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Evaluation of Anti-Anxiety and Anti-Depressant Activities of Sadamanjil Chooranam Extract (*Nardostachys Jatamansi*) In Mice

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ABSTRACT

In Siddha system of medicine, emotions and thoughts are considered to have a direct impact on a person's physical health. Because of the importance placed in the minds of Siddha system of medicine, many psychotropic drugs from this traditional system help often very specifically to treat the mental illness very effectively. One of such drug mentioned in Siddha system of medicine is Sadamanjil Chooranam (*Nardostachys jatamansi* DC).This plant used in Siddha system of medicinein the treatment of excitement, insomnia and depressive illness. In the present study, an attempt has been made to explore the anti-anxiety and anti-depressant potential of the aqueous extract of *Sadamanjil Chooranam* (SMCE)in Elevated plus maze model, Forced Swim testand Tail suspension testin the mice model. Two dose levels of trial drug SMCE (100mg/kg and 200mg/kg body weight) were administered in mice. EPM result showed that the time spent of the mice after the administration of SMCE 100mg/kg and 200mg/kg showed the higher percentages of time in the open arms and the percentage of open arm entries which were statistically significant.TST and FST results showed significant decreases in the immobility period when compared with control group. The greater the immobility time observed with mice treated with higher dose of SMCE (200mg/kg) which showed the dose dependent activity of the trial drug. From the result, it is concluded that SMCE extract appeared to possess potent antianxiety and antidepressant effects and both the effects are apparently dose-dependent.

Keywords: Anti-anxiety, Anti-depressant, Elevated plus maze, Forced swim test, Tail suspension test, Sadamanjil Chooranam, *Nardostachys jatamansi*.

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INTRODUCTION

Mental health is an essential element of quality of life, performance and social participation. For the quality of life, psychological well-being is just as important as a healthy body. Mental illness can affect anyone. Impairments of mental health are widespread and range from mild restrictions on the psychological well-being to severe mental disorders. Due to their prevalence in the population, in particular depression, anxiety disorders, addiction disorders and dementias have great public health relevance. Mental disorders are often still misunderstood or not taken seriously. Mental health problems are manifested in various symptoms with different causes. But some of the mental health problems are common, which include anxiety and depression disorders. According to World Health Report, about 450 million people suffer from a mental or behavioral disorder [1].This amounts to 12.3 % of the global burden of disease, and predicted to rise up to 15 % by 2020 [2]. Anxiety and depression are burdensome psychiatric disorders that can change the normal chemistry of the brain due to lack of certain neurotransmitters include serotonin, dopamine and norepinephrine and affect the physical health, mood, thoughts and activities [3]. If left untreated, depression can lead to suicide. Because most of the suicide or suicidal attempts are always associated with untreated or severe depression. These facts highlight the importance of accurate diagnosis, effective and systematic treatment of depression [4].There are various depression medications and psychotherapies that can be used to treat depressive disorders. But most of the psychotropic drugs may cause side effects such as headache, nausea, dry mouth, constipation, bladder problems, blurred vision, sexual problems, poor efficacy and tolerability. Since psychiatric disorders are on the rise, clinicians are looking for alternative remedies and herbal medications for the treatment of neurobehavioral disorders [5]. In recent decades, researchers are turning to the traditional remedies because of their several beneficial effects in the treatment of neurological disorders. Many researches in plant origin, modern methods of isolation and identification of chemical constituents have been progressed remarkably worldwide and demonstrating the pharmacological effectiveness of different species of plants by various animal experiments [6]. In Siddha system of medicine, emotions and thoughts are considered to have a direct impact on a person's physical health, but also mental and physical health are equally valued. Because of the importance placed in the minds of Siddha system of medicine, many psychotropic drugs from this traditional system help often very specifically to treat the mental illness very effectively. One of such drug mentioned in Siddha system of medicine is Sadamanjil Chooranam (*Nardostachys jatamansi* DC -Family: valerianaceae) is

commonly known as Indian spikenard or musk root and it is a native of Himalayan region, available in Deccan plateau also [7].This plant is often used in Siddha system of medicine for various ailments include hypertension, respiratory disorders, peripheral edema, epilepsy, anxiety, insomnia, depression and other neurological disorders [8]. More than 25 active principles have beenisolated from the rhizome part of this plant which includes jatamansic acid, jatamansone and nardostachone [9-11].Jatamansone is the principle sesquiterpenoid and the renders majority of the biological activity [12]. From all the above facts, it was aimed to explore the anti-anxiety and anti-depressant potential of the aqueous extract of Sadamanjil Chooranam(SMCE)in Elevated plus maze model, Forced Swim test and Tail suspension test in the mice model.

