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RESEARCH ARTICLE

COMPARATIVE STUDY OF ANTIDEPRESSANT EFFECT OF HYDROALCOHOLIC EXTRACT OF ALOE VERA AND ZINGIBER OFFICINALE WITH FLUOXETINE ON MICE

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ABSTRACT

The antidepressant effects of Aloe vera and Zingiber officinale hydro alcoholic extract at different concentrations were compared with the fluoxetine-treated and the control groups of mice using forced-swimming, FST and TST tests. The mice were evaluated in six groups (control, taking aloe vera at the dosage levels of 150 mg/kg, 300 mg/kg, Zingiber officinale the dosage levels of 175 mg/kg, 350 mg/kg and finally fluoxetine at a dose of 10 mg/kg) by the FST and TST tests on 1st, 7th, and 14th days. The results of FST and TST test indicate the antidepressant effects of Aloe vera and Zingiber officinale even at low doses and it was found that the effect of fluoxetine at a dose of 10 mg/kg was approximatly equivalent to the effect of aloe vera at a dose of 150 mg/kg for the reduction in immobility time in mice in FST and TST test. According to the results obtained from FST and TST test, with regard to the experiments performed at different times, all the evidence pointed to the conclusion that the antidepressant effect of Aloe vera and Zingiber officinale was more than the control group and the antidepressant effect of Zingiber officinale was more than the Aloe vera. Based on the results of the FST and TST tests, Aloe vera and Zingiber officinale extract at different doses, has favourable antidepressant effects on mice as compared to the fluoxetine-treated and the control groups and the better effects were seen by increasing the dose and duration of drug use.

Keywords: *Antidepressant effects; Aloe vera; Zingiber officinale; Fluoxetine; FST; TST.*

INTRODUCTION

Depression is a disorder of major public health importance, in terms of its prevalence and the suffering, dysfunction, morbidity, and economic burden. The report on Global Burden of Disease estimates the point prevalence of unipolar depressive episodes to be 1.9% for men and 3.2% for women, and the one-year prevalence has been estimated to be 5.8% for men and 9.5% for women. It is estimated that by the year 2020 if current trends for demographic and epidemiological transition continue, the burden of depression will increase to 5.7% of the total burden of disease and it would be the second leading cause of disability-adjusted life years, second only to ischemic heart disease[1]. It is responsible for the largest proportion of disease burden attributable to non-fatal health outcomes, accounting for almost 12% of total years lived with disability worldwide[2]. Patients with depression have decreased social, occupational, and

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educational functioning. Moreover, they have high medical morbidity and are often plagued with more pain and physical illness than the general population. It has been estimated that 15% of patients with severe depressive episodes commit suicide. An accurate diagnosis followed by effective treatment can improve this outcome[3]. Depression shows a good response to pharmacological and behavioural treatments, individually or in combination. Among the various pharmacological agents selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) are most commonly used but have a lot of distressing adverse effects as they are often used for very long period of time. Moreover, most of the patients respond to a single drug (most commonly a SSRI or a TCA) but only about 30% achieve remission (complete normalization of symptoms), thus, combination therapy of antidepressants with different mechanism of action or those having mixed effects on serotonin (5HT) and catecholamines i.e., norepinephrine (NE) and dopamine (DA) levels in brain are often required[4]. This also adds up to the adverse effects of individual drugs. Therefore, search for antidepressants with broader spectrum of action and a benign profile of adverse effects continues.

In Ayurveda, the Indian system of medicine have a number of single and in combination antidepressant drugs, which have proved antidepressant effect and very less adverse effect profile[5]. So they can be beneficial for humanity. Herbal drugs are easily available and very cheaper than modern drugs In present study we are going to compare the antidepressant activity of Aloe vera and Zingiber officinale with fluoxetine on mice. Aloe vera is a very common home garden herb and Zingiber officinale is also very common kitchen herb. Both have shown depressant activity in the previous pre-clinical studies. This study can be helpful in terms of comparative value, cost, efficacy and ADR profile of antidepressant drugs.

