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Evaluation Of Anti-Depressant Effect Of Fruits Of *Emblica officinalis* In Adult Male Albino Mice.

S Saraswathi[1], Mathivani M[2]*, and XA Prasanna[3].

[1]Tutor, Department of Pharmacology, Government Medical College, Virudhunagar, Tamil Nadu, India.
[2]Associate Professor, Department of Pharmacology, Government Medical College, Virudhunagar, Tamil Nadu, India.
[3]Assistant Professor, Department of Pharmacology, Government Medical College, Virudhunagar, Tamil Nadu, India.

ABSTRACT

According to World Health Organisation depression affects more than 350 million of all ages and the incidence is shifting to younger years of age. *Emblica officinalis* primarily contains Tannins which might decrease the brain Mono amino oxidase A levels and hence be effective in depression. To study the antidepressant effect of aqueous extract of fruits of *Emblica officinalis* in adult male albino mice. The present study is to evaluate the antidepressant effect of aqueous extract of fruits of *Emblica officinalis* in male albino mice by tail suspension method and forced swim test. The control drug used was C. Fluoxetine. The results obtained were expressed as Mean± S.D. Statistical analysis of difference between groups was carried out using one- way Analysis of variance (ANOVA). Probability(P) value of < 0.05 was taken as the level of statistical significance. Antidepressant activity was demonstrated on day 8 and day 15 of both 2mg/kg and 4mg/kg of the extract. In this study it was observed that at day 15 the test drug had significant antidepressant activity comparable to that of the standard drug fluoxetine.

Keywords: Depression, *Emblica officinalis*, tail suspension method, Forced swim test, fluoxetine.

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Corresponding author

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INTRODUCTION

Depression, a serious mood disorder is characterised by anhedonia, the reduced ability to experience pleasure, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue, feeling of worthlessness or guilt, difficulty in concentrating and repetitive thought of suicide [1].

According to World Health Organisation depression affects more than 350 million of all ages. Lifetime prevalence rate of depression is about 16% [2]. Also, the incidence of depression is shifting to younger years of age with its prevalence being 5.7% among 13-18 years old with female to male ratio of 1.3:1 [3]. The strongest risk factors for depression in adolescents are a family history of depression and exposure to psychosocial stress.

The treatment options for depression include

- Psychotherapy - which in general sense provide education, reassurance and encouragement
- Pharmacotherapy.

The main pharmacological agents include Tri cyclic antidepressants (TCAs), Monoamine oxidase inhibitors (MAOIs), Selective serotonin reuptake inhibitors (SSRIs), Serotonin and nor adrenaline reuptake inhibitors (SNRIs) and other newer agents.

These anti-depressants are not free from adverse effects and are often associated with anti-cholinergic or neurological effects such as dizziness, sedation, sexual dysfunction, insomnia and anxiety [4].

Emblica officinalis, commonly known as Indian Goose berry or Amla is an edible fruit obtained from medium sized deciduous tree of family Euphorbiaceae and is being used in many Ayurvedic formulations.

Emblica officinalis primarily contains tannins, alkaloids, amino acids, phenolic compounds, carbohydrates, gallic acid and vitamin-C [5]. Tannins might decrease the brain Mono amino oxidase A levels and hence be effective in depression.

METHODOLOGY

The study was carried out in the Institute of Pharmacology, Madurai medical college, Madurai after getting clearance from the Institutional Ethical Committee (Ref.No.6/3152018). 24 inbred male albino mice were obtained from Central Animal House of Madurai Medical college. The animals had free access to food and water ad libitum. They were divided into four groups of 6 each (control, standard, Test-1 and Test-2).

Control: Normal feed and water
Standard: Normal feed and Water + C. Fluoxetine (20 mg/kg) P.O.
Test-1: Normal feed and Water+ Aqueous extract of *Emblica officinalis* (2mg/kg) P.O.
Test-2: Normal feed and Water + Aqueous extract of *Emblica officinalis* (4mg/kg) P.O.

Drugs were given once daily in the morning using a oral feeding tube for a duration of 15 days as per the following table.

Tail Suspension Test

The tail suspension test was carried out on day 1, day 8 and on day 15 for all the groups (control, standard, test – 1 and test – 2) one by one. The test was performed 1 hour after the drug administration. Prior to the experiment the camera was set in position. Adhesive tapes were applied gently to the tail tip (to prevent stress and apprehension), leaving the last 2-3 mm free. The mice were then suspended by attaching free end of the tape to the top of a three walled rectangular chamber of height 55 cm × breadth 20 cm × depth 12 cm. The adequate size of the compartment prevented the mice from getting in contact with the side walls. The distance between the tip of nose and the table was 20 cm approximately. The test

was carried out for 6 minutes and the whole procedure was recorded. After the experiment the tapes from the tail of the animals were removed gently and they were placed in their respective cages.

