Phytochemical and Pharmacological Evaluation of Aegle Marmelos Plant for Antidepressant Activity in Laboratory Animals

Mr. Pravin A. Rathod, Dr. G. V. Bihani, Dr. K. R. Biyani

Abstract: India is the largest producer of medicines and medicinal plants and is rightly referred to as “the World’s Botanical Garden, and Pharmacy of World.” A variety of medicinal plants play a vital role in the health and vitality of humans and animals. The medicinal plant Aegle marmelos Linn. Belong to family Rutaceae, is commonly known as “bael” in Nepal and India, is a precious medicinal plant and is considered sacred by the Hindus and cultivated around the temples of lord shiva and it is having various spectrum of pharmacological activities. Depression is a common mental disorder and Globally estimated over the world. It is associated with persistent sadness, lack of interest, mood swings, pleasure in previously rewarding or enjoyable activities. The medicinal plant Aegle marmelos is having broad spectrum of pharmacological activities. Therefore, the objective of current investigation aims to evaluate the antidepressant activities of methanol extract of Aegle marmelos stem bark as well as its interaction with conventional antidepressant drugs using Forced Swim Test model and tail suspension test in mice.

Keywords: Antidepressant activity, Aegle Marmelos, Tail Suspension Test, Forced Swim test. Biological activity.

I. INTRODUCTION

According to Archaeologists and their evidence the use of medicinal plants dates back to the Paleolithic age, from 60,000 to 70,000 years ago. Written evidence of herbal remedies dates back over 5,000 years, to the Sumerians, who compiled lists of plants. A number of ancient cultures have written about plants and their medical uses in books called related Herbs. Over the past few decades alternative medicine has increased and a variety of studies, research has suggested that this use is greater in persons with symptoms or diagnoses of anxiety and depression, effects of some popular herbal remedies and dietary supplements, such as kava, has seems the potential and benefit greater than that for harm with short-term use in patients with mild to moderate anxiety. Hence, the evidence varies according to supplements and anxiety disorder also Doctors can collaborate with patients in dietary supplement strategies that minimize risks and maximize benefits.[1] Depression is a common and serious medical illness that negatively affects how you feel, the way you think and how you act. Fortunately, it is also treatable. Depression causes feelings of sadness or a loss of interest in activities you once enjoyed. It can lead to a variety of emotional and physical problems and can decrease your ability to function at work and at home.[2] It is a common mental disorder which is characterize by persistent sadness, lack of interest or pleasure in previously rewarding or enjoyable activities. It can also disturb sleep and appetite and lead to a variety of emotional and physical problems, and it can decrease your ability to function at work and home. The 280 million people in the world have depression and it leads to suicide. Over 700000 die due to suicide every year and suicide is the fourth leading cause of death in 15-30 years patients.[3] Aegle marmelos is also known as bael in indigenous system of medicine which is belongs to family Rutaceae and having various medicinal properties. also, it considered a sacred tree in the Indian traditional system and Hindus. Leaves are offered in prayers to shiva and Parvati since ancient time it shows various medicinal properties such as antimicrobial, anti-inflammatory, antipyretic, anti diarrheal, anticancer, anti diabetics, antifungal, analgesics etc. the methanol extract of aegle marmelos fruit shows the Immunomodulatory activity by increases in adhesion of neutrophils and an increase in phagocytic index in carbon clearance assay.[4]

Aegle marmelos having various synonyms such as bel, bael, stone apple, wood apple, holy fruit etc. it belongs into family Rutaceae Bael tree is an indigenous to India and are found in Bengal, South India, Himalayan regions, also found in Bangladesh, Nepal, Sri Lanka, Pakistan, Vietnam, Cambodia, Thailand, and Burma. In India the leaves of Aegle marmelos are offered to Indian god lord shiva and due to this reason trees are planted extensively around the temples.[33] The Hight of tree is up to 43 feet, fruit of aegle marmelos having diameter around 5 to 10 cm, flowers are pale green and 1.5 to 2cm in size also the color of bark is pale brown and or greyish. it is having the chemical constituents’ alkaloids, phenylpropanoids, terpenoids, coumarins, fatty acids, γ-sitosterol, aegelin, lupeol, rutin, marmesinin, β-sitosterol, flavone, glycoside.[34]

