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RESEARCH ARTICLE

An Investigation of Anti-Depressant Activity of *Cinnamomum Camphora* Oil in Experimental Mice

Jay Rabadia[1*], Satish.S[1], J.Ramanjaneyulu[1], Narayanaswamy VB[1]

[1]Karavali college of Pharmacy, Vamanjoor, Mangalore

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ABSTRACT

Depression is one of the leading causes for many disorders in both developed and developing countries. *Cinnamomum camphora* oil (CCO) has been referred in Indian traditional medicine system for the treatment of various diseases which includes its antidepressant activity. Evaluation of antidepressant activity was done by using 3 doses of CCO in 2 invivo models. Group I received normal saline, group II received standard drug, group III received 250 mg/kg, group IV 500 mg/kg and group V 750 mg/kg of CCO. Animals treated with 3 doses of CCO showed decrease in their immobility times in Forced Swim Test (FST) & Tail Suspension test (TST) which was significant when compared with control.

Keywords: *Cinnamomum camphora* (CCO), Antidepressant models, Swiss albino mice.

1. INTRODUCTION

The human central nervous system is an extremely complex structure, having more than 12 billion nerve cells. Together with the endocrine system, it coordinates and regulates the functioning of all body organs[1]. Depression is highly prevalent condition, affecting approximately 350 million people worldwide according to WHO 2012[1]. It is a clinically and biologically heterogeneous disease. It is one of the most prevalent and costly psychiatric disorder worldwide, with 10-30 % of woman and 7-15% of men likely to suffer from depression in their life time[2]. Furthermore, the World Health Organization revealed that depression is the fourth leading cause of disability worldwide exceeded by lower respiratory infections, prenatal conditions and HIV/AIDS[3]. There are a number of formulations available in the modern medicines that are effective against mental and physical disorders in depression. Modern medical practitioners prescribe antidepressant drugs which are intended for symptomatic relief rather than dealing with the root cause of stress and depression. Herbal formulation has been in use for many years not only in Asian countries but also globally for human well being. The herbal formulation claimed to enhance physical endurance, mental function and non specific resistance of the body because of their antioxidant property[4].

Since the depressive disorders are having a huge impact on our lives, it is worth evaluating the alternative forms of medicines which can be used for its treatment. So in this study, an effort was made to investigate the antidepressant effect of *Cinnamomum camphora* Oil in experimental animals using different type of models of depression. *Cinnamomum camphora* is a massive broad leaved evergreen tree that grows to 75 m tall with a broad sweeping crown. The tree has thick scabrous bark, strong branches, young shoots, speckled greeny orange. The bark is rough and brownish-grey. it is found in much of east Asia including India, China, Indochina, Taiwan, Korea. It grows in warm temperature and subtropical forest on mountains and further north in coastal forests[5]. The major components of essential oil of *C. camphora* as determined by GC-MS are reported as fenchone (34.82%), camphene (23.77%), α-thujene (17.45%), L-limolene (7.54%) and cis-p-menthane (5.81%). Being volatile in nature, the essential oil of C. camphora may be easily emitted from the treated raw materials during sun drying[6].

*Corresponding author: Jay Rabadia | Karavali college of Pharmacy, Vamanjoor, Mangalore | email: smarty_jigo@yahoo.co.in

Cinnamomum camphor leaves, flowers, seeds, roots, bark and fruits are utilized to treat infections, skin diseases. Camphor is widely used in cooking (mainly for dessert dishes such as kheer or paal paayasm) in India where it is known as *pachha karpooram* (literally meaning "green camphor"). It is widely available at Indian grocery stores and is labeled as "edible camphor". The oil can be used in the manufacture of foam booster, glycerol and cosmetics. The therapeutic properties of camphor oil are analgesic, antidepressant, anti-inflammatory, antiseptic, cardiac stimulant, carminative, diuretic, febrifuge, antihypertensive, insecticide, laxative, rubefacient, stimulant, sudorific, vermifuge and vulnerary[5].

Camphor oil can be used in the treatment of nervous depression, acne, muscular aches and pains, sprains, rheumatism, bronchitis, coughs, colds, fever, flu and infectious diseases . Camphor absorbs easily into the skin and produces a cooling, soothing effect[7].

