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Psychotropic Activity of *Sphaeranthus indicus* Linn. In Experimental Animals

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ABSTRACT

Sphaeranthus indicus Linn. (Asteraceae) is a branched herb with purple color flowers, distributed in wet places. The present study evaluated the neuropharmacological effects of the hydroalcoholic extract of *S. indicus* (SIE) in rats and mice. Effect of SIE (100, 200 and 500 mg/kg, p.o.) on spontaneous motor activity, pentobarbital-induced sleeping time, motor coordination, exploratory behaviour and apomorphine-induced stereotypy were investigated in mice. SIE (100, 200 and 500 mg/kg, p.o.) induced catalepsy and effect of SIE on haloperidol induced catalepsy were studied in rats. The SIE showed significant reduction of spontaneous motor activity, exploratory behaviour and prolonged pentobarbital sleeping time in the mice. Neuroleptic potential of SIE was observed by the results in which SIE antagonized apomorphine-induced stereotypy in mice, produced catalepsy and potentiated haloperidol-induced catalepsy in rats. Further, SIE had no effect on motor-coordination as determined by the rota rod test. These results provide evidence that the hydroalcoholic extract of *Sphaeranthus indicus* may contain psychoactive substances that are sedative in nature with possible neuroleptic properties.

Keywords: Apomorphine-induced stereotypic behaviour, Exploratory activity, Haloperidol-induced catalepsy, Pentobarbital sleep, *Sphaeranthus indicus Linn.*, Spontaneous motor activity.

INTRODUCTION

Sphaeranthus indicus Linn. (Asteraceae) commonly known as 'Gorakhmundi' is a highly branched herb distributed throughout the plains in India in wet places. In folk medicine, the entire herb is used in insanity, epileptic convulsions, vomiting and hemicrania (1). The entire herb is valued as an aphrodisiac and nervine tonic (2, 3). Previous phytochemical studies reported the presence of sesquiterpene lactones (4, 5), steroids (6,7), flavanoids (8–10) and essential oil (11) in the *S. indicus*. Isolation of number of eudesmanolides was also reported from this plant (4, 12–14). The herb was reported to have antibacterial, antifungal (15), immunomodulator (13), antioxidant (16) and hypoglycemic (19) activities. Neuroleptic (17) and anxiolytic (18) activity of flowers of the plant was reported. Traditional uses and reported study suggested that this entire herb of *Sphaeranthus indicus* may have action on the central nervous system. Various activities of entire herb have reported but no scientific data available for neuropharmacological action of entire herb of *Sphaeranthus indicus*. In the light of above information and folklore uses, the present study was designed to determine acute toxicity test and to evaluate the psychotropic activity of whole herb of *Sphaeranthus indicus* using various experimental models.

MATERIALS AND METHODS

Animals

Albino wistar mice (25–30 g) and rats (200–250 g) of either sex bred in Central Animal House facility of the

institute were used. The animals were housed under standard conditions, maintained on a 12 h light/dark cycle and had free access to food and water up to the time of experimentation. The animals were acclimatized to the laboratory environment 1 h before the experiments. Animals were randomly distributed into groups of 10 animals each. All experiments were conducted during the light period (08.00–16.00 h). All the protocols were approved by the Institutional Animal Ethical Committee (IAEC) and conducted according to the guidelines of CPCSEA (Committee for the Purpose of Control and Supervision of Experiment on Animals).

Plant material and preparation of extract

The fresh, fully grown flowering herbs of *Sphaeranthus indicus* were collected from Vallabh Vidyanagar in the month of November 2004. The herbs collected were authenticated by a Taxonomist, Department of Bioscience, Sardar Patel University, Vallabh Vidyanagar, Gujarat. A specimen of plant is kept in the herbarium of our institute (Voucher No. ARGH7). The plant material was completely dried under shade and powdered. The powdered material was extracted exhaustively with 50% ethanol by maceration for 2 days at room temperature with occasional shaking. Crude (hydroalcoholic) extract was filtered and dried under reduced pressure at 40°C (Yield-11.1% w/w).

