INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com ISSN 2230 – 8407
Research Article

ANTIDEPRESSANT ACTIVITY OF HYDROALCOHOLIC EXTRACT OF *ZINGIBER OFFICINALE*

Singh Rudra Pratap[1], Jain Ritesh[1], Mishra Rahul[2], Tiwari Prashant[1]*
[1]School of Pharmacy, Chouksey Engineering College, Bilaspur- 495004, India
[2]Department of Pharmaceutical Sciences, Birla Institute of Technology, Mesra Ranchi-835215, India

Article Received on: 17/12/11 Revised on: 17/01/12 Approved for publication: 09/02/12

*Email: ptc_ptc15@rediffmail.com

ABSTRACT
The present study was design to evaluate the effect of *Zingiber officinale* hydro-alcoholic extract as well as its interaction with conventional anxiolytic and antidepressant drugs using tail suspension test and forced swim test (FST) and to evaluate the possible mechanisms involved in its actions. The rhizomes of ginger were collected and authenticated. Extraction of dried rhizomes was carried out using soxhlet apparatus to obtain its Hydro alcoholic extract. The extract of *Zingiber officinale* showed the significant antidepressant activity comparable to the standard drug. The oral administration of *Zingiber officinale* extract at 150 mg/ kg and 300 mg/kg respectively as compared to the control treated group showed an antidepressant activity comparable to that of standard drug. The antidepressant effects of *Zingiber officinale* extract seem to be mainly associated with the activation of dopamineergic system and possess potential anxiolytic and antidepressant activities.
Key words: Antidepressant activity, *Zingiber officinale*, forced swimming test, tail suspension test.

INTRODUCTION

Depression is an important global public-health issue and is associated with substantial disability [1, 2]. It is a chronic illness that affects mood, thoughts, physical health and behavior of any individual and has been estimated to affect upto 21% of the world's population [3]. Synthetic antidepressants taken in appropriate doses are often associated with their anticipated side effects like dry mouth, inability in driving skills, constipation and sexual dysfunction [4] and majority of patients are reluctant to take this treatment. Accordingly, natural medicinal plants may be important sources of novel antidepressant drugs and the usage of plant extracts may be proven better in the management of stress and depression. In oriental countries, many medicinal plants from natural resources, especially Chinese medicine, such as *Plantago asiatica, Scrophularia ningpoensis,* and *Hypercarium perforatum* were successfully used to treat or prevent depression-like disorders [5, 6].

Ginger, the rhizome of *Zingiber officinale*, is one of the most widely used species of the ginger family (Zingiberaceae) and is a common condiment for various foods and beverages. Ginger has a long history of medicinal use dating back 2,500 years in China and India for conditions such as headaches, nausea, rheumatism, and colds [7]. Characterized in traditional Chinese medicine as spicy and hot, ginger is claimed to warm the body and treat cold extremities, improve a weak and tardy pulse, address a pale complexion, and strengthen the body after blood loss[8]. Ginger contains a number of pungent constituents and active ingredients. Steam distillation of powdered ginger produces ginger oil, which contains a high proportion of sesquiterpene hydrocarbons, predominantly zingiberene[9]. The major pungent compounds in ginger, from studies of the lipophilic rhizome extracts, have yielded potentially active gingerols, which can be converted to shogaols, zingerone, and paradol[10]. The compound 6-gingerol appears to be responsible for its characteristic taste. Zingerone and shogaols are found in small amounts in fresh ginger and in larger amounts in dried or extracted products.

The mechanism underlying ginger's anti-emetic activity is not clearly understood, but the aromatic, spasmolytic, carminative, and absorbent properties of ginger suggest it has direct effects on the gastrointestinal tract[11]. No study indicates ginger influenced within the vestibular or oculomotor system[12]. A mechanism involving the central nervous system cannot be ruled out, considering several of ginger's components antagonize serotonin type-3 receptors; however, this has not been clearly demonstrated[13-15]. The compounds 6-gingerol and 6-shogaol have been shown to have a number of pharmacological activities, including antipyretic, analgesic, antitussive, and hypotensive effects[10]. Ginger extracts exhibit inhibition of platelet aggregation and thromboxane synthesis *in vitro*[11-15] which has led to concerns ginger extracts may prolong bleeding; however, several European studies using ginger orally did not find any significant anticoagulant effects *in vivo* [16]. Daily consumption of 15 gm raw ginger rhizome or 40 gm cooked rhizome by healthy volunteers for two weeks failed to decrease platelet cyclooxygenase activity[17]. Similarly, differences were not found in bleeding time, platelet count, and platelet functioning when eight healthy volunteers were given a single 2-gram dose of the dried rhizome or placebo [18]. In continuation of our research on *Zingiber officinale*, we have investigated the probable mechanisms of antidepressant-like activity of *Zingiber officinale* in behavioral models of depression using laboratory rats. The study would possibly help to establish that hydro alcoholic extract of the *Zingiber officinale* rhizomes which have potential therapeutic value for the management of depressive disorders.

