



ANTIDEPRESSANT ACTIVITY OF AQUEOUS EXTRACT OF ALLIUM SATIVUM LINN. IN ALBINO RATS

Pharmacology

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ABSTRACT

The present study was undertaken to investigate the effect of the aqueous extract of *Allium sativum* L. (Family: Liliaceae), commonly known as garlic, on antidepressant in albino rats. Aqueous extract of garlic (250, 500 and 1000 mg/kg) was administered orally for 20 successive days to young albino rats of either sex and antidepressant-like activity was evaluated employing tail suspension test (TST) and Forced swim test (FST). The efficacy of the extract was compared with standard antidepressant drugs like imipramine. Garlic extract significantly decreased immobility time in a dose-dependent manner in both TST and FST, indicating significant antidepressant activity. The efficacy of the extract was found to be comparable to imipramine (15 mg/kg p.o.) in both TST and FST treated group. Garlic extract administered orally for 20 successive days showed significant antidepressant-like activity.

KEYWORDS

Allium sativum, Depression, Forced swim test, Tail suspension test

INTRODUCTION

Depression is one among the most important form of psychiatric disorders and a leading cause for morbidity and mortality¹. Various Misconceptions towards mental disorders and the prevailing attitude among the general public and health professionals constitute major barriers in the recovery of mentally ill patients. It is a common problem affecting about 120 million people world-wide². It occurs in persons of all genders, ages, and back-grounds. It is almost twice as common in females as males. It also poses a significant economic burden to society as it leads to reduced productivity, treatment costs and loss of human life by suicide. How do we now approach depression, a condition that has been identified since antiquity but is still conceptualized as a common and complex disorder of unknown etiology. A triad of symptoms clinically characterize depression: low mood, anhedonia and low energy levels. Other symptoms, such as sleep disturbances, guilt feelings, low self-esteem, suicidal tendencies, and food-intake irregularity, are also often present. **Because, each of the above symptoms are not qualitatively different from experiences all of us have at some point in our lives, depression is frequently not detected or misdiagnosed.** There are now dozens of approved drugs, which belong to four different classes: tricyclic drugs, selective serotonin reuptake inhibitors, MAO-inhibitors and miscellaneous antidepressants. Each drug has a success rate of about 60%. When patients do not respond to one particular drug, they are switched to another one, usually of a different class, until various classes of antidepressants are tried. At present, the choice of medication is completely arbitrary and often based on their side effect profile³.

Recent estimates have suggested that only 10% patients with depression are likely to receive adequate treatment. It has been repeatedly reported that 40-50% patients suffering with depression do not seek treatment for their illness. **Depression costs the US economy, directly and indirectly, over 43 billion dollars per year and it is a leading cause of disability worldwide.** Suicide, which is usually a consequence of depression, is the eighth leading cause of death in the United States. The rate of suicide is even more alarming, when it is examined as a function of age. Suicide is the sixth leading cause of death in the 5-14 age group, the third leading cause of death in the 15-24 age groups, and the fourth leading cause of death in the 25-44 age group. The patients resort to alternative systems of medicine for depression because they

- i) entail a lack of satisfaction with allopathic medicines and/or
- ii) they desire to avoid side effects and/or
- iii) they are scared of the stigma attached to conventional treatment.

Since allopathic medicines attack selected symptoms of depression & exhibit adverse effects, complementary therapies such as Herbal Therapy are becoming popular⁴. During the past few years, herbal therapy has increasingly been used as a tool for the investigation of

human cognition and its underlying brain mechanisms. Thus there is a constant need to identify newer natural antidepressants with greater efficacy, fewer side effects and to explore their potential over synthetic antidepressants. Various plants and their extracts have been reported to possess antidepressant-like activity. In the search for new molecules useful for the treatment of psychiatric disorders, medicinal plant research, worldwide, has progressed constantly, demonstrating the pharmacological effectiveness of different plant species in a variety of animal models⁵. The concomitant use of botanical supplements along with conventional medications has engendered a growing medical concern over possible herb-drug interactions. Recent surveys indicate that 24-36% of all consumers use botanical products on a regular basis⁶⁻⁸. Still other surveys indicate that herbal supplement usage is prevalent among patients taking prescription medications⁹ with many individuals greater than 65 years of age. Garlic (*Allium sativum*) family (Liliaceae) originated in China, it is functional food and is very nutritionally complete containing numerous mineral substance and trace elements e.g. calcium, copper, bromide, magnesium, phosphorus etc. Practically all existing vitamins A, B1, B2, B3, an essential oil whose main active ingredient (allicin) possesses particularly valuable property numerous natural antibiotic that are easily used by the Organism. Garlic is one of the most powerful medicinal plants for combating high blood pressure, protecting heart also effective in combating diabetes and cholesterol. Garlic extract has been reported to contain active components like allicin, alliin, allyl methyl thiosulfinate, γ -glutamyl-S-allyl cysteine, γ -glutamyl-S-cis-1-propenyl cysteine¹⁰.

