Afr. J. Med. Med. Sci. (2018) 47, 133-140

Antidepressant activity of ethanol extract of *Albizia adianthifolia* (Schumach) W. F. Wight leaf in mice

N Unumadu[1], AO Aderibigbe[1] and OA Adeoluwa[2]

Department of Pharmacology and Therapeutics[1], College of Medicine, University of Ibadan, Ibadan and Department of Pharmacology[2], College of Medicine and Health Sciences, Afe Babalola University Ado-Ekiti, Nigeria

Abstract

Background: *Albizia adianthifolia* (Mimosoideae) is a medicinal plant used in the management of infections and central nervous system disorders. The presented study evaluated the antidepressant properties of the ethanol extract of *Albizia adianthifolia* leaves (EEAAL) in mice.

Methods: Pulverised leaves of *Albizia adianthifolia* were extracted with 50% ethanol by cold maceration and concentrated to dryness. Swiss mice were divided into five groups and treated with distilled water (10 mL/kg), EEAAL (1.25, 2.50, 5.00 mg/kg, i.p.) and imipramine (12 mg/kg). Antidepressant activity was assessed by force swim test (FST), tail suspension test (TST), reserpine-induced depression model and yohimbine-induced lethality test. Open field paradigm was used to screen the false results in FST and TST.

Results: The EEAAL (1.25, 2.50 mg/kg) significantly reduced immobility time in FST at dose 1.25 mg/kg (40.8 ± 13.1) and 2.50 mg/kg (42.4 ± 9.7) compared to control (170.0 ± 10.1) [$p<0.05$]. Similarly, 1.25 mg/kg of the extract significantly reduced immobility time in TST (85.2 ± 8.9) compared to control (142.6 ± 3.9) [$p<0.05$] without causing changes in spontaneous motor activity in open field. EEAAL reversed diarrhoea, ptosis, and hypothermia induced by reserpine compared with control groups and did not potentiate yohimbine-induced lethality.

Conclusion: It was concluded that the extract has antidepressant like properties which supports its ethnomedicinal use in the treatment of depression.

Keywords: *Immobility, antidepressant, Albizia adiantifolia, imipramine, reserpine*

Résumé

Contexte: Albizia adianthifolia (Mimosoideae) est une plante médicinale utilisée dans la gestion des infections, et des troubles du système nerveux central. L'étude présentée a évalué les propriétés antidépressives de l'extrait à l'éthanol des feuilles d'*Albizia adianthifolia* (EEFAA) chez les souris.

Méthodes : Des feuilles pulvérisées d'*Albizia adianthifolia* ont été extraites avec de l'éthanol à 50% par macération froide et concentrées à sec. Des souris suisses ont été divisées en cinq groupes et traitées avec de l'eau distillée (10 ml / kg), de l'EEFAA (1,25 ; 2,50 ; 5,00 mg / kg, i.p.) et de l'imipramine (12 mg / kg). L'activité antidépressive a été évaluée par le test de nage à force (TNF), le test de suspension de la queue (TSQ), modèle de dépression induite par la réserpine et le test de létalité induite par la yohimbine. Le paradigme du champ ouvert a été utilisé pour filtrer les faux résultats dans TNF et TSQ.

Résultats : L'EEFAA (1,25 ; 2,50 mg / kg) a significativement réduit le temps d'immobilité dans le TNF à la dose de 1,25 mg / kg (40,8 ± 13,1) et de 2,50 mg / kg (42,4 ± 9,7) par rapport au témoin (170,0 ± 10,1) [$p<0,05$]. De même, 1.25 mg / kg de l'extrait réduit significativement le temps d'immobilité dans le TSQ (85,2 ± 8,9) par rapport au témoin (142,6 ± 3,9) [$p<0,05$] sans provoquer de modifications de l'activité motrice spontanée en champ ouvert. EEFAA a inversé la diarrhée, la ptose et l'hypothermie induites par la réserpine par rapport aux groupes témoins et n'a pas potentialisé la létalité induite par la yohimbine.

Conclusion: Il a été conclu que l'extrait a des propriétés antidépressives qui soutiennent son utilisation ethno-médicinale dans le traitement de la dépression.

