Antidepressant activity of *Piper nigrum* fruit extract and comparison with Imipramine in mice models


1. Department of Pharmacology, Samskruti college of Pharmacy, Ghatkesar, Hyderabad-560 034, Andhra Pradesh, India
2. QPS Bioserve India (P) Ltd, Balanagar, Hyderabad-500037, Andhra Pradesh, India

Received on: 07-04-2012; Revised on: 12-05-2012; Accepted on: 16-06-2012

ABSTRACT

Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration. Depressed patients usually respond to antidepressant drugs. Medicinal plants form the major system of medicine in India. Herbs are natural remedies for the disease with higher safety profile and efficacy. Approximately a dozen animal tests for antidepressant agents are commonly used. The Forced swim test and Tail suspension test in mice were mostly used. Hence in the present study Forced swim test and Tail suspension test were used as animal models of depression. In present study immobility time in Forced swim test and Tail suspension test was significantly decreased for *Piper nigrum* fruit extract and Imipramine treated groups compared to control group. High dose extract activity was comparable to standard drug Imipramine, but the low dose was less effective. Gross motor activity test demonstrated that treatment does not modified the locomotor activity of mice, which indicates that the plant extract exerts antidepressant effects without modifying significantly locomotor activity. Therefore, it is probable that these effects are not related to the stimulation of general motor activity. Hence the present study confirms the aqueous extract of *piper nigrum* fruit having antidepressant activity. Further studies should be conducted to confirm whether the antidepressant activity is due to piperine or other chemical constituents are also involved. Further studies may help to find new antidepressant constituents in *piper nigrum* fruits.

Key words: *Piper nigrum*, Piperine, Imipramine, Antidepressant, Tail suspension test, Forced swimming test

INTRODUCTION

Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration. These problems can become chronic or recurrent and lead to substantial impairments in an individual’s ability to take care of his or her everyday responsibilities. As per WHO report Depression is common, affecting about 121 million people worldwide1.

Depression can be treated by antidepressants and Talk therapy called psychotherapy other treatments for depression are Electroconvulsive therapy (ECT), Transcranial magnetic stimulation (TMS) and Light therapy may relieve depression symptoms in the winter time2,3.

Medicinal plants form the major system of medicine in India. Studies have acknowledged the value of medicinal plants as potential source of bioactive compounds. Phytochemicals from medicinal plants serve as lead compounds in drug discovery and design. Herbs are natural remedies for the disease with higher safety profile and efficacy4.

Black pepper (*Piper nigrum* L.) the king of spices originated in the Western Ghats of India and subsequently spread to other countries. It is the largest foreign exchange earner among spices and the average quantity exported from India accounts for more than 70 per cent of the total Production5.

The fruits are traditionally used for treatment of various diseases. The various chemical constituents in *Piper nigrum* includes approximately 5–9% alkaloids structurally related to piperine, including piperridene, piperretine, pipelongummine, guineensine and pipericine, as well as 2–4% volatile oils containing safrole6.

Piperine a principle constituent of *piper nigrum* and pipert longum reported to possess antidepressant activity6,7 but there are no reports for the *piper nigrum* antidepressant activity. Present study was conducted to evaluate antidepressant activity of *piper nigrum* fruit aqueous extract.

METHODOLOGY

Animals

Male albino mice weighing between 20-25 gm were used. Animals were maintained under standard conditions in the animal house of Samskruti College of Pharmacy. The study was approved by Institutional Animal Ethics Committee (1625/PO/a/12/CPCSEA).

Chemicals: Imipramine gift sample was obtained from Aurobindo Pharma Limited, Hyderabad.

Extraction of *Piper nigrum* fruits

The dried fruits of *Piper nigrum* were purchased from local market. They were reduced to coarse powder in a mechanical grinder. The powdered material obtained was then extracted with water by using Soxhlet apparatus to obtain aqueous extract.

Acute toxicity studies

The acute toxicity for the fruits of *Piper nigrum* was determined in albino mice (20-25 g) by adopting fixed dose method of CPCSEA (OECD guidelines No. 420). Animals were administered with increasing dose of methanol extract (5, 50, 300, 2000 and 5000 mg/kg body weight) to determine changes in parameters for assessing toxicity. The animals were observed for behavior

* Corresponding author.

*G. Srinivas Rao*
Assistant professor
Department of Pharmacology
Samskruti college of Pharmacy,
Ghatkesar, Hyderabad-560 034,
Andhra Pradesh, India
profile, neurological profile and autonomic profile till fourteen consecutive days. Correspondingly dose used for pharmacological activity was finalized for aqueous extract.

Antidepressant activity
Antidepressant activity of *Piper nigrum fruit extract* was evaluated by force swimming test and tail suspension test compared with standard antidepressant imipramine. The interference of antidepressant activity with motor activity was determined by using Actophotometer.

A total of 24 animals were used in study. They were divided into 4 groups of 6 animals each. Test drugs were administered orally for 14 days.

**Treatment groups**
Group 1: Normal control (saline)
Group 2: *Piper nigrum* aqueous extract high dose (500 mg/kg, p.o.)
Group 3: *Piper nigrum* aqueous extract low dose (250 mg/kg, p.o.)
Group 4: Imipramine (10 mg/kg, p.o.)

