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Pharmacological screening and effect of *Elettaria cardamomum* extract on depression-like behaviour in rat model

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Abstract

Depression is a heterogenous mood disorder that has been classified and treated in variety of ways. Although a number of synthetic drugs are being used as standard treatment for clinically depressed patient, they have adverse effects that can compromise the therapeutic treatment. Thus, it is worthwhile to look for antidepressant from plants with proven advantage and favorable benefit to risk ratio. A number of medicinal plants and medicine derived from these plants have shown antidepressant properties by virtue of combined effect of their medicinal constituents. The causes of depression are decreased brain levels of monoamines like noradrenaline, dopamine and serotonin. Therefore, drugs restoring the reduced levels of these monoamines in the brain either by inhibiting monoamine oxidase or by inhibiting reuptake of these neurotransmitters might be fruitful in the treatment of depression. The present review is focused on the medicinal plants to investigate the possible effect of *Elettaria cardamomum* seed extract on depression-like behavior using experimental model in laboratory animals.

The present study was undertaken to assess the antidepressant effect of crude methanolic extract of seed of *Elettaria cardamom* at doses 200mg/kg and 400mg/kg using forced induced swimming test (FST) imipramine (20mg/kg, body weight) was used as standard. Significant dose dependent decline in immobility time was observed in doses in FST of *Elettaria cardamom* extract exhibited effectual results.

Keywords: Depression, medicinal plants, antidepressants, herbal medicine, monoamine oxidase, forced induced swimming test

Introduction

Depression is not just a form of extreme sadness. It is a disorder that affects both brain and body, including cognition, behavior, the immune system and peripheral nervous system. Unlike a passing sad mood, depression is considered a disorder because it interferes with ordinary functioning in work, school, or relationships. Unlike normal grief, which comes in waves, it is constant and oppressive. Depression is an affective (not natural) very common and serious disorder. It is also called mania depression syndrome, It can occur at any age, but the highest rate is in the age group of 25-45 years. The incidence of depression is about 2-3 times more common in females than in males. Type-1. Manic Depression- It is characterized by opposite behavior, like- enthusiasm, rapid thoughts, disturbed speech pattern and extreme self-confidence with impaired judgment. The manic depression is further of two types- unipolar depression (up and down mood) and bipolar depression (cyclization of mood). Type-2. Endogenous Depression- It can be classified into four categories- true depression (delusion, sleep disorder), neurotic (depression with anxiety and fear), obsessive (suicidal tendencies), involuntional depression (helplessness and unhappy emotional state) [1] Depression is a heterogeneous disorder that affects a person's mood, physical health and behavior. Antidepressant drugs such as tricyclic anti-depressant and selective serotonin re-uptake inhibitor (SSRI) are used to treat depression showing various side effects and thus, the search for a new anti-depressant without side effects is deemed important [2]. Major depressive disorder (MDD) is commonly referred as depression. That is characterized by sad mood, loss of interest, unhappiness, change of appetite, somatic complaints (e.g., aches and pains), psychomotor changes (e.g., agitation), decreased energy and tiredness, a sense of worthlessness or guilt. Impaired concentration, suicidal ideation and cognitive deficits Moreover, depression in the most common of the affective disorders; it may vary from very mild condition, bordering on normality, to severe psychotic depression accompanied by hallucinations and delusions. Depression is a state of low mood and aversion to activity or apathy that can affect a person's thoughts, feelings, behavior and sense of well-being.

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It is a very serious and disabling psychiatric condition that occasionally leads to suicide or premature death due to unattended physical problems. The annual prevalence of major depressive disorder is 6.6 % and the lifetime prevalence of depression is 16.2% [1]. An estimated 676 million (one in ten people) are affected by depression. Worldwide, 804,000 people committed suicide in 2012, making depression one of the leading causes of death in young adults (15-29 years) second to road traffic accidents [1, 3]. Persons with major depression have a 40% greater chance of dying prematurely than the general population [2]. The association between depression and increased risk of death and morbidity is an obvious indicator of the severity of the condition, which is usually clear when reflecting upon the WHO data on life expectancy and the causes of death. The World Health

Organization estimated that by 2020 unipolar major depression will become the second largest cause of global disease problems in the world, only behind ischemic heart disease. Because the mechanism of depression is quite complex, many currently available synthetic chemical antidepressants have low rates of response and remission and even severe adverse effects [4]. The majority of patients are often reluctant to take synthetic antidepressants in their appropriate doses due to their anticipated side effects including inability to drive a car, dry mouth, constipation, sexual dysfunction and so on. Therefore, finding more effective and less toxic agents is a serious and urgent problem. Furthermore, natural plants may be some of the most attractive sources of new drugs with lower side effects than those of synthetic antidepressants [2]. (W.H.O, 2017) [5].

