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ANTIDEPRESSANT EFFECTS OF FRUIT EXTRACT OF *ELAEOCARPUS GANITRUS* IN FORCE SWIM TEST

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ABSTRACT: The present study was designed to evaluate antidepressant effects of fruit extract of *Elaeocarpus ganitrus* (75% ethanol) on albino mice. Albino mice of either sex, weighing 25-30g were divided into seven groups and each group contains six animals. The animals were housed in polypropylene cages (38×23×10cm^3) with not more than six animals per cage. Group I, II and III were administered orally with distilled water, fluoxetine and imipramine respectively. Group IV, V, VI and VII were administered orally with different doses (20, 40, 60 and 80 mg/kg body weight) of *Elaeocarpus ganitrus* fruit extract (EGFE). Antidepressant effect of EGFE assessed by forced swim test. The (EGFE) (20 and 40mg/kg) significantly decreased the immobility time and it also increased climbing and swimming time significantly. Duration of immobility of mice increased (246.00±1.73) at high dose (80mg/kg) as compared to vehicle (228.00±4.28). It is concluded that the EGFE exhibit antidepressant effect in tested animal model at low dose but at high dose it is sedative.

INTRODUCTION: Plant derived medicinal products have been used throughout the world. *Elaeocarpus ganitrus* belongs to family Elaeocarpaceae. Genus *Elaeocarpus* contains approximately 350 species and distributed in India, Southeast Asia, Japan, Australia, Malaysia, Southern China, New Zealand, Fiji and Hawaii in the east. The greatest concentration of species is found in the islands of Borneo and New Guinea [1, 2]. *Elaeocarpus ganitrus* is commonly known as Rudraksha and grows in India, South-East Asia, Indonesia, New Guinea, Australia, Guam, and Hawaii [3].

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The fruits of *Elaeocarpus ganitrus* is covered by arduous endocarp and used as religious jewellery throughout India and Southeast Asia [4]. Fruit of Rudraksha contain alkaloids [5, 6] flavonoids, tannins [7] and fatty acids [8]. After development of advance techniques like HPTLC new flavanoid Quercetin have been determined [9] Rudraksha fruits are thermogenic, sedative and are useful in anorexia, bronchitis, neuralgia, cephalagia, migraine, manic conditions and other brain disorders [10]. The pulp of stony fruit may be useful in epilepsy and other mental disorders [11]. Moreover, some other studies reported that it exhibit various pharmacological activities i.e analgesic [12, 13], antiasthamatic [14], anti-inflammatory [15], antihypertensive[16] hypoglycemic [17], smooth muscle relaxant and hydrocholeretic [18], antiulcerogenic [19], anticonvulsant [20], antimicrobial [21]. Earlier the fruits of Rudraksha used to be employed as auspicious and for getting rid of bad spirit [22].

The biological and pharmacological properties of many plants are still unknown [23]. Therefore, the present study was designed to explore the antidepressant effect of *Elaeocarpus ganitrus* in mice.

MATERIALS AND METHODS:

Plant material and extraction: *Elaeocarpus ganitrus* (Family: Elaeocarpaceae) were identified by Department of Botany, University of Rajasthan, Jaipur. The specimen preserved in the Herbarium (Voucher specimen: RUBl21124) for the reference. Ripened fruits of plant were shade dried, powdered and extracted with 75% ethanol for 24 to 36 h by soxhlet extraction method. Then, ethanol was separated under reduced pressure to obtain solid mass. The hydro-alcoholic extract was dried and stored in air tight amber-colored bottle in refrigerator until further use.

Animals: Albino mice of either sex, weighing 25-30g were housed individually under diurnal light conditions (12 h light/12 h dark) in polypropylene cage and testing was carried out during the light phase. The animals were fed with food pellets, germinated/sprouted gram and wheat seeds as an alternative feed. Tap water was supplied *ad libitum*. The animals were handled as per guidelines of committee for the purpose of control and supervision on experimental animals (CPCSEA), Government of India. Animals were acclimatized to laboratory conditions before testing. The study was conducted according to the Indian National Science Academy Guidelines for the use and care of experimental animals.