Depression is the most common of the affective disorders (defined as disorders of mood rather than disturbances of thought or cognition); it may range from a very mild condition, bordering on normality, to severe (psychotic) depression accompanied by hallucinations and delusions. Worldwide, depression is a major cause of disability and premature death. In addition to the significant suicide risk, depressed individuals are more likely to die from other causes, such as heart disease or cancer[6].

Mood and anxiety disorders are the most common mental illnesses, each affecting up to 10% of the general population at some time in their lives[7].

Symptoms of depression –

1. Biological – retardation of thought & action, sleep disturbance, anorexia.
2. Emotional – misery, apathy, low self esteem, feeling of guilt, loss of motivation.

There are two distinct types of depressive syndrome, namely *unipolar depression*, in which the mood swings are always in the same direction, and *bipolar affective disorder*, in which depression alternates with mania. Mania is most respects exactly the opposite, with excessive exuberance, enthusiasm and self-confidence, accompanied by impulsive actions, these signs often being combined with irritability, impatience and aggression, and sometimes with grandiose delusions of the Napoleonic kind. As with depression, the mood and actions are inappropriate to the circumstances[6]. Causes of depression – decreased brain levels of monoamines e.g.- Noradrenaline, Dopamine, Serotonin etc[8-10].

Treatment - Presently a number of synthetic drugs are being used clinically, as standard treatment for depression, but most of them have adverse effects i.e.- dry mouth, fatigue, GI or respiratory problems, drowsiness & cardiac arrhythmias. So there is possibility, for alternative treatment of depression by the use of medicinal plants or by plant based antidepressant formulations.

Drugs restoring the reduced levels of these monoamines in brain either by inhibiting monoamine oxidase or by inhibiting reuptake of these neurotransmitters, might be fruitful in the treatment of depression. The decision to treat with an antidepressant is guided by the presenting clinical syndrome, its severity, and by the patient's personal and family history[7].

MATERIAL AND METHODS

All the experiments were performed after the prior permission from the Institutional Animal Ethics Committee (IAEC), NIMS Medical College, Jaipur, India (Approval number is NIMS/MC/PO/2013/158). 36 Swiss albino mice three / four months of age (20 to 35 g) of either sex were procured from the central animal house of the institute. The treatment groups will be divided into 6 groups, in Group A (control) - distilled water[11]. Group B - hydroalcoholic extract of Aloe vera at the 150 mg/kg dosage[11]. Group C – hydroalcoholic extract of Aloe vera at 300 mg/kg[11]. Group D - hydroalcoholic extract of Zingiber officinale at 175 mg /kg dosage [12]. Group E – hydroalcoholic extract of Zingiber officinale at 350 mg/kg dosage [12]. Group H - Fluoxetine at 10 mg/kg dosage given to the mice[11].

The antidepressant like activity of hydroalcoholic extract of aloe vera and zingiber officinale with fluoxetine was evaluated by forced swimming test (FST)[13] in glass jar and tail suspension test (TST)[13] after drug doses in mice. The drugs will administered once daily for 2 weeks and 20 min before the tests[11]. Route for drug administration is i.p. – for Aloe vera, Zingiber officinale & Fluoxetine. All the tests were done in six groups of animals with at least six animals in each group. In every 6 groups, the mice will be evaluated after i. p. injection (medicine) on 1st, 7th and 14th days by FST and TST.

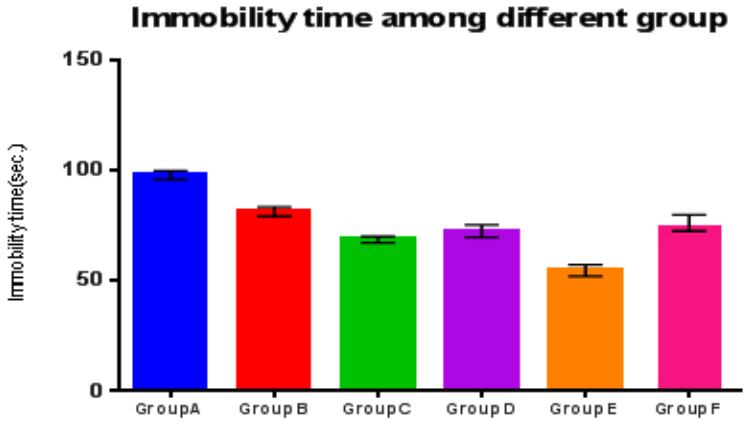
RESULTS

FORCED SWIM TEST (FST)