2. MATERIALS & METHODS:

2.1. Drugs and Chemicals :

Ethanol, Chloroform, 5 % Tween 80, Imipramine (15 mg/kg), Diazepam (1 mg/kg)

2.2. Instruments:

Glass cylinder, Tail Suspension Appartus, Stop Watch.

2.3. Collection of bark:

The wood of *Cinnamomum camphora* belonging to the family Lauraceae were collected from Ecotech Technologies (I) Pvt Ltd, Mumbai, Maharashtra. It is preserved in the departmental library for future reference.

2.4. Preparation of dose:

Woods were washed 2 or 3 times with tap water so that it was made free from all dust materials. They were cut into small pieces and dried under shade till they were brittle. The dried pieces of wood were powdered with the help of mixer grinder and 100g of powder is used for extraction. Steam distillation is a process employed to extract essential oils from organic plants by passing steam generated through the plant material.

2.5. Experimental Animals:

Swiss albino mice weighing 18-30 gm, were used for the study. The mice were inbred in the central animal house of the Department of Pharmacology, Karavali College of Pharmacy, Mangalore, under suitable conditions of housing, temperature, ventilation and nutrition were used for antidepressant activity. They were kept in clean dry cages week before the beginning of the experiment to acclimatize with the experimental conditions. The animals were fed with standard pelleted diet (Lipton India Ltd., Mumbai) and distilled water *ad libitum* was maintained at 21^0C-23^0C under a constant 12hrs light and dark cycle. The animal care and experimental protocols were in accordance with CPCSEA /IAEC.

2.5. Standard Drug:

Imipramine (15 mg/kg) is used for antidepressant activity as a standard drug.

2.6. Experimental Design:

Experimental mice are randomly divided into five groups and each groups contain six animals:

Group I – Received 0.05ml/10g of Normal saline intra peritoneally.

Group II – Received 15 mg/kg Imipramine intra peritoneally.

Group III – Received 250 mg/kg *cinnamomum camphora* Oil orally.

Group IV – Received 500 mg/kg *Cinnamomum camphora* Oil orally.

Group V – Received 750 mg/kg *Cinnamomum camphora* Oil orally.

2.7. Statistical Analysis :

Results are prepared as Mean ± SEM. One way ANOVA was used for multiple comparison followed by Dunnett's multiple comparison tests. For all tests a "P" value of 0.05 or less was considered for statistical significance.

3. EXPERIMENTAL MODELS:

3.1. Forced Swim Test[8]:

Forced swim test, the most frequently used behavioral model for screening antidepressant-like activity in rodents, was first proposed by Porsolt., et. al. The procedure was same as followed previously. Mice were individually forced to swim in open glass chamber (25 × 15 × 25cm) containing fresh water to a height of 15 cm and maintained at 23-25 °C. At this height of water, animals were not able to support themselves by touching the bottom or the side walls of the chamber with their hind-paws or tail. Water in the chamber was changed after subjecting each animal to FST because "used water" has been shown to alter the behavior. Each animal showed vigorous movement during initial 2 min period of the test. The duration of immobility was manually recorded during the next 4 min of the total 6 min testing period.

Mice were considered to be immobile when they ceased struggling and remained floating motionless in water, making only those movements necessary to keep their head above water. Following swimming session, mice were towel dried and returned to their housing conditions.

3.2. Tail Suspension Test[9,10] :

Tail suspension test commonly employed behavioral model for screening antidepressant-like activity in mice, was first given by Steru .,et.al. Animals were moved from their housing colony to laboratory in their own cages and allowed to adapt to the laboratory conditions for 1-2 hr. Each mouse was individually suspended to the edge of a table, 50 cm above the floor, by adhesive tape placed

approximately 1 cm from the tip of the tail. Each animal under test was both acoustically and visually isolated from other animals during the test. The total period of immobility was recorded manually for 6 min. Animal was considered to be immobile when it didn't show any body movement, hung passively and completely motionless. The test was conducted in a dim lighted room and each mouse was used only once in the test. The observer, recording the immobility of animals, was blind to the drug treatments given to the animals under study.

