National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Evaluation of the antidepressant activity of *Tricholepis glaberrima* bark alone and in combination with *Mimosa pudica* root extract

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Received: April 29, 2019; **Accepted:** May 24, 2019

ABSTRACT

Background: The incidence of depressive disorder statistics has increased in every year; it differs from county to county and risk factor is also differed between country and lifestyle modification, cultures. Depression is a serious health problem in worldwide including India. Due to the present utilizing antidepressant drugs, a variety of upsetting symptoms. Amid the most recent decade, the disclosure of more secure stimulant natural cures is on the rise. *Tricholepis glaberrima* has been utilized in ancient people prescription different diseases incorporating central nervous system disorders in Ayurveda. **Aims and Objectives:** The study was aimed to investigate the persistent behavioral antidepressant activity of *T. glaberrima* bark alone and in combination with *Mimosa pudica* root extract. **Materials and Methods:** Ethanolic extract of *T. glaberrima* bark and *M. pudica* root extracts was prepared followed by analysis of phytochemical constituents was determined using appropriate biochemical method, acute toxicity studies also performed, and the biological investigation of both plants extracts was conducted through pharmacological screening models (forced swimming test and tail suspension test) in Swiss albino mice. Sixty trained animals were divided into six groups, each group six animals allotted (n = 6), Groups-1 and 2 served as vehicle control and imipramine (15 mg/kg), respectively, Groups-3 and 4 were treated 200 mg/kg and 400 mg/kg of Ethanolic extract of *T. glaberrima* bark (ETGB), and Group-5 was treated ETGB 100 mg/kg and Ethanolic extract of *M. pudica* root (EMPR) 100 mg/kg extracts; Imipramine was used as reference standard control. Following 14 days chronic treatment with acute restrain stress induced. All animals were tested using behaviors depression screening models. **Results:** The study shown significant ($P < 0.0001$ [at 1% level]) improvement in chronically treated mice in both screening models. Group V shown significant improvement compare to alone ETGB treated groups. **Conclusion:** The results suggest that this combination groups can be potential antidepressant effect. However, further mechanistic studies are required to confirm the cellular action and therapeutic efficacy of ETGB and EMPR against depression.

KEY WORDS: Antidepressant; *Mimosa pudica; Tricholepis glaberrima;* Forced Swimming Test; Tail Suspension Test

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2019.9.0518724052019	

INTRODUCTION

Tricholepis glaberrima (Greek word meaning thrix, trichos = hair, and lepis, lepidos = scale; Archives de Botanique 2:515.1833) belongs to *Asteraceae* family. It is conspicuously used by ancient healers as an aphrodisiac, wound healing, and inflammation. It is rather termed with

a *phrase* "poor man's sex tonic" by numerous traditional healers. The plant distributed around hills of Mysuru, Mahabaleshwar, West Rajputana, Mount Abu, Central India Konkan, and Western Ghats in Bombay.[1]

T. glaberrima is a forceful, glabrous, very smooth, grayish, purple, bracts erect, motabor yearly herb and is famously known as Brahmadandi leaves sessile, 2.5–6.3 cm by 3–6 mm, linear, elliptical or lanceolate, intense whole, spinous, and bristle. Flowers small and slender, more or less penciled, florets few purple in terminal head Florets few purple in terminal head. *Corollas* 1.25–1.4 cm long purple.[2]

In Ayurvedic, it is *Ushna veerya* (hot in nature) *dravya* with *Tikta* (bitter), *Katu rasa* (taste) in nature. It has been stated to possess *katuvipaka* which diminishes the *kapha* and *vata dosha* predominated diseases like *Shopha* (inflammations). In the *Guhyarogadhikar* chapter of Ayurvedic treatment book *Vaidyamanorama,* the Brahmadandi has been used in distinct way.[3] It produces high-quality pleasure to male accomplice whilst intercourse. In addition, ash is mixed with oil for treating chronic non-healing wound. It is also claimed to be beneficial in hematuria such as condition, blurring micturition, and maintaining the natural color of urine in Unani systems. Review literature revealed little part of the work done in pharmacognosy, phytochemistry, and pharmacology including anticancer activity with respects to *T. glaberrima*.[4]