MATERIALS AND METHODS

Antidepressant activity was assayed using tail suspension test and forced swim test and an antipsychotic model was assayed in Amphetamine stereotype in mice.

Plant materials

The plant material *Nardostachys jatamansi* was procured from the Country drug shop, Parrys Corner, Chennai. After collection, plant material was identified and authenticated by the botanist, Government Siddha Medical College, Arumbakkam, Chennai. A specimen sample was deposited at the herbarium for future reference. The roots were washed and disinfected. They were dried in a shady ventilated room. After complete drying the roots were pulverized to make Sadamanjil Chooranam as per Siddha classical text [13] and 100 g of these extracted with one liter of water. The aqueous extract was lyophilized to 10% was obtained and one gram per 100 ml.

Animals

The experimental animals used in this study were Swiss albino mice of either sex weighing between 25-30 g obtained from animal house of Department of Pharmacology, Vel's University, Chennai. They were kept under controlled conditions, 24 ± 0.5 ^{o} C, relative humidity 50-60%, in a 12 h: 12 h light-dark cycle alternate. All the animals were fed with standard pellet diet and water ad libitum. All experimental protocols were approved by the Institutional Animal Ethical Committee (IAEC) and CPCSEA guideline for laboratory animal care was adhered during the maintenance and experiments. Prior to each experiment, the animals were fasted for 12 hours with free access to water. All the experiments were carried out between 11:00 to 17:00 hours.

Drugs & chemicals

Diazepam (Lupin Pharmaceuticals, Mumbai, India) was used reference standard for anti-anxiety activity. Fluoxetine hydrochloride (Cadila Pharmaceuticals, Ahmadabad, India) and imipramine

hydrochloride (Psycho Remedies, Ludhiana, India) were used reference standards for anti-depressant activity.

Behavioral tests

Elevated plus maze is an animal model of anxiety disorder following unconditioned reflex. It is a well-validated animal model to anxiogenic and anxiolytic effects of drugs to assess which was developed and modified by Kulkarni et al [14]. The test apparatus is a plus-shaped cross of two open (16 x 5 cm) and two enclosed arms (16 x 5 x 12 cm) opposite each at an angle of 90^0 connected with a central area called neutral zone elevated with 25 cm from the floor [15].

Method

The experimental animals were divided into four groups of six animals each. The first group considered as a control group and was treated with vehicle (Normal saline) only. The second group considered as standard group which was treated with reference drug (Diazepam 2 mg/kg body weight). The third and fourth groups were considered as test groups and were treated with SMCE at the dose levels of 100mg and 200mg/kg body weight respectively. Animals were fasted 18 h prior to the experiment. An adaptation period of about forty five minutes after the drug treatment, the experimental animals were placed individually in the center of a platform facing one of the arms was closed, because animals naturally prefer the enclosed arms, as the aversion against the open arms predominates. Then the animal was observed for 5 minutes, recording the number of times that entered into the open or closed arms, and the average time spent by the animal was recorded.

Average time was calculated by the following formula.

Average time = total duration in the arms / number of entries.

During the experiment, all the animals were allowed to socialize to avoid unnecessary anxiety. After each animal, the test apparatus was carefully cleaned.

Antidepressant activity

Experimental protocols

Mice were randomly selected to form groups of 6 each. The animals were acclimatized one hour before for behavioral tests.

Group I – Control group received distilled water (1ml, p.o)

Group II – Standard groups received Imipramine (15mg/kg, p.o) for forced swim test and fluoxetine (20mg/kg, p.o) for the tail suspension test.

Group III – Test group 1 received SMCE 100 mg/kg, p.o

Group IV – Test group 2 received SMCE 200 mg/kg, p.o

Tail suspension test (TST)

The tail suspension test has been developed as an alternative to forced swimming test and based on a similar concept. The tail suspension test was originally developed by Steru et al [16]. This behavioral despair test commonly employed experimental model for screening psychotropic drugs for its antidepressant, sedative like activity in mice. In this method, mice suspended by the tail hook using a piece of adhesive tap causing no pain in animals and the hook are connected to a sensor which records changes in movement for 6 minutes. The measuring principle is based on the behavior of a rodent trying to escape an uncomfortable situation. The magnitude of this immobility is considered correlated with depression, and is significantly reduced by antidepressants. Mouse movements are analyzed in terms of activity, energy and power developed in time.

