

To evaluate and compare antidepressant activity of *Centella asiatica* in mice by using forced swimming test

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ABSTRACT

Background: *Centella asiatica* is a great multipurpose miracle herb used in Oriental medicine that has several therapeutic (such as sedative and hypnotic) effects. It also heals depression, grief, nervous stress and tension. In the present study we evaluated antidepressant-like effect of *Centella asiatica* using forced swimming test (FST). The forced swim test is a commonly used stressor test, where mice are forced to swim in specially constructed tanks for a particular period where there is behavioural activation characterized by vigorous swimming and diving to search for alternate routes to escape. Animal health including human has been shown to be affected by the stressful events of life inducing situation which alters cognition, learning memory and emotional responses, causing mental disorders like depression and anxiety and stress in mice.

Methods: The experiment was carried out with 24 healthy albino mice of either sex weighing about 25-30 gm. These were acclimatized to their environment for one week prior to experimentation. Two doses of aqueous extract (10 and 20 mg/kg) was injected intraperitoneally. After 30 min of injection, immobility and swimming times were measured and compared with control (negative control) and imipramine (positive control).

Results: In the present study *Centella asiatica* in the doses of 10 mg and 20 mg/kg significantly decreased the immobility time compared to the control than standard, thereby proving that it has anti-depressant activity. The dose of 20 mg/kg body wt. showed anti-depressant activity almost similar to the standard drug imipramine (10 mg/kg).

Conclusions: Due to lack of certain records, it is envisaged that the change of medicine both discontinuation as well as addition was done because of blood glucose control, cost factor (in case of pioglitazone) as well as patient's compliance.

Keywords: *Centella asiatica*, Mice, Immobility time, Anti-depressant like effect

INTRODUCTION

Centella asiatica is a great multipurpose miracle herb used in oriental medicine.¹ Botanical synonyms include *Hydrocotyle asiatica*.² It is native to India, Sri Lanka, northern Australia, Indonesia, Iran, Malaysia, Melanesia, Papua New Guinea, and other parts of Asia.³ Its Indian name is 'Brahmi' which means 'Bringing knowledge of the Supreme Reality' and it has long been used there medicinally and as an aid to meditation.²

In India it is chiefly valued as a revitalizing herb that strengthens nervous function and memory, it increases concentration and intellectual ability in children, It reduces

inflammation and fever, improves wound healing and immunity.^{4,5} It is used in the treatment of leprosy, various skin diseases, chronic and obstinate eczema, Psoriasis, ulcers and venereal diseases like syphilis and gonorrhoea.⁶ It is used in insanity. It has been successfully employed in amenorrhoea. Externally, the herb is applied to wounds, hemorrhoids and Rheumatic joints.^{2,7}

The medicinal properties have been ascribed to three Terpeninoids, asiatic acid, asiaticoside and madecassic acid.⁸

Studies have stated that *Centella asiatica* has neuroprotective and anti-depressant property. The present

study is conducted on animal models to evaluate anticonvulsant and antidepressant property of *Centella asiatica*.⁹

METHODS

Plant material and preparation of extract of *Centella asiatica*

Plants were obtained from Tirumala hills, chitoor district, Andhra Pradesh. The plant was authenticated for their correct botanical identity by the chief botanist. The whole plant was dried and coarsely ground with a grinder. For the preparation of the aqueous extract, the coarse powder of the plant was extracted with 8 parts of water under boiling for 5 hours and was filtered through a 400-mesh cloth to collect the extract. The extract was concentrated and finally spray dried to get a powder of greenish brown. The percentage w/w yield of extract was 41. The extract was preserved in deep freezer in air tight container.¹⁰

Animals

Swiss albino mice weighing 25-30 grams of either sex were obtained from the central animal house of Narayana Medical College, Nellore. They were housed in standard polypropylene cages with paddy husk as bedding and kept under controlled room temperature (21-23°C; relative humidity 60-70%) in a 12h light-dark cycle. Animals were given a standard laboratory diet and water ad libitum. All experiments were performed between 09:00 AM and 3:00 PM in order to minimize the effect of circadian rhythms. Animals were acclimatized to laboratory conditions one week prior to initiation of experiments.

Force swimming test¹¹

Albino mice of either sex weighing from 25 to 30g were used in this study. These were acclimatized to their environment for one week prior to experimentation. The animals were randomly distributed into four different groups. Each experimental group consisted of a 6 animals. Each group is caged separately after recording its body weight and the animals were marked with marker for identification.

Equipment: Glass chamber, Stop watch.

Experimental groups

The experimental animals were weighed, and randomly divided into four groups, each group consisting of six animals (n=6) were used.

Group I - Control group (Saline)-0.5 ml.

Group II - Standard group (Imipramine)-10 mg/kg.

