Research Article

Evaluation of effect of ethanolic leaf extract of Ocimum sanctum in experimental models of depression

Manu G[1*], Hema N G[2], Parashivamurthy B M[3], Kishore M S[4]

[1]Assistant Professor, Department of Pharmacology, Adichunchanagiri Institute of Medical Sciences, BGS Nagar, Nagamangala Taluk, Mandya district-571448, Karnataka, INDIA.
[2]Professor, [3]Professor and Head, [4]Assistant Professor, Department of Pharmacology, Mysore Medical College and Research Institute, Mysore, Karnataka, INDIA.
Email: drmanugigu@gmail.com

Abstract

Introduction: Depression affects 121 million people worldwide. It can affect a person's ability to work, form relationships and destroy their quality of life. Various drugs are available for the treatment of depression. Approximately two-thirds of the depressed patients respond to the currently available treatments but the magnitude of improvement is still disappointing. Since the depressive disorders are having a huge impact on our lives, it is worth evaluating the alternative forms of medicines which can be used for its treatment. So in this study, an effort was made to investigate the antidepressant effect of ethanolic extract of leaves of Ocimum Sanctum. **Aims and Objectives:** To evaluate the anti depressant activity of Ocimum Sanctum in albino mice. **Material and Method:** Swiss albino mice weighing 20 to 40gms of either sex were divided into 3 treatment groups, each group containing 6 animals and orally administered with 1% Gum acacia (control), Ocimum Sanctum 4mg/kg and 8mg/kg (test drug). A total of 36 animals were used. The duration of immobility was observed for 6minutes in Tail suspension test and Forced swimming test on a separate set of animals on 1st day, 8th day and 15th day. **Results:** The data was analyzed for statistical significance by using unpaired t test. The ethanolic extract of leaves of O. Sanctum in the above mentioned doses significantly reduced the immobility time ($p < 0.05$) in both Forced Swimming test model and Tail Suspension test models compared to control. **Conclusion:** The alcoholic extract of leaves of Ocimum Sanctum has significant antidepressant activity in acute animal models of depression.

[*]**Address for Correspondence:**
Dr. Manu G, Assistant Professor, Department of Pharmacology, Adichunchanagiri Institute of Medical Sciences, BGS Nagar, Nagamangala Taluk, Mandya district-571448, Karnataka, INDIA.
Email: drmanugigu@gmail.com
Received Date: 07/09/2014 Accepted Date: 26/09/2014

Access this article online

Quick Response Code:

Website: www.statperson.com

DOI: 27 September 2014

INTRODUCTION

Depression affects 121 million people worldwide. It can affect a person's ability to work, form relationships and destroy their quality of life. At its most, severe depression can lead to suicide and is responsible for 850,000 deaths every year. Major Depressive Episode (MDE) were elevated in high income countries (28% compared to 20%) and were especially high (over 30%) in France, the Netherlands and America. The country with the lowest incidence was China at 12% but, in contrast, MDE were very common in India (at almost 36%) [1]. Various drugs are available for the treatment of depression. They include monoamine oxidase inhibitors, selective and non selective monoamine reuptake inhibitors and selective serotonin reuptake inhibitors. These medications work by normalizing the levels of neurotransmitters, notably serotonin and nor-epinephrine. Approximately two-thirds of the depressed patients respond to the currently available treatments but the magnitude of improvement is still disappointing.[2] Indian physicians practicing Ayurveda recognized the contributions of rejuvenating herbs 5000years ago. Adaptogenic herbs are considered phytomedicines or natural product remedies based on plants. An adaptogen has the ability to increase the body's resistance to stress by stimulating a nonspecific self regulation response in adapting to stress. Adaptogens also produce an increase in the power of resistance against multiple (physical, chemical or environmental)

How to site this article: Manu G, Hema N G, Parashivamurthy B M, Kishore M S. Evaluation of effect of ethanolic leaf extract of Ocimum sanctum in experimental models of depression. *MedPulse – International Medical Journal* September 2014; 1(9): 599-602. http://www.medpulse.in (accessed 28 September 2014).

