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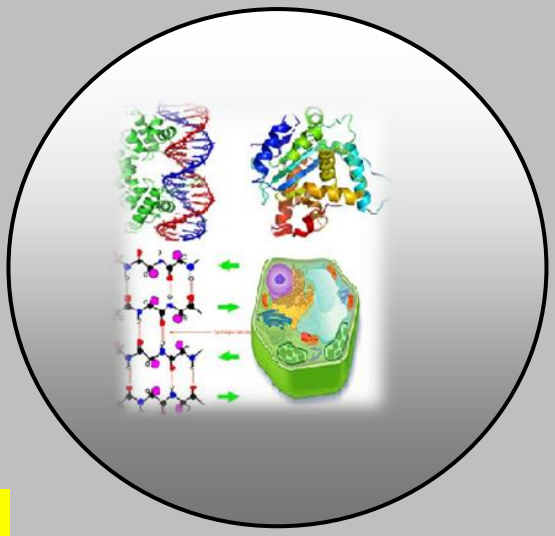

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Some Pharmacological Studies of *Centella asiatica* Linn. (Brahmi/ Mandookparni)

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ABSTRACT

Centella asiatica has been described to be useful in "Grahni roga" (abdominal disturbances) like diarrhoea in ancient texts of Ayurveda. It has also been described to be a nervine tonic and has been reported by various workers as a CNS active medicine. In the present study general pharmalogical CNS activity and toxicity were evaluated for the lot of this drug collected from Sitapur district U.P. It has no overt effect on general behavior and muscular co-ordination in rota rod test; however it possessed mild sedation and reduced the activity of mice as judged by photoactometer. As it is known to be effective in intestinal disorders its effect on intestinal transit was studied in albino rats (invivo). The drug reduces the intestinal transit conforming its Ayurvedic concept for its usefulness in diarrhoeal condition. The range of safely ratio (LD_{50}/ED_{50}) of the CAE was quite high proving the innocuous nature of the drug.

Key words: Centella asiatica, Grahni roga, CNS activity and toxicity

INTRODUCTION

The plant *Centella asiatica* belongs to family umbeliferae known as Brahim/ Mandookparni in Sanskrit/Hindi has been described as Nervine Tonic in Carak Samhita (2700-600 B.C.). Recent studies shows memory enhancing activity in the drug.

In Carak Samhita (2700-600 B.C.), and (Kirtikar and Basu, 1935) it has also been described to be useful in gastro-intestinal disturbances (Krimi Roga). (Tiwari et al., 1986) have described this plant to be useful in "Grahni Roga" which appears to have close resemblance to Giardiasis. A lot of research work has been done on its CNS activity however, as in medicinal plants the active constituents and activity differ from lot. to lot. Some studies on general behavior and CNS effects and studies specially related to G.I.T. and toxicity were carried out with a view to assess its G.I.T effects in vivo, not reported earlier LD_{50} and ED_{50} were assessed to evaluate the innocuous nature of the drug. 70% alcoholic *Centella asiatica* extract (CAE) of whole plant was taken for the study in animal models.

MATERIAL AND METHODS

Plant was collected from the areas around the chestnut ponds near Namisharayan a holy place in Sitapur district, Uttar Pradesh. There was thoroughly washed and dried in shade, made in roughly crushed powder. Then this powder was extracted with 70% ethyl alcohol in soxhlet apparatus. The alcohol was evaporated on a water bath and the residue thus obtained suspended in normal saline and administrated by oral route to animals for pharmacological studies.

Albino mice weighing between 20-30 gms and albino rats of 100 to 120 gms of same age group were divided into different groups of equal body weights. The drug was administered orally by a feeding canula to all the animals. ED_{50} for motor activity in photoactometer in mice and intestinal transit in rats was calculated using the method of Litchfield and Wilcoxon, 1949 and LD_{50} was done by the method of Smith 1960.

Experimental studies

General Behavioral Studies

CAE administered up to dose of 500 mg/kg p.o. did not induce any overt behavioral effect. However, the animals only appeared to be less active and had mild sedation. Larger dose up to 1200 mg/kg p.o. could not produce loss of righting reflex. The heart rate and respiration were not affected.

Central Nervous System (CNS) Studies

Effect on motor activity: The spontaneous motor activity was observed following the photoelectric cell method of Dews, 1953. This was observed by photo-actometer. The study was carried out in 4 groups of mice, 10 animals in each group. Group I was administered with normal saline and served as control. Group II, III, and IV were given CAE in doses of 25, 50 and 100 mg/kg p.o. one hour before the experiment. The results are summarized in Table 1. There was reduction in their activity as judged by the countings of movement in photo-actometer. The drug showed a dose dependent effect in all three groups of animals treated with CAE. These findings were significant (p value< 0.05).

