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

ISSN 2349-8870
Volume: 4
Issue: 12
634-639
Year: 2017

PHARMACOLOGICAL SCREENING OF ANTIDEPRESSANT ACTIVITY OF PLANT *TRICHOLEPIS GLABERRIMA*

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Article Received on 14/10/2017 **Article Revised on 05/11/2017** **Article Accepted on 25/11/2017**

ABSTRACT
Tricholepis glaberrima (Asteraceae), popularly known as "Brahmdandi" has been used for the treatment of variety of disease. The main objective of this research work was to evaluate the antidepressant activity of Tricholepis glaberrima in rats. The study was undertaken to evaluate the possible antidepressant effect of *Tricholepis glaberrima* aerial parts using forced swimming test and tail suspension test models of depression. Imipramine has been taken as a standard drug with a dose of 10mg/kg, Group-1(untreated), group-2 (standard) received imipramine orally. Group 3, 4 and 5 received METG at the doses of 200, 400 and 600mg/kg respectively. Methanolic extract of aerial parts of *Tricholepis glaberrima* produced significant antidepressant like effect at the dose of 600mg/kg in both models of FST and TST which indicated reduction in immobility time. The efficacy of METG at 600mg/kg found to be comparable to that of standard drug Imipramine at 10mg/kg. The results of present study indicated that methanolic extract of aerial parts of *Tricholepis glaberrima* possesses significant antidepressant activity compared to that of standard drug imipramine.

KEYWORDS: *Tricholepis glaberrima*, Forced swimming test, Tail suspension test, Methanolic extract of *Tricholepis glaberrima*, Imipramine.

INTRODUCTION
Depression is a heterogeneous psychiatric disorder.[1] This causes changes in mood, behaviour, thoughts and physical health. It is a common but serious disorder that can take away a person's ability to enjoy life and also decrease in capacity to undertake the simplest daily tasks.[2] The diagnosis of depressive disorder is carried out by changes in mood, which is characterized by either sadness or irritability and causes several psychophysiological changes, like disturbances in sleep, appetite, constipation, loss of the ability to experience pleasurable work, suicidal thoughts and both slowing of speech and actions. These changes must last a minimum of 2 weeks and interfere considerably with work and family relation.[3,4] The most common treatment for depression is medication. For example, selective serotonin reuptake inhibitors (ssris) are drugs that provide relief from some forms of depression.[5,6] By inhibiting reuptake of serotonin by serotonin transporters, Selective serotonin reuptake inhibitors (ssris) prolong the activity of this neurotransmitter at synapses in the brain. Ssris include fluoxetine (Prozac), paroxetine (paxils) and sertraline (Zoloft).[7]

Medicines from herbal sources still remain the widespread choice in the developing countries due to their ease of availability, lesser side effects and lower cost.[8] Herbal medicine has been a reasonable alternative for both treatment and management of mental disorders such as depression, anxiety and dementia etc.[9] Most antidepressants are developing from herbal sources due to their therapeutic efficacy and lower incidence of side effects.[10]

Tricholepis glaberrima belonging to the family of Asteraceae and it is popularly known as "Bhramdandi". It has been exhibited several pharmacological properties such as antioxidant[11], nervine tonic[12], aphrodisiac[13] and hepatoprotective[14] effects in experimental animal models. Aerial parts of *Tricholepis glaberrima* used in several types of diseases. Thus, the present study was designed to screen the antidepressant activity of aerial parts of *Tricholepis glaberrima.*

MATERIAL AND METHODS
Collection and authentication of plant materials
Fresh aerial parts of *Tricholepis glaberrima* were collected from the Tirupathi, and authenticated by botanist Dr. K. Madhava Chetty, at Sri Venkateshwara University, Tirupati, A.P India.

Preparation of plant extract of *Tricholepis glaberrima*
The aerial parts of *Tricholepis glaberrima* were chopped and dried in shade. It was then subjected to size

reduction by mechanical grinder. The powdered plant material was subjected to extraction by using continuous soxhlet apparatus and methanol was used for the extraction. The extract obtained was then evaporated under reduced pressure through rotary evaporator. The concentrated extract was dried on water bath then it was kept in an amber coloured container.

Drugs and chemicals

Imipramine (10mg) was used as a standard drug. All other chemicals and reagents were used for phytochemical analysis of methanolic extract of *Tricholepis glaberrima*.

Experimental animals

Healthy Albino rats 30 weighing between 200-250grams were used for the study. They were kept in polypropylene cages and allowed to acclimatize to the environment for two weeks before the commencement of the experiment. The animals were fed with standard animal pellet grower mash and allowed access to water ad libitum.