Mots-clés: *Immobilité, antidépresseur, Albizia adiantifolia, imipramine, réserpine*

Introduction

Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, decreased energy, feelings of guilt or low self-worth, disturbed sleep or appetite, and poor concentration. Sometimes, it also comes with symptoms of anxiety. These problems can become chronic or recurrent and lead to substantial impairments in an individual's ability to take care of his or her everyday responsibilities. At its worst,

Correspondence: Dr. A.O. Aderibigbe, Department of Pharmacology and Therapeutics, College of Medicine, University of Ibadan, Ibadan, Nigeria. E-mail: adebee738@yahoo.com; ao.aderibigbe@ui.edu.ng

depression can lead to suicide [1]. It is also associated with serious impairment of social, marital and occupational functioning as well as prominent and interpersonal distress [2]. According to Kessler *et al.* [2], depression is one of the most common psychiatric disorders with a life time prevalence of 10% - 20% in the general population. Women are twice at the risk of developing depression compared to men, and it is the leading cause of disease burden for women in most countries irrespective of the economic or income status [3].

Drugs used in management of depression such as monoamine oxidase inhibitors, tricyclic antidepressants, selective serotonin reuptake inhibitor, norepinephrine and dopamine reuptake inhibitors etc, act by blocking the reuptake or degradation of monoamine neurotransmitters. However, only 50-70% of the patients exhibit acceptable responses to treatment [4]. For those that do respond, therapeutic effect develops slowly (which is the major drawback in their usage), usually over several weeks of treatment [5, 6] constituting a major setback. Also, the adverse effects associated with antidepressant therapy frequently leads to discontinuation of treatment. In the search for new therapeutic products for the treatment of neurological disorders, medicinal plant research, worldwide, has progressed constantly, demonstrating the pharmacological effectiveness of different plant species in a variety of animal models [7].

Albizia adianthifolia (Schumach) W. F. Wight (Mimosoideae), known as *ayinreta* or *igbabo* in Yoruba and *kawo* in Hausa, is a big tree found in moist and tropical forest zones as well as areas that are transitional to woodland [8]. It is used ethnomedicinally to treat mental illness, pain associated with labour, river blindness, conjunctivitis, arthritis, rheumatism, parasitic infection, toothache, stomachache, allergic reactions, diarrhoea, gonorrhoea, wounds and sore feet [9, 10, 11]. In addition, some of the pharmacological activities exhibited by *A. adianthifolia* have been documented. The root extract has been shown to possess antibacterial, anti-inflammatory and anticholinesterase effects [12]. Memory-enhancing activity of the aqueous leaf extract in the 6-hydroxydopamine-lesion rodent model of Parkinson's disease has also been documented [13]. Tamokou *et al.* [14] demonstrated the antioxidant and antimicrobial activities of ethyl acetate extract, fractions and compounds from stem bark. Previous studies have shown presence of certain phytochemicals such as alkaloids, glycosides, saponins, steroids, tannins, astringents [15] and three flavonoids: okanin, melanoxetin and dihydroflavonol [16]. The aim of this study was to evaluate the antidepressant effect of ethanol extract of *A. adianthifolia* leaves (EEAAL) in mice.

Materials and methods

Collection of plant materials

The leaves of *A. adianthifolia* were collected at the Botanical Garden of the University of Ibadan, Ibadan, Oyo state, Nigeria in April, 2014. The taxonomical identification and authentication of the plant was carried out at the herbarium section of the Forestry Research Institute of Nigeria (FRIN), Ibadan, Nigeria. A voucher specimen with identification number 109833 was deposited and compared with the reference specimen.

Preparation of extract

The fresh leaves were washed in clean water and air-dried under shade for five weeks. One hundred grammes (100 g) of the air-dried leaves were pulverized and soaked in 50% ethanol (2 L) for 48 hr. The filtrate was concentrated with a rotary evaporator to give a semisolid residue and evaporated to dryness to form solid residue (23 g). It was kept in the desiccator until use. The dried extract was dissolved in distilled water and administered intraperitoneally.

Experimental animals

One hundred and fifty female Swiss mice weighing between 20 – 25 g used in this study were obtained from the Laboratory Animal Centre of the College of Medicine, University of Ibadan, Nigeria. The animals were kept in hygienic and well-ventilated compartments, maintained under standard environmental conditions and fed with standard rodent pellet (Livestock Feed PLC, Lagos, Nigeria) and water ad *libitum*. The experimental procedures adopted in this study were in accordance with the United States National Institutes of Health Guidelines for Care and Use of Laboratory Animals in Biomedical Research (NIH, 1985).