MATERIALS AND METHODS

Collection and Preparation of extract

Zingiber officinale was collected from Bilaspur, India. The rhizomes were washed; air dried under shade and powdered with the help of Grinder at School of Pharmacy, Chouksey Engineering College, Bilaspur, India. Powdered rhizomes were weighed and packed in soxhlet. Solvent used for soxhletion was mixture of methanol and water in the ratio of

50:50 respectively. Extraction was continued at the temperature of 50°C till clear solvent was observed in siphon tube. Extract was concentrated in water bath at 40°C. Concentrated extract was dried at 40°C in hot air oven. Dried extract was packed in an air tight container.

Animals

The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC). Regd.No. 1275/ac/09/CPCSEA of School of Pharmacy, Chouksey Engineering College, Bilaspur, India. Adult male Swiss Albino rats weighing 150-200 gm from our breeding stock were used in this study. They were housed in polypropylene cages under standard conditions (23 ± 2 .C, humidity 60–70%, 12 h light/dark cycles). They had free access to food and water *ad libitum*. The animals were acclimatized for a period of 7 days before the study. The study was conducted according to the Indian National Science Academy Guidelines for the use and care of experimental animals.

Acute dermal toxicity – fixed dose procedure

The acute dermal toxicity study was carried out in adult female albino rats by "fix dose" method of OECD (Organization for Economic Co-operation and Development) Guideline No.434. Latex of the rhizomes of *Zingiber officinale* was given orally at dose level 2000 mg/kg.

Selection of Dose and standard drug preparation

For the assessment of antidepressant activity, dose level was chosen in such a way that, dose was approximately one tenth of the maximum dose during acute toxicity studies (150-300mg/kg/day). Imipramine was used as the reference drug for evaluating the antidepressant activity. Imipramine was powdered and made into suspension in distilled water using.

Forced Swim Test (FST)

The method described in the literature was used in our study[19]. Each animal was placed individually in 5 liter glass beakers, filled with water upto a height of 15 cm and were observed for duration of 6 minutes. The duration of immobility was recorded during the last 4 minutes of the observation period. The mouse was considered immobile when it floated motionlessly or made only those moments necessary to keep its head above the water surface. The water was changed after each test.

Tail suspension test (TST)

The method described by *Steru et al.* was used in our study. The animals were hung by the tail on a plastic string 75 cm above the surface with the help of an adhesive tape. The duration of immobility was observed for a period of 8 minutes. The duration of immobility was recorded during the last 6 minutes of the observation period. Mice were considered to be immobile only when they hung passively and were completely motionless [20].

Groping of Animal

Animals were divided in to three groups, each group consisting of 6 rats.

Group I: Received no treatment and served as control, 1% gum acacia (10ml/kg)

Group II: Received test drug *Zingiber officinale* (150 mg/kg/) per orally

Group III: Received test drug *Zingiber officinale* (300 mg/kg/) per orally

Group IV: Received standard drug i.e. imipramine (10mg/kg)

Statistical analysis

The mean ± S.E.M. statistical significance of difference of control and test data was determined by using ANOVA followed by Dunnet's multiple comparison test. $P< 0.05$ was considered to be significant. A probability value of 0.05 or less was taken to indicate statistical significance.

