International Journal of Pharmacy and Biological Sciences
ISSN: 2321-3272 (Print), ISSN: 2230-7605 (Online)
IJPBS | Volume 8 | Issue 3 | JUL-SEPT | 2018 | 38-42
Research Article | Pharmaceutical Sciences | Open Access | MCI Approved| ज्ञान-विज्ञान विमुक्तये
|UGC Approved Journal |

ANTIDEPRESSANT ACTIVITY OF LEAF METHANOLIC EXTRACT OF N-BUTANOL FRACTION *VITEX NEGUNDO*

Kanakam Vijayabhaskar*[1], Jimidi Bhaskar[2], M. Arunadevi[3], and Ambala Rajanikanth[4]

[1]Department of Pharmacognosy, Sahasra Institute of Pharmaceutical Sciences, Warangal Telangana, India 506007.
[2]Avanthi Institute of Pharmaceutical Sciences, Gunthapally, Hayathnagar, Rangareddy Telangana, India 501512.
[3]Sri Balalaji college of Pharmacy, choppadhandi college of pharmacy, Karimnagar, Telangana, India
[4]Department of Pharmaceutics, Sahasra Institute of Pharmaceutical Sciences, Warangal Telangana, India 506007.

***Corresponding Author Email: bhaskar3743@yahoo.com**

ABSTRACT

Introduction: *Depressive disorder is a prevalent psychiatric disorder, which affects 21% of the world population. The presently using drugs can impose a variety of side-effects including cardiac toxicity, hypopiesia, sexual dysfunction, body weight gain, and sleep disorder. During the last decade, there is a growing interest in the therapeutic effects of natural products on mental disorders. Vitex negundo was investigation for antidepressant activity.* ***Methods:*** *Antidepressant activity of leaf methanolic extract of N-butanol fraction Vitex negundo (Bf-VN) was investigated by using Forced swimming test (FST) and Tail suspension test (TST) models. Escitalopram and Imipramine were used as reference standards.* ***Results:*** *It has been observed from our study that both the BFVN at higher concentration showed significant ($p<0.01$) reduction in immobility in tail suspension and forced swim model of depression comparable to Escitalopram and Imipramine.* ***Conclusion:*** *However further study is needed to understand mechanism of action and to identify active component responsible for antidepressant like activity.*

KEY WORDS

Vitex negundo, Escitalopram and Imipramine, methanol, N-Butanol.

1. INTRODUCTION

According to the World Health Organization report, mood disorders are the second leading cause worldwide of disability adjusted life years and the leading cause of years lived with disability in all ages. Each drug used to treat this disorder has a success rate of about 60%. In addition, most therapies require several weeks of treatment before improvement of signs and symptoms is observed and there are numerous side effects caused by antidepressants1. Thus, the high prevalence of depression and the fact that a significant proportion of individuals do not respond well to any currently marketed antidepressants or treatments support the need for new therapeutics to treat depression. Numerous antidepressant compounds are now available, presumably acting via different mechanisms including serotonergic, noradrenergic and/or dopaminergic systems2. Medical plant therapies may be effective alternatives in the treatment of depression and has progressed significantly in the past decade[3].

The world is gradually turning to herbal formulations which are known to be effective against a large repertoire of diseases and ailments. More importantly, they are not known to cause any notable derogatory effects [4]; and are readily availabile at affordable prices [5-6]. however, add a note of caution stating that plant remedies are effective and without side-effects,

provided they are selected properly and taken under proper medical supervision. The active component, most often a secondary metabolite, varies in quality and quantity for a given plant species growing in different locations. *Vitex negundo* Linn. (Verbenaceae) is a woody, aromatic shrub growing to a small tree. It commonly bears tri- or penta-foliate leaves on quadrangular branches, which give rise to bluish-purple coloured flowers in branched tomentose cymes. Demands of the scientific community have necessitated experimental evidence to further underline the medicinal importance of *Vn* described above. Taking cue from these traditional and folk systems of medicine, scientific studies have been designed and conducted in order to pharmacologically validate these claims. Anti-inflammatory and analgesic activity[7], Effect on oxidative stress[8], Enzyme-inhibitory activity[9], Effect on reproductive potential[10], Histomorphological and cytotoxic effects[11], Drug potentiating ability[12], Anti-bacterial[13], Anti-filarial[14], Anti-fungal[15], Anti-larval[16], Anti-viral[17], Insecticidal[18], Larvicidal[19], Mosquito repellant [20].