Ethanopharmacological survey and the traditional usage of these herbs reveal the treatment of the various diseases from the immemorial. Based on these views, the present combination of polyherbal was chosen for antidepressant evaluation. This study is aimed to test and validate the antidepressant activity of *T. glaberrima* alone and in combination of *Mimosa pudica* roots extracts, which is existing proven antidepressant agents.[5]

M. pudica is belonged to the Leguminosae family. It is a small medium-small size tree about 1.5 m in height cultivated throughout India. In Ayurvedic, whole plants are used as different ailments such as treating open wounds, bacterial infections, and a source cosmetic oil and their many places still are using cooking for its oil obtained from whole plant.

M. pudica (Chui-Mui) is one such herbal product having various pharmacological effects including antiepileptic activity, antidiabetic, antioxidants, antihepatotoxic, antioxidant, and wound healing.[6]

According to the WHO organization, depressive disorders are the next foremost cause in worldwide of inability to adjust the normal social life in all the ages.[7] Anticipated from last many years, the main pathology to illustrate and manage the depressive disorders has been based on the available pharmaceutical antidepressants drugs on monoamine hypothesis, serotonin, and norepinephrine reuptake inhibitors (SNRIs).[8] Nevertheless, the duration of lag period for a therapeutic efficacy has led to the hypothesis that cellular and molecular adaptations following therapy are necessary for their antidepressant effects. Various pharmacological agents such as antidepressants including selective serotonin reuptake inhibitors, SNRIs, and tricyclic antidepressant therapies, increase the neurogenesis and synaptic connectivity in the cortical area such as hippocampus.[9]

Psychoactive drugs, predominantly anxiolytics, and antidepressants are do not influence the therapeutic efficacy for patients with psychiatric and comorbid psychiatric ailments, it's not safe in higher doses and it produced drug-induced toxicities, unwanted side effects are listed, especially these drugs are incredible benefits and moderate costs. Natural occurring sources including plants are one of the easily available sources to test and validate novel treatment for depression, anxiety, and other disorders.

MATERIALS AND METHODS

Plant Materials and Extract Preparation

T. glaberrima bark and *M. pudica* root were collected freshly during the months of April and May (2018) from Mysuru Chamundi hill. It was taxonomically identified and was authenticated by Dr. Mruthunjaya, Department of Pharmacognosy, JSS Pharmacy College, Mysuru, and herbarium of the plant is preserved for future references (Specimen Voucher No. SA-10601 TG/MP/Pharma). The collected flower was washed and dried under shade condition at room temperature for 5–7 days. The dried flower was coarsely powdered and fine powder was separated. The coarse powder of bark (800 g) and root (800 g) was imperiled to extraction using inorganic solvents such as ethanol by Soxhlet apparatus and solvents are removed and concentrated to dryness by vacuum apparatus. Before administration, the extract was freshly prepared with normal saline and three doses (200 mg/kg, 400 mg/kg, and 100 mg/kg) were selected based on the results of the previous studies.

Experimental Animals

Female mice weighing between 22 and 30 g were randomly selected from the breeding stock of Central Animal Facility of JSS Medical College, Mysore. All were held within polypropylene cages under proper temperature (25 ± 3°C), humidity 45%–55%, and 12/12 h light/dark cycle as per Committee for the purpose of control and supervision of experiments on animals (CPCSEA) animal husbandry guidelines. We provide access to water and food *ad libitum*. Experiment animals were accustomed and skilled for a period of 7 days before grouping. Before conducting the study, clearance was taken by the Institutional Animal Ethical Committee of JSS Medical College, JSS Academy of Higher

Education, Mysuru (JSSMC/PG/13B10601), registered under Committee for the Purpose of Control and Supervision of Experiments on Animals (261/PO/ReBi/2000/CPCSEA).

