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Evaluation of Anti-Depressant Activity of *Pogostemon Cablin* (Labiatae)

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Abstract: *Pogostemon Cablin* (Labiatae) is widely used in traditional Indian medicine as an antioxidant, anti-stress, anti inflammatory and diuretic. Although, there are reports of its neuropharmacological effect in Ayurveda, its use in psychological disorders like depression is not scientifically evaluated. In the present study aqueous and alcoholic extracts of PC were evaluated for acute oral toxicity in rats followed by anti depressant activity. The rats were administered aqueous and alcoholic extract of *Pogostemon Cablin* at doses of 250mg/kg, 500mg/kg, and 750mg/kg for a period of 14 days followed by evaluation of spontaneous locomotor activity and subjected to forced swimming test and tail suspension test. The extracts were found to be safe till a dose of 5000 mg/kg since no mortality and abnormal toxicity was observed at these doses. Alcoholic extract at the dose of 500mg/kg and 750mg/kg significantly reduced the duration of immobility in forced swimming test and tail suspension test indicating potential antidepressant activity.
Key words: Acute toxicity, FST, Antidepressant, *Pogastoman cablin* (Labiatae) and Tail suspension test.

Introduction

Depression is one of the most debilitating psychiatric disorders characterized by regular negative moods, decreased physical activity, feelings of helplessness along with sluggish thought and cognitive function. According to the WHO, depression is a medical and social problem affecting 340 million people worldwide.[1] The prevalence rate is about 5% annually[2] along with a recurrence rates of up to 85% have been reported.[3] Although, several classes of antidepressants are currently being used, due to clinical limitations and adverse effects there is critical interest in development of efficient and safe drugs for treatment of depression.[4] Medicinal plants have been established as the spring board in the discovery of new molecules useful in the treatment of CNS maladies. Plant sources such as Withania somnifera, Bacopa monniera and St. John's wort extract have been reported to have antidepressant activity and can be effective therapeutic alternatives for treatment of depression. [5, 6]

Pogostemon cablin (Labiatae),POC, commonly known as Patchouli, has been used as a traditional medicine in India for over 20 centuries, the leaves and roots are used as anti- stress, anti inflammatory, astringent, carminative, diuretic, fungicide, insecticide and sedative.[7] The plant was found to have protective effect on MPTP induced neurotoxicity and ROS scavenging potential in oxidant-induced cell death of human neuroglioma cells.[8] Chemically, POC contains sesquiterpene b-patchoulene, a-guaiene, caryophyllene, a-patchoulene, seychellene, a-bulnesene, norpatchoulenol, patchouli alcohol and pogostol.[9] Although there are scanty reports of its neuropharmacological effect in literatureits use in psychological disorders like depression is not scientifically evaluated. [10, 11, 12] Therefore the aim of the present study is to investigate the anti depressant potential of POC using forced swimming test and tail suspension test as animal models of depression along with its acute oral toxicity and effect on spontaneous locomotor activity.

Materials and methods

Plant Material

Leaves of *Pogastoman ca*blin were collected and authenticated from Indira Gandhi Agricultural University, Raipur (Chhattisgarh).

Preparation of the aqueous extract of Plant

The leaves were shade dried for 48 h and powdered so that all the material could be passed through a 0.5-mm mesh. The aqueous extract was obtained by maceration (yield = 16.1%, w/v) in water for 24 h, followed by filtration and evaporated to dryness under reduced heat (50-60c)

Preparation of the ethanolic extract of Plant

The powdered leaves were extracted with 70% ethanol using a soxhlet extractor. (yield14.2% w/v)

Chemical and Solvents

Fluoxetine (Prozac, Eli Lilly), 20mg tablet was procured from local market. All the solvents used for the extraction were procured from Samar chemicals, Nagpur.

Experimental animals

Male Wistar *rats*, weighing approximately 200-250 g were fed on standard pellet diet (Lipton) and were maintained in 12 hour light and dark cycle. All the procedures used in the study were performed in accordance with the Institutional animal ethics committee as per the guidelines laid by the CPCSEA.

Experimental design

The test animals were divided in the following groups.

Group I : Vehicle control, Normal saline *p.o.*

Group II : Positive control, Fluoxetine (10mg/kg) *p.o.*

Group III : POC aqueous extract 250mg/kg *p.o*

Group IV : POC aqueous extract 500mg/kg *p.o*

Group V : POC aqueous extract 750mg/kg *p.o*

Group VI : POC alcoholic extract 250mg/kg *p.o*

Group VII : POC alcoholic extract 500mg/kg *p.o*

Group VIII: POC alcoholic extract 750mg/kg *p.o*

Acute toxicity

Different doses of POC were orally administered (500–5000 mg/kg), while the control group received only the vehicle. The groups were observed for 48 h and at the end of this period mortality was recorded for each group.[13]

Forced Swimming test

The POC extracts were administered to the animals 1 hour prior to the experiments and swimming sessions were conducted for 5 min by placing rats in individual glass cylinders (45 cm high×20 cm in diameter) containing (25±2 °C) water 38 cm deep, so rats could not support themselves by touching the bottom with their feet. Following the swimming sessions, the rats were removed from the cylinders, dried with paper towels and then returned to their home cages. The immobility period in seconds was measured live in each test session by a blind observer.[14]