Therefore, the present work aimed to evaluate firstly the antidepressant-like effect of the leaf methanolic extract of N-butanol fraction *Vitex negundo* in the models predictive of antidepressant action,

2. METHODS

2.1. Collection of Plant Material and Extraction

The fresh plant of *Vitex negundo* Linn. was collected from Tirupathi hills, and was authenticated by Prof. Srinivas, Department of Botany, Kakatiya University. The whole plant was shade dried and coarsely powdered. The coarse powder was subjected to extraction with methanol by soxhlet apparatus and extract was concentrated to dryness in vacuum.

2.2. Animals

Male Swiss Wistar rats weighing 150-250 gm were acclimatized to the experimental room at temperature 23 ± 2 °C, controlled humidity conditions (50-55%) and 12 h light and 12 h dark cycle. They were caged with a maximum of two animals in polypropylene cage and were fed with standard food pellets (Kamadenu Enterprises, Bangalore) and water ad libitum. All the studies conducted according to prescribed guidelines of CPCSEA, Government of India (Reg. No. 117/1998/ CPCSEA).

2.3. Acute Toxicity Studies

Leaves methanol extract of N-Butanol fraction of *Vitex negundo* Linn (was studied for acute oral toxicity as per revised (2002) guidelines No. 423. Animals were observed for four hours hourly for behavior changes and daily for fourteen days. The extract was devoid of any toxicity in rats when given in dose up to 2000 mg/kg by oral route. Hence, for further studies 200-400 mg/kg doses of extract were used.

2.4. Antidepressant Activity

Experimental Design for anti-depressant activity:

The rats were divided five groups (n=6). Drugs/ vehicle were administered to the animals 60min prior to study.

Group I: Negative control, administer saline 2 ml/kg orally.

Group II: Positive control and receive standard drug Escitalopram (10 mg/kg orally).

Group III: Receive standard drug Imipramine (10 mg/kg orally)

Group IV: Receive (Bf-VN) 100 mg/kg orally

Group V: Receive (Bf-VN) 200 mg/kg orally

2.5.1. Forced Swim Test

For the forced swim test (FST), Rats of either sex were individually forced to swim in an open cylindrical container (diameter 10 cm, height 25 cm) containing 19 cm of water at 25±1°C. Treatment was given 60min prior to study as described by study design. All animals were forced to swim for 6 min and the duration of immobility was observed and measured during the final 4 min interval of the test. Each mouse was judged to be immobile when it ceased struggling and remained floating motionless in the water, making only those movements to keep its head above water. A decrease in the duration of immobility is indicative of an antidepressant like effect[21].

2.5.2. Tail Suspension Test[22]

The tail suspension method used in this study was similar to those described. Treatment was given 60 min prior to study as described by study design. Mice were suspended on the edge of the table, 50 cm above the floor, with the help of adhesive tape placed approximately 1 cm from the tip of the tail. The total duration of immobility induced by tail suspension was recorded during a 6 min of the 10 min period. Animal was considered to be immobile when it did not show any movement of the body, hanged passively and completely motionless.

2.5.3. Statistical Analysis

All the values were expressed as Mean ± S.E.M. the results were analyzed statistically by one-way ANOVA followed by Dunett Multiple comparison test, P<0.05 was considered significant.

3. RESULTS

3.1. Acute Toxicity Studies

Methanolic extract of *Vitex negundo* Linn. showed no behavioural changes nor mortality at dose 2000 mg/kg.

3.2. Antidepressant Activity

The antidepressant effects of leaf methanolic extract of N-butanol fraction *Vitex negundo* (100 and 200 mg/kg) and Escitalopram and imipramine were studied by observing the changes in the duration of immobility in the two models: Forced swim test (FST) and Tail suspension test (TST). In both TST and FST, (Bf-VN) 100 and 200 mg/kg, p.o. produced significant reduction (p<0.01) in the immobility period when compared with that of control group animals that received only the vehicle. The results are tabulated in Table 1.

Table 1. Effect of leaf methanolic extract of N-butanol fraction *Vitex negundo* on immobility time in Forced swim test and Tail Suspension test

Treatment	Dose (mg/kg)	forced swim test duration of immobility (sec)	Tail suspension method duration of immobility (sec)
Control	100	140.33± 6.6	152.1±0.55
Escitalopram	4	70.98±0.74	90.8±0.88
Imipramine	4	74.5±0.12	91.5±0.57
BF-VN	100	52.1±0.65	108.9±0.645
BF-VN	200	78.5±0.95	132.8±0.9

Each value represents Mean ± S.E.M., n=6. **p< 0.05 compared with control.