Drugs and chemicals

Yohimbine (Sigma- Aldrich St.Louis, MO, USA), reserpine (Pfizer Inc., New York, NY, USA), imipramine (Shanghai Zhongxi Pharmaceutical Co., Ltd. Shanghai, China). The chemicals were purchased by the institution from respective companies.

Acute toxicity test

The method described by Lorke [17] was used to determine the LD_{50} using thirteen female mice (20 – 25 g). This method involved an initial dose finding

procedure, in which the animals were divided into three groups of three animals each. Doses of 10, 100 and 1000 mg/kg were administered intraperitoneally (i.p.), one dose for each group. The treated animals were monitored for 24 hr for mortality and general behaviour. From the results obtained, four different doses of (200, 400, 600 and 800 mg/kg) were chosen and administered i.p. respectively to four groups of one mouse each. The treated animals were monitored for 24 hr. The LD_{50} was then calculated as the geometric mean of the highest dose showing no death and the lowest dose showing death.

Antidepressant assays

Force swimming test (FST)

The force swim test was carried out according to the method described by Porsolt *et al.* [18] and Matsuzaki *et al.* [19] with a minor modification. Female mice (20 - 25g) were assigned to five different groups of five animals each. Group 1 received distilled water (10 mL/kg), groups 2- 4 received EEAAL (1.25, 2.5 and 5 mg/kg, i.p.) respectively while group 5 which served as positive control received Imipramine (15 mg/kg, i.p.).The animals were forced to swim a day before the study in a Plexiglas cylinder (25 cm height, diameter 10 cm) containing water to a height of 10 cm maintained at a temperature of 25°C for 15 min (pre-session). On the following day (test session), thirty minutes after treatment, mice were placed back into the cylinder individually and forced to swim for 6 min. After an initial period of vigorous activity for two minutes, each animal assumed a typical immobile posture. A mouse was considered to be immobile when it remained floating in the water without struggling and making only minimum movements of its limbs necessary to keep its head above the water. The total duration of immobility was recorded during the last 4 min of the total test duration of 6 min.

Tail suspension test

The total duration of immobility following tail suspension was measured according to the method described for evaluating potential antidepressants [20]. Another set of female mice (20 - 25g) were assigned to five different groups (n = 5) and treated as in FST. Thirty min later mice were suspended on the edge of a table, 50 cm above the floor with the help of an adhesive tape placed approximately 1 cm from the tip of the tail. Immobility time was recorded during the last 4 min of the total duration of 6 min in different groups Mice are considered to be immobile when they hang passively and completely motionless.

Open field test (OFT)

In order to rule out any nonspecific locomotor effect of *A. adianthifolia* on the observed antidepressant effect in the FST and TST, mice were evaluated in the open-field paradigm after pre-treatment with the same regimen as in the FST or TST. Their locomotor activities (crossing activity) were evaluated in the open field paradigm. Before each test, animals were kept in the test room at least 1 hr before the open-field test (OFT) for habituation. The ambulatory behaviour was assessed in open-field test as described by Rodrigues *et al.* [21]. The main apparatus consisted of square arena (50 cm × 50 cm × 40 cm) with grey surface covering every wall. The floor of the arena was divided equally into twenty-five squares (10 cm × 10 cm) marked by black lines. All animals were used only once in this test. Mice (20 - 25 g) were assigned to five different groups (n = 5) and treated as in FST. Thirty minutes after, each mouse was placed individually at the centre of the arena and allowed to explore freely. The number of squares crossed with all paws (crossing activity) were observed and counted in 5 min. The square arena was cleaned with a solution of 70% alcohol between tests and dried after occupancy by each mouse in order to hide animal clues and to prevent each mouse from being influenced by the odours present in the urine and faeces of the previous mouse.

Reserpine-induced depression

Five groups of animals were treated with reserpine (2.5 mg/kg, i.p.) 30 min after the respective drug and extract administration as stated previously in FST. The initial rectal temperature of all animals was determined before administration of reserpine. The acute effects of *A. adianthifolia* and Imipramine on reserpine-induced ptosis, hypothermia and diarrhoea were observed and recorded at 60, 120, 180 and 240 min after reserpine injection. The degree of ptosis was rated according to the following rating scale : 0, eyes open; 1, eyes one-quarter closed; 2, eyes half closed; 3, eyes three-quarters closed; 4, eyes completely closed [22]. The rectal temperature was determined by insertion of a digital thermometer to a constant depth of 2 cm into the anus of each animal. Diarrhea was assessed as previously described by Qing-Qiu [22]

Yohimbine-induced lethality test

To evaluate the involvement of noradrenergic system in the antidepressant-like effect of the extract, the yohimbine-induced lethality test was performed [23]. Mice were assigned to five different groups (n = 10) and treated as previously described for FST 30 min prior to yohimbine administration (35 mg/kg, i.p.).