stressors. Ocimum Sanctum (Tulsi) has been used successfully in the treatment and prevention of many stress disorders.[3] Ocimum Sanctum (OS) linn, belongs to the family Labiatae popularly known as Tulsi in Hindi and Holy Basil in English.[4] Tulsi has been recognised for thousands of years to be one of India's greatest healing herbs. Tulsi in Sanskrit means **"one that is incomparable"**. It enhances general health and well being, having positive overall effects on the body and mind.[3] the entire plant of OS has medicinal value although mostly the leaves are used. The plant has hypoglycemic, hypolipidemic, antioxidant, adaptogenic, antiepileptic, hepatoprotective, antifertility, anticancer, antiasthmatic, antiemetic, diaphoretic, radioprotective, antiviral, analgesic and anti-inflammatory properties. It is also effective against dementias, antistress, Alzheimer's disease and anxiety.[4] since the depressive disorders are having a huge impact on our lives, it is worth evaluating the alternative forms of medicines which can be used for its treatment. So in this study, an effort was made to investigate the antidepressant effect of ethanolic extract of leaves of Ocimum Sanctum.

AIMS AND OBJECTIVES

To evaluate the anti depressant activity of Ocimum Sanctum in albino mice.

MATERIAL AND METHODS

Study Design

The present study was conducted at department of Pharmacology, Mysore Medical College and Research Institute, Mysore with aim to evaluate the anti depressant activity of Ocimum Sanctum in albino mice.

Materials and Solutions

1. **Chemicals:**
   a. **Ocimum Sanctum (OS):** Ethanolic extract of leaves of Ocimum Sanctum was procured from Himalaya Drug Company, Bangalore. Extraction is usually carried out by hot extraction.[5]
   b. **Gum Acacia:** it is a dried exudate from Acacia Senegal (a small tree) and certain other species of Acacia. It comes as a white powder. It is a suspending agent.[6] Used as control in the dose of 0.1 ml/10 g (1%), administered by oral route. Used as a vehicle, to suspend test drug (OS extract).
2. **Animals:** Swiss albino mice weighing around 20 to 40 g of either sex were randomly selected from central animal facility, MMC and RI, Mysore with following inclusion and exclusion criterion.

Inclusion criteria:

1. Albino mice weighing 20 to 40 g of either sex.
2. Age 3-4 months.
3. Animals acclimatized to the experimental conditions for 2 days.
4. Healthy with normal behaviour and activity.

Exclusion criteria:

1. Mice <20 g and >40 g and age <3 months and > 4 months.
2. Pregnant animals.
3. Diseased animals.
4. Animals previously used in other experiments.

The experiment was conducted in central animal facility, MMC and RI, Mysore, between 9:00 A.M. to 3:00 P.M. The experiment room was equipped with standard fluorescent lighting. The food and water was removed for the duration of test. Animals were weighed and appropriate dose of drug was administered to different groups. The experiment was conducted 1 hour after administrating the drug. A total of 36 animals (n=36) were used. They were divided into 6 groups of 6 animals each.

Methods

The methods employed here to study the antidepressant activity in albino mice are:

a. **Forced swimming test (FST)[7]**

Group I: Received 0.1 ml/10 g of gum acacia orally (Control).
Group II: Received 4 mg/kg of ethanolic extract of leaves of OS orally.
Group III: Received 8 mg/kg of ethanolic extract of leaves of OS orally.

b. **Tail suspension test (TST)[8]**

Group IV: Received 0.1 ml/10 g of gum acacia orally (Control).
Group V: Received 4 mg/kg of ethanolic extract of leaves of OS orally.
Group VI: Received 8 mg/kg of ethanolic extract of leaves of OS orally.
Data was collected analyzed by calculating mean, standard deviation and unpaired t test.

RESULTS

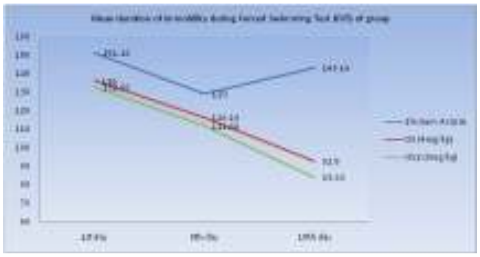
Table 1A: Mean duration of immobility during results of Forced Swimming Test (FST) of group

Day	Group I 1% Gum Acacia Mean ± SD	Group II OS (4mg/kg) Mean ± SD	Group III OS (8mg/kg) Mean ± SD
1st day	151.16 ± 17.16	136 ± 6.19	132.66 ± 11.82
8th day	129 ± 13.43	116.16 ± 13.36	111.66 ± 9.24
15th day	143.16 ± 8.95	92.5 ± 12.98	83.83±8.47

Table 1B: Comparison between control and test group on different days using unpaired t test

	Group I and II	Group I and III	Group II and III
1st day	0.069	0.054	0.553
8th day	0.127	0.026*	0.512
15th day	0.000*	0.000*	0.200

*statistically significant



ON DAY 1

There were no significant differences in durations of immobility among different groups.