4. DISCUSSION

Depression is an important psychiatric disorder that affects individuals' quality of life and social relations directly. Depression is characterized by emotional symptoms such as hopelessness, apathy, loss of self-confidence, sense of guilt, indecisiveness, and amotivation, as well as biological symptoms like psychomotor retardation, loss of libido, sleep disturbances, and loss of appetite. When the symptoms are very severe, major depression is considered.

Medications such as tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), selective reversible inhibitors of monoamine oxidase A (RIMAs), and specific serotonin–noradrenaline reuptake inhibitors (SNRIs) are clinically employed for drug therapy [23]. However, these drugs can impose a variety of side-effects including cardiac toxicity, hypopiesia, sexual dysfunction, body weight gain, and sleep disorder [24-25]. Escitalopram is classical selective serotonin reuptake inhibitors SSRIs, it is bound at the primary site of pre-synaptic serotonin transporter (SERT) with a very high affinity, and it has higher serotonergic activity than the classical SSRIs [26]. Imipramine prevents reuptake of nor adrenaline and serotonin resulting in their increased availability in the synapse and therefore an increase in adrenergic and serotonergic neurotransmission[27].

In this study, we used two animal models, FST and TST. Both the paradigms are widely accepted behavioral models for assessing pharmacological antidepressant activity[28]. Characteristic behavior scored in these tests is termed immobility, reflecting behavioral despair as seen in human depression[29]. In addition, it is well known that many antidepressant drugs are able to reduce the immobility time in rodents. BFVN produced a marked reduction in immobility time at doses of 100 and 200 mg/kg in the rat FST and TST, with a profile comparable to that observed for the classical antidepressant drug ESC and imipramine. FST has not traditionally been viewed as a consistently sensitive model for detecting selective serotonin reuptake inhibitor activity, whereas these antidepressants are generally reported as active in the TST [30]. Moreover, TST is proposed to have a greater pharmacological sensitivity as compared with FST [31].

CONCLUSION

The present study provides the first evidence indicating that leaf methanolic extract of N-butanol fraction *Vitex negundo* showed significant antidepressant activity in

TST and FST models of depression. Further research is required to know the mechanism of its action.

ACKNOWLEDGMENT

The authors are thankful to Sri T.Ramesh Chairman, Sri T. Dheeraj Director, Sahasra Institute of Pharmaceutical Sciences, Waranagal, Telanagana (India) for providing facilities to carry out the research work.