Preliminary phytochemical screening

Preliminary phytochemical screening was performed using standard procedures for detection of phytoconstituents (20) present in the extract.

Drugs

Diazepam (Calmpose®, Ranbaxy, India) was used as reference drug for spontaneous motor, muscle relaxant, exploratory and sedative activities. Haloperidol (Torrent, India) was used as positive control for apomorphine induced stereotypy in mice and cataleptic response in rats. It was administered in the form of suspension using Tween 80 (0.2% v/v) as the suspending agent. Apomorphine hydrochloride (Sigma, St. Louis, MO, USA) and sodium pentobarbital (Sigma, St. Louis, MO, USA) were used for induction of stereotypy and sleep respectively. They were dissolved in 0.9% saline solution prior to administration.

Treatment

Freshly prepared aqueous solution of dried extract (SIE) in suitable dilution was administered orally in the test animals. SIE was also administered intraperitoneally in the mice for acute toxicity test. For the neuropharmacological activity, animals were divided in to five groups each group consisting of ten animals. Group 1 served as control group received distilled water (vehicle) 1 ml/kg, p.o., group 2–4 served as test groups received SIE (100, 200 and 500 mg/kg, p.o.) and group 5 served as positive control received reference drugs. Diazepam (2 mg/kg, i.p.) and Haloperidol (1 mg/kg, i.p.) were administered in a positive control group for above mentioned experimental models. 1 h after oral and 30 min after intraperitoneal administration, each animal was submitted to various behavioural testing.

Acute toxicity test

Different doses (100–5000 mg/kg) of SIE were administered intraperitoneally to five groups of mice (6 in each) and orally to another five groups of mice (6 in each). Mortality within 24 h was recorded (21). The LD_{50} was estimated from the graph of probit against log-dose of the extract.

Neuropharmacological activity
Spontaneous motor activity

The spontaneous motor activity was measured using an actophotometer. The movement of the animal cuts off a beam of light falling on the photocell and a count was recorded and displayed digitally. Each mouse was placed individually in the actophotometer for 10 min and basal activity score was obtained. Mouse was placed again in the actophotometer after treatment for recording the activity score (22).

Effect on motor coordination

The effect on motor coordination was examined by rotarod apparatus (23). The mice were placed on a horizontal rotation rod set at a speed of 25 rpm. Mice that were able to remain on the rod longer than 180s were selected. Fall off time was recorded for selected animals after treatment. The test was considered positive if a mouse is unable to remain on the rod during the 3 min trial.

Pentobarbital induced hypnosis

Pentobarbitone sodium (35 mg/kg, i.p.) was administered to all pretreated animals. The interval between the administration of pentobarbital until the loss of the righting reflex was recorded as on set of sleep, while the time from the loss to regaining of the righting reflex as the duration of sleep (24).

Exploratory activity

Exploratory activity was measured using hole-board apparatus. Hole-board is a wooden board with 16 evenly spaced holes. The board was elevated so that the mouse could peep through holes. Each mouse was placed individually on the corner of the board and observed for a period of 3 min. The number of head dips in to hole by each mouse was noted (25).

Catalepsy in rats

Rats were tested for catalepsy by placing both front paws over an 8 cm high horizontal bar (26). The time elapsing between paw placement and the first movement of either paw (descent latency) was measured in second. Animals were tested for catalepsy 15, 30, 60, 90, 120, 180, 240 and 300 min after treatment. Furthermore, the animals whose catalepsy score was more than 10 seconds were considered to be cataleptic.

For observing the effect of SIE on the Haloperidol induced catalepsy, Haloperidol (1mg/kg, i.p.) was injected to control and SIE treated and positive control animals. Catalepsy score (descend latency) in seconds of each animal in the group, at the respective testing time interval, was measured.

Apomorphine induced stereotypy

Stereotypy was induced by Apomorphine hydrochloride (2 mg/kg, i.p.) to all groups of mice after treatment. The mice were individually placed in glass containers of 250 ml capacity. Continuous sniffing, rearing, licking and gnawing were observed as stereotypic behaviour at 0, 15, 30, 45 and 60 min after apomorphine administration. The intensity of stereotypy was recorded by scoring system (27). For each mouse, a global score was calculated by averaging the five stereotype scores obtained at mentioned time interval.