Tail suspension test

The "tail suspension test" has been described as a facile means of evaluating potential antidepressants. The procedure was used as described by Vogel G. H, 1997**.** Rats were treated with the POC extracts 60 minutes prior to testing. For the test the animals were suspended on the edge of a shelf 58 cm above a tabletop by adhesive tape placed approximately 1 cm from the tip of the tail. The duration of immobility was recorded for a period of 5 minutes. Rats were considered to be immobile when they hung passively and completely motionless.[15]

Spontaneous locomotor activity

After 60 min of POC administration, the rats were placed in the photoactometer (Techno, Lucknow, India) and acclimatized for 10 min. The interruptions of 16 photo beams spaced 2.5 cm apart and 2.5 cm above the floor were detected and scored.[16] Activity counts were recorded live for 10 min after acclimatization by a blind observer.

Statistical Analysis

The data was analyzed using Prism Graph Pad software and represented as mean±S.D. Comparison between control and drug treated groups were made by one-way analysis of variance (ANOVA) followed by Dunett's test, *P* values of less than 0.05 were considered to be significant.

Table 1: Effect of POC on the duration of immobility in despair swimming test

Groups	Duration of immobility in seconds
Vehicle control	*46.5±1.7*
Fluoxetine,10mg/kg	*30.3±0.55***
POC aqueous extract, 250mg/kg	*47±0.60*
POC aqueous extract, 500mg/kg	*40.6±0.49*
POC aqueous extract, 750mg/kg	*38.6±0.21*
POC alcoholic extract, 250mg/kg	*38.9±0.73*
POC alcoholic extract, 500mg/kg	*32.8±0.70***
POC alcoholic extract, 750mg/kg	*27.5±0.42***

Each value is expressed as mean± SEM for six rats in each group *, P< 0.05; **, P< 0.01; in comparison to vehicle control

Table 2: Effect of POC on the duration of immobility in tail suspension test

Groups	Duration of immobility in seconds
Vehicle control	*182.5±0.82*
Fluoxetine,10mg/kg	*90.3±1.2***
POC aqueous extract, 250mg/kg	*190±1.6*
POC aqueous extract, 500mg/kg	*186±2.1*
POC aqueous extract, 750mg/kg	*173.2±0.63*
POC alcoholic extract, 250mg/kg	*142.3±0.93**
POC alcoholic extract, 500mg/kg	*137.2±0.30***
POC alcoholic extract, 750mg/kg	*119.2±0.72***

Each value is expressed as mean± SEM for six rats in each group *, P< 0.05; **, P< 0.01; in comparison to vehicle control

Table 3: Effect of POC on the spontaneous locomotor activity

Groups	Spontaneous motor activity (counts)
Vehicle control	*56±0.56*
Fluoxetine,10mg/kg	*52.2±0.76*
POC aqueous extract, 250mg/kg	*46.2±0.52*
POC aqueous extract, 500mg/kg	*51.2±0.21*
POC aqueous extract, 750mg/kg	*61.2±0.82*
POC alcoholic extract, 250mg/kg	*48.2±0.36*
POC alcoholic extract, 500mg/kg	*58.2±0.34*
POC alcoholic extract, 750mg/kg	*43.2±0.40**

Each value is expressed as mean± SEM for six rats in each group *, P< 0.05; **, P< 0.01; in comparison to vehicle control

Result and Discussion

The acute oral toxicity studies were carried out according the OECD guidelines no.423. The extracts of POC did not show mortality and any visual symptoms of toxicity during the 48 hour observation period and hence were considered to be safe till the oral dose of 5000mg.

Forced swimming model also known as Despair Swim test and tail suspension test are among the most common animal models for screening behavioural depression in animals. When animal is subjected to compulsive swimming or suspended downwards with its tail, a state of despair similar to depression is observed which is characterized by immobility. A drug with potential antidepressant activity is able to significantly reduce the duration of immobility.[17, 18]

In the present study, standard anti-depressant Fluoxetine at the dose of 10mg/kg significantly reduced the duration of immobility (P<0.01) as compared to the vehicle control group. Aqueous and alcoholic extracts of POC were administered to rats at the doses of 250,500 and 750mg/kg for 14 days. As shown in the table 1 and 2, the alcoholic extract of POC at the doses of 500mg/kg and 750mg/kg significantly reduced the immobility time in rats (P<0.01) as compared to the vehicle control while

POC alcoholic extract at the doses of 250mg/kg and POC aqueous extracts did not show any significant changes in the duration of immobility in rats.

Further, the effect of the POC on spontaneous locomotor activity is shown in Table 3. Dunnets test reveals that the alcoholic extract of POC at the dose of 750mg/kg significantly decreased spontaneous locomotor activity($P<0.05$) as compared to the vehicle treated group. POC aqueous extract did not show any effect on the spontaneous locomotor activity.

Based on the above findings, the present studies reveal that alcoholic extract of *Pogostemon Cablin* possess potential antidepressant activity. These important and significant preliminary finding can be taken as the basis upon which further studies should be carried out to delineate the detailed profile of these neuropharmacological actions of *Pogostemon Cablin.* Subsequent studies can comply (1) other extract and preparation of POC. (2) mechanistic models of depression (3) phytochemical analysis and last but not least (4) controlled clinical trial applying the principles of reverse pharmacology.

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