ABSTRACT

Depression is a common symptom of the present day world which is widespread psychiatric disorder affecting a large number of population. It is often difficult to predict the cause and also to treat depression. In the traditional systems of medicine, many plants and formulations have been used to treat depression for thousands of years. The water extract of *Terminalia chebula* (TC) contains total phenolic and tannin content. The water extract appeared to have good antioxidant activities. It is believed that tannins have neuroprotective functions capable of reversing 6-hydroxydopamine-induced toxicity. The tannins has shown promise as a potential therapeutic agent, which may be beneficial in patients with neurological disease.

Therefore, the present study was undertaken to evaluate the antidepressant potential of acute of TC in forced swim test (FST). Inbred adult male Swiss Albino rats weighing 150-200gm were used in the study. Standard drug (imipramine) and aqueous extract of test drug (TC). The vehicle (10ml/kg, p.o), imipramine (10mg/kg, p.o) and TC (9mg/kg, 18mg/kg, 36mg/kg, p.o. respectively) were administered through prior to acute study. Duration of immobility was noted. In our study, both imipramine and TC significantly reduced the duration of immobility forced swim test (FST) as compared to the animals in the control group. The antidepressant activity of TC was comparable to that of standard drug imipramine. The results of the present study indicate the potential for use of TC as an adjuvant in the treatment of depression.

Keywords: Depression, *Terminalia chebula*, Forced swim test.

INTRODUCTION

Mental depression is a chronic illness that affects a person’s mood, thoughts and physical and behaviour and may range from very mild condition, bordering on normality to severe depression.

Depression is an affective disorder, defined as disorders of mood rather than disturbances of thought or cognition; it may range from a very mild condition, bordering on normality, to severe psychotic depression accompanied by hallucinations and delusions. The primary clinical manifestations of major depression are significant depression of mood and impairment of function. Some features of depressive disorder overlap those of the anxiety disorders, including panicagoraphobia syndrome, severe phobias, generalized anxiety disorder, social anxiety disorder, posttraumatic stress disorder, and obsessive-compulsive disorder.

Along with the classical theory of decrease in the neurotransmitter levels in the brain leading to the pathogenesis of clinical depression, recent studies have also shown the involvement of oxidative stress in the phenomenon. Recent evidence suggests that depression may be associated with neurodegeneration and reduced neurogenesis in the hippocampus. Despite the development of new molecules for pharmacotherapy of depression, it is unfortunate that this disorder goes undiagnosed and untreated in many patients. Although the currently prescribed molecules provide some improvement in the clinical condition of patients, it is at a cost of having to bear the burden of their adverse effects.

Ayurveda, the Indian traditional system of medicine, mentions a number of single and compound drug formulations of plant origin that are used in the treatment of psychiatric disorders. *Terminalia chebula* an important medicinal plant is distributed in the sub-Himalayan tracks, and the eastern, western and southern parts of India. Its fruits are extensively used as an adjuvant in medicines for various diseases with special reference to Ayurvedic medicaments. The pericarp of the dried ripe fruit is used in the preparation of many Ayurvedic formulations for infectious diseases.

*T. chebula* is reported to promote digestive power, wound healing, and is curative of ulcers, local swelling, anemia, diabetes, and chronic and recurrent fever. The fruits are astringent, purgative, laxative, gastro protective and are used to alleviate asthma, piles and coughing. *T. chebula* has been reported to exhibit a variety of biological activities, such as anti-diabetic, anti-cancer, anti-mutagenic and anti-viral activity. The water extract of *Terminalia chebula* (TC) contains total phenolic and tannin content. The water extract appeared to have good antioxidant activities. It is believed that tannins have neuroprotective functions capable of reversing 6-hydroxydopamine-induced toxicity. The tannic acid has shown promise as a potential therapeutic agent, which may be beneficial in patients with neurological disease.

Since oxidative stress and neurodegeneration is known to play a key role in depression and *T. Chebula* has antioxidant property and neuroprotective function, the present study was undertaken to evaluate the antidepressant potential of acute and chronic administration of TC in forced swim test (FST) in rats.

MATERIALS & METHODS

Animals

The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) of Yenepoya Medical College, Yenepoya University, and Mangalore, India. Adult male Swiss Albino rats weighing 150-200gm from our breeding stock were used in this study. The animals were housed at 24±2°C with 12:12 hr 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 obtained from Al Thary Enterprises, Mangalore. 1% gum acacia (vehicle).

Experimental design

On the day of the experiment, the animals were divided randomly into control and experimental groups (n=6). Group 1 received the vehicle, 1% gum acacia (10ml/kg) and served as the control group. Groups 2, 3 and 4 received the test drug (TC) in doses of 9, 18, 36mg/kg, and group 5 received the standard drug imipramine.
(10mg/kg) per orally. Drugs/vehicle was administered to the animals 60 minutes prior to the behavioural evaluation in acute study. For chronic study, a new set of animals were used. They were grouped as in acute study and were administered the drug/vehicle for a period of 10 days. Behavioural evaluation was carried out 60 minutes post drug/vehicle administration on 10th day. The antidepressant activity of the test drug was evaluated using the following experimental model of depression FST.