Drugs and Treatments: Imipramine hydrochloride (IMP) and Fluoxetine hydrochloride (M/s.Alkem, Ltd.Mumbai, India) were used as reference standard drugs (positive controls). The drug was dissolved in distilled water and administered to animals through oral intubations at doses of 15 and 20 mg/kg body weight. Negative control group received distilled water. Animals were intended into seven groups containing six animals each (n=6). All solutions were prepared freshly on the test days and administrated orally in a volume of 300µl per 30g of the body weight of mice. Group I and II, III served as negative and positive controls. The animals of group IV, V, VI and VII were treated with EGFE of 20, 40, 60 and 80 mg/ kg body weight, respectively.

Experimental design: The mice were divided into 7 groups

Group	Treatment
I	Untreated Control received vehicle (Distilled water) only
II	Control (Fluoxetine) 20 mg/kg body weight
III	Control (Imipramine) 15 mg/kg body weight
IV	EGFE 1 20 mg/kg body weight
V	EGFE 2 40 mg/kg body weight
VI	EGFE 3 60 mg/kg body weight
VII	EGFE 4 80 mg/kg body weight

*EGFE - *Elaeocarpus ganitrus* fruit extract

Forced swimming test: The test was performed according to a modification [24] of the traditional method [25]. Mice were placed individually in a transparent glass cylinder (25 cm height x 18cm in diameter) filled with 25^{o}C water to a 15-cm depth. Two swim sessions were conducted. An initial 15-min pre-test was performed by placing mice into water, the mice were then removed from the water, dried and placed in their home cages with paper towels and heat lamp. Distilled water, fluoxetine, imipramine and different doses of EGFE (20, 40, 60 and 80 mg/kg body weight) were administered after 24hrs of pre-test and prior to the FST.

During the 7-min test, the climbing, swimming and immobility behaviors of the mice were recorded at 5 second intervals. Initial 2 minutes were discarded. Increases in climbing or swimming and reduction in immobility were considered as behavioral responses consistent with an antidepressant-like action [24].

Statistical analysis: Statistical evaluation of the results was made with SPSS 14.0 (SPSS Inc. Chicago, Illinois, USA). All values were expressed as mean ± SEM. The differences in the mean of activity counts per 5 minutes and the mean of immobility, climbing and swimming counts among different treated groups were statistically analyzed by one-way ANOVA followed by Post hoc Dunnett t test.

In view of the exploratory nature of the study, probability values P≤0.1 were regarded as statistically significant[26, 27].

RESULT AND DISCUSSION: In this study FST test was performed to evaluate antidepressant activity of EGFE in mice. It was observed that low dose (20mg/kg) of EGFE exerted antidepressant activity, whereas high dose (80mg/kg) of EGFE showed sedative effect. FST is suitable and widely used model for assessing antidepressant activity in rodents[25, 28]. Relatively this test is more sensitive to all major classes of antidepressant drugs including trycyclics, serotonin selective reuptake inhibitors, and MAO inhibitors [24, 29].

Along with reduction of immobility antidepressant drugs also produce two distinct active behavioral patterns i.e. swimming and climbing [24]. Post hoc tests included to determine the statistical significance between all groups, in case of climbing except Group II i.e. Fluoxetine (p=0.998) rest of all groups had shown significant difference with Group I i.e. Vehicle control. Compression of Group III i.e. Imipramine with group IV i.e. EGFE 1 (p=0.940) had shown no statistically significant difference whereas all other groups (Group I, II, V&VI) had shown significant difference **(Fig. 1 and 2).**