Behavioural Analysis

Behavioural analysis was done from the video recordings. Immobility period was calculated for the entire 6-minute duration. Mobile and immobile period was taken into account as follows:

Movement of all the four limbs, attempt to touch side walls, running like movements, shaking the body were considered as mobility. Whereas, small movements of the forelimbs without any hindlimb movement and the oscillatory movement of the tape due to the momentum gained by the previous movement of the animal were taken as immobility. The results were tabulated and statistically analysed.

Forced Swim Test

After a wash out period of 15 days, the same 24 mice were procured from the Central Animal House of Madurai Medical College. They were grouped and given Standard and test drugs as done previously for the Tail suspension test. Forced swim test was done on day 1, day 8 and day 15 one hour after the drug administration.

Transparent cylindrical tanks made of plexiglass of height 30 cm × diameter 20 cm was taken and water of temperature 25^0 C is filled up to 15 cm from the bottom. Video recording is started and the mice is held gently by its tail and it is slowly placed in the water and then the tail is released so as to prevent the head of animal being submerged in water. The animal is allowed to swim for 6 minutes and then the animals are taken and dried and placed in their respective cages.

Behavioural Analysis

With the video recordings the immobility period was calculated for the last 4 minutes. This is because most of the mice are very active during the initial 2 minutes and it may obscure any beneficial effects produced by the drug. Mobility was taken as any movement other than that needed to balance the body and keep the head above the water. The results were tabulated and statistically analysed.

RESULTS

Statistical Tests Used

One-way ANOVA (Analysis Of Variance)

In this study four independent groups were compared, so ANOVA was used as the statistical test which is considered as an extension of student t test (done for the comparison of two groups). One-way ANOVA was used as there was an independent variable and a single dependent variable.

Post Hoc Test

Bonferroni post hoc test

Once it was found that there was difference existing between the means among the four groups, to determine where the difference is present Bonferroni post hoc test was applied. It is used where a list of paired comparison is made that is One group(control) is compared with all the other groups (standard, test 1 and test 2 groups).

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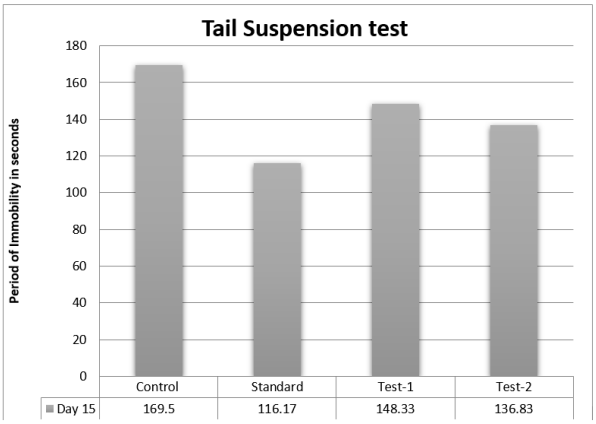
Table 1: Mean ± SD immobility period in seconds on Day 1, Day 8 and Day 15 for tail suspension method

DAY	CONTROL	STANDARD	TEST I	TEST II
Day 1	169.17 ± 19.22	153.67 ± 7.92	166.17 ± 10.36	162.67 ± 13.56
Day 8	168 ± 16.61	119.17 ± 14.98**	150.67 ± 9.95	140.33 ± 18.33*
Day 15	169.5 ± 21.08	116.17 ± 11.97**	148.33 ± 9.24*	136.83 ± 14.59**

Table 2: Mean ± SD immobility period in seconds on Day 1, Day 8 and Day 15 for forced swim test

