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Antidepressant activity of ethyl acetate extract of *Mollugo pentaphylla* in mice

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Abstract
Mollugo pentaphylla is a well-known indigenous plant. The ethyl acetate extract of aerial parts of *M. pentaphylla* was administered orally to the mice at 200 and 400 mg/kg for 14 days were able to elicit dose-dependent relation of immobility reduction in the forced swimming test and tail suspension test in mice as compared to vehicle control. It was observed that the extract at the dose of 400 mg/kg produced a significant ($P \leq 0.01$) and better therapeutic activity, resulting in 46.4 and 51.6% immobility reduction respectively. Fluoxetine showed significant ($P \leq 0.01$) antidepressant activity by decreasing immobility time in both the animal models. The activity of the extract at both the doses 200 and 400 mg/kg may be due to probable inhibition of MAO B in animal brain. The result demonstrated that *M. pentaphylla* had antidepressant effects *in vivo*.

Keywords: *Mollugo pentaphylla*, Fluoxetine, Tail suspension, Forced swimming

1. Introduction
Depression is an important global public health problem due to both its relatively high lifetime prevalence and the significant disability that it causes. Without treatment, depression has the tendency to assume a chronic course, to recur, and to be associated with increasing disability over time. Depression is a prevalent psychiatric disorder with estimates reaching as high as 13-20% [1]. For nearly 2,500 years, depression has been described as one of the most common illness of humankind, but only recently it has commanded major public health interest. It is manifested by a depressed mood, loss of pleasure in daily activities, sleep disturbances, cognitive difficulties, and psychomotor disturbances. Commonly used drugs for depression are monoamine oxidase inhibitors and tricyclic antidepressants (TCAs). They increase the synaptic concentration of at least two of three neurotransmitters, namely 5-HT and dopamine (DA). The combined effect of Serotonin selective reuptake inhibitor (SSRI) and serotonin reuptake transporter (SERT) inhibitor increases synaptic concentration of 5-HT and its duration of action. The major problems of existing allopathic antidepressant drugs include serious side-effects, and a response rate of less than 50 percent [2]. As compare to allopathic medication the herbal or plant products are having minimal side effects. Therefore the research work is undertaken for the evaluation of anti depressant activity from plant derivative i.e. *Mollugo pentaphylla* belonging to family molluginaceae. The plant is reported to contain flavones (apigenin and mollupentin), carotene, mollugogenol A, triterpenoid, mollugogenol B, mollugogenol D, oleanolic acid and a steroid the β- sitosterol[3]. It has been reported that the plant possesses antimicrobial [4], whooping cough [5], hepatitis [6], anticancer [7], spermicidal [8], antibacterial [9] and antifungal activity [10]. The ethyl acetate extract of the plant was taken for anti depressant activity.

2. Materials and methods
Preparation of extracts
The aerial parts of fresh *M. Pentaphylla* were collected from Satupally, Khammam district of Telangana state, India and authenticated by Y. S. Parameswari, P.L.T.S. Agricultural University, Telangana state, India. The plant was washed in running tap water and made shade dried in the room temperature. The dried plants were made course powder and subjected to extraction with n-hexane in order to remove the fatty substances and chlorophyll. The marc was further extracted 10 times with ethyl acetate by using Soxhlet Extractor. The extract was filtered and then concentrated in vacuum into residues. Fluoxetine (Crescent) was suspended in 1% gum acacia.

Chemicals
N-hexane was purchased from Finar chemicals Ltd., Ahmadabad and ethyl acetate was purchased from Sd fine chem. - Ltd., Mumbai. All other reagents used in the study were of analytical grade.

Animals
Male albino mice weighing 22-26 g, were purchased from the Laboratory Animal Center (Maheveer Hydrabad, CPCSEA Reg No: 146/99/CPCSEA) were housed in a quiet room under a 12-h light: 12-h dark cycle at 25±2 ^{0}C for 5 days before experimentations. All the animals were given standard chow and water *ad libitum*, except during observation periods. The experiment has been performed in the CPCSEA approved laboratory of Mother Teresa Pharmacy College, Sankethika Nagar, Kothuru, Sathupally-507303, Dist. Khammam, T.S. India (Regd.1769/PO/E/S/14/CPCSEA) with the approval no. 01/2017 of the Institutional animal ethics committee.

Acute toxicity study
The acute toxicity of *M. pentaphylla* was determined as per the OECD guideline no. 420 (fixed dose method). It was observed that the test extracts shows no mortality even at 2000 mg/kg dose hence, 1/10th (200 mg/kg) and 1/5th (400 mg/kg) of this dose were selected for further study.

Drug administration
The animals were randomized into control and experimental groups and divided into five groups of 6 animals each. Animals in group I were administered with 1% gum acacia. Animals in group II were administered with fluoxetine at the dose of 20 mg/ kg. Animals in group III and IV were administered with the extracts of *M. Pentaphylla* at the doses of 200 and 400 mg/kg. All the drugs were orally administered at 16:00/16:30 h for 14 days except groups II which was administered with fluoxetine only 1, 7 or 14 days, respectively. The behavioural tests were conducted 1 h after the last treatment, respectively.