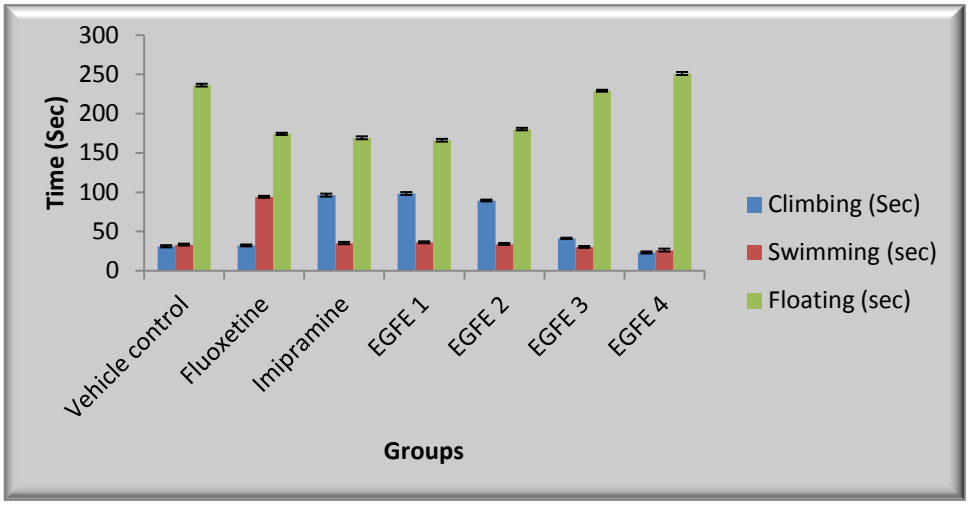

FIG. 1: COMPARISON OF STANDARD AND *ELAEOCARPUS GANITRUS* FRUIT EXTRACT (EGFE) TREATED ANIMALS IN THE FORCED SWIMMING TEST. DATA REPRESENTS MEAN ± SEM OF THE MEAN ACTIVITY COUNTS PER 5 MIN DURING 20-MIN TEST PERIOD. COMPARISONS WERE MADE USING ONE-WAY ANOVA FOLLOWED BY POST HOC DUNNETT TEST

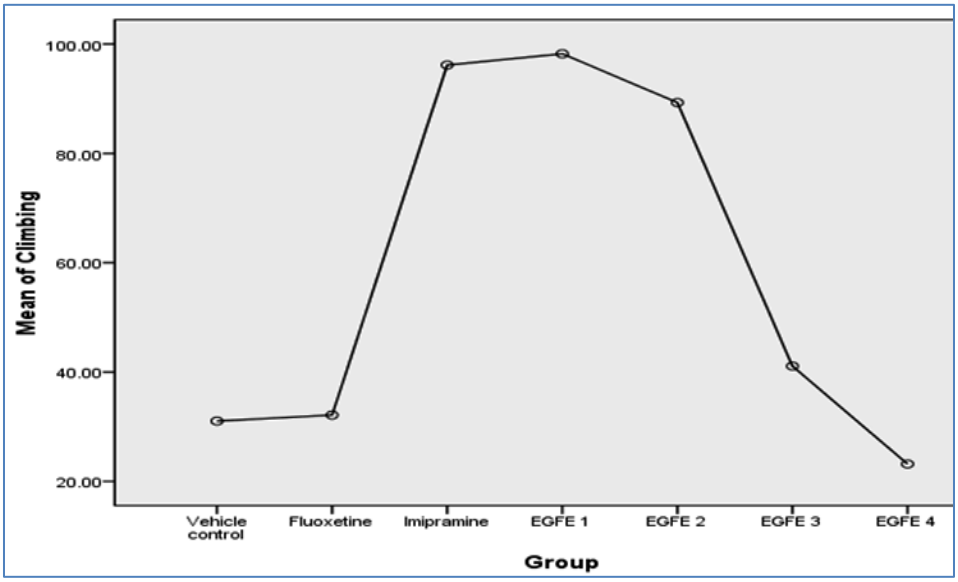

FIG. 2: EFFECTS OF EGFE 20-80 MG/KG BODY WEIGHT ON ACTIVE BEHAVIORS IN THE FST. DATA REPRESENTS MEANS ± SEM OF THE CLIMBING COUNTS DURING THE 5 MIN TEST SESSION (n=6 mice per group). Comparisons were made using one-way anova followed by post hoc dunnett test

Multiple Comparisons of all groups in swimming revealed that Imipramine (p=0.947), EGFE 1 (p=0.730), EGFE 2 (p=0.999) and EGFE 3 (p=0.710) had shown no significant difference with control vehicle treated animals whereas, mice administered EGFE 4 (p=.015) had shown significant difference as compared to control vehicle **(Fig. 1 and 3).**

