World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

ASSESSMENT OF ANTIDEPRESSANT EFFECT OF LEAVES FROM *PAULLINIA PINNATA* ON MICE

Bakou Niangoran François*[1], B. A. Abdoulaye[2], Guiro Hamidou[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: Bakou Niangoran François
Unit of Animal Physiology, Jean Lorougnon Guede University, Daloa, (Côte D'ivoire).

Article Received on 14/07/2020 **Article Revised on 04/08/2020** **Article Accepted on 25/08/2020**

ABSTRACT

Objective: The aim of the present study is to evaluate the antidepressant-like effect of hydro alcoholic extract of leaves from *Paullinia pinnata* in mice. Materials 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 alcohol extract of *PP* (50, 100, and 200 mg/kg) was used for two weeks treatment. To assess the antidepressant-like effect of *PP* 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 *ML* 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 *Paullinia pinnata* leaves may possess an antidepressant effect.

KEYWORDS: *Paullinia pinnata*, antidepressant, activity, mice.

INTRODUCTION

Depression is the second leading psychiatric disorder where 21 % of the world population suffers from this disease.[1] The age range is markedly decreasing from 40–50 years age range to 25–35 years age range which observed worldwide.[2] In last few decades, several drugs have been discovered to treat depression such as tricyclic antidepressants, monoamine oxidase inhibitors.[3] 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.[4] Several African medicinal plants have been reported to be useful in the treatment, management, and/or control of infectious disease, including diarrhea.[5] *Paullinia pinnata* from the *Sapindaceae* family Linn leaf, root and bark extracts are widely used in African folk medicine to treat several diseases including rheumatism, weakness, impotence,[5] ulcers, haemorrhoids, wounds,[6] malaria,[7] fever, hypertension, contraceptive,[8] syphilis,[9] convulsion,[10] typhoid,[11] and diarrhea.[12] Previous works have reported the antianalgesic and anti-inflammatory activities,[13] anxiolytic,[14] antibacterial and antioxidant,[15,16,17] antityphoidal,[18] and antidiarrheal properties of *P pinnata*.[19] The acute and subacute toxicity of the methanolic extract of the leaves of *P pinnata* was reported as well as the repeated toxicological study and cardiotoxicity of hydroalcoholic root extract.[20,21] Phytochemical studies of *P pinnata* have demonstrated the presence of phenols, alkaloids, flavonoid, sterols, tannins, and other classes of secondary metabolites.[22,23,24] Despite the fact that *P pinnata* has been intensively screened for pharmacological activities, no scientific report regarding the in vivo antidepressant activity of *P pinnata* extract has been published. That's why, the present study was undertaken to assess the possible antidepressant effects following single administration of leaves extract from *P pinnata* in mice. For this purpose, we used the forced swim test (FST), open field tests (OFT) and the tail suspension test (TST).

MATERIALS AND METHODS

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.

Extract preparation

A 100 g sample of crushed *P pinnata* 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.

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.

Drugs and chemicals

The standard drugs amitriptyline was 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).

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 [25, 26]. 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 [26] for 15 min (pretest). 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*. [26, 27]. 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 [28]. 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

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 *PP* (50, 100, and 200mg/kg body weight i.p). A single dose of *PP* 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 14^{th} 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).

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 $p < 0.001$.

RESULTS

The hydro alcohol extract of *P pinnata* showed antidepressant-like effects in animal models, namely forced swimming, measurement of locomotor activity and tail suspension tests. The extract of *P pinnata* (50, 100 and 200 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 extract 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 (50 and 200 mg/kg) was shown the satisfactory locomotion effect. At the doses of 100 and 200 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 alcohol extract of *Paullinia pinnata* in forced swimming test.

Treatment	Doses (mg/kg)	Immobility time (s)
Distilled water	0,1ml/mouse	210,5±3,58
Amitriptyline	20	38,18±1,43*
PP	50	75,3±2,15*
PP	100	63,4±1,73*
PP	200	49,5±2,12*

Table 2: Antidepressant effects of hydro alcohol extract of *Paullinia pinnata* in tail suspension test.

Treatment	Doses (mg/kg)	Immobility time (s)
Distilled water	0,1ml/mouse	201,5±2,38
Amitriptyline	20	30,08±1,49*
PP	50	71,3±2,15*
PP	100	58,4±2,53*
PP	200	60,5±2,48*

Table 3: Antidepressant effects of hydro alcohol extract of *Paullinia pinnata* in measurement of locomotor activity.