Effect on motor coordination: It was observed on Rota-rod by method of Kinnard & Carr, 1957. 4 groups of animals (mice) each consisting of 10 animals were taken group I served as control, II, III and IV groups were given CAE in doses of 25, 50 and 100 mg/kg p.o. one hour before the experiment. The animals of each group were mouted on the rota-rod mouting time (when the animal was put on the rota-rod and when it fell from it) of each animal was noted. The mean time of mouting was calculated from this data for each group. The muscular coordination activity was not significantly affected in the doses administered in the test.

Analgesic effect: Observed by pinna reflex and tail clip pressure method. There was no analgesic effect as judged by pinna reflex and tail clip method. Thus the CAE was devoid of any analgesic activity.

G.I.T. Studies Effect on intestinal transit was studied in rats by method of Dhasmana et al., 1987 and Singh et al., 1991 by charcoal transit.

Effect on intestinal transit

Four groups of animals (Rats) were taken for the study; each group consisted of 10 rats. One group served as control and was given normal saline 0.5 ml per rat p.o. Groups II, III and IV were given the CAE produced inhibition of intestinal transit in a dose related manner as compared to normal control. The results are summarized in Table2. Thus CAE can be a useful agent in emotional disturbances in man, where stress can be factor responsible for increased intestinal motility. The results of this study were significant (p value < 0.05).

Toxicological studies

Approximate lethal dose in 50% animals (ALD_{50}) was determined by the method of (Smith, 1960). First the drug was administered in different doses to pairs of mice and rats and the

dose killing one animal out of the pair was taken as $ALD_{50.}$ It was found to be 8.29 gm & 2.39 gm/kg p.o. in mice and rats respectively. On the basis of ALD_{50} the test to determine the exact LD_{50} was conducted in 30 mice and 30 rats these were divided in groups of 10 animals each (Group I, II & III).

A dose nearer to ALD_{50} dose; one dose higher than this and one dose lower than this i.e. 4, 8 and 12 gms/kg body weight was administered p.o.in groups I, II & III in both mice and rats respectively. The lethal effect of the drug was observed from the mortality in each group of mice and rats at the end of 48 hours. A log dose response curve was plotted on graph paper and LD_{50} was calculated both in mice and rats. It was found to be 8.511$\pm$ 0.2 and 7.079 $\pm$ 0.4 gm/kg p.o. in mice and rats respectively table 3 and 4. The safely margin of CAE was calculated in both mice and rats using formula LD_{50} / ED_{50}.

Safe margin in mice and rats was found to be 130 and 93 respectively.

Table 1. Effect on motor activity in mice

Groups	Drug	Dose/kg / oral	No. of Animals	Movement count/min (mean $\pm$ S.E.)	% Reduction	ED_{50} /kg/oral
I	Control	5 ml	10	32$\pm$ 3.8	100.00	
II	CAE	25 ml	10	26$\pm$ 4.6	18.75	65.31 mg.
III	CAE	50 ml	10	20 $\pm$ 3.4	37.50	
IV	CAE	100 ml	10	10 $\pm$ 2.8	68.78	

***p <0.05 as compared to control**

Table 2. Effect on Intestinal transit in rats

Groups	Drug	Dose/kg/ oral	Mean total length mm	Mean charcoal length mm	% Decrease	ED_{50} /kg/oral
I	Control	5 ml	1004	770	100.00	
II	CAE	25 ml	989	631	16.88	75.86 mg.
III	CAE	50 ml	967	535	28.57	
IV	CAE	100 ml	1002	260	66.20	

***p <0.05 as compared to control**

Table 3. 48 hours mortality in mice

Groups	Drug	Dose/kg/ oral	No. of animals	48 hrs. mortality no. of animals	% Mortality	LD_{50} /kg/oral
I	CAE	4 gms	10	3	30	
II	CAE	8 gms	10	4	40	8.511 gm.
III	CAE	12 gms	10	7	70	

Table 4. 48 hours mortality in rats

Groups	Drug	Dose/kg/ oral	No. of animals	48 hrs. mortality no. of animals	% Mortality	LD_{50} /kg/oral
I	CAE	4 gms	10	3	30	
II	CAE	8 gms	10	5	50	7.079 gm.
III	CAE	12 gms	10	8	80	

DISCUSSION

Centella asiatica which has been described to posses CNS activity by other workers earlier was found to posses' mild sedative activity in our tests. This activity appears to be persistant in *Centella asiatica* from different places in different climate. Since the drugs have been used in Gastrointestinal disorders in ancient literature and its effects were not studied earlier on the mobility and peristalsis of intestine in vivo. Thus it was a new facet of the study where the drug was studied in albino rats by charcoal meal test. The drug was found to reduce the intestinal transit in a dose dependent manner. Thus its ancient use in Ayurveda in Grahni Roga which is associated with diarrhea and increased peristalsis is confirmed by our experimental study. The detail toxicity studies provide proof to the fact that the drug had a very wide margin of safely both in rats and mice and so is very innocuous in nature. Further, our study is indicates its use in common abdominal disorders like diarrhea in man.

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