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Research Article

Antidepressant Activity of *Linum usitatissimum* Extract

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ABSTRACT

In present study the effect of *Linum usitatissimum* extract in animal models of depression has been reported. Locomotor activity, forced swimming test and tail suspension test were used for assessing antidepressant activity. 05ml/kg and 10 ml/kg body weight dose were used for the present study. At both doses duration of immobility in both models of depression decreased significantly. The effect of extract was although less significant than standard drug, presence of omega 3 fatty acid may be the reason for antidepressant activity of *Linum usitatissimum*.

Keywords: *Linum usitatissimum*, antidepressant effect, Locomotor Activity, tail suspension test, forced swimming test.

INTRODUCTION

As research continues to mount, it is becoming clear that neurobiology/physiology, genetics, life stressors, and environmental factors can all contribute to vulnerability to depression. While much attention has been given to genetics and life stressors, only a small group of international researchers have focused on nutritional influences on depressive symptoms. Collectively, the results of this relatively small body of research indicate that nutritional influences on depression are currently underestimated[1]. Omega-3 fatty acids in particular represent an exciting area of research. Detailed reviews of the possible neurobehavioral mechanisms of omega-3 fatty acids have been previously published[2].

Flaxseed, also known as linseed, is derived from the flax plant (*Linum usitatissimum*), of the family Linaceae, which is cultivated worldwide for its fiber and oil. Flaxseed contains 6% mucilage or soluble fibers, insoluble fibers 18%, proteins 25%, and oil 30-40%, with alpha-linolenic acid (ALA) making up about 50-60% of the total fatty acids [3]. ALA is a precursor of omega-3 fatty acids, which makes flaxseed the leading source of plant-derived omega- 3 fatty acids[4]. Several experimental and clinical studies have demonstrated that ALA reduces total cholesterol [5], coronary heart diseases [6] and colon cancer [7]. The lignan constituents of flaxseed possesses *in vitro* antioxidant and possible estrogen receptor agonist/antagonist properties, prompting hypotheses on its utility in the treatment of breast cancer [8], prostate cancer [9], inflammatory bowel disease [10], lupus nephritis [11], and type 2 diabetes [12].

Linseed oil contains linolenic acid has beneficial effect in reducing inflammation leading to atherosclerosis. Linseed oil may reduce cardiovascular risk through platelet function and inflammation [13], has positive effect on femur bone mineral content, bone mineral density and lumbar vertebrae [14]. Linseed oil supplementation was found to achieve a greater reduction in lung and total metastases [15].

MATERIAL AND METHOD

Extraction - *Linum usitatissimum* seeds were collected locally from Rayagada, Orissa. Seeds were crushed and kept at room temperature. Crushed seeds were macerated with Petroleum ether and ethyl acetate (1:1) for 8 days at room temperature with regular stirring. Extract was evaporated using rotary vacuum evaporator. The oil was obtained as extract. The oil was kept in well closed tight container for further studies.

Animals - Male Wistar rats (300-450 gm, 14 weeks old) were obtained from animal house of Orissa University of Agriculture and Technology, Bhubaneswar, Orissa and

were housed in group of 5 per cage in standard metal cages at 22 ± 2° C on 10:14 h light - dark cycle. All animals were given access to standard food pellet and water *ad libitum*. All conditions were maintained as per CPCSEA guidelines.

Drugs - Fluoxetine, Chlorpromazine and Imipramine were used as standard drug. DMSO was used as solvent. 05 ml/kg and 10 ml/kg body weight of extract were selected as dose for the study. Route of administration was oral (p.o.).

Experimental protocol - All rats were randomly divided into 4 groups. Each group contained 5 rats. The first group was control group treated with DMSO only which was used as vehicle. The second group was treated with the extract at dose of 05 ml/kg body weight p.o.. The third group was treated with the extract at dose of 10 ml/kg body weight p.o.. The doses used in this study are based on the preliminary studies on extract. Fourth group was treated with fluoxetine or, Chlorpromazine or, Imipramine as per the protocol.

Methods: Forced-swimming test – Measurement of immobility time was carried out by observing the motor activity of the rats, which were placed in a pool of water. A glass cylinder, 25 cm in diameter, height 23 cm, was