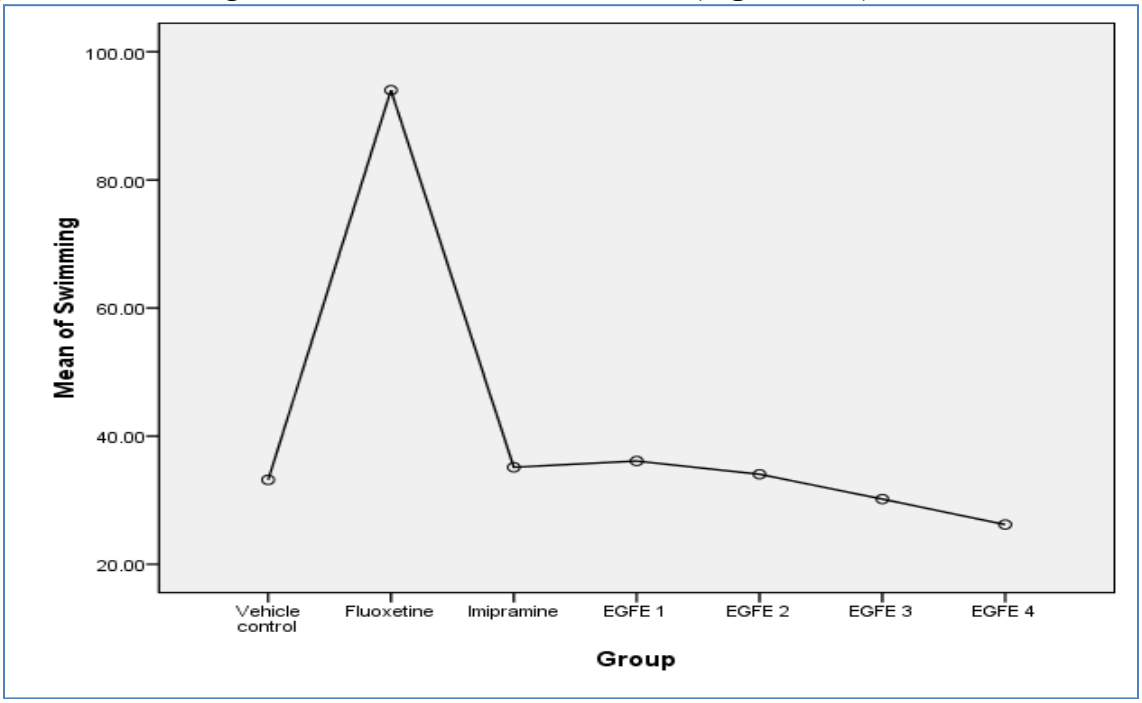

FIG. 3: SWIMMING COUNTS DURING THE 5 MIN TEST SESSION (N=6 MICE PER GROUP). COMPARISONS WERE MADE USING ONE-WAY ANOVA FOLLOWED BY POST HOC DUNNETT TEST

In case of Floating, EGFE 3 treated mice (p=.093), had shown no significant difference with Vehicle control. Imipramine (p=.382), EGFE 1 (p=.051) and EGFE 2 (p=.144) had also shown no significant difference with Fluoxetine treat animals whereas, EGFE 4 showed a significant difference as compared to Fluoxetine treated animals, indicated the sedative effect of high dose of extract on mice. When group III i.e. Imipramine compared to Fluoxetine (p=0.382) and EGFE 1 (p=0.875) treated animals there was no significant difference observed in case of floating **(Fig. 1 and 4).**

