Print ISSN 2319-2003 | Online ISSN 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

doi: 10.5455/2319-2003.ijbcp20140817

Research Article

Evaluation of anti-depressant effect of lemon grass (*Cymbopogon citratus*) in albino mice

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Received: 23 May 2014
Accepted: 10 June 2014

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ABSTRACT

Background: Depression is a common serious psychiatric disorder and the available anti-depressant treatments are associated with many unwanted side-effects. Thus, various herbal products have been tried. The advantages of herbal treatments would include its complementary nature to the conventional treatment, thus making the latter a safer and cheaper option for depressive disorders. The objective of the present study was to evaluate the anti-depressant activity of lemon grass (*Cymbopogon citratus*) in albino mice and compare it with Imipramine.
Methods: A total of 60 Swiss albino mice weighing around 20-40 g of either sex were divided into 10 groups (n=6). They were orally administered with tween 80, as a control, 20 mg/kg imipramine (standard), 5 mg/kg and 10 mg/kg *C. citratus* (test drugs), and combination of imipramine (10 mg/kg) and *C. citratus* (10 mg/kg). Duration of immobility was observed for last 4 mins of total 6 mins period in groups 1-5 for forced swimming test (porsolt test) and groups 6-10 for tail suspension test each on 1st, 8th and 15th day and recorded as mean±standard error of the mean. Results were analyzed by one-way analysis of variance, followed by Tukey's post-hoc test.
Results: Lemon grass at the above doses significantly reduced the immobility time in both the tests compared with the control (<0.05). The reduction in the duration of immobility at the dose of 10 mg/kg was comparable to imipramine.
Conclusions: The essential oil of lemon grass (*C. citratus*) has significant anti-depressant activity comparable to imipramine.

Keywords: Anti-depressant, Imipramine, *Cymbopogon citratus*

INTRODUCTION

Depression and anxiety disorders are the most common mental illnesses, each affecting in excess of 10-15% of the population at some time in their lives. Both anxiety and depressive disorders are amenable to pharmacological treatments that have been developed since 1950s. The last half century has seen notable advances in the discovery and development of drugs for treating anxiety and depression.[1]

The current therapy includes monoamine oxidase inhibitors (MAOI) (tranylcypromine, clorgyline, moclobemide) tricyclics and related compounds (imipramine, amitryptyline, desipramine, fluoxetine, and fluoxamine). However, the typical anti-depressants are some of the most toxic psychopharmacological agents.[2] They produce unusual side-effects such as MAOIs-insomnia, hypotension, anorgasmia, weight gain, hypertensive crisis, and tyramine cheese reaction. Tricyclic anti-depressants-anti-cholinergic side-effects (dry mouth, tachycardia, constipation, urinary retention, and blurred vision), sweating, tremor, postural hypotension, cardiac conduction delay, sedation, weight gain. Selective serotonin re-uptake inhibitors-headache, nausea, other gastro intestinal effects, jitteriness, insomnia, and sexual dysfunction.[3]

Since depressive disorders have a tremendous impact on our lives, it is worth evaluating the alternative forms of medicines which are better tolerated, more efficacious and cost-effective like herbal products. Herbal medicine is a major component in all indigenous peoples' tradition, a common element in ayurvedic, homeopathic, naturopathic, traditional, oriental and native American Indian medicine.

Cymbopogon citratus, commonly known as lemon grass, is a tropical plant from Southeast Asia, which is often sold in stem form. It contains various active principles like myrcene, citrondiol, citronellol, citronellal, and geraniol

which impart various actions and benefits, making the plant multifunctional. Extracts of both leaves and stalks are used as herbal medicine to treat nervous conditions and inflammation.[4]

Traditional Indian medicine employs lemon grass for fever, infection and sedation (Lawless, 1995). It is also commonly used as an antitusive, anti-rheumatic, anti-septic agent, an insecticide and food flavoring agent (Julia, 1992). In the Malay Peninsula, *C. citratus* is recommended in folk medicine for common colds, pneumonia and gastric problems (Carlini et al., 1986). In Brazil, it is used in folk medicine for nervous conditions or gastro intestinal disturbances (Carlini et al., 1986; Suzana et al., 2001). In Thai, it is used in the treatment of fever, irregular menstruation, diarrhea and digestive problems. It is also used in Central and South America for nervous conditions and helps to regulate blood pressure (Lawless et al., 1995; Blumenthal, 1998).