REFERENCES

1. Wong, M., Licinio, J (2001). Research and treatment approaches to depression. Nat. Rev., Neurosci. 2, 343–351.
2. Elhwuegi, A.S (2004). Central monoamines and their role in major depression. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 28, 435–451.
3. Zhang, Z (2004). Therapeutic effects of herbal extracts and constituents in animal models of psychiatric disorders. Life Sci. 75, 1659–1699.
4. Kirtikar, K.R. and Basu, B.D. (1984) *Indian Medicinal Plants*, Bishen Singh Mahendra Pal Singh, Dehradun, 1984.
5. Sharma, A., Shanker, C., Tyagi, L.K., Singh, M. and Rao, C.V. (2008) 'Herbal medicine for market potential in India: An overview', Academic Journal of Plant Sciences. 1, 26-36.
6. Prajapati, D.S., Purohit, S.S., Sharma, A.K. and Kumar, T. (2004) *A Handbook of medicinal plants*, Agrobios India, Jodhpur, 2004.
7. Dharmasiri, M.G., Jayakody, J.R.A.C., Galhena, G., Liyanage, S.S.P. and Ratnasooriya, W.D. (2003) ' Anti-inflammatory and analgesic activities of mature fresh leaves of *Vitex negundo*', Journal of Ethnopharmacology. 87, 199-206.
8. Tiwari, O.P. and Tripathi, Y.B. (2007) 'Antioxidant properties of different fractions of Vitex negundo Linn', Food Chemistry. 100, 1170-1176.
9. Lodhi, A., Choudhary, I., Malik, A. and Ahmad, S. (2008) 'a-Chymotrypsin inhibition studies on the lignans from *Vitex negundo* Linn', Journal of Enzyme Inhibition and Medicinal Chemistry. 23, 400-405.
10. Bhargava, S. (1989) 'Antiandrogenic effects of a flavonoid-rich fraction of *Vitex negundo* seeds: A histological and biochemical study in dogs', Journal of Ethnopharmacology. 27, 327-339.
11. Tandon, V. and Gupta, R.K. (2004) 'Histomorphological changes induced by Vitex negundo in albino rats', Indian journal of pharmacology. 36, 176-177.
12. Tandon, V.R. and Gupta, R.K. (2006) 'Anti-inflammatory Activity and Mechanism of Action of Vitex negundo Linn', International Journal of Pharmacology. 2, 303-308.
13. Samy, R.P., Ignacimuthu, S. and Sen, A. (1998) 'Screening of 34 Indian medicinal plants for antibacterial properties', Journal of Ethnopharmacology. 62, 173-182.
14. Sahare, K.N., Anandhraman, V., Meshram, V.G., Meshram, S.U., Gajalakshmi, D., Goswami, K. and Reddy, M.V. (2008) 'In vitro effect of foue herbal plants on the motility of *Brugia malayi* microfilariae', Indian Journal of Medical Research. 127, 467-471.
15. Guleria, S. and Kumar, A. (2006) 'Antifungal activity of some Himalayan medicinal plants using direct bioautography', Journal of Cell and Molecular Biology. 5, 95-98.
16. Nathan, S.S., Kalaivani, K. and Murugan, K. (2006) 'Behavioural responses and changes in biology of rice leaffolder folowing treatment with a combination of bacterial toxins and botanical insecticides', Chemosphere. 64, 1650-1658.
17. Nguyen-Pouplin, J., Tran, H., Tran, H., Phan, T.A., Dolecek, C., Farrar, J., Tran, T.H., Caron, P., Bodo, B. and Grellier, P. (2007) 'Antimalarial and cytotoxic activities of ethnopharmacologically selected medicinal plants from South Vietnam', Journal of Ethnopharmacology. 109, 417-427.
18. Paneru, R.B. and Shivakoti, G.P. (2001) 'Use of botanicals for the management of pulse beetle (*Callosobruchus maculatus* F.) in lentil', Nepal Agriculture Research Journal. 4-5, 27-30.
19. Kamaraj, C., Rahuman, A. and Bagavan, A. (2008) 'Antifeedant and larvicidal effects of plant extracts against *Spodoptera litura* (F.), *Aedes aegypti* L. and *Culex quinquefasciatus* Say', Parasitology Research. 103, 325-331.
20. Karunamoorthi, K., Ramanujam, S. and Rathinasamy, R. (2008) 'Evaluation of leaf extracts of *Vitex negundo* L. (Family: Verbenaceae) against larvae of *Culex tritaeniorhynchus* and repellent activity on adult vector mosquitoes', Parasitology Research. 103, 545-550.
21. Porsolt, R.D., Bertin, A., Jalfre, M (1977). Behavioral despair in mice: a primary screening test for antidepressants. Arch Int Pharmacodyn Ther.229:327–36.
22. Steru, L., Chermat, R., Thierry, B., Simon, P (1985). The tail suspension test: a new method for screening antidepressants in mice. Psychopharmacology (Berl.) 85:367–70.
23. Fava, M (2003). Diagnosis and definition of treatment-resistant depression. Biol Psychiatry 53:649–59.
24. Antai-Otong, D (2004). Antidepressant-induced insomnia: treatment options. Perspect Psychiatr Care, 40:29–33.
25. Baldwin, D., Bridgman, K., Buis, C (2004). Resolution of sexual dysfunction during double-blind treatment of

major depression with reboxetine or paroxetine. J Psychopharmacol, 20:91–6.

26. Sanchez, C., Bogeso, K. P., Ebert, B., Reines, E.H., Braestrup, C (2004). Escitalopram versus citalopram: the surprising role of the R-enantiomer. Psychopharmacology 174, 163–176.
27. Tatsumi, M., Groshan, K., Blakely, R.D., Richelson,E(1997).Pharmacological profile of antidepressants and related compounds at human monoamine transporters. Eur J Pharmacol 340: 249–258.
28. Bourin, M (1990). Is it possible to predict the activity of a new antidepressant in animals with simple psychopharmacological tests. Fundam Clin Pharmacol. 4:49–64.
29. Willner, P (1984). The validity of animal models of depression. Psychopharmacology (Berl) 83:1-16.
30. Cryan, J.F., Mombereau, C., Vassout, A (2005). The tail suspension test as a model for assessing antidepressant activity: review of pharmacological and genetic studies in mice. Neurosci Biobehav Rev. 29:571–625.
31. Thierry, B., Steru, L., Simon, P., Porsolt, R.D (1986). The tail suspension test: ethical considerations. Psychopharmacology (Berl.) 90:284–5.

Received:04.05.18, Accepted: 08.06.18, Published:01.07.2018

***Corresponding Author:**
Kanakam Vijayabhaskar*
Email: bhaskar3743@yahoo.com