II. MATERIALS AND METHODS:

Preliminary phytochemical screening
1. Tests for Carbohydrates:
2. Test for alkaloids
3. Test for Phenolic compounds
4. Test of Saponins
5. Test of Flavonoids
6. Test of reducing sugars
7. Test for Tannins
8. Test for Phytosterols
9. Test for Cardiac glycoside
10. Test for Terpenoids
11. Test for Carbonyl
12. Test for Phlobatannins
13. Test for Steroids

**IAEC Approval**

In the present study, the antidepressant activity of *Aegle marmelos* was evaluated in male albino mice by force swim test and tail suspension test. Approval was obtained from Institutional Animal Ethical Committee of Anuradha College of Pharmacy, Chikhli, before commencing the experiment. Under approval number 751/PO/Re/S/03/CPCSEA

**Plant Material:**

The Steam of *Aegle marmelos* were collected from local region of Sindkhed raja buldhana district, Maharashtra, India. The species was identified and authenticated by Dr. Mustafa M. Dandu, Head of Botany Department, A.S.C. College, Badnapur and further processing was done at the Pharmacology department of Anuradha college of pharmacy Chikhli.

**Preparation of Extract:**

The Stem was dried at room temperature and made into powder using a grinding process. Powered 100g stem was extracted using soxhlation method. The filtrate obtained was concentrated under reduced pressure using rotavapor (Buchi model). The residue obtained was stored in refrigerator at 4°C until required. The extract was weighed and reconstituted daily, with distilled water according to the dosage needed (200mg/kg, & 400mg/kg) and administered orally for a period of 14 days during both models.

**Standard Drug:**

Imipramine tablets were used as a standard drug in the dose of 20 mg/kg, dissolved with distilled water and administered by oral route.

**Experimental Animal**

30 adult male albino mice weighing 20-25 g were procured from animal house of Anuradha college of pharmacy Chikhli were used for the experiment. The animals were housed in cages at room temperature with a 12 hours:12 hours light/dark cycle. They had free access to food and water. They were acclimatized to laboratory conditions for at least 1 week before starting the study. The study followed the principles of CPCSEA, and utmost care was taken while handling the animals and adequate care was provided to them during and after experimentation.

**Procedure**

The animals were divided into 4 groups of 6 animals in each group. Group I served as control, group II as standard, group III, and IV served as test groups respectively. Drugs were administered orally, using oral feeding tube fit on a 1 ml syringe, once daily in the morning for a period of 14 days, according to the groups as per the table below.

<table>
<thead>
<tr>
<th>GROUP NO.</th>
<th>GROUPS</th>
<th>SPECIES WITH GENDER (MICE)</th>
<th>NO. OF ANIMALS REQUIRED</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control Group</td>
<td>Male Albino Mice</td>
<td>06</td>
</tr>
<tr>
<td>2</td>
<td>Standard Group (Imipramine)</td>
<td>Male Albino Mice</td>
<td>06</td>
</tr>
<tr>
<td>3</td>
<td>Treatment group (200mg/kg p.o)</td>
<td>Male Albino Mice</td>
<td>06</td>
</tr>
<tr>
<td>4</td>
<td>Treatment group (400mg/kg p.o)</td>
<td>Male Albino Mice</td>
<td>06</td>
</tr>
<tr>
<td><strong>TOTAL NO. OF ANIMALS REQUIRED</strong></td>
<td></td>
<td></td>
<td>24</td>
</tr>
</tbody>
</table>

1. **Force Swim Test**

Forced swimming test (FST) or behavioral despair test is the most commonly used pharmacological model for assessing the antidepressant activity in mice. This method was adopted for the observation of animals exposed to a situation of forced swimming in which they become passive and immobile after a period of vigorous swimming activity, producing only the movements required to keep the head above the water. The forced swimming test was conducted in such a way that the mice could not support themselves by touching the bottom of the cylinder with their feet. Swimming sessions were conducted after administration of dose of drug on 1 day, 7 day and 14th day by placing mice in cylinder containing water having 27 cm depth. All mice were subjected to an initial 15 min pretest followed 25 h later by a 5 min test. The standard drug and extracts were administered three times during the period between these two sessions, first immediately after pretest session and then, after 6 and 23 h of the first dose. In both the swimming sessions, the mice were dried before placing them back in their cages. In the test period, 24 h later, the animals were exposed to experimental conditions for 5 min. The immobility period was recorded in the test session for 5 min and water in the cylinder was changed after every test. An animal is judged to be immobile whenever it remains floating passively in water in a slightly hunched but upright position with no activity but keeping its head just above the surface. All behavioral studies were recorded.
2. Tail Suspension Test