The number of dead mice was recorded during a 24 h period after the injection of yohimbine and percentage mortality determined.

Statistical analysis

All data are presented as Mean ± SEM. The results were analyzed by One way analysis of variance (ANOVA), Chi square and post hoc tests (Student's-Newman-Keuls) were carried out to determine the source of significance using GraphPadInStat® Biostatistics software. The level of significance for all tests was set at $p < 0.05$.

Results

Acute toxicity test

The LD_{50} of the crude extract of *Albizia adianthifolia* was found to be 282 mg/kg i.p. body weight in mice.

Effect of EEAAL on immobility time in forced swim test (FST)

The EEAAL at 1.25 and 2.5 mg/kg significantly reduced ($p< 0.05$) immobility time of mice in FST compared to the negative control (distilled water) while 5 mg/kg did not reduce immobility time in mice. In addition, the anti-immobility effect of EEAAL (1.25 and 2.5 mg/kg) and that of imipramine are comparable ($p > 0.05$) [Fig. 1].

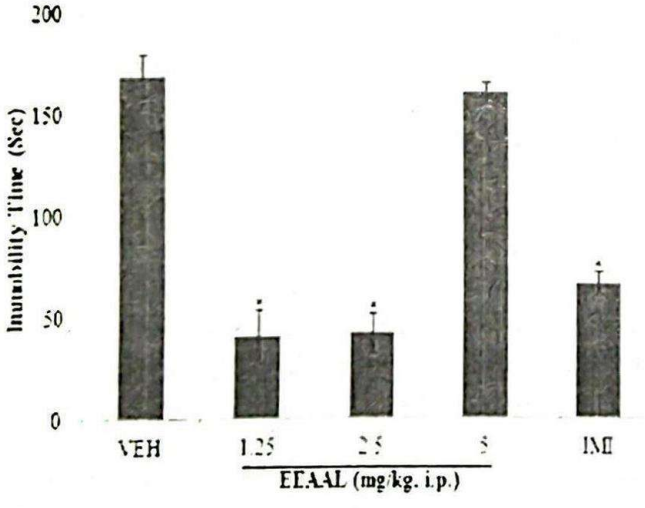

Fig. 1: Effect of *Albizia adianthifolia* on immobility time of Forced Swimming Test

* indicates significant difference from negative control ($p< 0.05$).**VEH**: Vehicle; **EEAAL**: Ethanol Extract of *Albizia adianthifolia;* **IMI**: imipramine (15 mg/kg, i.p.)

Effect of EEAAL on immobility time in tail suspension test (TST)

The EEAAL at 1.25 mg/kg significantly reduced ($p< 0.05$) immobility time of mice in TST compared to the negative control while doses at 2.5 mg/kg and 5 mg/kg did not reduce immobility time in mice. The antidepressant-like effects of EEAAL (1.25 mg/kg) and Imipramine are comparable ($p > 0.05$) [Fig. 2].

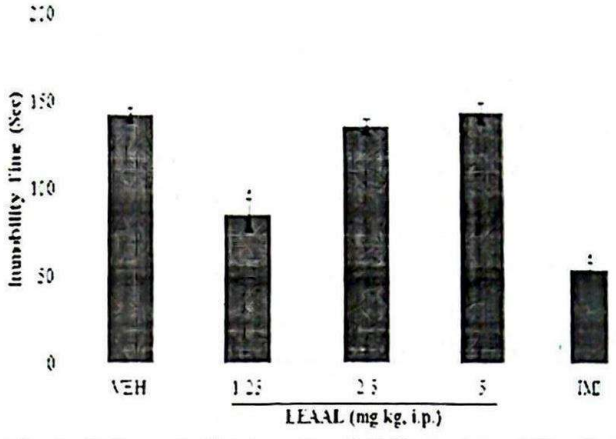

Fig. 2: Effect of *Albizia adianthifolia* on immobility time in Tail Suspension Test

* indicates significant difference from negative control ($p< 0.05$).**VEH**: Vehicle; **EEAAL**: Ethanol Extract of *Albizia adianthifolia;* **IMI**: imipramine (15 mg/kg, i.p.)