The experimental protocol was approved by the institutional animal Ethics Committee (IAEC) of CPSCEA (Committee For The Purpose of Control and Supervision of Experimental Animals). (**Reference number:** 1448/PO/Re/S/11/CPCSEA/02/2016).

Experimental study protocol

Overnight fasted animals were selected randomly on the day of experiment for administration of vehicle, standard drug (Imipramine 10mg/kg) and the test drug at the doses of (200mg/kg, 400mg/kg and 600mg/kg) respectively. The animals were acclimatized one hour before the study.

For the purpose of this study 30 Albino rats with body weights of (200-205gm) were divided into five groups, each group containing 6 animals in each, which showed in the below Table no. 1.

Table 1: Experimental study protocol of methanolic extract of *Tricholepis glaberrima.*

S.NO	Groups	Treatment	Dose (once daily) oral
1	Group-1 Control	Normal saline	0.5 ml
2	Group-2 Standard	Imipramine	10mg/kg
3	Group-3 Test -1	Methonolic Extract of *Tricholepis glaberrima* (METG1)	200mg/kg
4	Group-4 Test-2	Methonolic Extract of *Tricholepis glaberrima* (METG2)	400mg/kg
5	Group-5 Test-3	Methonolic Extract of *Tricholepis glaberrima* (METG3)	600mg/kg

Antidepressant activity

Forced swimming test (FST)

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.

Tail suspension test (TST)

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.

Statistical analysis

The values were expressed as Mean±SEM. The obtained data were analyzed by using one way ANOVA followed by Dunnett's test to calculate the significance difference among the groups. The levels of statistical significance expressed as $p<0.001$, $p<0.01$ and $p<0.05$.

RESULTS

Preliminary phytochemical examination of extract

The preliminary phytochemical analysis was done for the obtained methanolic extract of *Tricholepis glaberrima* aerial parts and the extract showed the presence of Alkaloids, carbohydrates, glycosides, tannins, steroids and flavonoids in the methanolic extract of aerial parts of *Tricholepis glaberrima*.

Effect of METG on immobility period in Tail suspension test

In this test animals were treated with three doses of METG (200mg/kg, 400mg/kg and 600mg/kg) for the screening of antidepressant effect of plant extract, and results were presented in the below **Table no. 2.** Results evaluated that the animals treated with the both doses of 200mg/kg and 400mg/kg of the crude extract showed increased in the duration of immobility when compared to that of standard drug Imipramine (10mg/kg). On the other hand the animals treated with the dose of 600mg/kg showed significant decreased in the duration of immobility and the extract exhibited its highest effect at this dose. When compared with standard drug. Moreover, less statistically significant difference were observed between the effects produced by Imipramine and 600mg/kg of the extract.

Table 2: Effect of Methonolic extract of *Tricholepis glaberrima* (METG) on Immobility time in Tail suspension test model in rats.

Group	Dose	Immobility time
Control (Normal saline)	----------	125.3 ± 13.54***
Standard (Imipramine)	10 mg/kg	59.7 ± 9.11
METG – 1	200mg/kg	89.56 ± 16.21*
METG – 2	400mg/kg	62.14 ± 11.25**
METG – 3	600mg/kg	52.62 ± 15.36**

*Values expressed Mean± SEM ***p< 0.001, **p< 0.01, *p< 0.05 when compared to Standard group. One-way ANOVA followed by Dunnett's test.*

Figure 1: Comparison graph of immobility period between control, standard and test groups.

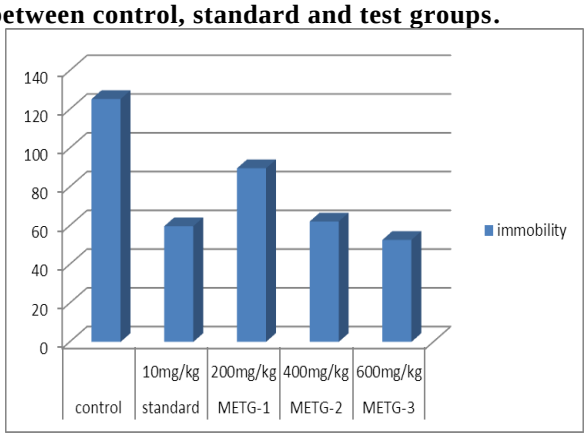

Figure 1: Comparison of the immobility time between untreated (control), standard (Imipramine 10mg/kg) and test methanolic extract of Tricholepis glaberrima (200mg/kg, 400mg/kg and 600mg/kg) groups in TST model.