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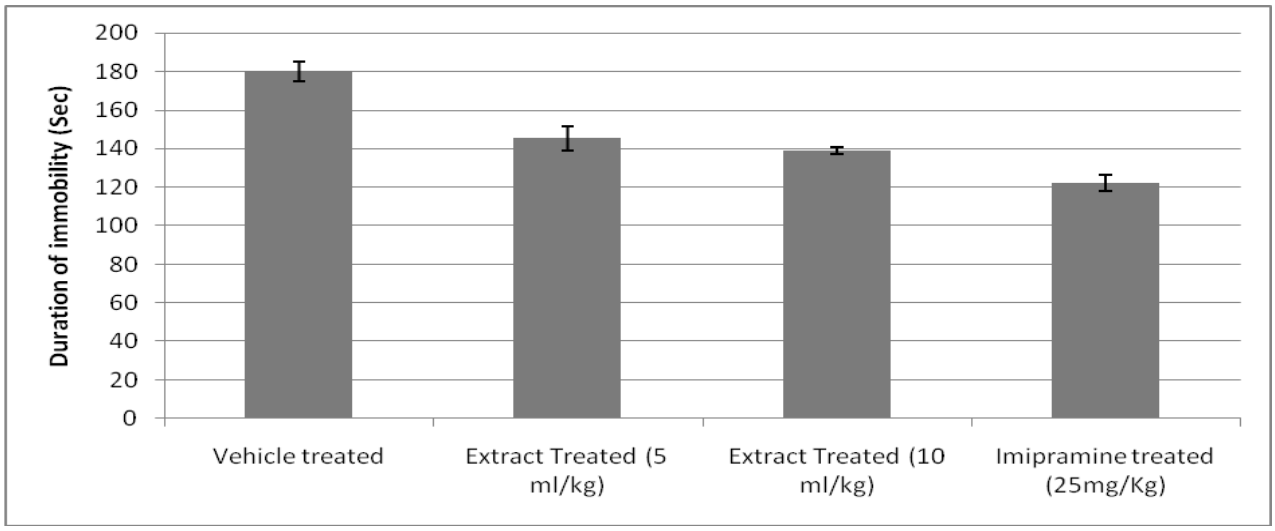
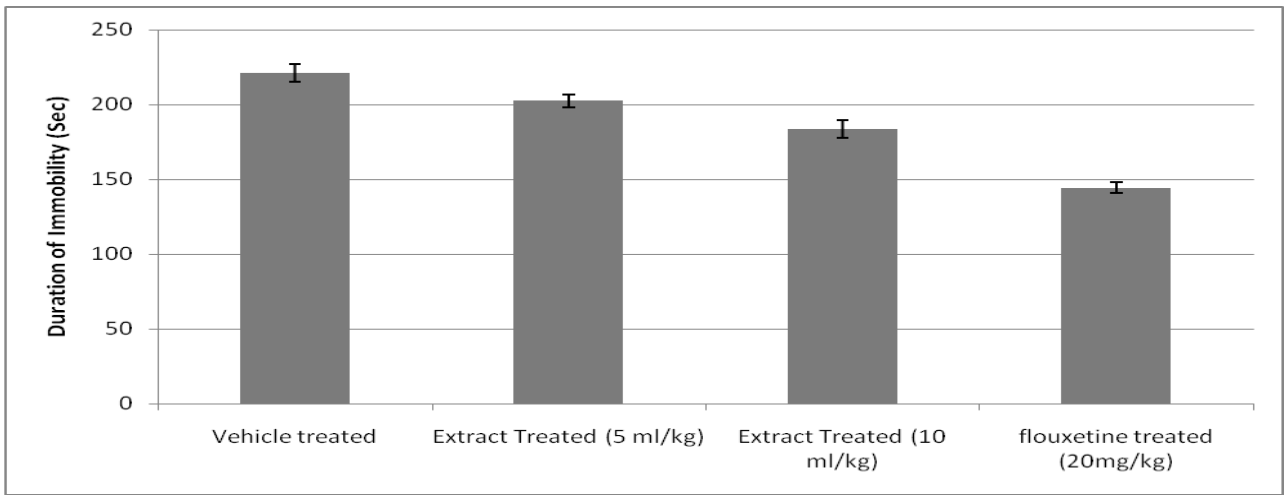


Graph 1 - Effect on immobility in forced swim test

Table 1 - Effect on immobility in forced swim test

Group	Duration of Immobility (Sec)
Vehicle treated	180±5.09
Extract Treated (5 ml/kg)	145.4±6.22
Extract Treated (10 ml/kg)	138.8±1.92
Imipramine treated (25mg/Kg)	122.2±3.96

filled with water to a height of 12 cm. The temperature of water was 23 ± 1 ºC. Each rat was injected once with a respective dose of the extract. Thirty minutes later, the animals were subjected to the test. Measurement was carried out for six minutes; the first two minutes the animal was allowed to adjust to the new conditions; after these two minutes, the immobility time that alternated with conditions of enhanced motor activity was measured. Immobility time was measured with a stopwatch for the next four minutes[16, 17]. Each time animals were removed from the water, dried with a soft towel and placed in separate cage. The water of cylinder was changed after each test.