After the 10 days washout period, tail suspension was carried out for the control one by one in group wise. On day 7 and on day 14, after one hour of drug administration the tail suspension test was carried out for all the 6 animals in standard, test I, test and II at a time. The tail suspension box is a rectangular chamber made of plywood painted in brown color to provide the contrast. The dimensions of the box were height 55 cm width 90cm and depth 11.5 cm. It was divided into six chambers by placing dividers, so that each chamber had a width of 15cm. There was a provision in the roof of each compartment to hang the mice. The space in each compartment was adequate to prevent the mouse from getting into contact with the wall. The distance between the floor and the tip of nose of the suspended mouse was around 2025cms. A detachable tray was placed in the bottom of each compartment to collect the excreta. Clear hollow cylindrical plastic tubes of dimension 4 cms x 1.5cms were introduced into the tail and used as climb stoppers. An adhesive tape of length 17cm was cut for each mouse and at 2 cm from one end a mark was made. The 2cm marked portion of the tape was applied to the tip of the tail leaving 2-3 mm free and it was adhered securely. It was done for all the six animals in a group consecutively. Care was taken so that the tape is strong enough to hold the mouse’s weight, and not too sticky while removing. The camera with a timer set up was positioned in a way so that the view of the tail suspension box was not obscured, and the recording would not be interrupted. All the six mice in the group were suspended back-to-back by attaching the free end of the adhesive tape that measures 15 cm to the hook at the roof of all six compartments. Without any interruption for the next six minutes the immobility time was recorded using the camera that was already positioned. The recordings were saved at the end of six minutes. The animals were taken off the chamber; the tapes were removed with proper care. They were placed back into their cage and observed for a week. Assessment of the behavior of all animals was done from the readings. The total observation period was six minutes. Immobility time was assessed. An important facet of this assessment was to differentiate between mobile and immobile state of the animal. Behaviors that were associated with escapism like all four limb movements, attempt to touch the side walls, shaking of the body, running like movements were considered as mobility. While small movements involving the forelimb without any hind limb involvement, movements due to oscillatory movement of the tail because of momentum gained by previous motion of the animal were considered as immobility. We have used the whole period of six minutes for assessment; because mostly in tail suspension test the mice tend to be immobile more during the early period of the test. The immobility period was recorded by this method in all the groups after the corresponding treatment, and the scores were analyzed statistically.

Statistical Analysis:

Results were analyzed using the statistical test. IBM SPSS (statistical package for social sciences) software version 20 was used for statistical analysis. One way ANOVA and Bonferroni post hoc test was applied. In this study four independent groups were compared, so One-way ANOVA was used for analysis. The difference between groups were considered significant at a level of P < 0.05 which is considered statistically significant. The data were expressed as mean ± SEM (n = 5).

III. RESULTS

Table 02 Data showing the nature of the phytoconstituents present in Aegle Marmelos

<table>
<thead>
<tr>
<th>Phytoconstituents</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate</td>
<td>+</td>
</tr>
<tr>
<td>Alkaloid</td>
<td>+</td>
</tr>
<tr>
<td>Phenolic Compound</td>
<td>+</td>
</tr>
<tr>
<td>Saponins</td>
<td>+</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>+</td>
</tr>
<tr>
<td>Reducing Sugar</td>
<td>-</td>
</tr>
<tr>
<td>Tannins</td>
<td>+</td>
</tr>
<tr>
<td>Cardiac Glycosides</td>
<td>+</td>
</tr>
<tr>
<td>Terpenoids</td>
<td>+</td>
</tr>
<tr>
<td>Carbony</td>
<td>-</td>
</tr>
<tr>
<td>Phlobatannins</td>
<td>+</td>
</tr>
<tr>
<td>Steroids</td>
<td>+</td>
</tr>
</tbody>
</table>

(+) Indicates the presence of chemical constituents.
(-) Indicates the absence of chemical constituents.

Acute Toxicity Study:

The acetone extract of aegle marmelos did not show any sign of toxicity till the oral dose of 2000 mg/kg hence the extracts were used in the range of 200 - 400 mg/kg orally assuming that LD50 dose is 2000 mg/kg.

