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## Comparing the Effects of Ginger's Extract and Imipramine on Cortisol Variation in Mice under Depression

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**Abstract** Depression is one of the most common psychiatric disorders that is classified as mood disorder. Medicinal plants have long been used as a treatment for depression. Ginger (*Zingiber officinale*) is widely used in traditional medicine as a nutritional supplements and also a drug. Sixty male mice in the weight range of 25-30g were divided into eight groups of control, depression, imipramine and 50,100, and 200mg/kg of ginger's extract. Mice were kept under controlled conditions of temperature and humidity, natural light cycles with sufficient water and food. 24 hours before test, mice transferred to the test site. On the morning of the test, Drug injections were done and after 55 minutes, tail suspension and forced swimming tests were performed. After that, blood samples were taken and cortisol amount was measured. Obtained data were analyzed using SPSS program. Ginger's extract in dose of 50mg/kg had different cortisol amount from imipramine and control groups ( $P<0.01$ ). 100 and 200mg/kg doses had different cortisol amount from depressed group ( $P<0.01$ ) but not from imipramine and control groups. According to results, hydroalcoholic extract of ginger in 100 and 200 mg/kg doses can increase cortisol amount and act similar to imipramine in depression.

**Keyword:** ginger, depression, imipramine, cortisol, mice

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### Introduction

All people sometimes feel discomfort or annoyed, but these feelings are usually transient and forgotten within a few days. But when the person has a depressing disorder, this depression affects life and usual activities and causes the suffering of the person and those who are in contact with him. Although depression appears to be normal but it is an important illness and most of people who experience it need recovery and treatment to improve. Many people with depression do not seek treatment; while, most of them, even those with the most severe depression, recover with treatment and treatment. Developed drugs, psychotherapy and new methods for treating people with this disabling disease are the result of researches focused on the disease [1]. Although many compounds such as monoamine oxidase enzyme inhibitors (MAOIs), triangular antidepressants (TCAs), and serotonin reuptake inhibitors (SSRIs) are used for the treatment of depression, most of these drugs cause several unwanted reactions including anticholinergic effects, blood pressure and arrhythmia [2-5].

Imipramine is from tricyclic anti-depressant drugs which its anti-depressant effect is due to the prevention of neurotransmitter reuptake of noradrenaline and today is prescribed more often for the treatment of children's nocturnal urine because of the anticholinergic properties [6, 7]. In the imipramine group, anticholinergic effects such as dry mouth and urinary retention are more than expected [8]. Therefore, more effective drugs with less toxicity are needed [9].



Herbal extracts are among the most attractive sources of new drugs and have shown promising results in treating depression [10-11]. *Zingiber officinale* is a perennial plant with about 1.3m height, with a tubercular creeping rhizome, bayonet or linear -bayonet narrow leaves without petioles, a circular inflorescence with a maximum height of 25 cm, oval bracts with a narrow, long, green tip, up to 2.5 cm in length. The components of the flower are: flower sepal (one centimeter) with a crescent margin, green-yellow flower bowl with about 2cm tube and equal lobes, sterilized petal like stigma (Purple with yellow spots), dark purple stigmas [12-13].

In a study by Kamalirousta et al. (2013) on essence oil of ginger, 17 compounds were identified which zingiberon (31.79%) was main component and arkorkoman, beta sesquiphellandrene and beta bisabolene (15.88, 15.57, and 9.29%) were in the next ranks [11].

Wide use of ginger in food and medicine of many countries has led to lots of pharmacological studies on this plant. Following effects in laboratory animals have been reported: decrease in blood glucose, increase and decrease in blood pressure, effects on cardiovascular system, Inhibition of prostaglandins and platelet aggregation, decreased blood lipids, bile production, decreased gastric acid secretion and even anti-parasitic properties [14-15]. These pharmacological properties have been investigated on various ginger compounds. For instance, the effect of gingerols on preventing the proliferation of human cancer cells from the pathway to apoptosis has been proven [16-17].

During stressful situations, Emotional stimuli and acute stress, secretion of stress hormones especially cortisol will be increased. Cortisol is from the most important glucocorticoids which is naturally secreted from the adrenal gland cortex. This hormone is essential for the normal activity of all types of cells in animals. In response to secretion of adrenocorticotropin from the anterior lobe of the pituitary, a Cortisol is released from the adrenal cortex and interacts with tissue receptors. Studies have shown that depression is often accompanied by impaired function of the hypothalamus-pituitary-adrenal axis and increased cortisol secretion [18]. High levels of stress have several consequences including anxiety, depression, physical-psychiatric disorders, sleep disorders, restlessness and irritability, forgetfulness, abnormal fatigue, decreased body resistance and frequent infections, headache, decreased focus, memory impairment and reduced ability to solve problems [19]. Furthermore, (Increased heart rate, high blood pressure and sweating, cold hands and feet, pupil opening, hearing sensitivity, secretion of cortisol, epinephrine and norepinephrine are signs of stress [20]. Based on mentioned points, current study was carried out to comparing the effects of ginger's extract and imipramine on cortisol variation in mice under depression.

### **Materials and Methods**

Sixty mature mice in the weight range of 25 to 30g were kept in standard cages made from polycarbonate with lattice steel ceilings. Animals were kept for two weeks to adapt to environment. Samples had free access to food and water, 20-22 °C temperature and 60% humidity. Cages floors were covered with sawdust which were replaced every two days. All animal care was carried out in accordance with the guidelines of Animal Care Committee of Vale do Paraiba University (Brasilia).