Treatment	Doses (mg/kg)	Rearing	Number of square traversed
Distilled water	0,1ml/mouse	21±1,48	107,5±1,23
Amitriptyline	20	34±2,09*	210,8±1,09*
PP	50	25±1,54	101±2,48*
PP	100	36±2,12*	127±1,45
PP	200	47±2,20*	162±2,18*

DISCUSSION

The aim of this study was assessed the antidepressant-like effect of *P pinnata* 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.[29] 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.[30] 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.[31] 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.[32,31] 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 *P pinnata* 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.[33]

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.[34] 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.[35]

The phytochemical screening of the ethanolic crude extracts of P. pinnata revealed the presence of active chemical compounds (phenols, tannins, alkaloids, saponins, anthraquinons, steroids and flavonoids) with antibacterial properties,[18] Moreover, the results obtained

by Afagnigni,[17] showed that P. pinnata leaves extract contain an important amount of total phenol responsible for its remarkable antioxidant activity exhibited. 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.[36] Meanwhile, treatment with antidepressants reduces the oxidative stress related to depressive disorder.[37,38] 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.[38,29] Therefore, it is possible that the antioxidant activity of the hydro alcohol extract from *P pinnata* may contribute to its antidepressant-like effect.

CONCLUSION

In the present study, we have reported antidepressant-like effect of *P pinnata* 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 *P pinnata* in the CNS, the pattern of effects were observed in these experiments suggest the involvement of norepinephrine neurotransmitters system on its antidepressant-like effect.

REFERENCES

1. Schechter LE, Ring RH, Beyer CE, Hughes ZA, Khawaja X, Malberg JE, Rosenzweig-Lipson S. Innovative approaches for the development of antidepressant drugs: current and future strategies. NeuroRx., 2005; 2: 590–611. doi: 10.1602/neurorx.2.4.590.
2. Nemeroff CB, Owens MJ. Treatment of mood disorders. Nat Neurosci, 2002; 5: 1068–70. doi: 10.1038/nn943.
3. Belmaker RH, Agam G. Major depressive disorder. N Engl J Med, 2008; 358: 55–68. doi: 10.1056/NEJMra073096.
4. 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.
5. Kiessoun K, Kassi Y, Oksana S, Marian B. Antidiarrheal and antimicrobial profiles extracts of the leaves from *Trichilia emetica* Vahl (Meliaceae). Asian Pac J Trop Biomed, 2015; 5: 242–248.
6. Addo-Fordjour P, Kofi AA, Durosimi BE, Akonnor D. Diversity and conservation of medicinal plants in the Bomaa community of the Brong Ahafo Region, Ghana. J Med Plants Res., 2008; 2: 226–233.
7. Agyare C, Asase A, Lechtenberg M, Niehues M, Deters A, Hensel A. An ethnopharmacological used of medicinal plants used for wound healing in Bosomtwi-Atwima-Kwanwoma area, Ghana. J Ethnopharmacol, 2009; 125: 393–403.
8. Adinortey MB, Sarfo JK, Adukpo GE, et al. Acute and sub-acute oral toxicity assessment of hydro-alcoholic root extract of *Paullinia pinnata* on haematological and biochemical parameters. Bio Med, 2012; 4: 121–125.
9. N'Guessan K, Kadja B, Zirihi GN, Traoré D, Aké-Assi L. Screening phytochimique de quelques plantes médicinales ivoiriennes utilisées en pays Kroubou (Agboville, Côte d'Ivoire), Science et Nature, 2009; 6: 1–15.
10. Focho DA, Nkeng EA, Lucha CF, Ndam WT, Afegenui A. Ethnobotanical survey of plants used to treat diseases of the reproductive system and preliminary phytochemical screening of some species of Malvaceae in Ndop Central Subdivision, Cameroon. J Med Plants Res., 2009; 3: 301–314.
11. Maiha BB, Magaji MG, Yaro AH, Hamza AH, Ahmed ST, Magaji RA. Anticonvulsant studies on *Cochlospermum tinctorium* and *Paullinia pinnata* extracts in laboratory animals. Nig J Pharm Sci., 2009; 8: 102–108.
12. Lunga PK, de Dieu Tamokou J, Fodouop SPC, Kuiate JR, Tchoumboue J, Gatsing D. Antityphoid and radical scavenging properties of the methanol extracts and compounds from the aerial part of *Paullinia pinnata*. Springerplus, 2014; 3: 302.
13. Afagnigni AD, Nyegue MA, Ndoye FC, Voundi OS, Fonkoua MC, Etoa FX. In vitro assessment of antibacterial and antioxidant activities of ethanolic leaves extracts of *Paullinia pinnata* Linn (Sapindaceae). World J Pharm Sci., 2016; 4: 173–182.
14. Dingom ATP, Keugni AB, Bendegue EAJ, Dzeufiet DPD, Kamtchouing P, Dimo T. Analgesic and acute inflammatory properties of the aqueous extract of dried leaves of *Paullinia pinnata* (Sapindaceae) Linn. Int J Phytomed, 2017; 9: 490–497.
15. Aliyu M, Anuka JA, Yaro AH, Magaji MG. Evaluation of the anxiolytic effect of methanolic leaves extract of *Paullinia pinnata* Linn in mice. Br J Pharm Res., 2014; 4: 1638–1646.
16. Annan K, Gbedema S, Adu F. Antibacterial and radical scavenging activity of fatty acid from *Paullinia pinnata* Linn (Sapindaceae). Pharmacogn Mag., 2009; 5: 119–123.
17. Njimoh FO, Sofidiya MO, Afoloyan AJ. Antioxidant properties of the methanol extract from the leaves of *Paullinia pinnata* . J Med Food., 2007; 10: 707–711.
18. Ikhane D, Banwo K, Omotade O, Sanni A. Phytochemical and antimicrobial activities of methanolic extract of *Paullinia pinnata* leaves on some selected bacterial pathogens. J Herbs Spices Med Plants., 2015; 21: 59–74.
19. Voukeng IK, Beng VP, Kuete V. Antibacterial activity of six medicinal Cameroonian plants against gram-positive and gram-negative multidrug resistant