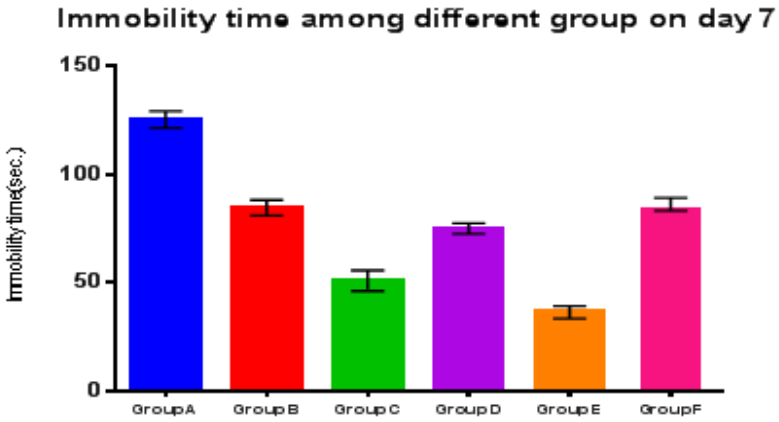
The results of FST test for the effect of hydroalcoholic extract of aloe vera at the dosage levels of 150, 300 and Zingiber officinale at the dosage levels of 175, 350

mg/kg and the control and fluoxetine-treated groups on 1st, 7th, and 14th days shown in Figure.

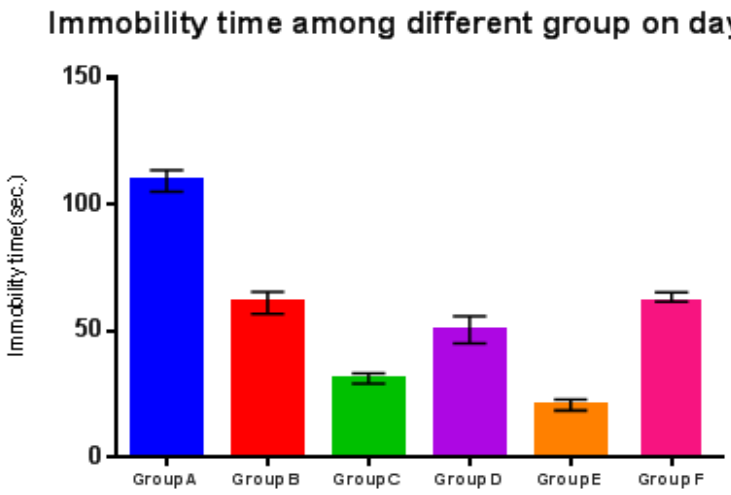
DAY 1 - In group A (control – distilled water) mean of immobility time is- 97.70, in group B (Aloe vera 150 mg/kg) - 83.13, in group C (Aloe vera 300 mg/kg) - 68.47, in group D (Zingiber officinale 175 mg/kg) - 72.41, in group E (Zingiber officinale 350 mg/kg) - 54.55 and in group F (Fluoxetine10 mg/kg) - 76.07 seconds.



DAY 7 - In group A (control) mean of immobility time is - 125.34, in group B (Aloe vera 150 mg/kg) - 84.57, in group C (Aloe vera 300 mg/kg) - 50.94, in group D (Zingiber officinale 175 mg/kg) - 75.08, in group E (Zingiber officinale 350 mg/kg) - 36.30 and in group F (Fluoxetine10 mg/kg) - 86.19 seconds



DAY 14 - In group A (control) mean of immobility time is- 109.23, in group B (Aloe vera 150 mg/kg) - 61.11, in group C (Aloe vera 300 mg/kg)-31.23, in group D (Zingiber officinale 175 mg/kg)-0.49, in group E (Zingiber officinale 350 mg/kg) - 20.74 and in group F (Fluoxetine10 mg/kg) - 63.38 seconds.

