable to the standard drug Amitriptyline. Amitriptyline acts by inhibiting norepinephrine (NE) reuptake and has been used as a standard drug in majority studies. The beneficial effect of Amitriptyline in the forced swimming test model seems to be due to increased availability of these neurotransmitters (NE) and serotonin (5HT) at the post synaptic site following reuptake inhibition.[20]

Initial hypothesis of depression has been formulated about 40 years ago, proposing that the main symptoms of depression due to functional deficiency of cerebral monoaminergic transmitters such as (NE), 5HT, and dopamine (DA) located at synapses.[21] Some studies have also shown the adaptogenic effect of the plant extract via normalization of the various stress parameters and monoaminergic levels which may provide a clue that the extract is bringing their possible antidepressant-like effect through restoration of normal monoaminergic neurotransmitters.[22]

Phytochemical screening of *Morinda lucida* leaf was found to include: Alkaloids, saponnins, tannin, anthraquinones, glycosides, anthraquinols, flavonoids, and steroids.[23,24,25,26] Saponins reduce bone loss and could act as antioxidant.[14,28] The antidepressant-like effect of the hydro ethanolic leaves from *Morinda lucida* could be due to the presence of saponins among the compounds of *Morinda lucida*. Indeed, recently, oxidative stress was linked with the pathophysiology of major depression, with significant correlations being found between the severity of depression and erythrocyte superoxide dismutase/lipoperoxidation levels.[29] Meanwhile, treatment with antidepressants reduces the oxidative stress related to depressive disorder.[30,31] Additionally, some species such as *Bacopa monneira*, *Withania somnifera* and *Asparagus racemosus*, all of which are reported to have antidepressant-like properties, also possess antioxidant activity.[32,33]

5 CONCLUSION

In the present study, we have reported antidepressant-like effect of hydro ethanolic extract of leaves from *Morinda lucida* in all the classic models such as forced swimming test (FST), measurement of locomotor activity test (OFT) and tail suspension test (TST), where it was found to possess significant antidepressant-like activity comparable to the standard drug Amitriptyline. Different kinds of the research must undertake to elucidate the mechanism of action of hydro ethanolic extract of leaves from *Morinda lucida* in the CNS, the pattern of effects were observed in these experiments suggest the involvement of norepinephrine neurotransmitters system on its antidepressant-like effect.

CONSENT

It is not applicable

Ethical Approval:

Animal Ethic committee approval has been collected and preserved by the author(s)

REFERENCES

1. World-mental-health-day. 2017. Accessed on 8 April 2019. Available https:/www.who.int/
2. Burden of Mental and Behavioural Disorders. 2001. Accessedon8April2019.Available: https:/www.who.int/
3. The Global Burden of Disease 2004. Accessed on 16 June 2012. Available online: http:/www.who.int/
4. Belmaker RH, Agam G. Major depressive disorder. N Engl J Med., 2008; 358: 55–68. doi: 10.1056/NEJMra073096.
5. Zhang ZJ. Therapeutic effects of herbal extracts and constituents in animal models of psychiatric disorders. Life Sci., 2004; 75: 1659–99. doi: 10.1016/j.lfs.2004.04.014.
6. Makinde JM, Obih PO. Screening of *Morinda lucida* leaf extract for antimalarial action on *Plasmodium berghei* in mice. *African Journal of Medicine and Medical Sciences*, 1985; 17: 59–63.
7. Karou SD, Tchacondo T, Ilboudo DP, Simpore J. Saharan Rubiaceae: a review of their traditional uses, phytochemistry and biological activities. *Pakistan Journal of Biological Sciences*, 2011; 14(3): 149–169.
8. Oliver-Bever B. *Medicinal Plants in Tropical West Africa*. Cambridge, Mass, USA: Cambridge University Press; 1986.
9. Joppa KM, Vovor A, Eklu-Gadegbeku K, Agbonon A, Aklikokou K, Gbeassor M. Effect of Morinda Lucida benth. (Rubiaceae) and Newbouldia leavis P. beauv. (Bignoniaceae) on sickling of red blood cells. *Medecine Tropicale*, 2008; 68(3): 251–256.
10. Oliver-Bever B. *Medicinal Plant in Tropical West Africa*. London, UK: Cambridge University Press, 2007.
11. SO Awe, OA Olajide, JO Adeboye, JM Makinde Some pharmacological studies on Morinda lucida Indian journal of pharmacology, 1998; 30(1): 38-42.
12. Cryan JF, Markou A, Lucki I. Assessing antidepressant activity in rodents: recent developments and future needs. Trends Pharmacol Sci., 2002; 23(5): 238–245. doi: 10.1016/S0165-6147(02)02017-5.
13. Porsolt RD, Le Pichon M, Jalfre M. Depression: a new animal model sensitive to antidepressant treatments. Nature, 2002; 266(5604): 730–732. doi: 10.1038/266730a0
14. 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: 571–625.
15. Souza G, Christina A, Cesar AB, WN. Diphenyl diselenide improves scopolamine-induced memory impairment in mice. Behav Pharmac, 2010; 21: 556-562.
16. Willner P. The validity of animal models of depression. Psychopharmacology (Berl), 1984; 83: 1–16. doi: 10.1007/BF00427414.
17. Porsolt RD, Bertin A, Jalfre M. Behavioural despair in mice: a primary screening test for antidepressants. Acrh Inter Pharmacodyn Ther., 1977; 229: 327–36.
18. Porsolt RD. Behavioral despair, Antidepressants: neurochemical, behavioral and clinical perspectives. In: Enna SJ, Malick JB, Richelson E editors. New York: Raven Press., 1981; 121–139.
19. Steru L, Chermat R, Thierry B, Simon P. The tail suspension test: a new method for screening antidepressants in mice. Psychopharmacol, 1985; 85: 367–70. doi: 10.1007/BF00428203.
20. Pal SN, Dandiya PC. Comparative study of imipramine, maprotiline, fluvoxamine, trazodone and Alprozolam in some animal models of depression. Indian J Pharmacol, 1993; 25: 204–8.
21. Schildkraut JJ. The catecholamine hypothesis of affective disorders. A review of supporting evidence. Am J Psychiat, 1965; 122: 509. doi: 10.1176/ajp.122.5.509.