Effect of EEAAL on locomotor activity in open field test (OFT)

Treatment with EEAAL at 1.25 mg/kg and imipramine significantly reduced duration of immobility in FST and TST while 2.5 mg/kg which significantly reduced duration of immobility in FST produced no significant difference in number of crossing activity of mice in OFT ($p > 0.05$). However, the extract at 5 mg/kg significantly reduced number of line crossed ($p < 0.05$). This shows that the extract at 1.25 mg/kg and 2.5 mg/kg and imipramine did not affect locomotor activity of the animals (Fig. 3).

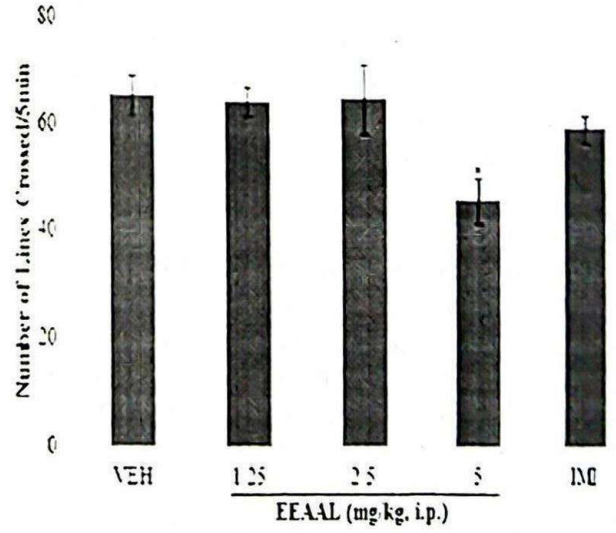

Fig. 3: Effect of EEAA on the locomotor activity of mice in open field test

* indicates significant difference from the negative control ($p< 0.05$).

VEH: Vehicle; **EEAAL**: Ethanol Extract of *Albizia adianthifolia*. **IMI**: imipramine (15 mg/kg, i.p.)

Effect of EEAAL in reserpine-induced depression

The EEAAL (1.25, 2.5, and 5 mg/kg) produced significant ($p< 0.05$) decrease in the mean watery faecal droppings (Table 1) and significantly antagonized reserpine-induced ptosis (Table 2) and hypothermia (Table 3) in all the groups compared to negative control.

Discussion

Antidepressant- like effect of ethanol extract of *A. adianthifolia* leaves was investigated in this study using the behavioural despair tests [forced swimming test (FST) and tail suspension test, (TST)], reserpine-induced depression and yohimbine induced lethality.

Table 1: Effect of EEAAL on reserpine-induced diarrhoea

Groups	DOSE(mg/kg)	Number of droppings at various time interval 60 min	120 min	180 min	240 min
VEH	10mL/kg	3.20 ± 0.66	4.20 ± 0.58	5.60 ± 0.68	6.00 ± 0.71
	1.25	2.60 ± 0.40	2.20 ± 0.37*	1.00 ± 0.45*	0.80 ± 0.20*
EEAAL	2.5	0.80 ± 0.37*	1.80 ± 0.58*	1.60 ± 0.75*	1.40 ± 0.60*
	5	1.00 ± 0.32*	1.60 ± 0.68*	1.60 ± 0.81*	1.60 ± 0.51*
IMI	15	0.80 ± 0.37*	0.80 ± 0.20*	1.60 ± 0.24*	1.60 ± 0.24*

** indicates significant difference from the negative control ($p< 0.05$).*
***VEH**: Vehicle; **EEAAL**: Ethanol Extract of Albizia adianthifolia; **IMI**: imipramine (15 mg/kg, i.p.)*

Table 2: Effect of EEAAL on reserpine-induced ptosis

Groups	Ptosis scores at various time interval Dose (mg/kg)	60 min	120 min	180 min	240 min
VEH	10mL/kg	3.20 ± 0.37	3.60 ± 0.24	3.60 ± 0.40	3.40 ± 0.40
	1.25	1.00 ± 0.55*	1.40 ± 0.60*	1.00 ± 0.45*	0.60 ± 0.40*
EEAAL	2.5	1.40 ± 0.60*	1.80 ± 0.37*	1.20 ± 0.58*	1.00 ± 0.63*
	5	1.00 ± 0.55*	1.40 ± 0.24*	1.20 ± 0.58*	1.40 ± 0.87*
IMI	15	1.00 ± 0.00*	1.00 ± 0.00*	1.00 ± 0.32*	1.00 ± 0.32*