Our study was aimed at studying the anti-depressant action of *C. citratus* and to compare it with the conventional anti-depressants available namely Imipramine. Studies proving this use of *C. citratus* are lacking and needs attention since depression is a growing problem of the modern world and use of indigenous medicines is welcome in its treatment.

Aims and objectives

1. To evaluate the anti-depressant activity of *C. citratus* in albino mice.
2. To compare the anti-depressant activity of *C. citratus* and imipramine in albino mice.
3. To compare the anti-depressant activity of:
    a. Combination of *C. citratus* and imipramine with imipramine alone
    b. Combination of *C. citratus* and imipramine with *C. citratus* alone.

METHODS

This study was conducted over a period of 15 days in the following manner.

Animals

Sixty Swiss albino mice of either sex weighing around 20-40 g were used. They were supplied from nearby Government Medical College. They were maintained under standard laboratory conditions (22±3°C, 12 hr light/dark cycle) supplied with standard pellet food and water given ad libitum in Government Medical college animal house.

The animals were cared in accordance with the guidelines provided by the CPCSEA and the Institutional Ethics Committee approved the entire study.

Plant extracts preparation

The plant was obtained from local ayurvedic college and following processing was done in pharmacology Department of Government Medical college.

The plant was dried and finely powdered. 100 g of this powder was soaked in 500 ml distilled water for 72 hrs. This mixture was filtered with sterile Whitman's no 1 filter paper. The filtrate obtained was stored in refrigerator at 4°C until required. This aqueous filtrate was freeze dried to reconstitute the extract into powdered form.[5]

Imipramine hydrochloride is used as a standard in the dose of 20 mg/kg, administered by the oral route. Tween 80 is used as the control in the dose of 0.1 ml/10 g (1%) administered by oral route.

General procedure

The mice were divided into10 groups of six each as follows.

1. Group 1: Tween 80
2. Group 2: Imipramine 20 mg/kg
3. Group 3: *C. citratus* 5 mg/kg
4. Group 4: *C. citratus* 10 mg/kg
5. Group 5: Combination of *C. citratus* 10 mg/kg and imipramine 10 mg/kg
6. Group 6: Tween 80
7. Group 7: Imipramine 20 mg/kg
8. Group 8: *C. citratus* 5 mg/kg
9. Group 9: *C. citratus* 10 mg/kg
10. Group 10: Combination of *C. citratus* 10 mg/kg and Imipramine 10 mg/kg.

Drug or *C. citratus* extracts are orally administered to the mice according to the group they belong to. After 1hr of oral administration, they were subjected to the following tests:

- Group 1 to 5 were subjected to forced swimming test.
- Group 6 to 10 were subjected to tail suspension test.

Forced swimming test

The adult mice are forced to swim in a cylinder (40×18 cm) with no escape. The mice become immobile after an initial struggling phase. Duration of immobility was observed for last 4 mins of total 6 mins period on day 1, 8 and 15.

Tail suspension test

Mice are rendered immobile by suspending from tail using an adhesive tape which is applied at the point, which is three-fourth of the distance from the base of the mouse's tail. Its nostril touches the water surface in a container. Initially the animal tries to escape by making vigorous movements, but is unable to escape and becomes immobile. The period of immobility during the last 4 mins of total 6 mins period is observed on day 1, 8 and 15.

Statistical analysis

All data were subjected to one-way analysis of variance using Statistical Package for the Social Sciences (SPSS) 18.0 software and in between groups were compared using Tukey's post-hoc test. $p \leq 0.05$ was considered as statistically significant.

RESULTS

Duration of immobility in the last 4 mins of the 6 mins duration of both the tests are recorded as mean±standard error of the mean on days 1, 8, and 15.