22. Rai D, Bhatia G, Palit G, Pal R, Singh S, Singh HK. Adaptogenic effect of *Bacopa monniera* (brami) Pharmacol Bio Chem Behave, 2003; 75: 823. doi: 10.1016/S0091-3057(03)00156-4.
23. Nweze EI, Okafor JI, Njoku O. Antimicrobial activities of methanolic extracts of Trema guineensus (schunm and Thorn) *Morinda lucida* (Benth) used in Nigeria. Bioresearch, 2004; 2: 39–46.
24. Akinyemi KO, Mendie VE, Smith ST, Oyefolu AO, Coker AO. Screening of some medicinal plants used in southwest Nigerian traditional medicine for anti-*Salmonella typhi* activity. J Herbal Pharmacother, 2005; 5: 45–60.
25. Ajayeoba FO, Abiodun OO, Falade MO, Ogbole NO, Ashidi JS, Happi CT, et al. *In vitro* cytotoxicity studies of twenty plants used in Nigerian antimalarial ethnomedicine. Phytomedicine, 2006; 13: 295–8.
26. Ebiloma GU, Omale J, Aminu RO. Suppressive, curative and prophylactic potentials of *Morinda lucida* (Benth) against erythrocytic stage of mice infective chloroquine sensitive *Plasmodium* berghei NK-65. Br J Appl Sci Technol, 2011; 1: 131–40, 201.
27. Odugbemi T. Lagos: University of Lagos Press; A Textbook of Medicinal Plants from Nigeria, 2008.
28. Kutalek R, Prinz A. African medicinal plants. In: Yaniv Z, Bachrach U, editors. Handbook of Medicinal Plants. New Delhi: CBS Publishers, 2007.
29. Bilici M, Efe H, Köroglu MA, Uydu HA, Bekaroglu M, Deger O. Antioxidative enzyme activities and lipid peroxidation in major depression: alterations by antidepressant treatments. J Affec Disord, 2001; 64: 43–51. doi: 10.1016/S0165-0327(00)00199-3.
30. Abdalla DS, Bechara EJ. The effect of chlorpromazine and Li2CO3 on the superoxide dismutase and glutathione peroxidase activities of rat brain, liver and erythrocytes. Biochem Mol Biol Int., 1994; 34: 1085–90.
31. Khanzode SD, Dakhale GN, Khanzode SS, Saoji A, Palasodkar R. Oxidative damage and major depression: the potential antioxidant action of selective serotonin re-uptake inhibitors. Redox Rep., 2003; 8: 365–70. doi: 10.1179/135100003225003393.
32. Sairam K, Dorababu M, Goel RK, Bhattacharya SK. Antidepressant activity of standardized extract of *Bacopa monniera* in experimental models of depression in rats. Phytomedicine, 2002; 9: 207–11. doi: 10.1078/0944-7113-00116.
33. Singh GK, Garabadu D, Muruganandam AV, Joshi VK, Krishnamurthy S. Antidepressant activity of *Asparagus racemosus* in rodent models. Pharmacol Biochem Behav, 2009; 91: 283–90. doi: 10.1016/j.pbb.2008.07.010.