Forced Swim Test

Forced Swim Test also called Porsolt test or behavioral despair test is widely used for assessing depression in animal models [17]. The test is frequently used to measure the effect of antidepressants drugs on behavior. Mice were individually placed in a glass chamber (25 ×15 × 25cm) containing 15 cm height of water maintained at 25± 2°C.Swim test training was carried out in each test animal 24 hours before the experiment for 15 minutes period. 30 minutes before the experiment, different doses of trial drug administered, distilled water control group. Mice were forced to swim in the tank. The test lasts 6 minutes, but only the last 4 minutes of the test are used to record the time swimming. Because each animal showed energetic movement during initial 2 minutes period of the test. The duration of immobility was manually recorded during the next 4 min of the total 6 min testing period.

Statistical Analysis

The results were expressed as mean ± S.E.M. The differences were compared using one way analysis of variance (ANOVA) and subsequently followed by Dunnet's multiple comparison test. $p < 0.05$ considered as significance level.

RESULTS AND DISCUSSION

Anti-anxiety activity

Elevated plus maze model of anxiety

Anxiolytic effect of SMCE on the behavior of rats in the elevated plus-maze was presented in Table 1 and Figure.1. The average time spent of the mice after the administration of SMCE 100mg/kg and 200mg/kg showed the higher percentages of time in the open arms (13.42± 0.85

and 10.08±0.34 respectively) and the number of open arm entries(6.58± 0.32 and 5.42± 0.43 respectively) which were statistically significant compared to control group. Here, at the doses tested, the greater effect was observed by 100mg/kg dose level than 200 mg/kg dose. The standard group received diazepam (0.5mg/kg) yielded highly significant responses of 14.75± 0.25and 7.75± 0.34in the frequency and time variables respectively. Control group had no significant effects on any of the parameters that were measured on the elevated plus maze method. In this model, the natural aversion of mice to height and open space is used as a fear stimulus. The entries in the open arms of the apparatus as well as the time spent are a quantitative measure of anxiety behavior. Anxiety in animals results in decreases the motor activity which is regained by anxiolytic drugs. This motor activity is measured by the time spent by the animal in the open arms[18]. From the present study it was found that SMCE significantly prolonged the time animals spent in the maze compared to that of the control group. Normally, when mice are placed ina maze they prefer to hide rather than explore, because they are anxious. In this test, mice generally nervous and fearful in the maze were trans formed by SMCE and mice treated with SMCE showed a quiet curiosityin exploring their environment. When mice treated with two doses of SMCE(100mg and 200mg/kg body weight) for a period of 10 days, SMCE in higher dose (200mg/kg) causes a significant reduction in locomotion due to its well-known sedative effect. Hence a small dose of SMCE extract can relieve anxiety without sleep.

Table 1. Anti-anxiety effect of Sadamanjil Chooranam extract (SMCE) in mice

Treatment	Dose	No. of entries in open arms (Mean±SEM)	Average time spent in open arms (Mean±SEM)
Control	Vehicle	3.22± 0.18	3.60± 0.21
Standard(Diazepam)	2mg/kg	7.75± 0.34*	14.75± 0.25*
SMCE 100	100mg/kg	6.58± 0.32*	13.42± 0.85*
SMCE 200	200mg/kg	5.42± 0.43*	10.08±0.34*

The data is expressed as Mean ± SEM.; ANOVA followed by Dunnet's Multiple comparison test. *P<0.05 vs Control.

Two types of behavior can be observed during the test. Tail Suspension Test (TST) and Forced Swim Test (FST) are two of the most commonly used behavioral tests in rodents for evaluating drugs having antidepressant-like activity. These tests are quite sensitive and relatively specific to all major classes of antidepressants.

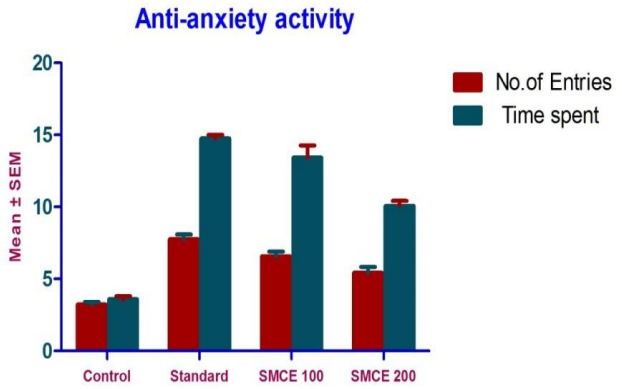

Figure:1. Showing the anti-anxiety effect of SMCE with two dose levels in rats Anti Depressant activity