Forced swimming test (Table 1)

1) On day 1: There is no significant reduction in the duration of immobility in any group when compared to the control.
2) On day 8: Significant reduction ($p \leq 0.05$) in the duration of immobility is observed in Groups 2 and 3 when compared to 1. Highly significant reduction ($p \leq 0.01$) in duration of immobility seen in Groups 4 and 5.
3) On day 15: There is significant reduction in duration of immobility in all groups compared to 1. Group 2 reduces duration of immobility more than Group 3 and Group 5, but less than Group 4. Group 3 is inferior to Group 4 and 5. Group 4 is more effective than 5 in reducing duration of immobility. Group 2, 4, and 5 are comparable.

Tail suspension test (Table 2)

1. On day 1: No significant reduction in duration of immobility in all the groups.
2. On day 8: No significant reduction in duration of immobility in any group. Compared with day 1, day 8 showed reduction in duration of immobility in all groups except group 6.
3. On day 15: Group 7 and 9 showed highly significant reduction in duration of immobility than Group 6. Group 7 showed more reduction in the duration of immobility than Group 8, but less than Group 9. Reduction in duration of immobility was maximum on day 15 compared to day 1 and 8.

DISCUSSION

Major depressive disorder is a mental disorder common in psychiatric practice wherein a patient presents with at least one of two major symptoms, constant sadness or anhedonia, accompanied by at least five secondary symptoms for at least 2 weeks.[5] The secondary symptoms include feelings of worthlessness, difficulty in concentrating, changes in diet and sleep patterns. It is a relapsing, remitting illness having >40% rate of recurrence over a 2 year period.[6]

Depression is multifactorial in origin. The various factors include familial factors, early life events, neuro-endocrine changes and genetics. The role of oxidative stress as a patho-physiological mechanism in depression, can be explained by the concept, sometimes referred to as the "oxygen paradox," that while oxygen is essential for aerobic life, excessive amounts of its free radical metabolic by-products are toxic.[7] These free radicals play integral roles in cellular signaling, physiological immunogenic responses and mitosis. However, being highly unstable molecules with unpaired electron they have differential oxidative strengths and hence potential to damage cellular proteins, lipids, carbohydrates and nucleic acids.[8]

Table 1: Forced swimming test.

Day	Group				
	1 (Tween 80)	2 (imipramine 20 mg/kg)	3 (*C. citratus* 5 mg/kg)	4 (*C. citratus* 10 mg/kg)	5 (imipramine 10 mg/kg+ *C. citratus* 10 mg/kg)
Day 1	140.37±3.79	134.5±3.79	137.33±3.79	134.83±3.79	136.0±3.79
Day 8	139.1±4.86	113.12±4.86*	116.5±4.86*	114.0±4.86**	110.5±4.86**
Day 15	130.67±3.89	85.57±3.89***	97.33±3.89***	83.5±3.89***	86.5±3.89***

Least square mean ± standard error of mean. *C. citratus: Cymbopogon citratus*

Table 2: Tail suspension test.

Day	Group				
	6 (Tween 80)	7 (imipramine 20 mg/kg)	8 (*C. citratus* 5 mg/kg)	9 (*C. citratus* 10 mg/kg)	10 (imipramine 10 mg/kg+ *C. citratus* 10 mg/kg)
Day 1	205.17±5.79	210.5±5.79	214.1±5.79	202.83±5.79	204.17±5.79
Day 8	196.5±7.11	170.67±7.11	185.83±7.11	171.83±7.11	184.33±7.11
Day 15	196.67±8.23	150.1±8.23**	163.17±8.23	149.33±8.23**	160.17±8.23

Least square mean ± standard error of mean, Not significant: $p > 0.05$, Significant: $p \leq 0.05$*, Highly significant: $p \leq 0.01$**, Extremely significant: $p \leq 0.001$***. *C. citratus: Cymbopogon citratus*