Phytochemical Analysis

The extract obtained from the powdered bark of *T. glaberrima* and *M. pudica* root was subjected to phytochemical tests to determine the presence of active metabolites using standard procedures.[10]

Acute Oral Toxicity Study

According to OECD guidelines (423 – acute toxic class method), acute oral toxicity was determined.[11] Twenty-four Swiss albino mice (25–30 g b.wt.) were divided into 4 groups for EMPR and 4 groups for ETGB, each group contained three animals. ETGB and EMPR solutions were administrated orally with a maximum dose of 2000 mg/kg (ETGB) and 4000 mg/kg (EMPR), weight of the mice was recorded before dosing and once a week till end of the experiment. Lethality and abnormal clinical signs were not observed on the day of dosing and thereafter for 13 days. No serious pathological changes were also observed at the end of the experiment.

Treatment Plane

- Group I: Control group (normal saline)
- Group II: Standard (imipramine 15 mg/kg p.o)
- Group III: ETGB 200 mg/kg
- Group IV: ETGB 400 mg/kg
- Group V: ETGB (100 mg/kg) + EMPR (100 mg/kg).

T. glaberrima and *M. pudica* root extracts were administered daily for 14 constitutive days with acute restrain stress-induced mice. In groups receiving the combination of standard drug and extract, the various doses were administered concomitantly. Within the chronic dose study, the behaviors of all groups were assessed for antidepressant activity 30 min after the last treatment dose on the 14th day. Totally different standardized depression models were used for behavioral tests to evaluate the antidepressant activity, such as forced swim test (FST) and tail suspension test (TST).

Acute Restrain Stress

The test was performed to induce by subsequent methods, i.e., continuous overnight illumination (24 h); intermittent illumination (light on and off every 2 h); tilting of cage (45° with 23 h: 1 h); soiled cage (100 ml of water spilled onto the bedding: 23 h); empty water bottles (23 h: 1 h); food or water deprivation (23 h: 1 h); and cold water swimming (4°C for 5 min). Stressor methods were employed individually each day for 14 days.

FST

The FST was done as per the method defined by Porsolt *et al*. (1977).

TST

The TST was done by as per the method defined by Steru *et al*. (1985).

Statistical Analysis

The statistical test was performed by GraphPad Prism version 7; initially, data were calculated with one-way ANOVA test followed by Dunnett's multiple comparison tests were applied using the software. Mean ± standard error of mean difference was considered to be significant ($P < 0.05$) and the results were denoted by graphical representation as below.

RESULTS

Preliminary and Phytochemical Screening

On preliminary phytochemical analysis, EMPR and ETGB showed the presence of alkaloids, flavonoids, saponins, glycosides, carbohydrates, phenolic compounds, and proteins [Table 1].

Acute Oral Toxicity Study

After administration of both the extracts as per standard procedure as per OECD, no abnormal clinical signs or treatment-related deaths observed in the tested animals at dose of 4000 mg/kg (EMPR) and 2000 mg/kg (ETGB) of the extracts. No gross pathological changes were observed in the major organs of all the experimental animals. LD_{50} of both the test drugs was found to be >4000 mg/kg b.wt and was found to be safe when administrated once orally to Swiss albino mice.

Effect of the Acute Treatment of ETGB Alone and in Combination of EMPR on Antidepressant Models in Mice

The result represented in Figures 1 and 2 showed that drugs given 14 constitutive days by oral route of administration reduced the time of immobility time in FST and TST models, a behavioral profile characteristic of antidepressant-like effect. One-way ANOVA revealed a significant effect of the extract for FST (F [4, 25] = 68.43, [$P < 0.0001$]) and for TST (F [4, 35] = 25.04, [$P < 0.0001$]). The corresponding Dunnett's multiple comparison test shown a significant reduction in the immobility time in FST caused by ETGB in dose of 200 and 400 mg/kg, ($P < 0.0300$) and ($P < 0.0467$), and combined group ETGB (100 mg/kg) and EMPR (100 mg/kg) ($P < 0.0017$) as compared to control group. In case of TST, ETGB elicited significant reduction in immobility