ON DAY 8

The inter group comparison between Group I, II and III showed that OS 4 mg/kg and OS 8 mg/kg showed reduction in duration of immobility than control group. There was no significant difference in reduction of immobility between OS 4mg/kg and control. But between OS 4mg/kg and control the difference was significant.

ON DAY 15

It was observed that there was reduction in duration of immobility than control group. There was significant difference in reduction of immobility between OS 4mg/kg and control group and OS 8mg/kg and control group.

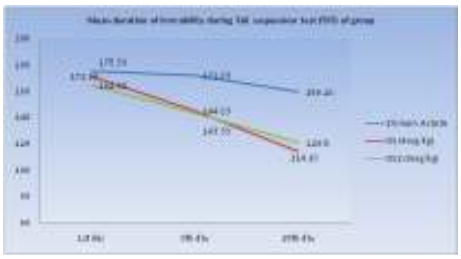
Table 2A: Mean duration of immobility during results of Tail suspension test (TST) of group

Day	Group IV 1% Gum Acacia Mean ± SD	Group V OS (4mg/kg) Mean ± SD	Group VI OS (8mg/kg) Mean ± SD
1st day	175.33 ± 11.63	171.33 ± 10.17	164.33 ± 9.22
8th day	171.83 ± 15.51	144.83 ± 13.1	143.33 ± 12.83
15th day	159.16 ± 15.67	114.16 ± 11.75	120.5 ± 10.36

Table 2B: Comparison between control and test group on different days using unpaired t test

	Group IV and V	Group IV and VI	Group V and VI
1st day	0.540	0.099	0.240
8th day	0.008*	0.006*	0.845
15th day	0.000*	0.000*	0.344

*Statistically Significant



ON DAY 1

There were no significant differences in durations of immobility among different groups.

ON DAY 8

The inter group comparison between Group IV, V and VI showed that OS 4mg/kg and OS 8 mg/kg showed highly significant reduction in duration of immobility than control group.

ON DAY 15

It was observed that there was reduction in duration of immobility than control group. There was highly significant difference in reduction of immobility between OS 4mg/kg and control group and OS 8mg/kg and control group.

DISCUSSION

The present study evaluated the antidepressant activity of ethanolic extract of leaves of Ocimum Sanctum (tulsi) in two different animal models of depression, Tail suspension test and Forced swim test. Both these methods are widely used for screening antidepressant drugs. There is a significant correlation between the potency of antidepressants in both forced-swim and Tail-suspension tests and clinical potency of the drugs[8]. These tests are quite sensitive and relatively specific to all major classes of antidepressants like tricyclics, selective serotonin reuptake inhibitors, monoamine oxidase (MAO) inhibitors and atypical antidepressants[8]. It has been argued that Tail suspension is less stressful than forced swim test and has greater pharmacological sensitivity[9]. The present study has shown that the ethanolic extract of Ocimum Sanctum at a dose of 4mg/kg and 8mg/kg significantly reduced the duration (time) of immobility of animals as compared to the control in both forced swim test and Tail suspension test of depression, showing that in both the doses, it has significant antidepressant activity. Both the tests showed consistent results in terms of reduction in the duration of immobility. The most prevalent theory for the pathogenesis of depression is "Monoamine hypothesis". Functional deficiency of central mono amines like noradrenaline, 5-hydroxytryptamine and dopamine are responsible for the symptoms of depression[10]. Many currently used antidepressants act by increasing the concentration of these neurotransmitters in the brain[11]. Evidence indicates