RESULTS AND DISCUSSION

In both the test i.e. Forced Swim Test (FST) and Tail suspension test (TST) the extract shortened the immobility period during the forced swimming test in comparison with control and exhibited a dose dependent antidepressant activity. A significant ($P<0.01$) decrease in duration of immobility was observed as compared to that of control. The extract at a dose of 300 mg/kg body weight is found to be effective nearly similar to that of conventional drug imipramine. The results are summarized in **Table 1**. Mood disorders are one of the most common mental illnesses, with a lifetime risk of 10% in general population. Prevalence of depression alone in general population is estimated to be around 5% with suicide being one of the most common outcomes [21-28]. Most of the drugs that are currently being used in the treatment of depression have adverse effects that affect the quality of life of the patient. This leads to patient's non-compliance to medication, which further complicates the problem [29-30]. Ayurveda mentions a number of single and compound drug formulations of plant origin that are used in the treatment of psychiatric disorders [31] and are claimed to have a better side-effect profile than conventional drugs.

Zingiber officinale (150 and 300 mg/kg) significantly ($P < 0.001$) and dose dependently decreased the immobility time as compared to control mice (Table 1). The extract at the dose of 300 mg/kg showed the almost same activity as imipramine ($P > 0.05$), in decreasing immobility period. Tail suspension test [26] represents the behavioural despair model, claimed to test is based on the observation that animals, following initial escape oriented movements, develop an immobile posture when placed in an inescapable chamber. The immobility is thought to reflect either a failure of persistence in escape-directed behaviour (that is, behavioural despair) or the development of passive behaviour that disengages the animal from active forms of coping with stressful stimuli [32]. It has been argued that the TST is less stressful than FST and has greater pharmacological sensitivity [33]. Remarkably, TST detects the anti-immobility effects of a wide array of antidepressants, including tricyclic antidepressants (TCA), selective serotonin reuptake inhibitors (SSRI), monoamine oxidase inhibitors (MAOI), electro-convulsive shock (ECS) and even atypical antidepressants. Thus, the activity of *Zingiber officinale* could involve one of the mechanisms of the established agents as described above.

Table 1. Effect of *Zingiber officinale* on duration of immobility time in the tail suspension test (TST) and Forced Swim Test (FST) using rats..

Group	Dose mg/kg/	(S), TST Duration of Immobility	(S), FST Duration of Immobility
1% gum acacia	(10ml/kg)	193±3.51	178±1.52
Zingiber officinale	150	141±5.06	146±1.73
Zingiber officinale	300	135±9.29	122±4.35
Imipramine	10	132±4.93	119±1.15

Values represented mean ± S.E.M. (n=6), P<0.05, P<0.01 vs. control (group 1).

CONCLUSION

As medicinal plants have their importance since ancient time, people using it from various ways as a source of medicine. From the above valuable animal study, we conclude that the plant extract *Zingiber officinale* show a significant antidepressant activity in TST and FST models of depression. Thus, we can say that *Zingiber officinale* significantly reduces the immobility period in both TST and FST.

