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Attenuation of depression on sub acute administration of *Terminalia bellerica* fruit in tail suspension test

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Abstract

Objective: The present study was undertaken to evaluate the sub acute antidepressant activity of aqueous extract of *Terminalia Bellerica* (AETB) fruit pulp in the tail suspension test (TST) as a model of depression in albino mice. **Methods:** Inbred adult male Swiss Albino mice weighing 25-30 g were divided into 5 groups of 6 animals in each. Group 1 (Control) received Gum acasia (10 ml/kg per oral), Group II received Standard drug Imipramine (10 mg/kg per oral), Group III, IV and V received the test drug AETB in doses of 9 mg/kg, 18 mg.kg and 36 mg/kg per oral respectively. All drugs were administered once daily for 10 days t. Duration of immobility was noted in the TST model. The results were analyzed using one way ANOVA with post hoc Dennett's test. **Results:** The results showed significant reduction in the immobility with group IV (AETB given 18 mg/kg) and group V (AETB given 36 mg/kg) in comparison to the control group (1% Gum acacia) when subjected to TST, suggesting an antidepressant like activity. **Conclusion:** The results of the present study indicate the potential for use of AETB as an adjuvant in the treatment of depression.

Keywords: Tail suspension test, *Terminalia bellerica*, Imipramine

Introduction

Clinical depression is a mood disorder in which feelings of sadness, loss, anger, or frustration interferes with everyday life for a longer period of time.[1] The most common manifestations of this disorder include low irritable mood, tiredness, and sleep disturbances, lack of activity and loss of appetite or overeating. More serious negative symptoms of depression like apathy, anhedonia, feelings of worthlessness, self-hate and guilt, suicidal ideations etc. require early attention and treatment.[2]

An estimated 121 million people around the world currently suffer from some form of depression. More than 36 % of cases of major depression are reported from India. The number of patients diagnosed with depression increases by 20 %every year.[3] The exact cause of depression is still unknown, yet there are many reasons attributable- social issues like stressful life events such as death, separation, unemployment, social isolation etc. and Organic damages induced by alcohol or drug abuse, medical comorbidities due to cancers, heart diseases, stroke, obesity, insomnia, chronic pain etc. Research over the last few decades has led to newer etiologies like nutritional deficiencies, hormonal imbalances, oxidative damage leading to neurotransmitter deficiencies etc.[4, 5]

A number of herbs and plants have demonstrable effects on mood, memory, and insomnia like *Withania somnifera*, *Hypericum perforatum*, *Areca catechu*, *Bacopa monieri* and polyherbal preparations like Triphala, Mentat, Eumiletc have been studied and proven as natural remedies that can be used in depressionby virtue of their antioxidant property.[6] Triphala is an Ayurvedic formulation consisting of equal parts of three myrobalans, taken without seeds Emblica officinalis, Terminalia bellirica, and Terminalia chebula, has been used for a wide variety of ailments for generations.[7] The antidepressant activity of components aqueous extract of fruits of Emblica officinalis in mice and Terminalia chebula in rats has been studied and proven.[8,9] The third component of Triphala, *T. belerica* (BelericMyrobalan in English, Bibhitaki in Sanskrit) locally known as Bahera in India, has many important phytoconstituents like Gallo-tannic acid , bellericanin, ellagic acid, gallic acid , termilignan, thannilignan, flavone and anolignan B, Tannins, ellargic acid, ethyl gallate, galloyl glucose and chebulaginic acid, phenyllemblin, sitosterol, mannitol, glucose, fructose and rhamnose.[10,11] The fruit extract of *T. belerica* found to possess antioxidant[12], antimicrobial[12] immumomodulatory[14] and organoprotective[15] properties etc. Acute administration of aqueous extract of *T. belerica* (AETB) demonstrated promising results as an antidepressant using the tail suspension test in mice in our previous study.[15] Hence In the current study, we aim at evaluating the sub acute antidepressant property of aqueous extract *of Terminalia billerica* (AETB) fruit pulp in using the tail suspension test as an animal model of depression in mice.

Materials and Methods

Animals

The experimental protocol was approved by the Institutional Animal Ethics Committee (Approval No. IAEC/02/2013/CPCSEA) dated 05/10/2013. Adult male Swiss Albino mice weighing 25-30 grams from our breeding stock were taken in this study. The animals were housed at 24±2^{o}C with 12:12 hour light and dark cycle. They had free access to food and water *ad libitum*. The animals were acclimatized for a period of 7 days before the study. The study was conducted according to CPCSEA guidelines.

Drugs and Chemicals

The standard antidepressant drug Imipramine was procured from Himedica laboratory. The test drug *Terminalia belerica* was provided by Shri Lakshmi Ayurvedic Dispensary, Mangalore

Plant Authentication

Terminalia belerica fruit was authentified by Prof. (Dr) Krishna Kumar.G, Chairman, Dept of Applied Botany, Mangalore University, and Mangalore.