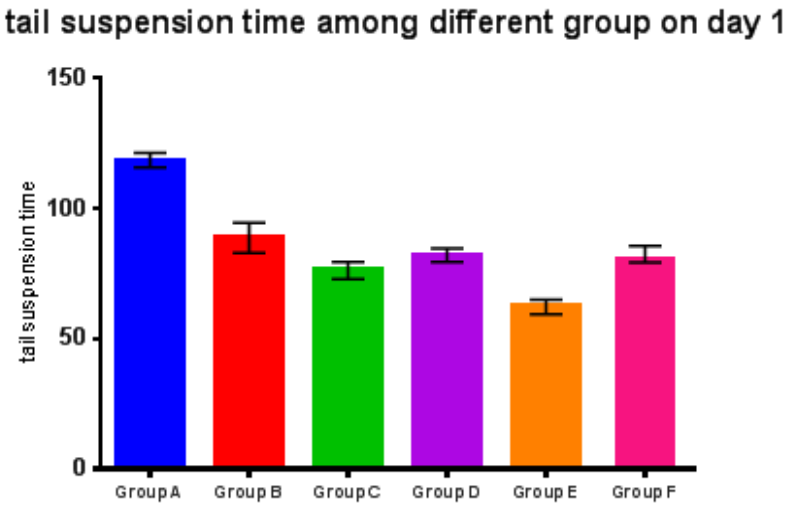


Analysis of variance (ANOVA test)[14] applied, and we find out the mean immobility time of forced swim test was significantly different, among different test groups on 1, 7 and 14th day.

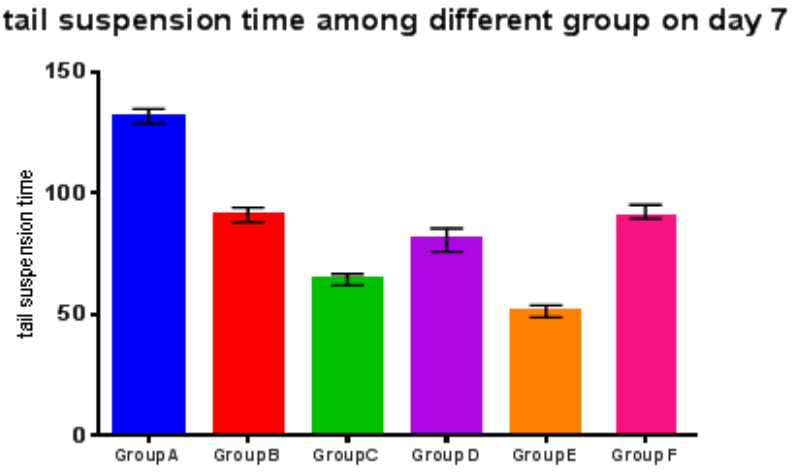
TAIL SUSPENSION TEST (TST):

The results of TST test for the effect of hydroalcoholic extract of aloe vera at the dosage levels of 150, 300 and Zingiber officinale at the dosage levels of 175, 350 mg/kg and the control and fluoxetine-treated groups on 1st, 7th, and 14th days shown in Figure.