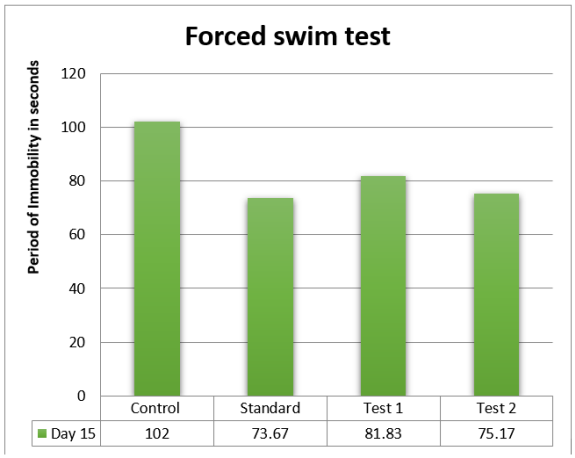
DAY	CONTROL	STANDARD	TEST I	TEST II
Day 1	101.83±7.49	98±8.92	99.67±6.62	98.67±3.39
Day 8	102.67±5.32	73.5±5.13**	83.5±5.79**	76.17±8.73**
Day 15	102±6.35	73.67±6.35**	81.83±6.74**	75.17±9.58**

Figure 1: The mean immobility period in seconds on day 15 in all group



On day 15 the decrease in the immobility time of standard and test-2 group were highly significant and that of test -1 group was significant.

Figure 2: The mean immobility period in seconds on day 15 in all groups



On day 15 there was a highly significant decrease in the immobility period in standard, test-1 and test-2 groups.

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DISCUSSION

The results of tail suspension method on day 15 shows that the duration of immobility was decreased to a highly significant extent by both the standard drug and the test drug in the dose of 4 mg/kg and significant reduction of immobility was observed with test drug in the dosage of 2 mg/kg. These finding shows that a lower dose of the test drug takes a longer time for its onset of action but still possesses anti-depressant activity.

Forced swim test showed both on day 8 and day 15 all the three groups, standard, test-1 and test-2 showed a highly significant reduction in period of immobility ($p< 0.01$). However, the duration of immobility reduction was greater in the standard group followed by the test-2 and then by test-1 groups.

In a study done previously by Pranav gupta *et al,* hydroalcoholic extract of fruits of *Emblica officinalis* was taken in a dose of 250 mg/kg and was tested in drug induced depression with phenobarbitone and the behavioural activity of the animal was tested in an actophotometer. The study showed that the test drug significantly opposed the depression produced by phenobarbitone sodium [6].

A study was done by Pawar Dattatray b *et al* in which antidepressant activity of aqueous extract of fruits of *Emblica officinalis* was done in behavioural models of depression and mechanism of action of *Emblica officinalis* was evaluated using prazosin, levosulpiride and P-CPA. Antidepressant activity of the test drug was reversed by prazosin and P-CPA in tail suspension test. This suggests that *Emblica officinalis* exerts its antidepressant effect by interacting with alpha-1 adrenoceptors and by increasing serotonin synthesis in the brain [7]. It was also observed that there was a decrease in brain MAO-A levels in animals pretreated with Emblica officinalis. This is because tannic acid which is a constituent of fruits of *Emblica officinalis* has shown to produce non selective inhibition of monoamino oxidase and hence increases the levels of monoaminergic neurotransmitters in brain.

Also increased pro-inflammatory markers such as CRP and IL-6 during childhood was associated with increased incidence of depression in early adulthood. Another evidence is that pro-inflammatory agents such as INF-ɑ given for the treatment of certain somatic disorders produced psychiatric symptoms such as depression. So, an agent with anti-inflammatory potential can decrease the symptoms of depression.

A study done by Mahaveer Golechha et al showed that extract of fruits of *Emblica officinalis* inhibits the synthesis, release, and action of inflammatory mediators like serotonin, histamine and prostaglandins which are involved in inflammation. It also inhibits NF-κB activation which is an important factor involved in chronic inflammation [8]. The anti-inflammatory effect could be due to Emblicanins A and B, ellagic acid and gallic acid which are powerful free radical scavengers. Moreover, Geraniin, Furosin and corilagin present in the fruits of emblica officinalis has NO scavenging property (NO reacts with superoxide anion and form peroxynitrite which is an oxidizing molecule eliciting lipid peroxidation). Hence fruits of *Emblica officinalis* with additional anti-inflammatory property can decrease the symptoms of depression.

CONCLUSION

In this study evaluation of antidepressant activity of aqueous extract of fruits of *Emblica officinalis* was done using tail suspension method and forced swim test and it was observed that at day 15 the test drug had significant antidepressant activity comparable to that of the standard drug fluoxetine. Hence the study objective has been achieved. *Emblica officinalis* can exert its antidepressant activity by multiple mechanisms such as through its alpha adrenergic and serotonergic activity and also through its anti-inflammatory activity.

Further animal studies with larger number of animals and other models of depression can help us further in better understanding of the mechanism of action of *Emblica officinalis* and it can be taken as a new lead molecule, from which promising drug can be generated for depression.

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