Evaluation of Antidepressant Activity by FST:

Table 1 shows antidepressant effects of control groups, standard control, and the test groups in the experimental animal. The control group animals remained immobile for long duration during test session. The stem bark extracts group III and group IV show some less significant reduction in the immobility time of mice as compared to control group. The standard drug Imipramine group animals (200 mg/kg p.o and ) evidently showed much less immobility time as compared to test and control. Thus, the antidepressant activity of AMAE was less significant effective as compared to group II i.e., Imipramine group.
Table 03: Effect of Aegle Marmelos Acetone extract on immobility period in FST

<table>
<thead>
<tr>
<th>Treatment groups</th>
<th>Immobility time in seconds Day 1 Mean ± SEM</th>
<th>Immobility time in seconds Day 7 Mean ± SEM</th>
<th>Immobility time in seconds Day 14 Mean ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>121.47 ± 4.79</td>
<td>120.51 ± 5.07</td>
<td>122.26 ± 6.03</td>
</tr>
<tr>
<td>Standard (Imipramine 20 mg/kg p.o.)</td>
<td>109.13 ± 5.94***</td>
<td>82.19 ± 6.56***</td>
<td>65.88 ± 6.44***</td>
</tr>
<tr>
<td>AMAE (200mg/kg p.o.)</td>
<td>120.41 ± 4.82***</td>
<td>101.23 ± 6.42***</td>
<td>87.76 ± 5.03***</td>
</tr>
<tr>
<td>AMAE (400mg/kg p.o.)</td>
<td>116.34 ± 3.83***</td>
<td>93.34 ± 3.90***</td>
<td>75.19 ± 4.05***</td>
</tr>
</tbody>
</table>

Value represents Mean ± SEM (n=6) *** p<0.01 vs control (Group 1)

Graph No. 01: Data of Antidepressant Activity using FST. Result of Time of Immobility In the Treatment groups, expressed as Mean ± Sem.

Evaluation of Antidepressant Activity by FST:
Table 2 shows antidepressant effects of control group, standard control, and the test groups in the experimental animal. The control group animals remained immobile for long duration during test session. The stem bark extracts group III and group IV show some less significant reduction in the immobility time of mice as compared to control group. The standard drug Imipramine group animals (200 mg/kg p.o.) evidently showed much less immobility time as compared to test and control. Thus, the antidepressant activity of AMAE was less significant effective as compared to group II i.e., Imipramine group.
Table No. 04 Percent Inhibition

<table>
<thead>
<tr>
<th>Groups</th>
<th>Day 1</th>
<th>Day 7</th>
<th>Day 14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Standard</td>
<td>10.1%</td>
<td>31.7%</td>
<td>46.11%</td>
</tr>
<tr>
<td>AMAE (200mg/kg p.o.)</td>
<td>0.87%</td>
<td>15.9%</td>
<td>28.6%</td>
</tr>
<tr>
<td>AMAE (400mg/kg p.o.)</td>
<td>4.2%</td>
<td>22.5%</td>
<td>37.6%</td>
</tr>
</tbody>
</table>

Table No. 05 Effect of Aegle Marmelos Acetone extract on immobility period in TST

<table>
<thead>
<tr>
<th>Treatment groups</th>
<th>Immobility time in seconds on Day 1 Mean ± SEM</th>
<th>Immobility time in seconds on Day 7 Mean ± SEM</th>
<th>Immobility time in seconds on Day 14 Mean ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Distilled water 10 ml/kg p.o.)</td>
<td>211.1 ± 15.03</td>
<td>212.7 ± 15.00</td>
<td>208.4 ± 16.02</td>
</tr>
<tr>
<td>Standard (Imipramine 20 mg/kg p.o.)</td>
<td>115.7 ± 6.13***</td>
<td>149.3 ± 7.06***</td>
<td>155.3 ± 6.02***</td>
</tr>
<tr>
<td>AMAE (200mg/kg p.o.)</td>
<td>154.3 ± 6.53***</td>
<td>168.6 ± 6.66***</td>
<td>177.4 ± 8.66***</td>
</tr>
<tr>
<td>AMAE (400mg/kg p.o.)</td>
<td>150.1 ± 7.86***</td>
<td>158.5 ± 8.06***</td>
<td>166.2 ± 7.56***</td>
</tr>
</tbody>
</table>

Value represents Mean ± SEM (n=6) *** p<0.01 vs control (Group 1)

Graph No. 2: Data of Antidepressant Activity using TST Result of Time of Immobility In the Treatment groups, expressed as Mean ± Sem on Day 1.
IV. DISCUSSION