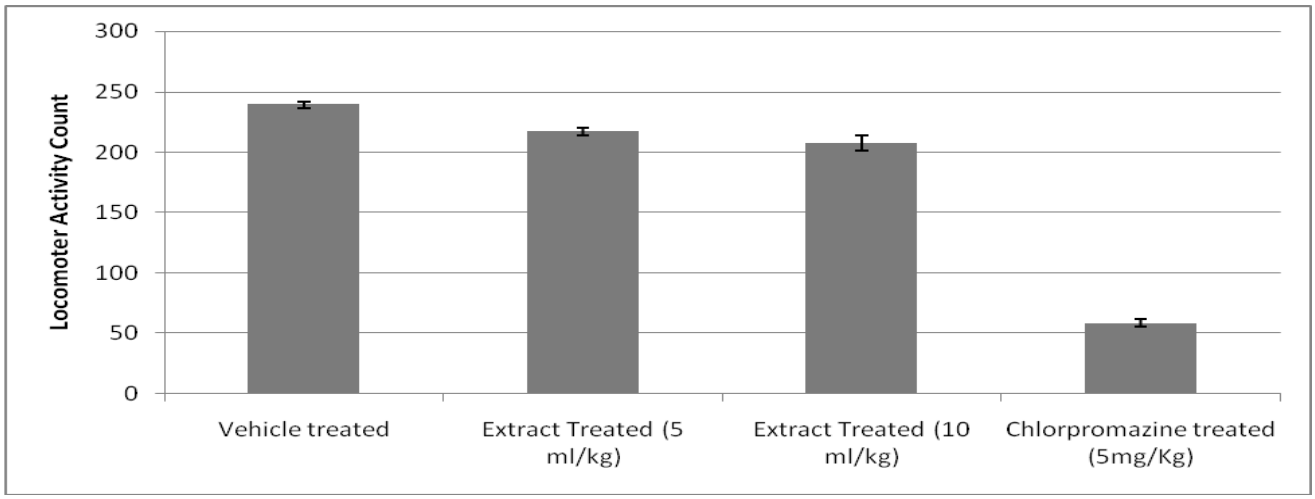
Graph 2- Effect on immobility in tail suspension test

Table 2- Effect on immobility in tail suspension test

Group	Duration of Immobility (Sec)
Vehicle treated	221.2±5.89
Extract Treated (5 ml/kg)	202.6±4.15
Extract Treated (10 ml/kg)	183.4±5.94
flouxetine treated (20mg/kg)	144.4±3.71

Immobility time is the time during which the animal floated on the surface with front paws together and made only those movements which were necessary to keep afloat. Shorter immobility time is an indication of the stronger antidepressant effect of the tested substance.

Tail-suspension test – The tail-suspension test was the second method for assessing the antidepressant effect of the extract. Thirty minutes after the single drug or vehicle injection, rats were subjected to the test. A cord of about 50 cm in length was stretched between two metal tripods



Graph 3 – Effect on spontaneous motor activity in rats

Table 3 – Effect on spontaneous motor activity in rats

Group	Count of Actophotometer
Vehicle treated	239.4±2.71
Extract Treated (5 ml/kg)	217±3.39
Extract Treated (10 ml/kg)	207.6±5.98
Chlorpromazine treated (5mg/Kg)	58.8±3.11

at a height of 70 cm, to which the rats were attached by the tail with sticky tape. After the initial period of vigorous motor activity, the rats became immobile and the immobility time was measured with a stopwatch, for a total duration of 4 minutes[18]. Rats were considered immobile when they hung passively and completely motionless.

Effect on spontaneous motor activity in rats – After 60 minutes of p.o. administration of each test drug locomotor activity was recorded with a photocell activity meter for 15 min.

Statistics: Results are presented as means ± SD and were evaluated by One way ANOVA followed by dunnett's test using primer software. A probability level of 0.05 or less was accepted as significant.

RESULTS

Effect on immobility in forced swim test – Mean duration of immobility in control group was found to be 180±5.09, whereas for the group treated with Imipramine it was 122.2±3.96. The decrease in immobility was found to be significant ($P<0.05$). In the groups treated with extract decrease in immobility was also found significant ($P<0.05$) for both dose. The total duration of immobility was found to be 145.4±6.22 and 138.8±1.92 respectively for 5 ml/kg and 10 ml/kg body weight (Graph 1).

Effect on immobility in tail suspension test - In control group mean duration of immobility was found to be 221.2±5.89, whereas in the group treated with fluoxetine it was 144.4±3.71. The decrease in immobility was found to be significant ($P<0.05$). The total duration of immobility was found to be 202.6±4.15 for 5 ml/kg body weight and 183.4±5.94 for 10 ml/kg body weight (Graph 2).In the groups treated with extract decrease in immobility was also found significant ($P<0.05$) for both dose as compared to that of vehicle treated group.

Effect on spontaneous motor activity in rats - In control group mean count was found to be 239.4±2.71, whereas in the group treated with Imipramine it was 58.8±3.11. The effect on locomotor activity was found to be significant ($P<0.05$). The total count was found to be 217±3.39 for 5 ml/kg body weight and 207.6±5.98 for 10 ml/kg body weight (Graph 3).In the groups treated with extract change in count was also found significant ($P<0.05$) for both dose as compared to that of vehicle treated group.

DISCUSSION

In this study, extract of *Linum usitatissimum* fruit was evaluated by actophotometer, forced swimming and tail suspension test. Extract showed significant antidepressant activity at both doses of 5 ml/kg and 10 ml/kg body weight.

Current research supports the theory that omega-3 fatty acid supplementation may be useful as an adjunct to current antidepressant therapy or alone. A number of studies have found decreased omega-3 content in the blood of depressed patients[19,20,21] . Seeds of *Linum usitatissimum* were reported to have omega-3-fatty acids. The possible explanation of antidepressant activity *Linum usitatissimum* seeds extract may be due to presence of omega-3-fatty acid. Although, further research is necessary to confirm and extend these results before application in humans.

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