MATERIALS and METHODS

Plant material and preparation of aqueous extract

Bulbs of *Allium sativum* were collected commercially, the collected bulbs of *Allium sativum* were chopped and packed. The extract concentrated by using Soxhlet's apparatus with water as solvent in the ratio of 1:4. The extraction continued till the solvent in the thimble becomes clear indicating the crude form of extract and evaporation of solvent to get semisolid 3-4 days, at ambient temperature and filtered. The crude extract was dried on a water bath and kept in a refrigerator till further use.

Animals

Albino rats of either sex, excluding three to four months of age and weighing around 120-150g were procured from Dr.S.N.M.C. Animal House (CPCSEA no. 692/02/a) our medical college. The animals had free access to food and water. However, food was withdrawn 1 hr. before and 2 hr. after the administration of the drugs. The animals were housed in an animal room, with alternating light-dark cycle of 12 hr each. The animals were acclimatized to the laboratory conditions for at least five days prior to the behavioral experiments. The experiments were carried in morning for proper monitoring of result. The Institutional Animal Ethics Committee (IAEC) approved the experimental protocol (S.NO./Pharma/MC/JU/15/189).

Study Design:**Forced swim test**

Dose of Garlic (250mg/kg, 500 mg/kg, 1000mg/kg P.O. was given¹¹ and imipramine was used as a standard drug 15mg/kg P.O.. in Albino rats weighing 120-150g were brought to the laboratory at least two day before the experiment after receiving the 14 days of treatment. Rats were individually forced to swim inside a vertical cylinder (height: 60 cm; diameter: 32c.m., containing 30 cm of water maintained temp. at 25 °C). Rats placed in the cylinders for the first time were initially highly active, vigorously swimming in circles, trying to climb the wall or diving to the bottom. The frequency and total duration were calculated for each of the following category by two observers behavioural score were:-

1. Struggling (with rhythmical simultaneous kicks and occasional pushes off legs)
2. Fast swimming (swimming with fast movement of hind limbs and fore limbs)
3. Slow movement (swimming with slow movement of legs)
4. Floating (floating on the surface of water without any movement of body escaping head out of water).

Immobile behavior during this 6 min period was observed for each rat considering slow movement and Floating period. After 6 min in the water the rats were removed and allowed to dry in a heated enclosure (32 °C) before being returned to their home cages^{12,13} Experiment were conducted during the period of 9 a.m. to 5 p.m.

Tail-suspension test: The total duration of immobility induced by tail suspension was measured according to the method described as a means of evaluating potential antidepressants. Rats were suspended on the edge of a table, 50 cm above the floor, with the help of an adhesive tape placed approximately 1 cm from the tip of the tail. Immobility time was recorded during a 5 min period. The animal was considered to be immobile when it did not show any movement of the body and hanged passively.

Experimental protocols

The animals were divided into ten groups and each group comprised a minimum of five rats Groups for Tail Suspension Test (TST):-

Group 1: Control group: Distilled water was administered orally for 14 successive days. At 90 min after administration on the 14th day, immobility period was recorded.

Group 2: Imipramine (15 mg/kg) was administered orally for 14 successive days. On the 14 day, immobility was recorded after 90 min in drug treated group

Group 3,4 and 5: Garlic extract (250, and 500, mg/kg .1000, respectively) was administered orally for 14 successive days. At 90 min after administration on the 14th day, immobility period was recorded.

Groups for Forced Swim Test (FST):-

Groups 6 to 10 are the same as groups 1 to 6 mentioned in the groups TST except that immobility period was recorded using FST.