Under physiological conditions, multiple tiers of defense exist to protect against these free radicals, including the restriction of their production through the maintenance of a high oxygen gradient between the ambient and cellular environments, their removal by non-enzymatic and enzymatic anti-oxidants, and the reparation of oxidative damages by structural repair and replacement mechanisms.[9] Oxidative stress occurs when red-ox homeostasis is tipped towards an overbalance of free radicals, due to either their over production or deficiencies in anti-oxidant defense.[10] The resultant cellular damage may range from cellular structural damage to mitotic arrest, to apoptosis and cell necrosis, depending on the level of oxidative stress severity.[11] The major classes of free radicals in living organisms are the reactive oxygen species, reactive nitrogen species, which are respective collective terms for oxygen and nitrogen derived radicals, as well as some non-radicals that readily convert into radicals.[12] A possible mechanism of anti-depressant action of lemon grass is the attenuation of this oxidative stress by monoterpenes and polyphenols present in it.

The present study evaluated the anti-depressant activity of aqueous extracts of *C. citratus* in two different animal models, tail suspension test and forced swim test. Both the models are widely used for screening anti-depressant drugs. There is a significant correlation between the potency of anti-depressants in both the tests and clinical potency of the drugs.

C. citratus at doses of 5 mg/kg, 10 mg/kg and in combination with Imipramine showed significant reduction in the duration of immobility in both the tests as compared to control, thus proving that it has significant anti-depressant activity.

C. citratus alone in the dose of 10 mg/kg is comparable to imipramine 20 mg/kg and is more effective alone than it's combination with Imipramine 10 mg/kg.

Furthermore, there was no significant reduction in duration of immobility in all the groups on the first day, but there was significant reduction on both days 8 and 15, more on day 15 when compared to day 8. This implies that chronic administration of *C. citratus* has anti-depressant activity.

Exact mechanisms underlying the anti-depressant action cannot be concluded at the moment due to the presence of a large number of phytochemicals in lemon grass oil. *C. citratus* grass contains about 0.4 % of volatile oil and that the oil contains 65-85% of citral and the concentration of citral depend on the geographical area grown (Carbajal *et al.,* 1989). Apart from citral, lemon grass oil also contains geraniol, myrcene, citronellal, citronellol, citronelyl, limonene, linalool and dipentene (Torres, 1996). The leaves also contain flavones like luteolin and its 7-O-β–Glucoside and 7-O-neohesperiodoside, iso-orientin and 2-O-rhamnosyl iso-orientin, chlorogenic acid, caffeic acid p-coumaric acid, fructose, sucrose, octacosanol and triacontanol (De Matouschek, 1991). The gas chromatography-mass spectrometry spectra of the essential oil separated by Tognolini et al., (2006) from leaves of *C. citratus* by steam distillation shows the occurrence of various compounds at different percentages like methyl-5-hepten-2-one-0.43%, myrcene - 15.48%, linalool - 1.28%, neral - 32.28%, geraniol - 3.35%, geranial - 41.28%.

They have also observed that percentage composition of non-oxygenated monoterpenes as 15.48%, oxygenated monoterpenes as 78.19% and hydrocarbons as 0.43%. The availability of flavonoids like luteolin and 6-C-glucoside has also been explained by Negrelle and Gomes, (2007).

It's anti-depressant activity may be attributed to the presence of 1,2 acetate of citronelyl. This action is mediated by an interaction with the noradrenergic system. However, interactions with other monoaminergic systems need to be investigated to assess that this plant can be alternative therapeutic approach in depression.[13]

Thus, *C. citratus* is multifunctional and the present work, though of preliminary nature is concentrated on its anti-depressant activity. Further elaborate research work involving more numbers of animals and different experimental models of anti-depressant activity are needed to elucidate the exact molecular and biochemical mechanism of action to develop more effective compound.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Animal Ethics Committee

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doi: 10.5455/2319-2003.ijbcp20140817
Cite this article as: Dudhgaonkar S, Mahajan M, Deshmukh S, Admane P, Khan H. Evaluation of antidepressant effect of lemon grass (*Cymbopogon citratus*) in albino mice. Int J Basic Clin Pharmacol 2014;3:656-60.