Group III - Test group (Aqueous extract of *Centella asiatica*) - 10 mg/kg.

Group IV - Test group (Aqueous extract of *Centella asiatica*) -20 mg/kg.

Principle

When an animal is forced to swim, it tries to escape by making rigorous movements. When it cannot escape from the glass chamber, the animal surrenders to the situation and floats making very little or no movements (immobility) in glass chamber. Thus forced swimming - induced immobility is considered as helplessness or a state of depression in animals. Antidepressant drugs reverse or reduce immobility period.

Procedure

Normal saline (oral), Imipramine in the dose of 10 mg/kg (oral) and *Centella asiatica* were administered daily for 7 days to mice of either sex at two different doses (10 and 20 mg/kg, orally). On day 7 of treatment forced swimming test was conducted after 1hr of drug administration. Mice were allowed individually to swim inside the glass tub (25-12-25 cm) containing water up to 15 cm height for 6 min at room temperature (25-27°C). Total immobility period is measured during the 6 min in all groups. Later immobility period is compared in all groups.

All the experimental procedures and protocols used in this study were carried out according to the guidelines of institutional animal ethical committee and ethical committee clearance was obtained from IAEC (Institutional Animal Ethics Committee).

RESULTS

The mean immobility time of control group was 204±8.595. For imipramine it was 148.66±6.28. Immobility time of *Centella asiatica* in the dose of 10 mg and 20 mg was 183.83±7.25, 160.16±5.11 respectively. The mean immobility time was decreased significantly ***p<0.001 with *Centella asiatica* compared to control.

Table 1: Antidepressant activity of *Centella asiatica* using forced swimming test.

Groups	Treatment Dose(mg/kg)Orally	Mean Immobility time (sec)
Control	Normal saline	204±8.595
Standard	Imipramine 10 mg/kg	148.66±6.28***
<i>Centella asiatica</i>	10 mg/kg	183.83±7.25***
<i>Centella asiatica</i>	20 mg/kg	160.16±5.11 ***

*** p<0.001 compared to control group.

The mean immobility time of control group was 204±8.595. For imipramine it was 148.66±6.28. Immobility time of *Centella asiatica* in the dose of 10 mg

and 20 mg was 183.83 ± 7.25 , 160.16 ± 5.11 respectively. The mean immobility time was decreased significantly *** $p < 0.001$ with *Centella asiatica* compared to control.

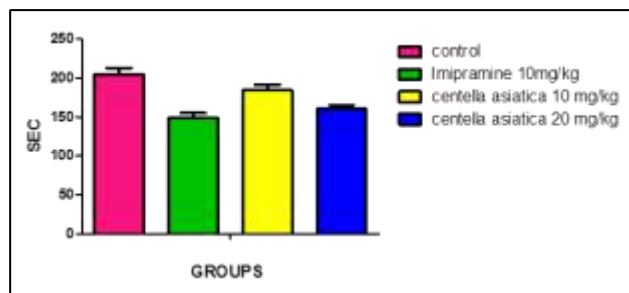


Figure 1: Antidepressant activity of *Centella asiatica* using forced swimming test Mean time of immobility time.

DISCUSSION

Porsolt's forced swimming test (Porsolt et al) is the animal model used in mice to check antidepressant properties. In this model immobility period was considered as a state of depression in mice Porsolt et al. proposed this behavioral model for the screening of new antidepressant compounds, concluded that the immobility time observed in the test reflected a state of lowered mood or hopelessness in animals, thus, this animal model is the most widely used tool for preclinical screening of putative antidepressant agents (Cryan et al).

In the present study *Centella asiatica* in the doses of 10 mg and 20 mg/kg significantly decreased the immobility time compared to the control than standard, thereby proving that it has anti-depressant activity. The dose of 20 mg/kg body wt. showed anti-depressant activity almost similar to the standard drug imipramine (10 mg/kg).

Our study is supported by Xin Liang et al showed antidepressant activity of *Centella asiatica* in mice using forced swimming test. The active principle involved in showing antidepressant activity is asiaticocicodide.¹²

Thamarai Selvi et al showed antidepressant activity of *Centella asiatica* in rats using forced swimming test. They proposed that increase in serotonin levels and inhibition of reuptake of serotonin levels in brain might be the responsible for antidepressant activity.¹³

The antidepressant activity of *Centella asiatica* is probably by increase in monoamine Neuro transmitters in brain.

CONCLUSION

Antidepressant activity of *Centella asiatica* was studied by forced swimming test in mice in the doses of 10 mg/kg and 20 mg/kg. This test shows that *Centella*

asiatica significantly decreased the immobility time in mice. The results suggest that *Centella asiatica* has dose dependent antidepressant activity comparable with imipramine. It is a valuable alternative therapy for depression and the mechanism of action involves increase in noradrenaline and serotonin levels in brain.

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