Procedure
Forced swimming test
The studies were carried out on mice according to the method of Porsolt [11]. The mouse was individually forced to swim individually for 6 min, in glass cylinders (20 cm in height; 14 cm in diameter), containing fresh water up to a height of 10 cm at 25±1 ^{0}C. The duration of immobility was manually recorded during the last 4 min of the session. A mouse was considered to be immobile when it floated or made only small movements necessary to keep its head above the water.

Tail suspension test
Mouse was individually suspended by the tail 50 cm above the floor with the help of an adhesive tape placed approximately 1 cm from the tip of the tail. Immobility time was recorded during 6 minutes period in different groups. The animal was considered to be immobile when it did not show any movement of the body and hanged passively [12]. Testing was carried out in a darkened room with minimal background noise. The duration of immobility was observed during the final 4 min interval of the test.

Statistics
Values are given as mean ± S.E.M and significances calculated using one-way analysis of variance following by Duncan's t -test by using prism soft ware.

3. Results
Effects of *M. Pentaphylla* in the mouse on forced swimming test
Effects of oral administration of the ethyl acetate extract of *M. Pentaphylla* and fluoxetine on the duration of immobility in the mouse forced swimming test were shown in Table-I. The extract showed significant (P≤0.01) change on 1 day treatment, and had the tendency to reduce the immobility time after 7-day. After a 14-day treatment, the extract at the doses of 200 and 400 mg/kg significantly (P≤0.01) decreased the duration of immobility in a dose-dependent manner as compared to vehicle control group, resulting in 38.3 and 46.4% immobility reduction, respectively. However, the reference antidepressant fluoxetine at the dose of 20 mg/ kg resulted in significant (P≤0.01) reduction as compared to vehicle control group.

Effects of *M. Pentaphylla* in the mouse on tail suspension test
Effects of oral administration of the ethyl acetate extract of *M. Pentaphylla* and fluoxetine on the duration of immobility in the mouse tail suspension test were shown in Table-II. The extract showed significant change (P≤0.01) on 1 day treatment, and had the tendency to reduce the immobility time after 7-day. After a 14-day treatment, the extract at the doses of 200 and 400 mg/kg significantly (P≤0.01) decreased the duration of immobility in a dose-dependent manner as compared to vehicle control group, resulting in 45.9 and 51.6% immobility reduction, respectively. However, the reference antidepressant fluoxetine at the dose of 20 mg/ kg resulted in significant (P≤0.01) reduction as compared to vehicle control group.

Table 1: Effects of the ethyl acetate of *M. Pentaphylla* and fluoxetine on the duration of immobility in the mouse forced swimming test (mean±S.E.M.)

Groups	Dose (mg/kg)	Duration of immobility (s)			% immobility
		Day-1	Day-7	Day-14	
Vehicle control(1ml/100g body weight of 1% gum acacia)	-	88.6±0.6	83±0.9	78.8±0.7	-
Fluoxetine	20	65.7±0.7**	46.9±0.6**	35.0±0.5**	55.5
M. Pentaphylla	200	68.1±1.2**	61.4±3.2**	48.6±0.7**	38.3
M. Pentaphylla	400	67.3±0.7**	59.0±1.6**	42.2±1.4**	46.4

**P≤0.01 when compared with vehicle control group.

Table 2: Effects of the ethyl acetate of *M. Pentaphylla* and fluoxetine on the duration of immobility in the mouse tail suspension test (mean ±S.E.M.)

Groups	Dose (mg/kg)	Duration of immobility (s)			% immobility
		Day-1	Day-7	Day-14	
Vehicle control(1ml/100g body weight of 1% gum acacia)	-	175.2±2.3	165.2±1.3	159.2±0.9	-
Fluoxetine	20	83.7±1.8**	76.1±0.3**	73.5±1.2**	53.8
M. Pentaphylla	200	124.7±1.6**	98.0±2.6**	86.0±2.2**	45.9
M. Pentaphylla	400	118.4±1.4**	83.4±5.0**	77.0±1.2**	51.6

**$P \leq 0.01$ when compared with vehicle control group.

4. Discussion

The tail suspension and forced swimming tests were two behavioural tests in rodent that predicted the clinical efficacy of many new types of antidepressant medication [11]. *M. Pentaphylla* consists of flavones (apigenin and mollupentin) are the constituents are responsible for controlling the oxidation. The extract at oral doses 200 and 400 mg/kg for 14 days significantly decreased the duration of immobility in the forced swimming test and the tail suspension test in mice. MAO is an important enzyme in the metabolism of a wide range of monoamine neurotransmitters, including noradrenaline, dopamine, and 5-hydroxytryptamine. MAO exists in two forms, A and B. MAO A is more important than MAO B in the metabolism of the major neurotransmitter monoamines.

These findings suggested that anti-depressant effects of *M. Pentaphylla* in animal models of immobility tests may be related to the inhibitory activity of MAO, especially to that of MAO A [13]. Further, more study is required in order to conform the mechanism and related active constituents.

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6. Conflict of interest

Authors declare no conflict of interest.

7. References

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