** indicates significant difference from the negative control ($P < 0.05$).*
***VEH**: Vehicle; **EEAAL**: Ethanol Extract of Albizia adianthifolia; **IMI**: imipramine (15 mg/kg, i.p.)*

Table 3: Effect of EEAAL on reserpine-induced hypothermia

Groups	Dose (mg/kg)	Rectal Temperature (°C) at various time interval 0 min	60 min	120 min	180 min	240 min
VEH		38.26 ±0.22	38.6 6± 0.17	38.26 ± 0.22	38.52 ± 0.21	38.1S8 ±0.13
VEH+ Reserpine	10mL/kg	38.70 ± 0.30	37.46 ± 0.25*	37.02 ± 0.25*	36.48 ± 0.18*	35.96 ± 0.12*
	1.25	38.56± 0.19	38.30 ± 0.21	38.48 ± 0.12	38.50 ± 0.04	38.58 ± 0.28
EEAAL	2.5	38.52 ± 0.24	38.52 ± 0.15	38.28 ± 0.25	38.58 ± 0.29	38.24 ± 0.23
	5	38.46 ± 0.15	38.52 ± 0.16	38.52 ± 0.12	38.42 ± 0.17	38.30 ± 0.19
IMI	15	38.46 ± 0.20	38.46 ± 0.15	38.70 ± 0.11	38.56 ± 0.14	38.30 ± 0.22

** indicates significant difference from the negative control ($p< 0.05$).*
***VEH**: Vehicle; **EEAAL**: Ethanol Extract of Albizia adianthifolia; **IMI**: imipramine (15 mg/kg, i.p.)*

Effect of EEAAL on Yohimbine induced-lethality test

EEAAL (1.25, 2.5,5 mg/kg) did not significantly potentiate yohimbine-induced toxicity in mice compared to negative control. However, imipramine (15 mg/kg) produced marked significant increase in the number of death ($p< 0.05$) as compared to negative control (Table 4).

The FST and TST are widely accepted behavioural models for screening antidepressants [18, 20, 21]. The characteristic behaviour evaluated in these tests, immobility reflects behavioural despair, similar to that seen in human depression and it is a well-established fact that antidepressants reduce the immobility time in rodents [18]. These tests are quite

Table 4: Effect of *Albizia adianthifolia* on Yohimbine-induced lethality Test

Group	Dose (mg/kg)	No of death	% mortality
VEH	10 mL/kg	2/10	20
EEAAL	1.25	2/10	20
	2.5	2/10	20
	5	0/10	0
IMI	15	7/10	70 *

** indicates significant difference from the negative control ($p< 0.05$)*
VEH: Vehicle; EEAAL: Ethanol Extract of A. adianthifolia; IMI: imipramine (15 mg/kg, i.p.)

sensitive and relatively specific to all major classes of antidepressants including tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs) and monoamine oxidase inhibitors [21, 24].

In the FST, EEAAL reduced immobility compared to that of VEH, a negative control. This result shows that EEAAL by increasing duration of swimming has antidepressant effect. In the same vein, TST study shows that EEAAL treated animals showed significantly reduced immobility time, but at the lowest dose. This may not be unconnected with the sedation caused by the higher doses as shown in the open field test. The standard drug also reduced immobility time. The TST has been argued to be less stressful than FST and shows greater pharmacological sensitivity [25]. The observation of EEAAL treated animals demonstrating more mobility time suggests that it might have antidepressant property which is comparable to imipramine.

Drugs/agents which stimulate locomotor activity or cause hyperkinesia produce false positive results in FST and TST, it is therefore important to assess the influence of the test substance on the baseline spontaneous motor activity of the animals. Antidepressants would not cause general increase in locomotor activity as psychostimulants will cause hyperkinesia and produce false positive result [27]. Antidepressants such as TCAs, SSRIs and SNRIs have been shown to reduce immobility time without altering locomotor activity [26]. Therefore there is the need to carry out the open field test in order to eliminate the bias that EEAAL exerts psycho-stimulant like action on animals. The fact that EEAAL did not increase the number of line crossed in open field compared to the negative control suggests that the antidepressant action is specific. Consequent upon this observation, it can therefore be inferred that the decrease in immobility time at various doses in FST and TST are associated with the antidepressant like effect and not the locomotor enhancing or stimulant effect.