Extraction

About 1000 gms of air dried crude powder of *Terminalia belerica* fruit pulp was extracted with water in a Soxhlet extractor for 36 hours. It was dried and reduced under controlled pressure and temperature (40-50^{0}C) using a rotatory evaporator. The aqueous extract yielded a brownish mass weighing 145 gms. The yield obtained was 14.5% w/w with respect to dried powder.[10]

Experimental design

On the day of the experiment, the animals were divided randomly into control and experimental groups (n=6). Group I received the vehicle, 1% gum acacia (10 ml/kg) and served as the control group, group II received the standard drug imipramine (10 mg/kg), group III, group IV and group V received the test drug (AETB) in doses of 9,18,36 mg/kg respectively *per orally* (Table 1). The above drugs were dissolved in 1% gum acacia. All the drugs were given once daily for 10 days. The antidepressant activity of the test drug was evaluated using Tail Suspension Test.[9]

Tail Suspension Test (TST)

Mice were hung on a plastic string 38cm above the table top with an adhesive tape placed approximately 1cm from the tip of the tail. Duration of immobility time was recorded for 8 minutes. The duration of immobility was recorded during the last 6 minutes of the observation period. Mice were considered immobile only when they hung passively and completely motionless.[16-18]

Table 1: groups and dose of the drug and route of administration

Group(n=6)	**Administered drug**	**Route of administration**
I – Control	1% gum acacia (10 ml/kg)	*Per oral*
II - Standard	Imipramine (10 mg/kg)	*Per oral*
III – Test Group	AETB (9 mg/kg)	*Per oral*
IV – Test Group	AETB (18 mg/kg)	*Per oral*
V – Test Group	AETB (36 mg/kg)	*Per oral*

Statistical analysis

All the data were expressed as mean±SEM.. The data were analyzed using one-way ANOVA followed by Dennett's multiple comparison test. $P<0.05$ was considered to be statistically significant.

Results

As shown in Table 2, Imipramine the standard antidepressant drug showed a high significant ($p< 0.001$) antidepressant property. On sub acute administration AETB at the dose of 9 mg /kg (group III) the duration of immobility was decreased as compared to the control (1% Gum Acacia) but it was not significant when compared to control. Whereas, AETB at the dose of 18 mg/kg (group IV) and 36 mg/kg (group V) showed a significant decrease in the duration of immobility in mice when compared to control (1% Gum Acacia).

Table 2: Effect of AETB on Immobility Time in TST

Group	**Mean Duration of immobility (in seconds)**
I (1% gum acacia 10.0 ml/kg)	223.67 ± 7.775
II (Imipramine 10.0 mg/kg)	144.83 ± 10.550****
III (AETB 9mg/kg)	197.50 ± 17.183
IV (AETB 18mg/kg)	162.50 ± 16.589*
V (AETB 36mg/kg)	161.33 ± 18.581*

Discussion

Extensive research has substantially increased the understanding of the pathophysiology of depression. Derangement of antioxidant defense system, leading to neurotransmitter deficiencies is one of the most important mechanism in Major depression.[19] The evidence of immune inflammatory process, increased monoamine catabolism leading to oxidative stress and lipid peroxidation further supports its role in causing depression.[20] *Terminalia Bellerica* being rich in antioxidant phytoconstituents like gallic acid, tannins, flavones etc can be beneficial in replenishing the antioxidant stores. Moreover, antidepressant like effect of AETB by increasing the levels of neurotransmitters like serotonin, dopamine and norepinephrine has already been proven in one of the previous studies.[17]

The understanding of depressive episodes depends on the availability of experimental models which potentially simulates the disease. In our previous study on acute treatment of AETB in Tail suspension test (TST) and Forced swim test (FST) models showed promising results.[15] In the present study of 10 days Tail suspension model was chosen based on the fact that it is less stressful and more pharmacologically sensitive compared to Forced

swim test (FST).[21] The animals when suspended by their tail, they are subjected to the short-term, unavoidable stress leading to an immobile posture.[2] Hence, antidepressant property of *Terminalia Bellerica* fruit was evaluated in terms of reversing the immobility and promoting the occurrence of escape-related behavior . The current study revealed a significant reduction in the immobility with group IV (AETB given 18 mg/kg) and group V (AETB given 36 mg/kg) in comparison to the control group (1% Gum acacia) when subjected to TST.

The exact mechanism of antidepressant property of AETB is not clearly understood. Attenuation of immobility time with AETB extract can be attributed to its antidepressant effect by antioxidant property as well as improvement in neurotransmitter release.

Conclusion

Hence AETB proves to be a potential pharmacological agent for treating depression .However, further studies are essential to substantiate these findings.

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