**Forced Swim Test (FST):** Each animal was placed individually in a 5 litre glass beakers, filled with water up to a height of 15 cm and were observed for duration of 6 minutes. The duration of immobility was recorded during the last 4 minutes of the observation period. The mouse was considered immobile when it floated motionlessly or made only those movements necessary to keep its head above the water surface. The water was changed after each test.

**Statistical analysis**

The means±SEM. values were calculated for each group. The data were analyzed using one-way ANOVA followed by Dunnet's multiple comparison test. *P<0.05* was considered to be statistically significant.

### Table: Effect of TC on immobility time in the Forced Swim Test (FST) using rats

<table>
<thead>
<tr>
<th>Group (Drug treatment)</th>
<th>Duration of Immobility (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acute Study</td>
</tr>
<tr>
<td>Group 1 (1% gum acacia 10.0 mi/kg))</td>
<td>11.6±2.58</td>
</tr>
<tr>
<td>Group 2 (TC 9mg/kg)</td>
<td>37.09±4.33**</td>
</tr>
<tr>
<td>Group 3 (TC 18mg/kg)</td>
<td>58.46±13.65**</td>
</tr>
<tr>
<td>Group 4 (TC 36mg/kg)</td>
<td>128.28±7.59*</td>
</tr>
<tr>
<td>Group 5 (Imipramine 10.0 mg/kg)</td>
<td>57.39±0.97**</td>
</tr>
</tbody>
</table>

Test solutions were administered orally 60 min prior to the test. Values represented mean±SEM. (n=6).*P>0.05, **P<0.01 vs. control.

### RESULTS

Results were given in table. A significant (P<0.01) decrease in the duration of immobility was seen with the standard drug imipramine. Whereas TC showed a significant (P<0.01) decrease in the duration of immobility at the doses of 9mg/kg and 18mg/kg as compared to the control in the acute study. In chronic study, TC in a dose of 9mg/kg has shown decrease in the duration of immobility compared to control.

### DISCUSSION

Mood disorders are one of the most common mental illnesses, with a lifetime risk of 10% in general population. Prevalence of depression alone in general population is estimated to be around 5% with suicide being one of the most common outcomes. Commonly used Antidepressants often cause adverse effects, and difficulty in tolerating these drugs is the most common reason for discontinuing an effective medication, for example the side effects of Selective Serotonin Reuptake Inhibitor (SSRIs) include: nausea, diarrhea, agitation, headaches. Sexual side-effects are also common with SSRIs. The Food and Drug Administration requires Black Box warnings on all SSRIs, which state that they double suicidal rates. Commonly used Antidepressants often cause adverse effects, and difficulty in tolerating these drugs is the most common reason for discontinuing an effective medication, for example the side effects of Selective Serotonin Reuptake Inhibitor (SSRIs) include: nausea, diarrhea, agitation, headaches. Sexual side-effects are also common with SSRIs. The Food and Drug Administration requires Black Box warnings on all SSRIs, which state that they double suicidal rates. Commonly used Antidepressants often cause adverse effects, and difficulty in tolerating these drugs is the most common reason for discontinuing an effective medication, for example the side effects of Selective Serotonin Reuptake Inhibitor (SSRIs) include: nausea, diarrhea, agitation, headaches. Sexual side-effects are also common with SSRIs. The Food and Drug Administration requires Black Box warnings on all SSRIs, which state that they double suicidal rates. Commonly used Antidepressants often cause adverse effects, and difficulty in tolerating these drugs is the most common reason for discontinuing an effective medication, for example the side effects of Selective Serotonin Reuptake Inhibitor (SSRIs) include: nausea, diarrhea, agitation, headaches. Sexual side-effects are also common with SSRIs. The Food and Drug Administration requires Black Box warnings on all SSRIs, which state that they double suicidal rates.

In the present study we have evaluated the antidepressant activity of TC in FST. The development of immobility when rodents are placed in an inescapable cylinder of water during FST reflects the cessation of their persistent escape-directed behavior. Conventional drugs reliably decrease the duration of immobility in animals during this test. This decrease in duration of immobility is considered to have a good predictive value in the evaluation of potential antidepressant agents.

In the present study, TC in the dose of 9mg/kg and 18mg/kg was superior to imipramine in acute and 9mg/kg in chronic study. Exact mechanisms underlying the antidepressant action cannot be concluded at the moment due to the presence of large number of Phytochemicals in the TC. However, the antidepressant activity may be attributed to the presence of tannic acid in the extract. Tannic acid has been shown to be a non selective inhibitor of monoamine oxidase, thereby increasing the levels of monoaminergic neurotransmitters in the brain. Another possible mechanism of action is the attenuation of oxidative stress produced during depression, by the polyphenols and tannic acid present in TC.

### REFERENCES