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Anti-Depressant Activity of *Camellia Sinensis* In Mice

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ABSTRACT

Depression is an affective disorder characterized mainly by change in mood and is associated with significant morbidity and mortality. A number of drugs are used for treatment but their adverse effects compromise the therapeutic effects. Thus search for an agent with minimal adverse effects and maximum therapeutic benefit is going on. In Asia, *Camellia sinensis* (CS) popularly known as green tea is widely used as a beverage and has been reported to have antioxidant property.On this basis, the present study was designed to evaluate the antidepressant activity of *Camellia sinensis* on albino mice. The antidepressant effect of *Camellia sinensis* was examined using two behavioral models, the forced swim test (FST) and tail suspension test (TST) in albino mice. The effect ofethanolicextract of *Camellia sinensis*in three different doses (3.3, 16.5 and 33mg/kg) was compared with the standard antidepressant, imipramine (10mg/kg). Antidepressant effect was studied both on acute and chronic administration (14 days) of *Camellia sinensis*. Acute and chronic treatment with *Camellia sinensis* reduced duration of immobility in FST in a dose dependent manner. In TST acute treatment with *Camellia sinensis* reduced duration of immobility at 3.3 & 16.5 mg/kg; whereas on chronic treatment CS reduced duration of immobility at 3.3 & 33 mg/kg. Acute & chronic treatment with *Camellia sinensis* produced antidepressant effect in both FST & TST models of depression in mice.

Keywords: Anti-depressants;*camellia sinensis*; forced swim test; tail suspension test

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INTRODUCTION

Depression is a major public health problem worldwide. Approximately 450 million people suffer from mental or behavioral disorders worldwide.[1]A number of synthetic drugs are being used in depressed patients but they have adverse effects that can compromise the therapeutic effects. Limitations to the use of available synthetic drugs open a way for alternative treatments for depression.

Plants have always been a source of drugs and herbal medicines are one of the ancient therapies that have stood the test of time. In Asia, *Camellia sinensis* popularly known as green tea is widely used as a beverage for centuries for its significant health-promoting effects.[2]From our laboratory, we have reported the antidepressant[3] and antianxiety activities[4] of a polyherbal product NR-ANX-C in rodents. *Camellia sinensis* is one of the major components (33%) of NR-ANX-C. In order to evaluate the contribution of *Camellia sinensis* in the antidepressant activity of NR-ANX-C, the present study was undertaken.

MATERIALS AND METHODS:

Adult albino mice (Swiss strain) weighing 25-30 grams, bred in our institutional animal house were used. They were housed in clean polypropylene cages in groups of three and maintained on a 12:12 hour dark/light cycle at an ambient temperature of 25±2^{o}C. They were fed with commercial pelleted chow and water *ad libitum.* Animals were acclimatized for seven days before exposure to the behavioral experiments. The study protocol was approved by the Institutional Animal Ethics Committee, Kasturba Medical College, Mangalore, and the study was performed according to the guidelines of CPCSEA.

The test drug, ethanolic extract powder of *Camellia sinensis* was supplied by Natural Remedies Pvt. Ltd, Bangalore, India. The standard drug, imipramine and test drug were suspended in 1% gum acacia (vehicle) before administration. All the drugs were given orally.

Animals were divided into five groups (n = 6 per group). Group I received vehicle (control), group II received imipramine (standard control), group III, IV and V received ethanolic extract of *Camellia sinensis* in doses of 3.3, 16.5 and 33mg/kg body weight respectively. For the acute study, sixty minutes after administration of drug/ vehicle the animals were exposed to the experimental procedures. For the chronic study, drug/vehicle was administered once a day for 14 days. The last dose was given sixty minutes prior to the experimental procedures.

The Forced Swim test (FST) was performed according to the method described by Porsoltet al.[5] Duration of immobility in the forced swim test was measured to evaluate the antidepressant potential of compounds. Sixty minutes after administration of drug/vehicle, animals were placed individually in a 5 liter glass jar (25 cm height x 12 cm diameter) filled with water to a height of 15 cm and the duration of immobility was recorded during the last 4 minutes of a 6 minutes test. A mouse is considered immobile when it is floating motionless or making only those movements necessary to keep its head above water surface. The water was changed after each test.

Tail suspension test (TST) was performed according to Steruet al.[6]Each mouse was suspended on a horizontal rod 50 cm above the surface of a table using an adhesive tape placed approximately one cm from the tip of the tail. Immobility duration was recorded for 6 minutes and mice were considered immobile only when they hung passively without any movements.

Statistical analysis was done between the groups and compared using One-way ANOVA followed by Dunnett's test. $P<0.05$ was considered significant.