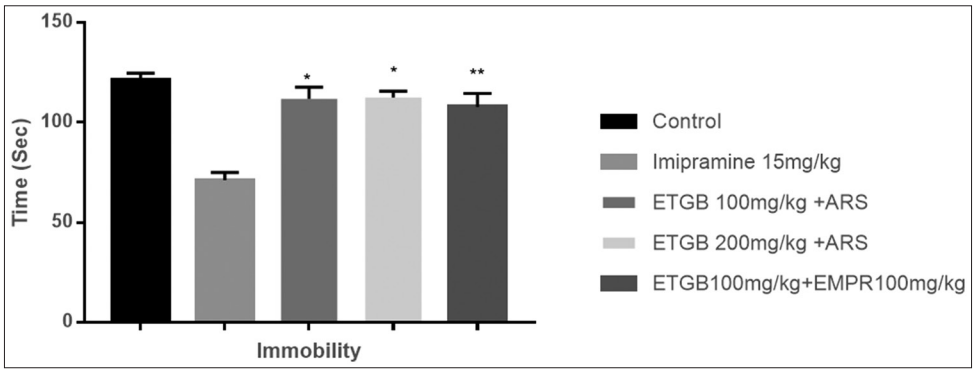

Figure 1: Result of repeated administration of ETGB (200, 400 mg/kg, and combination group p.o. [ETGB 100 mg/kg + EMPR 100 mg/kg] + acute restraint stress) for 14 days (p.o) in the forced swim test model. Each column represents the mean ± standard error of mean ($n = 6$). Statistical test was done by one-way ANOVA, followed by Dunnett's multiple comparison test. *$P < 0.01$ and **$P < 0.001$ as compared with the control group

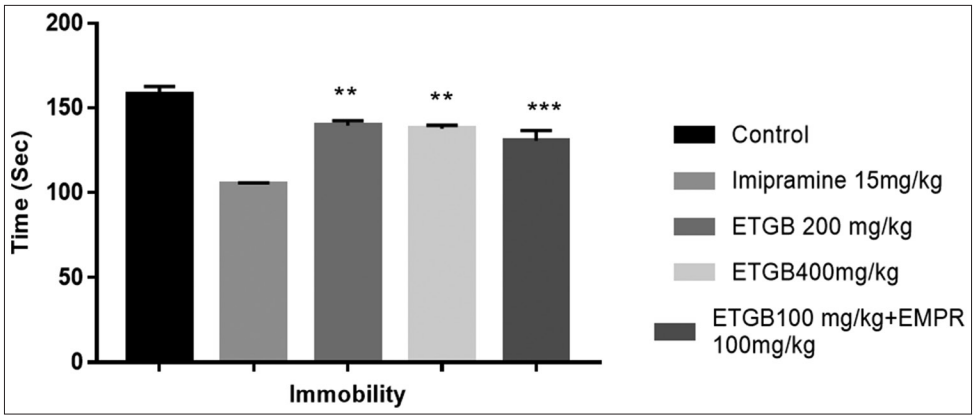

Figure 2: Result of repeated administration of ETGB (200, 400 mg/kg, and combination group p.o. [ETGB 100 mg/kg + EMPR 100 mg/kg] + acute restraint stress) for 14 days (p.o) in the forced swim test model. Each column represents the mean ± standard error of mean ($n = 6$). Statistical test was done by one-way ANOVA, followed by Dunnett's multiple comparison test. *$P < 0.01$ and **$P < 0.001$ as compared with the control group

Table 1: Biochemical analysis of the ethanolic extract of *Tricholepis glaberrima* and *Mimosa pudica* roots