#### **- Treatment groups**

1. Experimental groups: received 50, 100, and 200 mg/kg of ginger's extract (n=30)
2. Imipramine group: received 1.2 mg/kg of imipramine drug (n=10)
3. Depression group: received tetrabenazine intraperitoneal (n=10)
4. Control group: no injection (n=10)

#### **- Preparing hydro-alcoholic extract**

Ginger was cut to small pieces and grinded by mill. One hundred grams of this powder was weighed by digital scale and poured into a sterilized erlen plus 40cc of ethanol. Erlen was shaken well to mix powder and alcohol, then was sealed and placed in a cool place for 48 hours. After two days, erlen was shaken again for five minutes. Extract was filtered by using whatman paper. At first, paper was weighed. Then mixture was passed into a sterilized Becher.



Residuals were dried using oven (50 °C) for one and half an hour. Dried powder was weighed using a digital scale. Base extract was used to prepare desire doses (50, 100, and 200 mg/kg) [21-22].

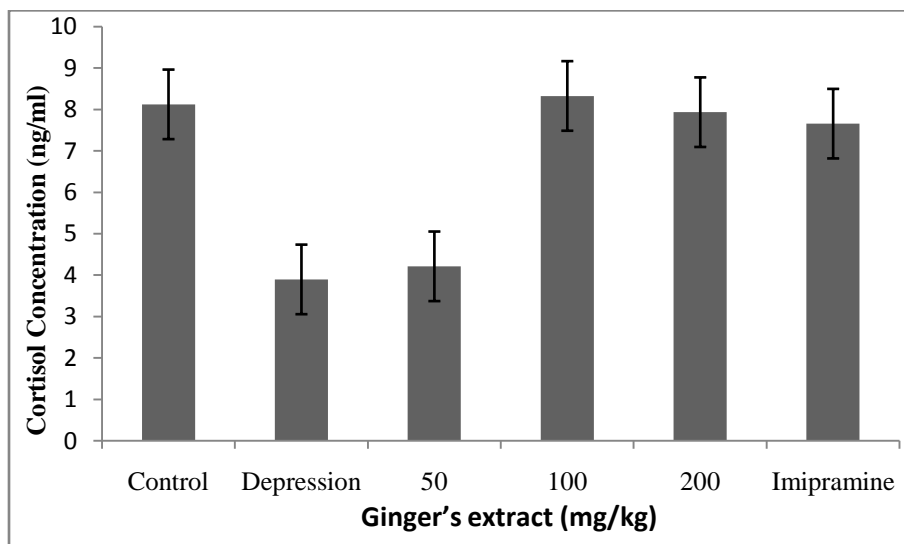
Tetrabenazine was used to induce the depression. At the end of period, blood samples were taken to measure cortisol hormone. Obtained data were analyzed using SPSS 22 program. At the descriptive level, the mean and standard deviations of the variables were calculated whereas one-way variance analysis plus Tukey test were used for inferential level.

## Results and Discussion

Results of measuring cortisol amount are presented in table 1 and Figure 1.

**Table 1:** Average and standard deviation of treatment groups

Groups	Cortisol Amount	
	Mean (ng/ml)	Standard deviation
Imipramine	7.45	1.12
Depressed	3.63	1.21
Control	8.49	1.38
50mg/kg	4.83	1.49
100mg/kg	8.71	1.65
200mg/kg	5.12	1.35



*Figure 1: Cortisol levels in treatment groups*

Current study was carried out to compare the effects of ginger's extract and imipramine on reducing depression symptoms. Sixty male mice in the weight range of 25-30g were divided into eight groups of control, depression, imipramine and 50, 100, and 200mg/kg of ginger's extract. After the last dose, tail suspension and forced swimming tests were performed and immobility duration was measured as depression Index. Obtained data were analyzed using SPSS program.

Hydroalcoholic extract of gingerin dose of 100 mg kg increased mobility time of mice in both tests significantly in proportion to control and imipramine groups, which is considered as an indicator of depression reduction. Therefore, findings of this study showed that gingers' extract in doses of 100 and 200 mg/kg can be a good alternative to imipramine in reducing symptoms of depression ( $P < 0.01$ ) the dose of 50 mg/kg lacked this ability.

Cortisol test showed that there was a significant difference between 50mg/kg group and imipramine or control groups. But the difference between these groups and depression group was not significant. The difference of 100mg/kg and 200 mg/kg groups from depression group were significant ( $P < 0.01$ ) but these groups were not



significantly different from imipramine and control groups. Accordingly, the extract in dose of 100mg/kg acts like the imipramine drug. It also increases the cortisol hormone. Some studies have reported a weak hormone response during three days of resistance training with carbohydrate supplementation.

Comparing the results of this study with previous studies showed that results of this hypothesis is consistent with previous results. For instance, Barzanjeh *et al.* (2016) in a study about the effects of ginger's root powder on inflammatory, anti-inflammatory responses caused by Delorme Resistance Exercise in volleyball men reported that pyramid resistance training plus ginger consumption did not change the cortisol index. Studies have reported a weak hormone response during three days of resistance training with carbohydrate supplementation [16].

Beti *et al.* (2007) and Gaeini *et al.* (2013) studied the effects of carbohydrate and protein supplementation and the response of cortisol to resistance training and reported that group which received carbohydrate supplement reached better hormone environment [17].

### Conclusion

Apparently, in the present study, cortisol hormonal concentration has been adjusted with doses of 100 and 200 mg/kg. As a result, it can be said that ginger's extract can affect cortisol production dose dependently via changing cortisol hormone precursors.

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