RESULTS AND DISCUSSION:

In the present study, ethanolic extract of *Camellia sinensis* was evaluated for antidepressant activity. The behavioral score of immobility (FST) in control, imipramine and *Camellia sinensis* treated groups are shown in table 1. Acute and chronic treatment with *Camellia sinensis* reduced duration of immobility compared to control and the effect was comparable to that of imipramine.

Table 1: Forced swim test - Duration of immobility

Groups	Dose (mg/kg)	Duration of immobility (seconds)	
		Acute	Chronic
Control	-	178.16 ± 23.50	153.5 ± 15.07
Imipramine	10	87.83 ± 18.12*	24.66 ± 2.30$^{\#}$
Camellia sinensis	3.3	64.83 ± 16.47**	109.16 ± 21.38$^{\$}$
Camellia sinensis	16.5	83.33 ± 25.99**	118.66 ± 25.14$^{\$\$}$
Camellia sinensis	33	99.5 ± 30.49*	34.66 ± 6.69$^{\#£€}$

All values are expressed as Mean±SEM, *p<0.05 vs control; **p<0.01 vs control; #p<0.0001 vs control, $^{\$}$ p<0.01 vs imipramine; $^{\$\$}$ p<0.0001 vs imipramine, $^{£}$ p<0.01 vs CS 3.3 group; $^{€}$ p<0.01 vs CS 16.5 group

Table 2: Tail suspension test - Duration of immobility

Groups	Dose (mg/kg)	Duration of immobility (seconds)	
		Acute	Chronic
Control	-	274.33 ± 30.31	271.16 ± 20.80
Imipramine	10	168.33 ± 13.91*	176.83 ± 25.73*
Camellia sinensis	3.3	200.83 ± 15.20**	212.5 ± 11.44**
Camellia sinensis	16.5	197.66 ± 22.03**	242.83 ± 8.12$^{€}$
Camellia sinensis	33	259.66 ± 12.18$^{\#\$£}$	142.5 ± 15.21***$^{\$\$¥}$

All values are expressed as Mean ± SEM, * p<0.01 vs control; **p<0.05 vs control; *** p<0.0001 vs control, $^{\#}$p<0.01 vs imipramine; $^{\$}$p<0.05 vs CS 3.3 group; $^{£}$ p<0.05 vs CS 16.5 group, $^{€}$ p<0.05 vs imipramine; $^{\$\$}$ p<0.01 vs CS 3.3 group; $^{¥}$ p<0.0001 vs CS 16.5 group

In TST acute treatment with *Camellia sinensis* reduced duration of immobility at 3.3 & 16.5 mg/kg only; whereas on chronic treatment *Camellia sinensis* reduced duration of immobility at 3.3 & 33 mg/kg only (Table 2).

Camellia sinensis reduced the duration of immobility of mice in both the experimental models studied. The maximum reduction of immobility in both the tests in the acute study were seen at lower doses (3.3 & 16.5 mg/kg), where as in the chronic study reduction of immobility in both the tests was better at high dose (33mg/kg). This may be because *Camellia sinensis* possibly lead to development of tolerance, either by induces its own metabolism, resulting in development of tolerance and hence a higher dose is required on chronic use.

Camellia sinensis contains antioxidant polyphenols/flavonoid catechins, carotenoids, tocopherols, and ascorbic acid.[7]The main catechins are epicatechin, epigallocatechin and epigallocatechingallate. Earlier studies have shown that epicatechin has been found to enhance learning & memory ability in mice.[8] Epigallocatechingallate increases protein kinase C in the membrane and cytosolic fractions of mice hippocampus which is the learning site of brain.[9] Theanine, one of the amino acids in *Camellia sinensis* has been found to have beneficial effects by increasing the brain levels of serotonin and dopamine since in depression the levels of these two neurotransmitters are decreased.[10,11] It has been established that reduction in immobility time in the FST and TST depends mainly on the enhancement of central 5-HT and catecholamine neurotransmission.[12] Hence it can be postulated that ethanolic extract of *Camellia sinensis*plausibly acts by the same mechanism. Moreover, due to its methyl xanthine content, *Camellia sinensis*may possess a stimulating effect in brain[13] which may add to its anti-depressant effect. The antidepressant effect of *Camellia sinensis*could be attributed to the above mechanisms but the precise mechanisms are not completely understood and have not been pursued in this study.

This study suggests that consumption of green tea (*Camellia sinensis*) may have beneficial effects on depressive symptoms and further clinical trials are required to ascertain whether it can be used as add on therapy in depression.

CONCLUSION:

Acute & chronic treatment with *Camellia sinensis* produced antidepressant effect in both FST & TST models of depression in mice.

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