4. RESULTS:

4.1. Forced Swim Test:

In FST, Table No.1shows that animals treated with three doses of CCO (250, 500 and 750 mg/kg) showed decrease in their immobility times, which was significant (116.7 ± 6.146, 110.8 ± 12.54; p<0.05 and 101.7 ± 9.458; p<0.01) when compared with control (146.0 ± 0.6325). Similarly, animals treated with imipramine (15 mg/kg), as expected, showed a significant decrease in the immobility time (41.00 ± 0.3651; p<0.001). Animals treated with high dose (750 mg/kg) show more significant decrease in immobility time when compared with low dose (250 mg/kg) and moderate dose (500 mg/kg).

Group No.	Drug Treatment	Dose (mg/kg)	Immobility period, mean ± S.E.M [n=6]
I	Control	0.05 ml/10 g	146 ± 0.6325
II	Imipramine	15	41.00 ± 0.3651***
III	CCO	250	116.7 ± 6.146*
IV	CCO	500	110.8 ± 12.54*
V	CCO	750	101.7 ± 9.458**

Values were mean ± S.E.M. for (n=6) expressed as the time (in sec) of 6 animals in each group. Data analysis was performed using Dunnett's test. *P < 0.05, **P < 0.01, ***P < 0.001 vs. control

Table No.1. Effect of CCO on Immobility time in FST :

Group No.	Drug Treatment	Dose (mg/kg)	Immobility period, mean ± S.E.M [n=6]
I	Control	0.05 ml/10 g	159 ± 0.6325
II	Standard	15	73.17 ± 0.4173***
III	CCO	250	133.3 ± 8.758*
IV	CCO	500	128.3 ± 8.33*
V	CCO	750	122.5 ± 8.342**

Values were mean ± S.E.M. for (n=6) expressed as the time (in sec) of 6 animals in each group. Data analysis was performed using Dunnett's test. *P < 0.05, **P < 0.01, ***P < 0.001 vs. control

Table No.2. Effect of CCO on Immobility time in TST :

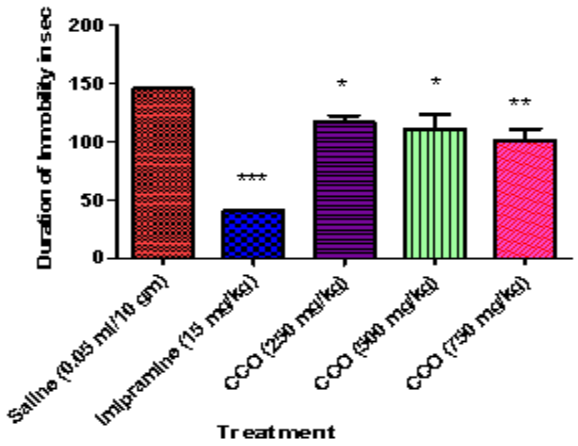

Fig .1.Comparative profile of immobility parameter in FST after oral administration of 250, 500 & 750 mg/kg of CCO.

4.2. Tail Suspension Test :

In TST, Table No.2 shows that animals treated with three doses of CCO (250, 500 and 750 mg/kg) showed decrease in their immobility times, which was significant (133.3 ± 8.758, 128.3 ± 8.33; p<0.05 and 122.5 ± 8.342; p<0.01) when compared with control (159.0 ± 0.6325). Similarly, animals treated with imipramine (15 mg/kg) as expected showed a significant decrease in the immobility time (73.17 ± 0.4173; p<0.001). Animals treated with high dose (750 mg/kg) shows more significant decrease in immobility time when compared with low dose (250 mg/kg) and moderate dose (500 mg/kg).

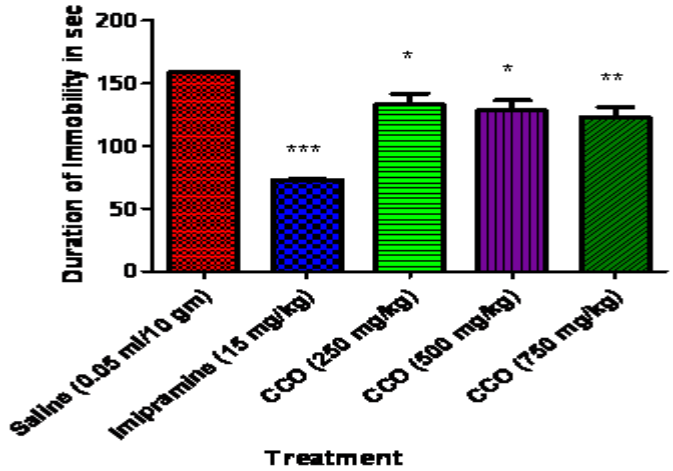

Fig 2.Comparative profile of immobility parameter in TST after oral administration of 250, 500 & 750 mg/kg of CCO.