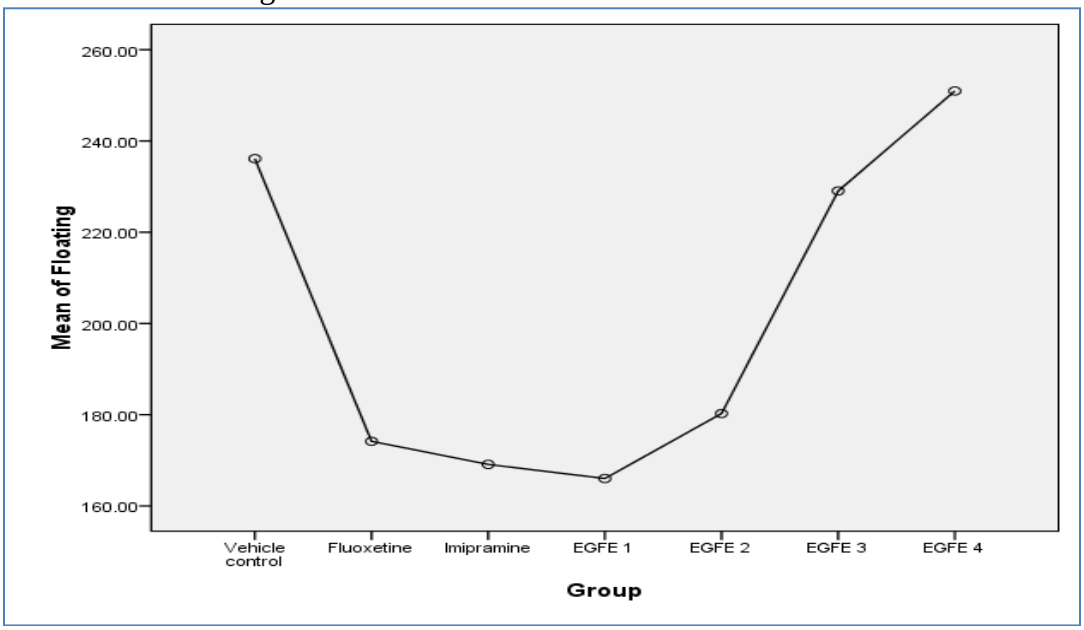

FIG.4: FLOATING COUNTS DURING THE 5 MIN TEST SESSION (N=6 MICE PER GROUP). COMPARISONS WERE MADE USING ONE-WAY ANOVA FOLLOWED BY POST HOC DUNNETT TEST

The study revealed that EGFE 1 treated animals showed better response as compared to the standard and all other groups. The EGFE 1 significantly reduced immobility and increased climbing at doses of 20 mg/kg, compared to vehicle control group. The EGFE 4 at the dose of 80 mg/kg increased the immobility in comparison to group II and III. Tukey post hoc comparison between different doses showed a significant effect of EGFE 4 (80 mg/kg) on immobility, compared to the dose of 20 mg/kg (p=0.01).

Serotonergic drug like fluoxetine, decreases immobility and increases swimming without changing duration of climbing. Whereas, drug such as imipramine increases level of dopamine and norepinephrine cause decreased immobility and increased climbing without changing the duration of swimming [24, 30].

The present study showed that the ethanolic fruit extract of *Elaeocarpus ganitrus* had significant antidepressant effects in mice. Different doses of the extract (20, 40, 60 and 80mg/kg) were administered to mice. Low doses (20, 40 and 60mg/kg) were able to reduce immobility and to enhance active behaviors, i.e. climbing, simultaneously. However, the effect of high dose (80mg/kg) on immobility and climbing were decreased. This effect is similar to the sedative effect which is shown by a reduction in general motor activity. There may be three major reasons for this effect.

The first reason may be due to interference of the phytoconstituents present in the extract with its antidepressant effect. Second may be due to the lack of dose-dependent effect of the extract on immobility and climbing behaviors. The third reason might be the doses itself used in this study which may have reduced plasma levels of tryptophan, an essential amino acid that is used for the synthesis of serotonin.

This substrate amino acid (for serotonin synthesis) is metabolized by the liver through the kynurenine pathway and only a small amount is transported into the brain actively and used for serotonin synthesis via the 5- hydroxytryptophan pathway [31]. They might not be in the linear portion of dose-responsive curve.

Nevertheless, the low doses of the extract showed antidepressant activity, close to that observed for IMP in this study. Since IMP is a standard tricyclic antidepressant, the extract may also play an important role in the management of depressive disorders. In addition high dose of the extract showed a sedative effect which was interpreted by a dose dependant reduction in spontaneous motor activity. Several studies have also shown sedative effect of fruit of *E. ganitrus* [18, 32]. This sedative effect of the extract ensures that the increment of climbing time in FST were caused by increment in general motor activity, not by possible CNS stimulating effect and confirms the specific action of extract as an antidepressant.

Since the pattern of behaviors showed by the extract in the FST is similar to those of imipramine, it suggested that this extract acts by enhancement of dopamine and nor-epinephrine. The fruit of *E. ganitrus* contains alkaloids, flavanoids, tannins and fatty acids may be responsible for this activity. Further studies are required to identify the active constituents of the plant extract responsible for the antidepressant effects.

CONCLUSION: This study had shown that the ethanolic fruit extract of *Elaeocarpus ganitrus* possess antidepressant effects. The present findings support the use of *Elaeocarpus ganitrus* as an antidepressant recommended in traditional medicine system and open an avenue to develop a new antidepressant agent from well-known herbal remedies.

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