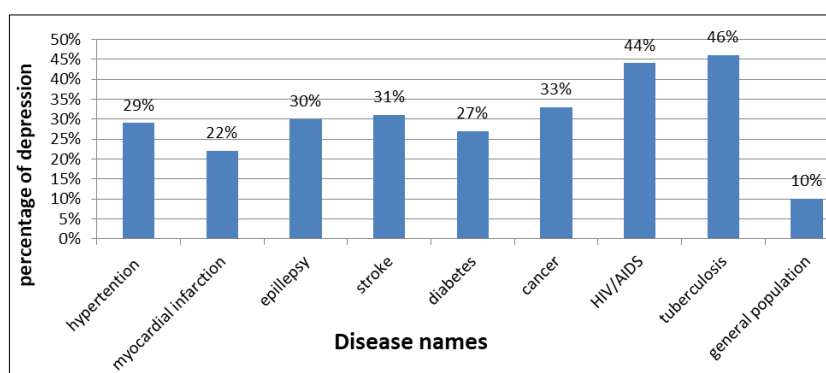


Fig 1: Prevalence of major depression in patients with physical illness

Objective of study

The objective of proposed study is to investigate the possible effect of *Elettaria cardamomum* seed extract on depression-like behavior using experimental model in laboratory animals.

Specific objectives

- To carryout extraction of *Elettaria cardamomum* fruits using suitable solvent and extraction procedure.
- To produce the appropriate depression-like behavior in animal using forced swim apparatus.
- To explore and determine the influence of *Elettaria cardamomum* on depression-like behavior.

Materials and Methods

Source of data

Data will be obtained from laboratory based studied by using experimental rats of either sex weighing between 150-200g, maintained at room temperature having free access to food and tap water. All the study will perform in accordance with the institutional animal ethics committee as per the guidelines laid by CPCSEA [2]

Method of collection data

Chemicals, reagents and glass wares will be procured from university lab. Extract of *Elettaria cardamomum* seed will be carried out using standard procedure. Forced swim test model will be used for interactive study.

Plant material and extraction

Dry *Elettaria cardamomum* seed will be purchased from the market. The plant seed will be identified by botanist at M.J.P. Rohilkhand University. A voucher specimen of the plant material will be deposited at the herbarium of botany department. The dried seed of plant (100g) will be grinded into fine powder using an electric grinder and extracted by percolation method and through using methanol (80%) for 72

h at room temperature. The solvent will be removed in a rotary evaporator, and after filtering, the extracts were concentrated to dryness [6].

Drugs and chemicals

The following drugs, chemicals, and materials will be used in the research work.

- Imipramine
- Distilled water
- Stopwatch
- Cloth towel
- Standard rat group housing cage
- Forced swimming apparatus
- Thermometer
- Normal saline
- Cannula

Experimental Model

The forced swimming test is most widely used pharmaceutical in-vivo model for assessing anti-depressant activity. The development of immobility when rats are placed in inescapable cylinder filled with water reflects cessation of persistent escape directed behavior. Rats when forced to swim in a restricted spaces, are induced to a peculiar behavior of immobility such as cessation in struggling to escape and they remained in motionless floating posture. This behavior reflects a state of despair which can reduce by several agents which are therapeutically effective in human depression. Decrease in time of immobility is considered as antidepressants action of drug¹. Forced swim test in glass jar will be performed as described by Porsolt *et al.* with few modifications. This test consists of two parts, an initial training period of 15 min followed by actual test for 5 min duration 24 h later. Rat will be individually forced to swim

inside a vertical glass cylinder (height: 40 cm; diameter: 18 cm; containing 30 cm height of water maintained at 25° C). The rats from each group I,II,III,IV, will be placed in the cylinder 24 h later after doses of *Elettaria cardamomum* seed extract and imipramine (20mg/kg p.o.) respectively and their activity will be recorded. The recordings will be analyzed to find the duration of immobility, swimming behavior and climbing behavior in the 5 min test period using stopwatch [7].