Extracts	Carbohydrates	Alkaloids	Flavonoids	Saponins	Phenols	Steroids	Glycosides	Proteins
ETGB	++	++	++	++	++	+	++	+
EMPR	++	++	+	+	++	−	+	+

+: Present, −: Absent, +++: Reaction intensity is high, ++: Reaction intensity is medium, +: Reaction intensity is normal, ETGB: Ethanolic extract of *T. glaberrima* bark, EMPR: Ethanolic extract of *M. pudica* root

at the doses of 200 mg/kg and 400 mg/kg ($P < 0.087$) and ($P < 00038$), and ETGB (100 mg/kg) and EMPR (100 mg/kg) ($P < 0.0001$) as compared to control group.

DISCUSSION

Depression is a serious ailment characterized by modification in mood, lack interest within the surroundings, psychomotor retardation, and depression. It is a disorder that can affect to anyone and their possibilities to occur in adult between the ages of 20 and 50 years. With no relations to race, education standard or financial gain 12 in line in the WHO, depression affects regarding 121 million individuals worldwide and it's among the leading reason behind incapacity. Depressions square measure typically results from a mixture of things adore biological science, biochemical, environmental, and psychological factors, and typically, it will appear without apparent reason or triggers.[12]

Minor stress is usually thought to be most valuable to test rodent antidepressant model, as it parodists numerous human depressive disorders and is more valuable for studying the molecular and cellular basis of depression. In the present work, we treated that ETGB and EMPR solutions administrated for daily for 14 days p.o. shown antidepressant-like effect in the FST and TST usually used antidepressant models that forecast the efficacy of antidepressant treatment.[13] These models are based on the despair or helplessness behavior developed in animals due to some inescapable state or restriction in a

confined space and are sensitive to various antidepressant drugs. The result is confirmed that repeated administration of ETGB (200, 400 mg/kg, and combination group) for 14 days p.o had an explicit significant antidepressant-like effect in both FST and TST in models compare to control groups. Furthermore, anti-immobility effect produced by ETGB aloe and in combination with EMPR shared some pharmacological mechanisms, with established antidepressant drugs and showed a dose-dependent effect. The combination group (ETGB 100 mg/kg + EMPR 100 mg/kg) extracts shown better efficacious than individual extracts group and comparable to reference standard imipramine 15 mg/kg. This result indicated repeated administration of ETGB alone and in combination with EMPR extracts for 14 days provides significant protection against acute restraint stress-induced increase the immobility time in both the antidepressant models, which supported the findings obtained in similar studies on assessment of antidepressant-like effects.

Antidepressant effect is due to the presence of different bioactive active secondary metabolite in plant extracts, numerous studies have conveyed the manifestation of flavonoids, saponins tannins, and triterpenoids/steroids in *T. glaberrima and Mimosa pudica* roots extract as revealed from their phytochemical analysis. Flavonoids, tannins, and triterpenoids are reported to have agonist/facilitatory activities at $GABA_A$ receptor complex, which led to hypothesis that they act as benzodiazepine-like molecule.[14]

ETGB and EMPR extracts are a rich dietary supplement of flavonoid, alkaloids, glycosides, carbohydrates, proteins, saponins, steroids, and phenolic compounds might responsible for to net enhancement of depression among the patients

CONCLUSION

Ethanolic extract of *T. glaberrima* extracts shown significant antidepressant activity alone and in combination with *M. pudica* roots highly efficacious than alone treated groups and comparable to reference standard drug imipramine. Our study is declared that polyherbal formulations are better choice for the treatment of depression. Further study is required to know the cellular action for exact antidepressant activity.

ACKNOWLEDGMENT

We acknowledge the help of all the authors and the institution for the smooth conduction of this study.

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How to cite this article: Shashikumara, Neetha CS, Prathima C. Evaluation of the antidepressant activity of *Tricholepis glaberrima* bark alone and in combination with *Mimosa pudica* root extract. Natl J Physiol Pharm Pharmacol 2019;9(8):775-779.

Source of Support: Nil, **Conflict of Interest:** None declared.