Statistical analysis

Data were expressed as mean ± S.E.M. The statistical significance of differences between groups was evaluated by one-way analysis of variance (ANOVA) followed by post hoc Dunnet's test. A probability level of 0.05 or less was accepted as significant.

RESULTS

Preliminary phytochemical screening

The results of preliminary phytochemical tests indicated the presence of sugars, proteins, steroids, saponins, tannins, flavanoids, coumarins and essential oil in the SIE.

Acute toxicity test

Oral administration of SIE did not show any toxic symptoms up to 5 g/kg dose in mice. The intraperitoneal LD_{50} of SIE was found to be 1258.9 mg/kg.

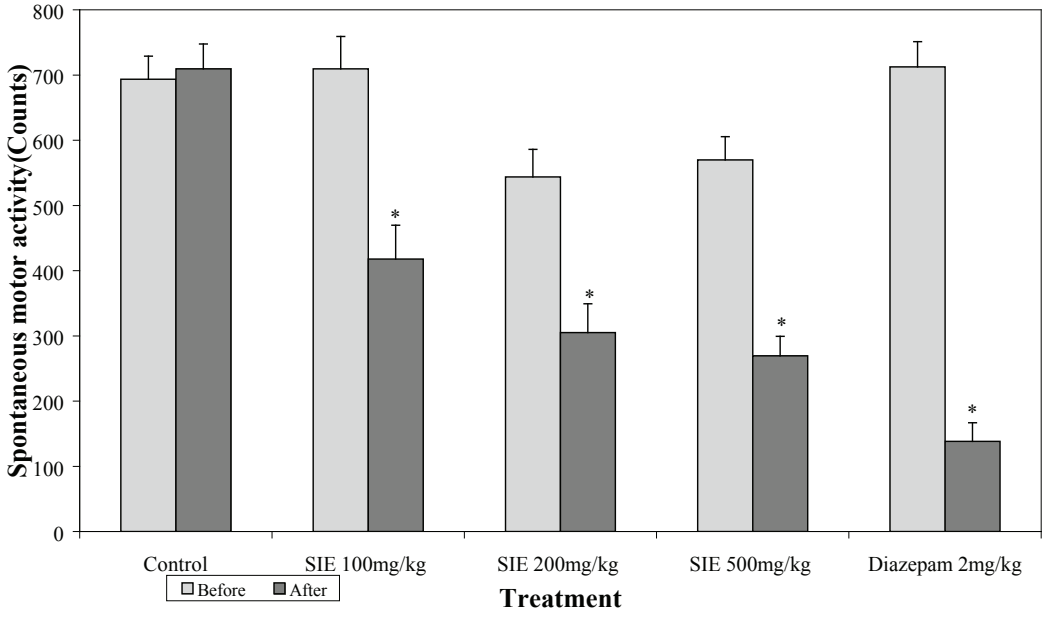

Figure 1: Effect of hydroalcoholic extract of *S. indicus* (SIE) on spontaneous motor activity. Each bar represents the mean ± SEM (n = 10). One way ANOVA followed by Dunnett's test, *p<0.05 when compared with control group.

Table 1: Effect of hydroalcoholic extract of S. indicus (SIE) on pentobarbital induced hypnosis in mice.

Treatment	Dose (mg/kg)	Onset of sleep (min)	Duration of sleep (min)
Control	-	3.9 ± 0.33	26.9 ± 2.31
SIE	100	4.6 ± 0.57	56.9 ± 4.07*
SIE	200	4.3 ± 0.32	60.6 ± 5.7*
SIE	500	4.4 ± 0.51	74.2 ± 6.59*
Diazepam	1	2.5 ± 0.16*	100.7 ± 2.94*

Values are expressed as mean ± SEM (n=10). One way ANOVA followed by Dunnett's test,
* $p<0.05$ when compared with control group.