5. DISCUSSION & CONCLUSION:

The purpose of this study was to evaluate the antidepressant effect of *Cinnamomum camphora* oil (CCO) by using antidepressant models. The main finding of present investigation suggests the antidepressant activity of CCO in different animal models of depression.

The review on pathophysiology of depression reveals that the depression occurs due to many reasons and many hypotheses have been proposed on it. But widely accepted mechanism involved in pathogenesis of

depression is mono amine deficiency. Certain biological monoamine like NA and 5-HT, dopamine especially decrease in NA and 5-HT causes depressive episodes in patients suffering from depression which makes their life miserable.

The current available drug therapies focus on increasing the availability of NA and serotonin which centres on the inhibition of MAO.

The incidence of depression in the community is very high and is associated with lot of morbidity. Hence, it is very important to address these problems and find effective remedies. Though several drugs are available, all are associated with some limitations and there is an urgent need for alternative medications for these disorders. Despite the widely popular use of CCO for treating nervous disorders, there is an absence of scientific reports about the evaluation of its pharmacological effects. In this work, it was demonstrated that the administration of different doses of CCO in mice was able to induce antidepressant effects.

In present study, behavioural models namely forced swim test and tail suspension test were employed. Both represent the behavioural despair models, claimed to reproduce a condition similar to human depression. The tests were based on the observation that animals, following initial escape oriented movements, develop an immobility posture when placed in an inescapable chamber. The immobility is thought to reflect either a failure of persistence in escape directed behavior or development of passive behavior that disengage the animal from active form of coping with stressful stimuli[11].

We observed that following oral administration of CCO demonstrated significant (compared to control treated group) dose dependent reduction in duration of immobility.

It has been established that the shortening of immobility time in the forced swimming and the tail suspension tests depends mainly on the enhancement of central 5-HT and catecholamine neurotransmission[12]. Early evidence of a role for noradrenaline in depression came from the discovery that drugs, either causing or alleviating depression, acted to alter the noradrenaline metabolism. Furthermore, depletion studies carried out in treated and untreated patients indicated a role for serotonin and noradrenaline in depression[13].

It has been recently shown that the regulation of α2-adrenergic receptor may be the major mechanism of this model. The results indicate that essential oil of *Cinnamomum camphora* may have an antidepressant-like effect and 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. The FST shows a strong sensitivity to monoamine alterations and is a very specific cluster of stress-induced behaviors that are not related to depression symptoms in humans, but which are nonetheless exquisitely sensitive to monoaminergic manipulations. It also provides a useful model to study neurobiological and genetic mechanisms underlying stress and antidepressant responses.

Forced swim test is most widely used test for screening of antidepressants involves placing mice in cylinder of water from where there is no escape and measuring the animal's behavior for several minutes. Initially, rodent's displays escape orientation behaviours, however, their behavior changes eventually into movement that are just sufficient to keep their head above the water-termed immobility. This was originally interpreted by Porsolt *et al* as "behavior despair"such that the animals has lost the motivation to perform escape oriented behavior. This behavioural immobility reflecting a state of despair is reduced by a broad spectrum of antidepressant drugs[14].

In tail suspension test, it has been argued that the TST is less stressful than FST and has greater pharmacological sensitivity. In this test, mice are suspended by their tail for defined period of time and duration of their immobility is assessed. Typically, animals are immediately engaged in escape oriented behavior followed by progressive increasing period of immobility. We observed that following oral administration of CCO demonstrated significant (compare to control) a dose dependent reduction in duration of immobility[15].

In both FST & TST, the results clearly revels tha fact that standard treated animals showed better response as compared to CCO & CCO treated animals showed good response as compared to control.