**Behavioral tests**

**Tail suspension test**
Tail suspension test commonly employed behavioral model for screening antidepressant-like activity in mice. Animals were moved from animal house to laboratory in their own cages and allowed to adapt to the laboratory conditions for 1-2 hr.

Each mouse was individually suspended to the edge of a table, 50 cm above the floor, by adhesive tape placed approximately 1 cm from the tip of the tail. The total period of immobility was recorded manually for 6 min.

Animal was considered to be immobile when it didn’t show any body movement, hung passively and completely motionless. The test was conducted in a dim lighted room and each mouse was used only once in the test. The observer, recording the immobility of animals, was blind to the drug treatments given to the animals under study.

**Forced swim test**
Forced swim test, the most frequently used behavioral model for screening antidepressant-like activity in rodents. Animals were moved from animal house to laboratory in their own cages and allowed to adapt to the laboratory conditions for 1-2 hr. Mice were individually forced to swim in bucket (25 × 25 cm) containing fresh water to a height of 15 cm and maintained at 26 ± 1°C. At this height of water, animals were not able to support themselves by touching the bottom or the side walls of the chamber with their hind-paws or tail. Water in the chamber was changed after subjectioning each animal to Forced swimming test because “used water” has been shown to alter the behavior. Each animal showed vigorous movement during initial 2 min period of the test. The duration of immobility was manually recorded during the next 4 min of the total 6 min testing period.

Mice were considered to be immobile when they ceased struggling and remained floating motionless in water, making only those movements necessary to keep their head above water. Following swimming session, mice were towel dried and returned to their housing conditions. The observer, recording the immobility of animals, was blind to the drug treatments given to the animals under study.

**Locomotor activity**
The Locomotor activity was monitored by using Actophotometer. Before subjectioning the animal for locomotor task they were individually placed in activity meter and the total activity count was registered for 5 min. The locomotor activity was expressed in terms of total photo beams count / 5 min per animal.

Statistical analysis
All the data represent mean ± S.E.M. values. The data were analyzed by means of analysis of variance (ANOVA). Whenever ANOVA was significant, further multiple comparisons were made using Tukey’s test as the post hoc test. Statistical analysis was performed using the GraphPad InStat software. The levels of statistical significance ranged from p<0.05 to p<0.001.

**RESULTS**

**Acute Toxicity studies:**
After using various dose levels in various groups the toxicological data was determined for aqueous extract of *Piper nigrum* fruits. No mortality was seen up to dose as high as 5 gm/kg body weight by following OECD guidelines. So dose well below the possibly toxic (approximately 1/10th) of 5 gm/kg body weight was taken i.e., 500 mg/kg body weight dose was taken as high dose and 250 mg/kg as low dose for further studies.

**Behavioral tests:**
After treatment for 14 days extract (high dose and low dose) and standard drug treated mice groups were shown significant decrease in immobility time in Forced swimming test and Tail suspension test compared to control group. This shows the antidepressant like activity of both extracts and standard drug.

**Forced swimming test:**
Control group mice shown immobility during test period (186.5±4.42). This immobility was significantly decreased when treated with extracts (high dose 136.0±4.65, low dose 159.5±6.70) and standard drug (132.8±6.26). The anti depressant activity of high dose extract was comparable but the low dose is significantly less activity compared to Imipramine group.

**Tail suspension test:**
Control group mice shown immobility during test period (198.8±5.65). This immobility was significantly decreased when treated with extracts (high dose 121.3±6.06, low dose 156.6±4.21) and standard drug (115.6±6.43). The anti depressant activity of high dose extract was comparable but the low dose is significantly less activity compared to Imipramine group.

**Gross motor activity:**
Gross motor activity test demonstrated that these products do not modify the spontaneous locomotor activity of mice, which indicates that the plant extract exerts antidepressant effects without modifying significantly this parameter. Therefore, it is probable that these effects are not related to the stimulation of general motor activity.

Table 1: Antidepressant activity and Gross motor activity results

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Tail suspension test (Immobility time in sec)</th>
<th>Forced swimming test (Immobility time in sec)</th>
<th>Gross motor activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>198.8±5.65</td>
<td>186.5±4.42</td>
<td>366.3±15.11</td>
</tr>
<tr>
<td><em>Piper nigrum</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aq extract high dose 500 mg/kg, p.o.</td>
<td>121.3±6.06***</td>
<td>136.0±4.65***</td>
<td>364.1±10.11</td>
</tr>
<tr>
<td>aq extract low dose 250 mg/kg, p.o.</td>
<td>156.6±4.21***</td>
<td></td>
<td>354.1±18.36</td>
</tr>
<tr>
<td>Imipramine</td>
<td>115.6±6.438***</td>
<td>132.8±6.26***</td>
<td>370.5±11.20</td>
</tr>
</tbody>
</table>

Values are expressed as Mean±SEM. Significance when compared to control group indicated with symbol * P<0.05, * P<0.01, * P<0.001. Compared to standard group indicated with symbol # P<0.05, ## P<0.01, ### P<0.001

**DISCUSSION**
Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed...
ACKNOWLEDGEMENT

The authors are thankful to Management of Samskruti College of pharmacy for providing facilities and support.

REFERENCES


Source of support: Nil, Conflict of interest: None Declared