Effect of METG on immobility period in Forced swimming test

The possible antidepressant effect of METG was screened by using Forced swimming test. In this test animals were treated with three different doses of METG (200mg/kg, 400mg/kg and 600mg/kg), 60min prior to the study and the immobility period was observed by the time intervals of 30min, 60min, 120min and 240min respectively and the results were showed in the below **Table no. 3.** Results revealed that there was a significant reduction in the duration of immobility time, when observed all groups of animals at the different time intervals. Thus, there was a significantly increased in the duration of immobility in groups treated with the doses of (200mg/kg and 400mg/kg) were seen, when compared to that of standard drug Imipramine (10mg/kg). Whereas the increase dose of 600mg/kg of METG was showed the significantly decreased in the duration of immobility which was compared with standard drug. Therefore, *Tricholepis glaberrima* was demonstrated significant antidepressant effect.

Table 3: Effect of Methonolic extract of *Tricholepis glaberrima* (METG) on Immobility time in Forced Swim test model in rats.

Groups	Dose	Immobility time MEAN ± SEM			
		30 min	60 min	120 min	240 min
Control (Normal saline)		135 ± 12.36*	132.2 ± 11.25*	129.2±12.3**	130.2± 15.26*
Standard (Imipramine)	10 mg/kg	75.3 ± 21.36	55.36 ± 26.54	56.32 ±19.51	65.36 ± 24.54
METG - 1	200mg/kg	98.21 ±11.45**	82.65 ± 5.25*	75.45 ± 8.21**	69.44 ± 5.56**
METG - 2	400mg/kg	88.21 ± 10.54**	78.84 ± 8.41*	70.47 ± 2.5**	65.44 ± 8.4*
METG - 3	600mg/kg	78.25 ± 11.5**	69.21 ± 10.4**	64.02 ± 5.05**	54.22 ± 4.20**

Values expressed Mean± SEM ***p< 0.001, **p< 0.01, *p< 0.05 when compared to Standard group. One-way ANOVA followed by Dunnett's test.

Figure 2: Comparison graph of immobility period between control, standard and test groups.

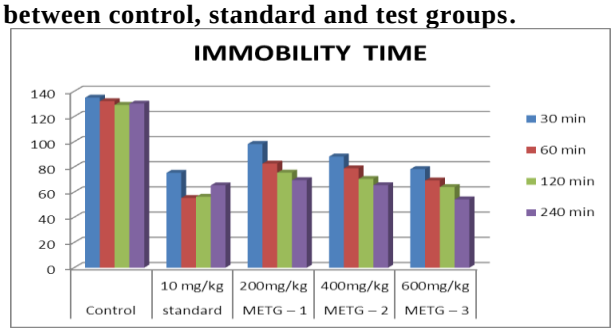

Figure 2: Comparison of the immobility time between control, standard (imipramine 10mg/kg) and test methanolic extract of Tricholepis glaberrima (200mg/kg, 400mg/kg, 600mg/kg) groups in TST model.

DISCUSSION

The prevention and management of psychiatric disorders remains a major clinical problem.[15] Depression is a heterogeneous, life threatening illness which is characterized by negative mood, decreased physical activity and feelings of helplessness and is caused by decreased levels of Monoamines like noradrenaline, dopamine and serotonin in brain.[16] These neurotransmitters are necessary for normal brain function, distruction of these neurotransmitters may cause chemical imbalance in the brain which leads to clinical condition called depression.[17] Therefore, the drugs which have the potential to enhance the reduced

levels of Monoamines (Noradrenaline, serotonin and dopamine) in the brain by both ways, first by inhibiting Monoamine oxidase enzyme and the second way is through inhibiting reuptake of those neurotransmitters which are necessary for normal brain function, may be effective in the treatment and management of depression.

Thus, now there is necessary to look for antidepressants from plants with proven advantage and favourable benefits. These plant based drugs are alternate sources of new drugs and have been shown promising results for the treatment of depression.[18]

On the basis of the above information *Tricholepis glaberrima* was selected for evaluating its antidepressant activity and the main aim of the study was to screen the pharmacological effect of the plant *Tricholepis glaberima* as an antidepressant drug.

For the purpose of the study phytochemical screening was done, indicated the presence of flavonoids, tannins, alkaloids and carbohydrates in the methanolic extract of *Tricholepis glaberrima*. It has been reported in many studies the presence of several biologically active phytochemicals such as flavonoids, glycosides, saponins and alkaloids etc, in different plant extracts were found to possess antidepressant like activity.[19]

On the basis of not only the clinical association of depression but also the stressful life events, different animal models are available for the evaluation of antidepressant drugs. The characteristic behaviour which is evaluated in those models are termed as immobility. The immobility behaviour of rodents models of depression is considered to be similar to that of depressive behaviour in human. Immobility period can be reduced by antidepressant drugs. Those drugs which can reduce the immobility period in rodent models of depression are therapeutically effective in human depression. Thus for this study both forced swim test (FST) and tail suspension test (TST) were used to screen antidepressant potential of *Tricholepis glaberrima.*

According to the results obtained from phytochemical screening of methanolic extract of *Tricholepis glaberrima* and the information collected from literature review on various plants which have been showed the therapeutic antidepressant effect, the antidepressant like potential might be due to the presence of phytochemical constituents such as alkaloids, flavonoids and glycosides. These phytochemical constituents are hydrolysed into their glycons through the mucosal and bacterial enzymes in the intestine and then converted into their conjugated metabolites during the absorption process. Transportation of these metabolites into the brain tissues through the blood brain barrier and their effect on the central nervous system (CNS) has been recently reported.[20,21] Thus these phytoconstituents might be responsible for the treatment of depression.