The exact mechanism underlying antidepressant effect of essential oil of *Cinnamomu camphora* is not clear but it may be apparently related to active compounds present in CCO are reviewed[6]. We cannot discard the possibility that more than one compound are the responsive for its antidepressant activity. Chemical studies have reported the presence of several monoterpenoid compounds in the essential oil of *Cinnamomum camphora*, primarily; β-pinene, β-thujone, limonene and also linalool are reported to have antidepressant activity[16].

Recently several studies have suggested the antidepressant effect of β-pinene which can increased the level of dopamine and depressed the activity of MAO in rabbits. Also some studies reported that many biologically active substances including monoterpenoids were claimed as a potent inhibitors of MAO-A & MAO-B. This might primarily account for the antidepressant activity and suggests applications in other CNS disorders[17].

The results indicate that essential oil of *Cinnamomum camphora* may have an antidepressant like effect.

However further experiments evaluating the levels of noradrenaline and serotonin in different regions of brain is necessary to confirm this hypothesis.

6. REFERENCES:

1. http://www.who.int/mediacentre/news/notes/2012/mental_health_day_20121009/en/index.html.
2. Malberg JE, Blendy JA. Antidepressant action: to the nucleus and beyond. Trends Pharmacol 2005; 26:631-8.
3. World Health Organization, the world health report 2001. Mental Health. New understanding, new hope. 2001, Geneva.
4. Singh N, Nath R, Mishra N, Kohli RP. An experimental Evaluation of Anti-Stress effect of Geriforte(An Ayurvedic Drug). *Q J Crude Drug Res* 1978; 3:125-9.
5. Haque rabiuli, Mondal Subbhasish, Ghosh Parag. Investigation of in vitro anthelmintic activity of *Cinnamomum Camphor* Leaves; IJDDR 2011; 3(1):295-300.
6. Priyanka Singh, Bhawana Srivastava & Ashok Kumar & N.K. Dubey. Fungal contamination of raw materials of some herbal drugs and recommendation of *Cinnamomum Camphor* oil as herbal fungitoxicant. Micro *Ecol* 2008; 56(3):555-60.
7. Hye Ja Lee. In vitro anti-inflamatory & anti-oxidative effects of *Cinnamomum Camphor* extracts. J Ethnopharmacol 2006; 103(2):208-16.
8. Porsolt DR, Pichon LM, Jalpre M. Depression : A model sensitive to antidepressant treatments. Nature 1997; 2666:730-4.
9. Santosh P, Venugopal R, Nilakash A S, Kunjibihari S, Dr.Mangalal. Antidepressant activity of methanolic extract of *passifora foetida* leaves in mice. Int J Pharm Pharm Sci 2011; 3(1):112-5.
10. Steru L, Chermat R, Thierry B, Simon P. The tail suspension test : A new method for screening antidepressant in mice. J Psychopharmacol 1985; 85:367-70.
11. Porsolt RD, Bertin A, Jalfre M. Behavioural despair in rats: a new model sensitive to antidepressant treatment. Eur J Pharmacol 1978; 47:379-91.
12. Borsini F, Meli A. Is the forced swimming test a suitable model for revealing antidepressant activity? Psychopharmacol 1988; 94:147–60.
13. Brunello N, Mendlewicz J, Kasper S, Leonard B, Montgomery S, et al. The role of noradrenaline and selective noradrenaline reuptake inhibition in depression. Eur J Neuropsychopharmacol 2002; 12:461–75.
14. Brocco M, Dekeyne A, Papp M, Millan MJ. Antidepressant-like properties of the anti-parkinson agent, Piribedil, in rodent: mediation by dopamine D-2 receptors. J Behav Pharmacol 2006; 17:559-72.
15. Thierry B, Steru L, Simon P, Porsolt RD. The tail suspension test: ethical consideration. Psychopharmacol 1986; 90:284-5.
16. Malaviya, M., Husain, R., Seth, P.K. and Husain, R. Prenatal effects of two pyrethroid insecticides on brain neuropterans Mitter function in the neonatal rat. Vet Hum. Toxicol. 1993; 35 (2): 119-22 .
17. Van Diermen, D., Marston, A., Bravo, J., Reist, M., Carrupt, P.A., Hostettmann, K. Monoamine oxidase inhibition by Rhodiola rosea L. roots. J. Ethnopharmacol. 2009; 122:397–401.

Conflict of Interest: None Declared

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