Spontaneous motor activity

As shown in the figure 1, the SIE (100, 200 and 500 mg/kg, p.o.) produced a significant ($p<0.05$) and dose dependent decrease in spontaneous motor activity. Similarly, positive control diazepam (2 mg/kg, i.p.) also produced significant reduction in spontaneous motor activity.

Effect on motor coordination

The SIE (100, 200 and 500 mg/kg, p.o.) did not exhibit significant effect on the rota-rod performance of the mice as all the animals stayed on the rod for 180 sec without falling. However, diazepam (2 mg/kg, i.p.) treated group showed an increase in the number of falls as compared to control (data not shown).

Pentobarbital induced hypnosis

The results are summarized in table 1. The SIE (100, 200 and 500 mg/kg, p.o.) significantly ($p<0.05$) prolonged the duration of pentobarbital sleeping time in mice with no effect on the onset of sleep. Positive control, Diazepam reduced onset of sleep and potentiated duration of sleep in significant manner.

Table 2: Effects of hydroalcoholic extract of S. indicus (SIE) on exploratory behaviour (Head dip test) in mice.

Treatment	Dose (mg/kg)	Number of head dips
Control	-	13.9 ± 0.82
SIE	100	8.7 ± 0.74*
SIE	200	7.0 ± 0.72*
SIE	500	5.4 ± 0.69*
Diazepam	1	2.9 ± 0.50*

Values are expressed as mean ± SEM (n=10). One way ANOVA followed by Dunnett's test,
* $p<0.05$ when compared with control group.

Table 3: Effect of hydroalcoholic extract of S. indicus (SIE) on apomorphine (2 mg/kg, i.p.) induced stereotypy in mice.

Treatment	Dose (mg/kg)	Score for stereotypy behaviour
Control	-	2.72 ± 0.09
SIE	100	1.82 ± 0.09*
SIE	200	1.48 ± 0.06*
SIE	500	1.34 ± 0.05*
Haloperidol	1	0.00 ± 0.0*

Values are expressed as mean ± SEM (n=10). One way ANOVA followed by Dunnett's test,
*$p<0.05$ when compared with control group.

Exploratory activity

As shown in the table 2, SIE (100, 200 and 500 mg/kg, p.o.) produced reduction of exploratory activity as indicated by significant ($p<0.05$) and dose dependent decrease in the number of head dips. Similarly, Diazepam caused a significant decrease in the number of head dips.

Catalepsy in rats

As shown in the figure 2, SIE in all the doses showed catalepsy at 30 min and 60 min of time intervals. SIE also showed catalepsy at 90 min (200 mg/kg and 500 mg/kg, p.o.) and 120 min (500 mg/kg, p.o.) of time intervals. Positive control, Haloperidol showed catalepsy for all time intervals.

As shown in the figure 3, Haloperidol induced catalepsy was significantly potentiated by 200mg/kg (at 15, 30 and 60 min) and 500 mg/kg (at all time intervals) dose of SIE.

Apomorphine induced stereotypy

As shown in the table 3, SIE (100, 200 and 500 mg/kg, p.o.) significantly attenuated apomorphine induced stereotyped behaviour in mice dose dependently. This effect was similar to that produced by haloperidol (1 mg/kg).

DISCUSSION

In this work, the effect of the hydroalcoholic extracts of *S. indicus* herb (SIE) was studied in several behavioral animal models for the evaluation of their possible psychotropic activity. The results of the present investigation showed that the hydroalcoholic extract of *S. indicus* (SIE) has some potent neuropharmacological activity. Assessment of acute toxicity is the first step in the toxicological investigation