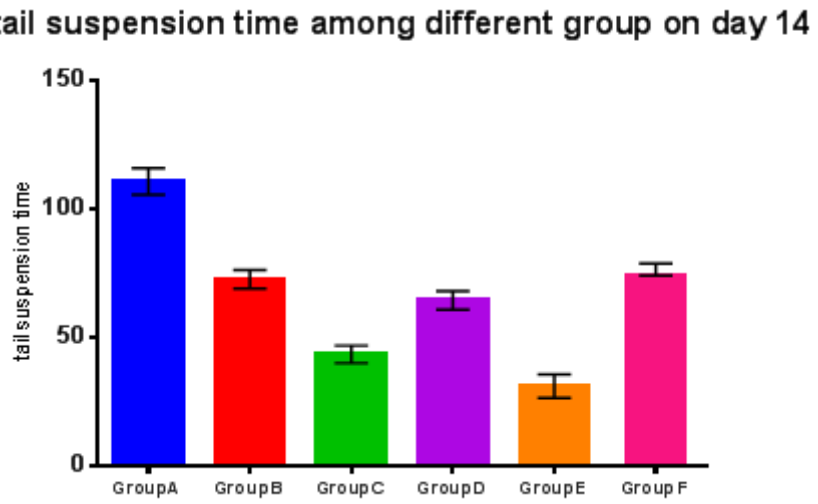
DAY 1 - In group A (control) mean of immobility time is- 118.58, in group B (Aloe vera 150 mg/kg) - 88.73, in group C (Aloe vera 300 mg/kg) - 76.30, in group D (Zingiber officinale 175 mg/kg) - 82.07, in group E (Zingiber officinale 350 mg/kg) - 62.22 and in group F (Fluoxetine10 mg/kg) - 82.44 seconds.



DAY 7 - In group A (control) mean of immobility time is- 132.03, in group B (Aloe vera 150 mg/kg) - 91.26, in group C (Aloe vera 300 mg/kg) - 64.46, in group D (Zingiber sofficinale 175 mg/kg) - 80.84, in group E (Zingiber officinale 350 mg/kg) - 51.31 and in group F (Fluoxetine10 mg/kg) - 92.49 seconds.



DAY 14 - In group A (control) mean of immobility time is- 110.57, in group B (Aloe vera 150 mg/kg) - 72.53, in group C (Aloe vera 300 mg/kg) - 43.34, in group D (Zingiber officinale 175 mg/kg) - 64.28, in group E (Zingiber officinale 350 mg/kg) - 30.90 and in group F (Fluoxetine10 mg/kg) - 76.28 seconds.



Analysis of variance (ANOVA test) applied, and we find out the mean immobility time of tail suspension test was significantly different, among different test groups on 1, 7 and 14th day.

CONCLUSION

Depression is a mental illness characterized by profound and persistent feeling of sadness or despair and/or loss of interest in things that were once pleasurable. The life time risk of depression varies from 5% to 12% in men and 10% to 25% in women[15]. Mood disorders such as depression can be treated with changing the function of neurotransmitters because the slightest change in the function of brain neurotransmitters can be effective in its function. Clinically various groups of drugs are used including typical and atypical antidepressant Allopathic drugs, but none of them are free of ADRs.

In this study, antidepressant effects of different doses of Aloe vera hydroalcoholic extract and Zingiber officinale hydroalcoholic extract were compared with the fluoxetine-treated and the control samples by FST and TST tests on the animal model (mice). According to the FST & TST results, most antidepressant effects were obtained from 300 mg/kg dose of aloe vera and 350 mg/kg of zingiber officinale as compared with other groups on 1st, 7th, 14th days. Also, antidepressants effects of Aloe vera and Zingiber officinale at different doses were more than the control groups.

Regarding the results obtained from the present study, it was found that the antidepressant effects of Aloe vera and Zingiber officinale hydroalcoholic extract increased with increasing the dose and duration of drug use. From the above animal study, we conclude that the plant extract of Aloe vera & Zingiber officinale and Fluoxetine shows a significant ($p < 0.0001$) antidepressant activity in FST & TST model of depression.

We can also say that the Zingiber officinale significantly ($p < 0.0001$) reduces the immobility period than the Aloe vera and Fluoxetine in both FST & TST. So according to the present study Zingiber officinale is a better antidepressant than the Aloe vera and Fluoxetine on particular dose. During the study no adverse effects were found.

Because the synthetic drugs (e.g. Fluoxetine) has many adverse effects like – gastrointestinal problems, nausea, weight gain, nervousness, restlessless, insomnia, anorexia, dyskinesia, headache and some drug interactions etc. Therefore there is a option of herbal drugs for the treatment of depression in comparison of allopathic drugs, which are safe and cheap. As medicinal plants have their importance since ancient time, people using it from various ways as a source of medicine, hence it can be beneficial in depression also. However further studies are required to substantiate these findings specially in clinical set up.

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