Reserpine is a vesicular re-uptake blocker which depletes catecholamines or lowers noradrenaline turnover in the brain to produce a depression like syndrome in animals [28]. Reserpine-induced depression is a model for assessing the mechanism of action of anti-depressants. Depletion of biogenic amines (noradrenaline, 5-hydroxytryptamine and dopamine) in the brain by reserpine produces effects such as ptosis, catalepsy, hypothermia and diarrhoea [29] which can be antagonized by antidepressants. Hypothermia induced by reserpine can also be antagonized by amphetamine like drugs, however, the time course is different: TCAs have a slow onset of action and a long lasting effect, whereas amphetamine like drugs have quick onset of action and a short lasting effect. In this study, reserpine-treated mice were observed for diarrhoea, ptosis and hypothermia. EAAL at all tested doses reversed these effects produced by reserpine over the period of 4 hr suggesting that its antidepressant action could be due to involvement of biogenic amines.

Potentiation of yohimbine toxicity has not only revealed antidepressant activity of compounds but also the participating system and has been reported for several antidepressants [30]. Yohimbine occupies central β_2-receptors and prevents noradrenaline from binding to these receptors leading to an increase in noradrenaline due to inhibition of the negative feedback mediated by β_2-receptors. Antagonism of α_2 receptors also causes an increase in the level of serotonin release which further contributes to the overall toxicity caused by yohimbine [31]. Simultaneous administration of yohimbine and antidepressant causes death of animal due to noradrenaline poisoning. The EAAL did not potentiate yohimbine action in this study thus precluding central adrenergic involvement in its antidepressant effect.

The antidepressant properties of the extract could be as a result of the presence of flavonoids. Though the phytochemistry of the extract was not done in the present study, previous studies have reported presence of three flavonoids: okanin, melanoxetin and dihydroflavonol [16].

Conclusion

The study has shown that the extract of the leaves of *A. Adianthiofolia* has antidepressant effect which could be due to involvement of biogenic amines. However, more studies are needed to identify the

bioactive compound and the exact mechanism of the antidepressant action.