Statistical analysis

All the results were expressed as Mean \pm Standard Error (SEM). Data was analysed using one-way ANOVA, followed by dunnett's test. The data for locomotor activity scores was subjected to paired t-test. $P < 0.05$ was considered as statistically significant.

RESULTS

Effect of garlic extract on immobility periods in TST and FST. Garlic extract (250, 500 and 1000mg/kg, P.O.) administered to rats for 14 successive days decreased immobility periods significantly in a dose-dependent manner, as compared to control in both TST and FST, indicating significant antidepressant activity. A dose of 1000 mg/kg P.O. of the extract showed the most potent antidepressant effect, as indicated by the highest decrease in the immobility period. The efficacy of the extract was found but less than imipramine (15 mg/kg) administered for two successive weeks in both TST and FST [Tables 1 and 2] and it can be used as an adjunct to antidepressant drugs.

Table 1:- Effect of aqueous extract of Allium Sativum on immobility period in Tail Suspension Test

S.N.	Treatment for 14 days p.o	No. of animals	Dose/kg	Immobility(sec) (Mean \pm SE)
1.	Control	5	10ml	164 \pm 5.1
2.	Imipramine	5	15mg	81 \pm 10.7
3.	Garlic extract	5	250mg	151 \pm 7.3
4.	Garlic extract	5	500mg	129 \pm 2.4
5.	Garlic extract	5	1000mg	98 \pm 3.7

Table 2:- Effect of aqueous extract of Allium Sativum on immobility period in Force Swimming Test

S.N.	Treatment for 14 days p.o.	No of animals	Dose	Immobility(sec) (mean \pm sem)
1.	Control	5	10ml	137.6 \pm 4.1
2.	Imipramine	5	15mg	65 \pm 3.2
3.	Garlic extract	5	250mg	84 \pm 11.2
4.	Garlic extract	5	500mg	71 \pm 7.6
5.	Garlic extract	5	1000mg	66 \pm 4.8

DISCUSSION

In the present study, aqueous extract of garlic (250, 500 and 1000mg/kg P.O.) administered to rats, for 14 successive days, showed significant antidepressant-like activity in Forced Swim Test (FST) and Tail Suspension Test (TST). The efficacy of garlic extract was found to be comparable to imipramine (15 mg/kg). FST and TST are two commonly used behavioural despair models of depression. The most potent effect is shown at a dose of 1000 mg/kg P.O. And can be used as adjunct with anti depressant drug. These tests are quite sensitive and widely employed in rodents to predict antidepressant potential by decrease of immobility period produced by several different classes of antidepressant drugs¹²⁻¹⁴. Among these two standard test TST is less stressful and has higher pharmacological sensitivity than FST¹⁵.

The measurement of FT was based on the original functional definition of Porsolt et al. (1977), that is the time during which the rat performed "only those movements necessary to keep its head above water." To elaborate on this definition, any slight movements of the tail, body, limbs or head, with the animal otherwise in a quiet state, were interpreted as floating. Therefore, floating was clearly differentiated from those behaviors that were escape attempts. Escape included the behaviors of vigorous movements of the whole body, climbing, swimming, diving; it also included head movements which appeared to indicate that the rat was searching for an escape, even when the rat's body remained in the same position within the tank. We expressed total FT in seconds and Immobility period of rat during this 5 min period was observed for each rat considering slow movement and Floating period. After 5 min in the water the rats were removed and allowed to dry in a heated enclosure (32°C) before being return to home cages. According to Dhingra D, Sharma A., that garlic extract might produce antidepressant-like effect through interaction with α 1-adrenoceptors, dopamine D2 receptors, serotonergic and GABAergic receptors, thereby increasing the levels of norepinephrine, dopamine, serotonin and decreasing GABA levels in the brain of mice. Garlic extract (1000mg/kg p.o.) administered to mice, for 14 successive days, significantly decreased brain MAO-A and MAO-B activities as compared to the control group. MAO inhibiting activity by the extract was comparable to imipramine. Thus, antidepressant-like activity of the extract might also be due to inhibition of MAO, resulting in increase in the brain levels of monoamines¹⁶.

CONCLUSION

In this study aqueous extract of Allium sativum (1000mg/kg, P.O.) significantly and dose-dependently decreased in immobility period in both tail suspension test (TST) and forced swim test (FST). Aqueous extract of Allium sativum Linn can be used as an adjunct to antidepressant drugs.

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