phenotypes. BMC Complement Altern Med., 2016; 16: 388.
20. Osarenmwinda I, Omonkhelin J, Ejiro D. Antidiarrhoeal activity of the methanolic extract of the leaves of *Paullina Pinnata* Linn (Sapindaceae). Int J Health, 2008; 9: 1–5.
21. Adeyemo-Salami AO, Makinde JM. Acute and sub-acute toxicity studies of the methanol extract of the leaves of *Paullinia Pinnata* (Linn) in Wistar albino mice and rats. Afr J Med Med Sci., 2013; 42: 81–90.
22. Mariame E, Aboudoulatif D, Povi LE, et al. Repeated toxicological study and cardiotoxicity of hydroalcoholic root extract of *Paullinia pinnata* L (Sapindaceae). J Appl Pharm Sci., 2016; 6: 24–28.
23. Lunga PK, Nkodo JM, Kuate JR, Gatsing D, Tchoumbe J. Post-treatment evaluation of the side effects of methanol leaf extract from *Paullinia pinnata* (Linn), an antityphoid plant. Pharmacologia., 2015; 6: 264–272.
24. Yusuf AZ, Zakir A, Shemau Z, Abdullahi M, Halima SA. Phytochemical analysis of the methanol leaves extracts of *Paullinia pinnata* Linn. J Pharmacogn Phytother, 2014; 6: 10–16.
25. 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.
26. Porsolt RD, Le Pichon M, Jalfre M. Depression: a new animal model sensitive to antidepressant treatments. Nature, 1977; 266(5604): 730–732. doi: 10.1038/266730a0.
27. 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.
28. 28 Souza G, Christina A, Cesar AB, WN. (2010) Diphenyl diselenide improves scopolamine-induced memory impairment in mice. Behav Pharmac, 2010; 21: 556-562.
29. Willner P. The validity of animal models of depression. Psychopharmacology (Berl), 1984; 83: 1–16. doi: 10.1007/BF00427414.
30. Porsolt RD, Bertin A, Jalfre M. Behavioural despair in mice: a primary screening test for antidepressants. Acrh Inter Pharmacodyn Ther., 1977; 229: 327–36.
31. 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.
32. 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.
33. 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.
34. 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.
35. 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.
36. 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.
37. 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.
38. 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.
39. 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.