On the other hand Monoamine oxidase (MAO) is a flavoenzyme, in the central nervous system the primary role of monoamine oxidase (MAO) lie in the metabolism of exogeneous amines and in the regulation of intracellular amine storages. It is believed that the pathophysiology of depression is due to the decrease levels of monoamines such as serotonin, dopamine and noradrenaline in the brain. Inhibition of this enzyme (MAO) causes a reduction in metabolism and subsequent increase in the concentration of biogenic amines.[22]

Thus the methanolic extract of *Tricholepis glaberrima* contains chemical constituents like alkaloids (ephedrine), flavonoids which may act as reversible monoamine oxidase inhibitors and improves the activities of dopamine and serotonin in the brain by blocking the enzymatic breakdown of the brain chemicals by monoamine oxidase inhibition and possesses antidepressant like activity. And they promotes the transport of both dopamine and serotonin precursors into the brain by increasing the permeability of the blood brain barrier to the precursors and eliciting the antidepressant potential.[23] These mechanisms of phytochemical constituents are responsible for the antidepressant effect, thus presence of these phytochemical constituents in the methanolic extract of *Tricholepis glaberrima* might be responsible for antidepressant effect of plant.

Results showed that the administration of the methanolic extract of *Tricholepis glaberrima* produced a decrease in the immobility time of rats exposed to the both in forced swimming test (FST) and tail suspension test (TST). In the present study methanolic extract of *Tricholepis glaberrima* (METG) (200mg/kg, 400mg/kg and 600mg/kg) was administered to rats, at the dose of 600mg/kg of methanolic extract of *Tricholepis glaberrima* produced significant antidepressant like effect in both FST and TST when compared to standard drug Imipramine (10mg/kg). The reduction of immobility period in animal models of depression is due to the enhancement of monoamine neurotransmitters. Neurotransmitters are chemical messengers that are responsible for the transmission of nerve impulses between neurons. Therefore, reduction in the activities of those neurotransmitters interferes in the neuronal communication.

It has been established that the shortening of immobility time in the forced swimming test (FST) and tail suspension test (TST) depends mainly on the enhancement of central serotonin (5-HT) and Catecholamine neurotransmissions. Therefore, one of the antidepressant mechanism of *Tricholepis glaberrima* is thought to be due to the presence of flavonoids and glycosides which reaches the brain tissues through the metabolizing process protecting brain function from central nervous system (CNS) disturbances and consequently exerting an antidepressant effect.

To relieve from depression and maintain a balanced mental state, the neurotransmitters in the brain need to be restored to normal levels. This can be done either by increase their synthesis or by preventing their breakdown by inhibiting monoamine oxidase enzyme, these effects are due to the presence of phytochemicals like alkaloids, flavonoids and glycosides. Thus the above studies indicated that methanolic extract of *Tricholepis glaberrima* may have potential therapeutic value for the management of depressive disorder. Further studies would be necessary to evaluate the contribution of other active chemical constituents for the observation of antidepressant activity and determine which components will be responsible for these effects.

5. CONCLUSION

The mood changes are part of our daily life, when reactions to these situations become extreme that leads to clinical condition called depression and it is associated with lots of morbidity. Hence, it is very important to address these problems and find effective remedies. Thus the antidepressant study of *tricholepis glaberrima* was done on different groups of white albino rats at the doses of (200mg/kg, 400mg/kg and 600mg/kg) by using forced swimming test (fst) and tail suspension test (tst). Results showed that the administration of the methanolic extract of *tricholepis glaberrima* (metg) produced a decreased immobility time of rats and at the dose of 600mg/kg produced significant antidepressant like effect in both FST and TST models of depression and their efficacies were found to be comparable to Imipramine (10mg/kg). The results concluded that the shortening of immobility time in the (FST) and (TST) mainly depends on the enhancement of central 5HT and catecholamine neurotransmitters, these effects are thought to be due to the presence of chemical constituents like, alkaloids, flavonoids and glycosides. Hence *Tricholepis glaberrima* aerial parts extract possesses antidepressant effect in animal models of depression. Further investigations in this line is essential to establish its other therapeutic benefits.

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