References

1. WHO World suicide prevention day 2012. Available from: URL: http://www.who.int/mediacentre/events/annual/world_suicide_prevention_day/en/Accessed 16th june, 2012.
2. Kessler RC, Berglund P, Demler O,*et al.* The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA 2003; 289: 3095 - 3105.
3. WHO. The Global Burden of Disease 2004 updates 2008. Available from: URL:http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004. Accessed 16th june, 2012.
4. Morilak DA and Frazer A. Antidepressants and brain monoaminergic systems: a dimensional approach to understanding their behavioural effects in depression and anxiety disorders. Int. J Neuropsychopharmacol 2004; 7: 193 - 218.
5. Nestler EJ, Gould E and Manji H. Preclinical models: status of basic research in depression. Biol Psychi2002; 52: 503-528.
6. Sonawalla SB and Fava M. Severe depression: Is there a best approach? CNS Drugs 2001; 15(10): 765–776.
7. Rodrigues AS, da Silva GL, Mateussi AS, *et al.* Involvement of monoaminergic system in the antidepressant-like effect of the hydroalcoholic of *Siphocampylus verticillatus*. Life Sci 2002; 70: 1347 -58.
8. Zabala NQ. *Albizia* and Paraserianthes species.Suriqao; del Sur, Philippines: Proceedings of an international workshop held in Bislig 1997; 13–19.
9. Lemmens RHMJ. *Albizia adianthifolia* (Schumach.) W.Wight. In: Louppe D, Oteng-Amoako AA, Brink M. (Editors). Prota 7 (1): Timbers/Bois d'œuvre 1. [CD-Rom]. PROTA, Wageningen, Netherlands 2006.
10. Focho DA, Ndam WT and Fonge BA. Medicinal plants of Aguambu – Bamumbu in theLebialem highlands, southwest province of Cameroon. Afr J Pharma Pharmaco 2008; 3(1): 1- 13.
11. Lawal IO, Uzokwe NE, Igboanugo ABI, *et al.* Ethno medicinal information on collation and Identification of some medicinal plants in Research Institutes of South-west Nigeria.Afr J Pharma Pharmaco 2010; 4(1): 001-007.
12. Eldeen IMS, Elgarashi EE and Van-Staden J.Antibacterial, anti-inflammatory, anti-cholinesterase and mutagenic effects of extracts obtained from some trees used in South African traditional medicine. J Ethnopharmaco 2005; 102: 457–464.
13. Beppe GJ, Alain BD, Harquin SF, *et al.* Memory-enhancing activities of the aqueous extract of *Albizia adianthifolia* leaves in the 6-hydroxydopamine-lesion rodent model of Parkinson's disease. BMC Comple Alter Med 2014 14: 142. http://www.biomedcentral.com/1472-6882/14/142
14. Tamokou, Jean de Dieu, Deke JSM, *et al.* Antioxidant and antimicrobial activities of ethyl acetate extract, fractions and compounds from stem bark of *Albizia adianthifolia* (Mimosoideae). BMC Comple Alter Med 2012; 12: 99.
15. Burkill HM. The useful plants of west tropical Africa, 1985 V3. Available from: URL:http://www.cababstractsplus.org/abstracts/Abstract.aspx?AcNo=19986770347
16. Orwa C, Mutua A, Kindt R, Jamnadass R and Simons A. Agroforestree Database: a tree reference and selection guide version 4.02009. Available from: URL:http://www.worldagroforestry.org/af/treedb/
17. Lorke D. A new approach to practical acute toxicity testing. Arch Technol 1983; 54: 275-282.
18. Porsolt RD, Bertin A and Jalfre M. Behavioral despair in mice: A primary screening test for antidepressants. Archives Internationales de Pharmacodynamieet de Therapie 1977; 229: 327-338.
19. Matsuzaki H, Yuta S, Naohiro I, *et al.* Antidepressant-like effect of a water-soluble extract from the culture medium of *Ganoderma lucidum* mycelia in rats. BMC Comple Alter Med 2013; 13: 370.
20. Steru L, Chermat R, Thierry B and Simon P. The tail suspension test: A new method for screening antidepressants in mice. Psychopharmaco 1985; 85: 367-370.
21. Rodrigues AL, Rocha JB, Mello CF and Souza DO. Effect of perinatal lead exposure on rat behavior in open-field and two-way avoidance tasks. Pharmacol Toxicol 1996; 79: 150–156
22. Qing-Qiu M, Siu-Po Ip, Sam-Hip T and Chun-Tao C. Antidepressant-like effect of peony glycosides in mice. J Ethnopharmaco 2008; 119: 272-275.

23. Voger HG and Voger WH. Drug Discovery and Evaluation-Pharmacological Assays; antidepressant activity; Springer-Verlag:Berlin Heidelberg 1997; 411.
24. Detke MJ, Rickels M and Lucki I. Active behavior in the rat forced swimming test differentially produced by serotonergic and noradrenergic antidepressants. Psychopharmaco 1995; 121: 66-72.
25. Thierry B, Steru L, Simon P and Porsolt RD. The tail suspension test: ethical considerations. Psychopharmaco 1986; 90: 284 - 285.
26. Porsolt RD, Anton G, Blavet N and Jalfre M. Behavioural despair in rats: a new model sensitive to antidepressant treatments. Eur J Pharmacol 1978; 47: 379–391.
27. Castagne V, Porsolt RD and Moser P. Use of latency to immobility improves detection of antidepressant-like activity in the behavioral despair test in the mouse. Eur J Pharmaco. 2009. 616. 128-133.
28. Carlsson A, Lindquist M and Magnusson T. "3. 4-Dihydroxyphenylalanine and 5-hydroxytryptophan as reserpine antagonists. Nature 1957; 180: 1200.
29. Bourin M, Poncelet M, Chermat R and Simon P. "The value of the reserpine test in psychopharmacology," Arzneimittel-Forschung/ Drug Res 1983; 33 (8): 1173–1176.
30. Malick JB. Potentiation of Yohimbine-induced lethality in mice: predictor of antidepressant potential. Drug Dev Res 1983; 3: 357–363.
31. Quiuton RM. The increase in toxicity of yohimbine induced by imipramine and other drugs in mice. Br J Pharmaco 1963; 21: 51-66.