Experimental Design

The animals will housed for 1 week in a laboratory room for acclimatization they will grouped into four, containing six animals each group. Rat will be divided into 4 groups (n=6).

- Group I - served as control (as vehicle 0.9% wt/vol.)
- Group II - animals treated orally with low dose of *Elettaria cardamomum* seed extract.
- Group III - animal treated orally with high dose of *Elettaria cardamomum* seed extract.
- Group IV - animals treated with imipramine at a dose of 20mg/kg p.o.

The rats will be divided into four groups and named or tagged properly. The first group will be controlled group will treated with normal saline (0.9% wt/vol.) as vehicle (Slsttery and Cryan., 2012) the second group will be test 1 group will treated with 200mg/kg of body weight. The third group will be test 2 group will treat with 400mg/kg of body weight. The fourth group will be the standard group will be treated with imipramine 20mg/kg p.o. [6].

Experimental protocols

- (day-0): if animals are ordered from a supplier, they arrive and are rehoused in single cages or into groups of 2-4; leave them for at least 7 days to habituate to the conditions. Next (days 7–11), handle the animals for 4 days to reduce the stress of the injections.
- (day-12): perform the pretest.
- (days- 13-19): administration of drugs.
- (day-19): perform the swim test (day 19 onward) perform the analysis of the swim test [8].

Behavioral coding

An animal will be judged to be immobile whenever it remains floating passively in the water in a slightly hunched but upright position, its nose just above the surface, with no additional activity other than that necessary to keep its head above water. Swimming is defined as active movement throughout the swim chamber, which includes crossing into another quadrant. Climbing activity (also termed thrashing) consist of upward directed movements of the forepaws along the side of the swim chamber. The data obtained will be compared between control, standard and test [7].

Result

Table 1: Test-1 (*Elettaria cardamom* seed extract 200mg/kg) and Test-2 (*Elettaria cardamom* 400mg/kg)

Treatments	Immobility (7 th day) Mean±sem
Control	161.4±5.02
Test-1	52.99±2.41
Test-2	24±1.76
Standard	4.33±0.51

Table- Effect of Control (2ml/kg normal saline), Test-1 (200mg/kg), Test-2 (400mg/kg) and standard (Imipramine 20mg/kg) on forced swim apparatus

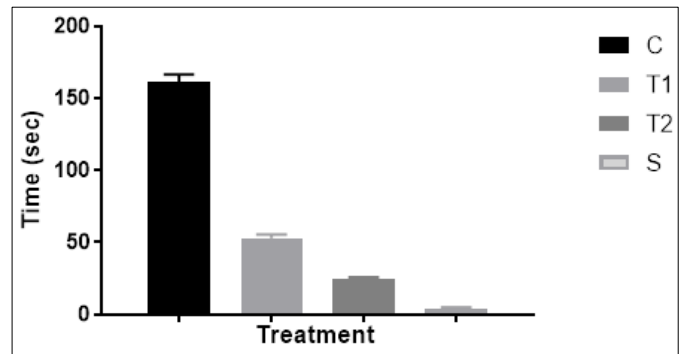


Fig 2: Show treatment

Test-1 (*Elettaria cardamom* seed extract 200mg/kg) and Test-2 (*Elettaria cardamom* 400mg/kg) and standard (imipramine 20mg/kg) administered group was found to significant decrease in immobility as compared to control (2ml/kg normal saline) during behavior coding on 7th day. It shows that test -1 (200mg/kg), test-2 (400mg/kg) and standard (imipramine 20mg/kg) was less immobile (less depressive) than control (2ml/kg normal saline). The values are represented as mean±sem one way anova followed by $p < 0.05$.