that OS and its active principle ursolic acid are known to increase the level of noradrenaline, 5HT and dopamine level in the brain[12, 13]. Thus, the antidepressant like activity of OS might be due its modulatory effect on central monoamines. However, the exact mechanisms underlying the antidepressant action cannot be concluded at the moment due to the presence of large number of phytochemicals viz, euginol, aigenin, luteolin, apigenin 7-glucuronide, luteolin-7-O-glucuronide, orientin, mollusdistin and two flavonoids, orientin and vicenin140 in the OS and further studies are being carried out to elucidate the same. O. sanctum has been shown to possess cortisol sparing immunostimulant and antioxidant activities. This cortisol sparing immunomodulatory activity of O. sanctum may also contribute to the behavioural disinhibitory activity[14]. The precise mechanisms by which O. sanctum produced antidepressant-like effects are not completely understood. Various antidepressant drugs, either by inhibiting MAO enzyme or by inhibiting reuptake mechanism, increase the central monoamine levels or reverse the stress-induced depressive-like behaviour. Previous studies have shown that administration of O. sanctum had a normalizing action on noise stress-induced alteration in brain monoamine neurotransmitters (norepinephrine, epinephrine, dopamine and serotonin) and controlled the alteration in neurotransmitter levels due to stress[15]. Therefore, the antidepressant activity of O. sanctum may be correlated with these studies.

CONCLUSION

In the present study, the ethanolic extract of leaves of tulsi (Ocimum Sanctum) has showed considerable antidepressant activity, in two animal models of depression i.e. forced swimming test and Tail suspension test.

REFERENCES

1. Evelyn Bromet, *et al*. Cross-National Epidemiology of DSM-IV Major Depressive Episode. BMC Medicine, July 2011.
2. Laurence L Brunton. Drug Therapy of Depression and Anxiety Disorders. Goodman and Gillman, the Pharmacological basis of Therapeutics, 11th edition, Mc Graw Hill Co 2005, 447-448.
3. Dr. Narendre Singh, Dr. Yamuna Hoette, Dr. Ralph Miller. Tulsi: The Mother Medicine of Nature. International Institute of Herbal Medicine (Lucknow, India): 2002.
4. Nadkarni K M. Indian Materia Medica. Popular Prakashan Pvt. Ltd., Bombay 1993, vol. 1: 865-866
5. N. Gopalan Kutty, G.K. Sudhakar, Extraction of phytoconstituents from plant materials, Study designs for evaluation of drugs acting on central nervous system in animals, 2009, Manipal press, 51-52
6. Cooper and Gunn's, Suspensions, Dispensing for pharmaceutical students, 1987, 12th edition, CBS publishers, 103-105.
7. Porsolt RD, Bertin A, Jalfre M. Behavioral despair in mice: a primary screening test for antidepressants. Arch Int Pharmacodyn Ther. 1977; 229(2):327-36.
8. Steru L, Chermat R, Thierry B, Simon P. The Tail suspension test: a new method for screening antidepressants in mice. Psychopharmacology (Berl). 1985; 85(3):367-70.
9. Thierry B, Steru L, Simon P, Porsolt RD. The Tail suspension test: ethical considerations. Psychopharmacology (Berl). 1986; 90(2):284-285.
10. Schildkraut JJ. The catecholamine hypothesis of affective disorders: a review of supporting evidence. Am J Psychiatry 122, 1965,: 509-522.
11. Schechter LE, Ring R. H., Beyer C. E., Hughes Z. A., Khawaja X. Malberg J. E., Rosenzweig-Lipson S. Innovative approaches for the development of antidepressant drugs: current and future strategies. NeuroRx. 2(4)2005, 590- 611.
12. Rajan Ravindran, Rathinasamy Sheela Devi, James Samson and Manohar Senthilvelan. Noise stress induced brian neurotransmitter changes and the effect of *Ocimum sanctum* (Linn) treatment in albino rats. J Pharmcol Sci 98, 2005, 354-360.
13. Delini- Stula A, Radeke E, Van Riezen H. Enhanced functional responsiveness of the dopaminergic system—the mechanism of antiimmobility effects of antidepressants in the behavioural despair test in the rat. Neuropharmacology.27 (9), 1988, 943-947.
14. Matsuoka Y, Hasegawa H, Okuda S, Muraki T, Uruno T, Kubota K. Ameliorative effects of tea catechins on active oxygen-related nerve cell injuries. J Pharmacol Exo Ther 1995; 274:602-8.
15. Ravindran R, Rathinasamy SD, Samson J, Senthilvelan M. Noise stress induced brain neurotransmitter changes and the effect of *Ocimum sanctum* (Linn) treatment in albino rats. J Pharmacol Sci 2005; 98:354-60.

Source of Support: None Declared
Conflict of Interest: None Declared