REFERENCES

1. Grant KL, Lutz RB. Alternative therapies: Ginger. Am J Health Syst Pharm 2000; 57:945-947.
2. Chang CP, Chang JY, Wang FY, Chang JG. The effect of Chinese medicinal herb *Zingiberis rhizoma* extract on cytokine secretion by human peripheral blood mononuclear cells. J Ethnopharmacol 1995; 48:13- 19.
3. Govindarajan VS. Ginger – chemistry, technology, and quality evaluation: part 1. Crit Rev Food Sci Nutr 1982; 17:1-96.
4. Govindarajan VS. Ginger – chemistry, technology, and quality evaluation: part 2. Crit Rev Food Sci Nutr 1982; 17:189-258.
5. Tyler VE. Some recent advances in herbal medicine. Pharm Int 1986; 7:203-207.
6. Holtmann S, Clarke AH, Scherer H, Hohn M. The anti-motion sickness mechanism of ginger. A comparative study with placebo and dimenhydrinate. Acta Otolaryngol 1989; 108:168-174.
7. Phillips S, Hutchinson S, Ruggier R. *Zingiber officinale* does not effect gastric emptying rate: A randomised, placebo-controlled, crossover trial. Anaesthesia 1993; 48:393-395.
8. Micklefield GH, Redeker Y, Meister V, et al. Effects of ginger on gastroduodenal motility. Int J Clin Pharmacol Ther 1999; 37:341-346.
9. Lumb AB. Mechanism of antiemetic effect of ginger. Anaesthesia 1993; 48:1118.
10. Suekawa M, Ishige A, Yuasa K, et al. Pharmacological studies on ginger. I. Pharmacological actions of pungent constituents, (6)-gingerol and (6)-shogaol. J Pharmacobiodyn 1984; 7:836-848.
11. Kiuchi F, Shibuya M, Sankawa U. Inhibitors of prostaglandin biosynthesis from ginger. Chem Pharm Bull (Tokyo) 1982; 30:754-757.
12. Kiuchi F, Iwakami S, Shibuya M, et al. Inhibition of prostaglandin and leukotriene biosynthesis by gingerols and diarylheptanoids. Chem Pharm Bull (Tokyo) 1992; 40:387-391.
13. Srivastava KC. Effects of aqueous extracts of onions, garlic and ginger on platelet aggregation and metabolism of arachidonic acid in the blood vascular system: *in vitro* study. Prostaglandins Leukot Med 1984; 13:227-235.
14. Srivastava KC. Isolation and effects of some ginger components of platelet aggregation and eicosanoid biosynthesis. Prostaglandins Leukot Med 1986; 25:187-198.
15. Srivastava KC. Effect of onion and ginger consumption on platelet thromboxane production in humans. Prostaglandins Leukot Essent Fatty Acids 1989; 35:183-185.
16. Bordia A, Verma SK, Srivastava KC. Effect of ginger (*Zingiber officinale* Rosc.) and fenugreek (*Trigonella foenumgraecum* L.) on blood lipids, blood sugar and platelet aggregation in patients with coronary artery disease. Prostaglandins Leuukot Essent Fatty Acids 1997; 56:379-384.
17. Janssen PL, Meyboom S, van Staveren WA, et al. Consumption of ginger (*Zingiber officinale* roscoe) does not affect *ex vivo* platelet thromboxane production in humans. Eur J Clin Nutr 1996; 50:772-774.
18. Lumb AB. Effect of dried ginger on human platelet function. Thromb Haemost 1994; 71:110-111.
19. Goodwin FK, Bunney WE. Depressions following reserpine: a re-evaluation. Sem Psychiatry 1971; 3:435-484.
20. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: global burden of disease study. Lancet 1997; 24: 1498-1504.
21. Paykel ES. Depression: major problem for public health. Epidemiol Psychiat Soc 2006; 15: 4-10.
22. Sarko J. Antidepressants, old and new. A review of their adverse effects and toxicity in overdose. Emer Med Clin North A 2000; 18: 637-654.
23. Schulz V. Safety of St. John's Wort extract compound to synthetic antidepressants. Phytomedicine 2006; 13: 199-204.
24. Sanchez-Mateo CC, Bonkaka CX, Prado B, Rabanal RM. Antidepressant activity of some *Hypercarium perforatum* L. fil. extracts in the forced swimming test in mice. J Ethnopharmacol 2007; 112: 115-121.
25. Porsolt RD, Bertin A, Jalfre M. Behavioural despair in mice : a primary screening test for antidepressants. Arch Int Pharmacodyn Ther 1977; 229:327-336.
26. Steru L., Chermat R, Thierry B., Simon P. The tail suspension test: A new method for screening antidepressants in mice. Psychopharmacology 1985; 85:367-370.
27. WHO. Mental and Neurological Disorders.1998 Fact sheet No.25. World Health Organization.
28. Stahl SM. Essential Psychopharmacology: Neuroscientific basis and Practical; Applications. Cambridge Univertsity Press; Cambridge; 1998.
29. Tripathi KD. Essentials of medical Pharmacology. 6th ed. Medical Publishers (P) Ltd: New Delhi, India; 2008.
30. Hardman JG, Limbird LE, Goodman Gilman A. Goodman Gilman's; The Pharmacological Basis of Therapeutics. 11th ed The McGraw Hill Companies, Inc: New York; 2007.
31. Sembulingam K, Sembulingam P, Namasiyam A. Effect of Ocimum sanctum Linn on noise induced changes in plasma corticosterone level. Indian J Physiol Pharmacol 1997; 41:139-143.
32. Lucki I. The forced swimming test as a model for core and component behavioural effects of antidepressant drugs. Behav Pharmacol 1997; 8:523-532.
33. Thierry B, Steru L, Simon P, Porsolt RD. The tail suspension test: ethical considerations. Psychopharmacology 1986; 90:284-285.

Source of support: Nil, Conflict of interest: None Declared