Discussion and Conclusion

Elettaria cardamom is investigated for its antidepressant activity in rats. The forced swim apparatus exposes the animal to the stress and fear which causes the animal to escape the situation and develops depression in the animal. Depression is a low mood that lasts for a long time, and affects your life every day. In its mildest form, depression can mean just being in low emotional state. A depressive person does not stop his work but makes everything harder to do and seem less valuable and the most severe, depression can be life-threatening because it can make the person feel suicidal or simply give up the will to live. Depression is more than just feeling sad or going through a rough patch. It is a serious mental health condition that requires understanding and medical care. Just like with any mental illness, people with depression experience symptoms differently. But for most people, depression changes how they function day-to-day. Changes in sleep, Changes in appetite, Lack of concentration, Loss of energy, Lack of interest, Low self-respect, Hopelessness, Changes in movement, Physical aches and pains are the some common symptoms of depression. Depression is a heterogeneous mood disorder which influences the cognition and causes mental disturbances in the subject. It can be also characterized as the persistently depressed mood or loss of interest in activities, causing significant impairment in daily life. A combination of causes contributes to the disorder including biological, psychological and social sources of distress. The state affects the daily to daily life at broad scale and hinders individual thinking.

Treatment of the depressive disorders with various types of medications and therapies is not optimal till date and requires development of more effective newer drugs. Most widely prescribed drugs for the treatment are tricyclic antidepressants. The use of these drugs is declined due to the side effects like addiction, dry mouth, hives, increased heart rates and blurred vision [9, 10, 11]. So it's high time to switch over to the herbal medications which have proven its efficacy in the disorder. In the present study *Elettaria cardamom* is investigated for its antidepressant activity. The drug is also used for the treatment of anxiety, stress, cognitive disorder,

intestinal spasm, constipation and loss of appetite. To evaluate the antidepressant activity various animal models are available. Therefore, Forced swim apparatus is selected for the study. The apparatus is simple, reliable, less time consuming and presents good results. The apparatus is used to evaluate the swimming behavior of the rats. The development of immobility when rats are placed in inescapable cylinder filled with water reflects cessation of persistent escape directed behavior. Rats when forced to swim in a restricted spaces, are induced to a peculiar behavior of immobility such as cessation in struggling to escape and they remained in motionless floating posture. This behavior reflects a state of despair which can reduce by several agents which are therapeutically effective in human depression. Decrease in time of immobility is considered as antidepressants action of drug. Forced swim test in glass jar will be performed as described by Porsolt with few modifications. This test consists of two sessions, an initial training period of 15 min followed by actual test for 5 min duration 24 h later. Rat will be individually forced to swim inside a vertical glass cylinder (height: 40 cm; diameter: 18 cm; containing 30 cm height of water maintained at 25° C). On the basis of the evaluation methods following results are obtained from various groups of rats by Forced swim apparatus.

Control group consists of six animals was treated with normal saline (2ml/kg,p.o.) and *Elettaria cardamom* extract groups was treated with the extract at dose of 200mg/kg and 400mg/kg 30min. prior to the depression experiment. Control group animals were immobile for the most of the experiment time whereas the extract group animals were less immobile(less depressive) as compared to the control group. The anti-depressive activity of the drug is due to the linalool present in the *Elettaria cardamom* [12].

The standard drug (Imipramine) group was given at a dose of 20mg/kg, p.o. and *Elettaria cardamom* extract groups were given doses at 200mg/kg and 400mg/kg p.o. and six animals were taken in each of the groups. When both the groups were compared it was noted that the animals of the both the groups were less immobile(less depressive) and they showed swimming behavior for most of experiment time period i.e. 5min. The behavior exhibited by the animals depicts the antidepressant effect of the drugs [7].

Elettaria cardamom groups treated at 200mg/kg and 400mg/kg, p.o. when compared at the forced swim apparatus showed that the animals which were administered at dose of 400mg/kg were very less immobile as compared to the animals of the group treated at dose of 200mg/kg. The animal is mobile throughout the experimental time period and this shows the antidepressant effect is more prominent in the 400mg/kg group. The animals were administered freshly prepared drug extract 30min. before the experiment [6].

Control group, Imipramine group (standard drug) and *Elettaria cardamom* extract groups when compared for their effects on the behavior exhibited by the rats on the forced swim apparatus shows that the herbal drug *Elettaria cardamom* proved to be significantly effective in relieving rats from the depression provoked by the forced swim apparatus. *Elettaria cardamom* shows this effect may be due to the linalool which interacts with the monoaminergic system including serotonergic and nonadrenergic system. The decrease in the immobility time period is the indication of the antidepressant effect of the drug. The following study proved that the *Elettaria cardamom* is effective in relieving in the depression.

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