Tail suspension test (TST)

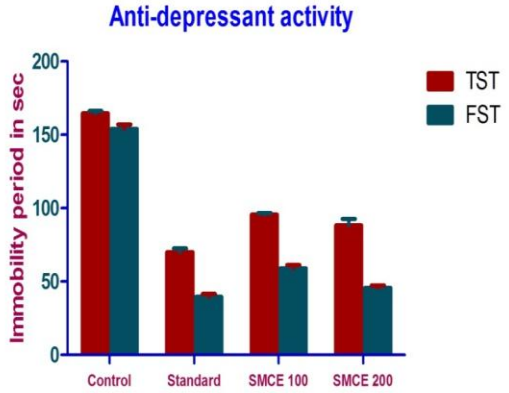

Figure:2. Showing the anti-depressant effect of SMCE with two dose levels in rats

Table 2: Effect of Sadamanjil Chooranam extract (SMCE) on locomotion of mice during Tails suspension and Forced swim tests

Treatment	Immobility period in Tail suspension test (sec)	Immobility period in Forced swim test (sec)
Distilled water 2 ml	164.5±1.82	154±3.12
Imipramine 15 mg	70.00±2.54*	39.5±2.09*
SMCE 100mg	95.50±1.31*	59.16±2.14*
SMCE 200mg	88.33±4.46*	45.83±1.60*

Statistical analysis of data was carried by one-way ANOVA followed by Dunnet's multiple comparisons test. *$p < 0.05$ vs Control

Table 2 and Figure.2 showed the result of the effect of SMCE on locomotion of mice during the tail suspension test. Two dose level of trial drug SMCE (100mg/kg and 200mg/kg body weight) treated mice showed significant decreases in immobility period of 95.50±1.31 and 88.33±4.46when compared with control group (164.5±1.82). The greater the immobility time

observed with mice treated with higher dose of SMCE (200mg/kg) which showed the dose dependent activity of SMCE. Similarly, standard drug Imipramine treated mice, as expected showed a significant decrease in the immobility period (70.00±2.54). This antidepressant effect probably due to an increase in transmission monoaminergic, result from inhibition of the reuptake of monoamines, which may be related to its content of flavonoids.

Forced swim test (FST)

The forced swimming test represents a state of stress induced in the mice that has the ability to move. This behavior shift is related to an adrenergicneur on activity. The non-depressed mice, even when they are unable to escape cylinder half filled with water, will try to swim and fight to escape beakers. But depressive mice will stop trying earlier than non-depressed mice, and begin to float in the cylinders, demonstrating a behavioral despair. Time floating or immobility during the forced swim test is an accurate indication of antidepressant and anxiolytic effects. The forced swim test result is presented in Table 2 and Figure.2. From the result, it was observed that, the swimming time was significantly higher in the group treated with test drug SMC Eat the dose level of 200mg/kg (45.83±1.60) when compared with control group (154±3.12). Mice group treated with SMCE at the dose level of 100mg/kg showed no significant periods of swimming time (59.16±2.14). Regarding the standard group treated with Imipramine showed highly significant increases in swimming time (39.5±2.09) related to the control group. World Health Organization (WHO) states that depression is the leading cause of disability as measured by Years Lived with Disability (YLDs) and the third leading contributor to the global burden of disease[19-20].Various studies have shown that under activation of serotonergic and noradrenergic systems play a major role in the pathogenesis of depression [21].SMCE according to our findings significantly reduces immobility time in the forced swim test showing its antidepressant effect. The antidepressant activity of Sadamanjil Chooranam extractcan be attributed to its inhibitory effect on MAO enzyme [22]. Inhibition of this enzyme causes reduction inthe metabolism of biogenic amines and subsequent increase in the levels of catecholamine and indoleamines [23]. Antioxidant activity of Sadamanjil Chooranam can be another reason for its antidepressant activity [24].

CONCLUSIONS

In our present experiment, the extract of Sadamanjil Chooranam (*Nardostachys jatamansi*) validated for its antianxiety and antidepressant effect in both experimental models of anxiety and depression. The Sadamanjil Chooranam achieved two different objectives such as the reduction

of anxiety and depression to feel better emotionally and mentally. From the result, it is concluded that the Sadamanjil Chooranamextract appeared to possess potent antianxiety and antidepressant effects and both the effects are apparently dose-dependent. Further clinical studies have to be conducted to extend these results and confirm its traditional use as antianxiety and antidepressant potentials.

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