Commonly known as Bael or Bilva, Aegle marmelos has been known for centuries for its medicinal value, spiritual value, ecological significance, and financial prospects. For many years, scientists have studied almost all parts of this plant for its great medicinal benefits, such as antibacterial, antifungal, antiviral, anti-inflammatory, anti-inflamatory, anti-inflammatory, anti-inflammatory -inflammatory, anti-inflammatory, anti-inflammatory, anti-inflammatory, anti-inflammatory electrical protection, sperm protection, etc. Extensive research has been carried out on this plant to further demonstrate its medicinal properties, isolate the plant components contained in it, demonstrate, and prove their relationship with various medicinal properties found in plants, and verify and validate the structure of various plant components. Methods used in job search. This paves the way for clinical trials of drugs; when finished, the industry could develop drugs to treat these diseases. According to the book "Food and Brain Health", because AM contains many plant species, AM has proven to be a powerful drug in the treatment of many diseases in the brain and can be used as a powerful psychotropic drug with no side effects on the brain, body. In the future, which is different from the synthetic drug model. A recent AM study found that the essential oil was extracted from the stems when taken at a dose of 25-100 mg/kg. It showed significant anxiolytic and antidepressant activity at all doses, and anticonvulsant and sedative effects were observed at higher doses. These activities are produced by serotoninergic and GABAergic pathways. Depression is a lifelong mental health problem and is an important health problem with a prevalence of 5% in the world and a life expectancy of 15-20%. It is estimated that depression will cause one in three serious illnesses by 20231.2. Interestingly, the AMAE 400 mg/kg group showed similar results to the imipramine 20 mg/kg group. When mice were treated with AMAE 200 and 400 mg/kg, the mean duration of absence was reduced compared to control treated with 10 ml/kg distilled water. However, the AMAE 400 mg/kg group showed a similar dose to the imipramine 20 mg/kg group. The results showed that when administered to rats at a dose of 400 mg/kg, acetone extract of AM stems showed significant anti-anxiety effects in the TST and FST models, respectively, compared to the 200 mg/kg dose. The presence of phytochemicals such as alkaloids, coumarins, phenolics, terpenoids, tannins, and flavonoids can be attributed to stress from the acetone extract of AM bodies. Scopeolenin, a phenolic coumarin isolated from various plants, including AM, has shown therapeutic potential for anxiety, epilepsy, depression, and Alzheimer's disease, so the herb may be responsible for the anxiolytic and antidepressant activities of AM bodies as coumarins. The presence of phytochemicals such as alkaloids, coumarins, phenolics, terpenoids, tannins and flavonoids can be attributed to stress from acetone extracts of AM bodies. Scopeolenin, a phenolic coumarin isolated from a variety of plants, including AM, has been shown to have therapeutic potential in the treatment of anxiety, epilepsy, depression, and Alzheimer's disease. Flavonoids, saponins, marmine, tannic acid, phenols etc. It can also be hypothesized that the electrical properties of AM indicate anxiety and stress, possibly due to high monoamine levels in the postsynaptic sites. The presence of phytochemicals such as alkaloids, coumarins, phenolics, terpenoids, tannins and flavonoids can be attributed to the anti-depressant properties exhibited by the acetone extract of AM stems. Scopeolenin, a phenolic coumarin isolated from various plants, including AM, has therapeutic potential in the treatment of anxiety, epilepsy, depression, and Alzheimer's disease. AM stress in the body can be caused by the GABA factor. The drug contains herbal components that improve sex life. Flavonoids, saponins, marmine, tannins, phenols, etc. includes. The psyche neuroparmacological activity observed in the AM lobes can be attributed to serotonergic and GABAergic pathways. Flavonoids attributable to the stress and anxiety of plants.

V. CONCLUSION

The following conclusions can be drawn from this study called Phytochemical and Pharmacological Evaluation of the Antidepressant Activity of Aegle Marmelos in Animals.

✓ Therefore, this botanical study supports the use of acetone extract of Aegle marmelos for its anti-depressant properties.
✓ In addition to discussing some functions, the absence of toxicity may offer new hopes for treatment.
✓ Preliminary phytochemical studies have shown that the acetone extract of Aegle marmelos contains carbohydrates, proteins, steroids, flavonoids, alkaloids, saponins, tannins and amino acids.
The results of this study show that the acetone extract of Aegle marmelos (2000mg/kg.p.o.) showed the best results against FST and TST. the combination of (200mg/kg, p.o.) and (400mg/kg, p.o.) showed significant antidepressant effects compared to standard imipramine.

In future studies, it will be possible to understand the functional groups responsible for the anti-anxiety properties of Aegle Marmelos acetone extract and to clarify the full mechanism of action of the study showing a great work with no toxicity and no better treatment.

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