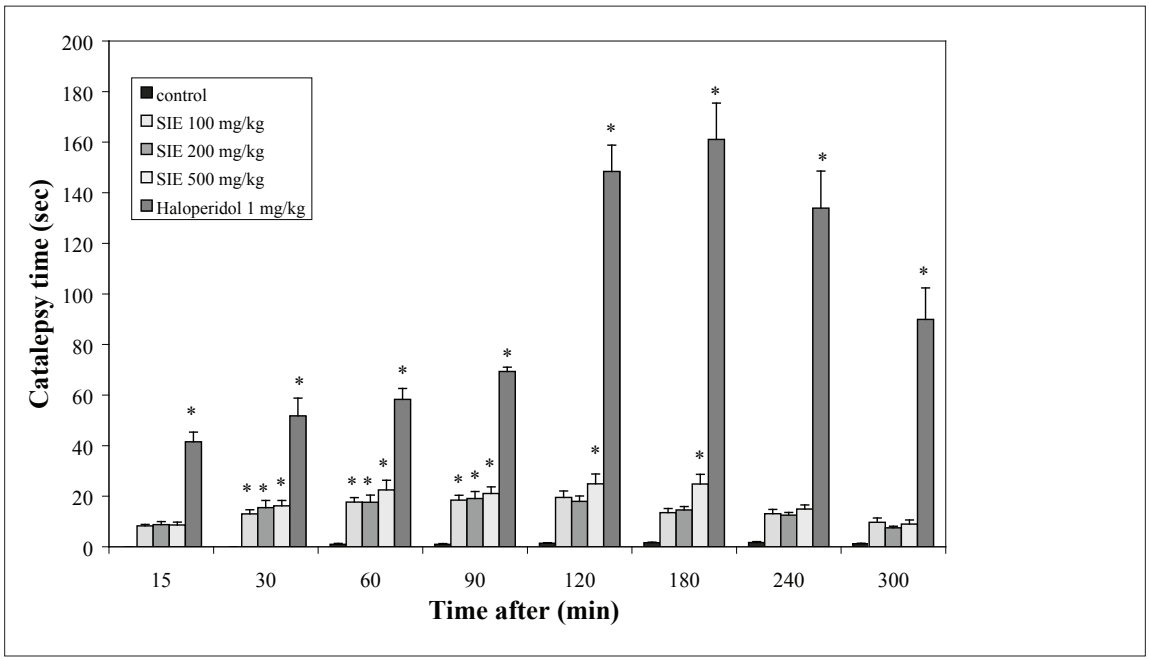

Figure 2: Effect of hydroalcoholic extract of *S.indicus* (SIE) on catalepsy in rats. Each bar represents the mean ± SEM (n = 10). One way ANOVA followed by Dunnett's test, *p<0.05 when compared with control group.

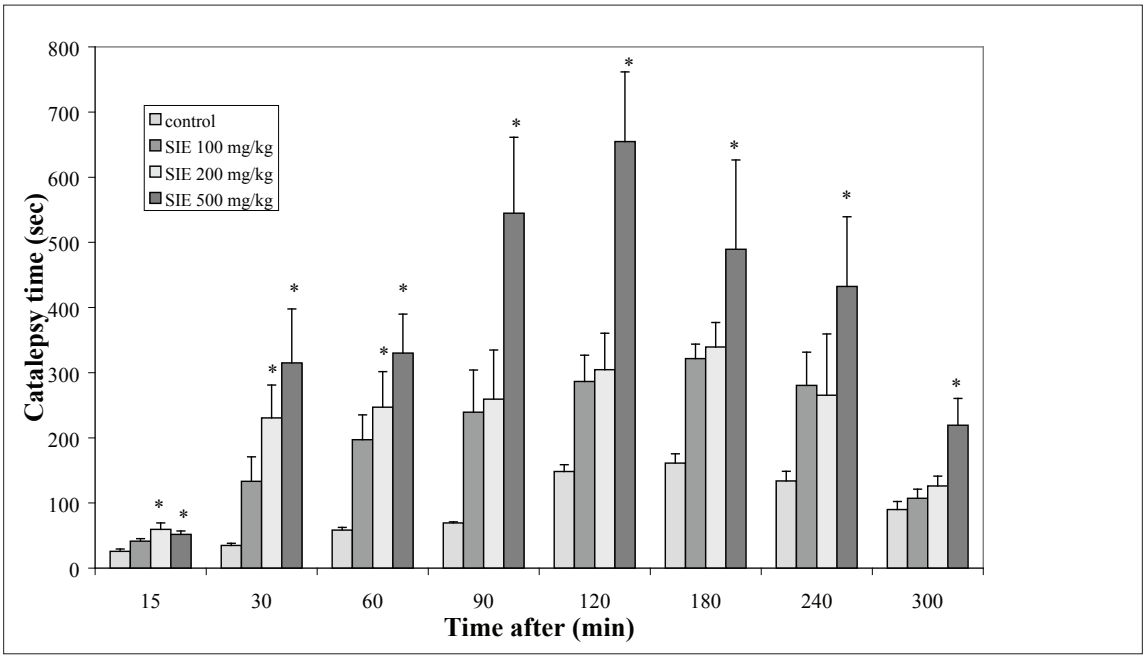

Figure 3: Effect of hydroalcoholic extract of *S. indicus* (SIE) on haloperidol induced catalepsy in rats. Each bar represents the mean ± SEM (n = 10). One way ANOVA followed by Dunnett's test, *p<0.05 when compared with control group.

of an unknown substance. The hydroalcoholic extract of *S. indicus* was well tolerated by mice and there were no signs of acute (during 2 h observation period) or delayed (24 h after extract treatment) toxicity by oral administration. Increasing doses of the hydroalcoholic extract of *S. indicus* up to 5 g/kg (p.o.) was not lethal, the LD_{50} value for this extract was estimated to be higher than 5000 mg/kg for oral administration. Thus, suggesting that this administration route is adequate and secure to produce its neuropharmacological effects.

Reduction in the spontaneous motor activity leads to sedation (28) as a result of reduced excitability of the central

nervous system (29). Prolongations of pentobarbital hypnosis were due to sedative and/or hypnotic property (30) attributed to an action on the central mechanisms involved in the regulation of sleep (31) or an inhibition of pentobarbital metabolism (32). The hydroalcoholic extract of *S. indicus* (SIE) significantly reduced spontaneous motor activity and prolonged pentobarbital induced hypnosis in mice. Thus, suggesting that the hydroalcoholic extract of *S. indicus* might be acting as mild neurosedative agents. Hole-Board test is a measure of exploratory behaviour (33) and an agent that decreases this behaviour reveals sedative (34) activity. The hydroalcoholic extract of *S. indicus* also reduced exploratory behaviour, further confirming sedative or central nervous depressant nature of *S. indicus*.

Neuroleptics, which have an inhibitory action on the nigrostriatal dopamine system known to induce catalepsy (26) while neuroleptics with little or no nigrostriatal blockade produce relatively little or no cataleptic behavior (35). Compounds which prevent apomorphine induced stereotypy also antagonize dopamine receptors in the nigrostriatal system (36). Haloperidol induces catalepsy and antagonizes apomorphine-induced stereotypies by blocking the postsynaptic striatal D_2 and D_1 dopamine receptors (37). The neuroleptic potential of the hydroalcoholic extract of *S. indicus* (SIE) was confirmed by the results in which it produced catalepsy, potentiated haloperidol induced catalepsy and antagonized apomorphine induced stereotypies.

Furthermore, the inability of the extract to affect motor coordination is additional evidence of centrally mediated actions and not blockade of neuromuscular system (38). The efficacy of most herbal remedies is attributed to various active principles in combination. The observed pharmacological actions of hydroalcoholic extract of *S. indicus* (SIE) may be due to the presence of steroids, saponins, tannins, flavanoids, coumarins, triterpenes and essential oil as indicated by the results of preliminary phytochemical screening. Since triterpenoids (39,40), saponins (41,42), flavanoids (40,42) and essential oil (43) from other plants have reported to display depression of central nervous system. It is therefore suggested that fraction of the components which is present in the hydroalcoholic extract of *S. indicus* might contribute in providing observed CNS effects. At present, it is not clear which of the chemical constituents of the plant is responsible for the observed pharmacological effects in the present study.

In conclusion the results of present study provide evidence that the hydroalcoholic extract of *Sphaeranthus indicus* may contain some psychoactive principles, which are sedative and neuroleptic in nature.

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