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Preclinical evaluation of antidepressant activity of *Boswellia serrata* by Tail Suspension Test

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The objective of present study is to evaluate the antidepressant activity of *Boswellia serrata* and compare with imipramine in Swiss albino mice by Tail Suspension Test. A total of 30(n=30) Swiss albino male mice were used in the present study. They were divided into five groups of six mice in each. Control group received normal saline 10mg/kg, imipramine 10mg/kg for standard and test groups received *Boswellia serrata* in three different doses 50/kg, 100mg/kg and 200/kg per orally. They were evaluated for antidepressant activity by Tail Suspension Test (TST), after 60 minutes of drug administration. Duration of immobility was noted for six minutes for each mouse in all groups. Results were analyzed by ANOVA followed by Dunnet's multiple comparison test. *Boswellia serrata* at the dose of 100 mg/kg significantly reduced the immobility period in Tail Suspension Test model (TST) compared to the control group ($p < 0.001$). Present study shown *Boswellia serrata* has significant antidepressant activity at the dose of 100mg/kg in acute models of depression.

Keyword: Anti-Depressant, *Boswellia serrata*, Tail Suspension Test.

1. Introduction

Depression is a psychiatric disorder characterized by state of low mood and aversion to activity that can affect a person's thoughts, behavior, feelings and sense of well-being. Depressed people feel sad, anxious, empty, hopeless, worried, helpless, worthless, guilty, irritable, and sometimes restless[1]. Depression is a major cause of morbidity in worldwide[2]. Lifetime prevalence varies widely, from 3% in Japan to 17% in the United States. In India prevalence of depression is estimated to be 15%. In most of the countries number of people who would suffer from depression during their lives falls within an 8–12% range[3,4]. In North America the probability of having a major depressive episode within a year-long period is 3–5% for males and 8–10% for females[5,6]. Population studies have consistently shown major depression to be about twice as common in women as in men[7].

Depression can be associated with number of infectious diseases, neurological conditions including hypoandrogenism, Addison' s disease, stroke, cancer, Lyme disease, multiple

sclerosis, diabetes, chronic pain, and sleep apnea[8-11].

Decreased levels of monoamines like serotonin, noradrenaline and dopamine in nervous system is the most accepted theory for the etiopathogenesis of depression. And the drugs that inhibits monoamine reuptake, leading to an increased concentration of monoamines in the synaptic cleft, has been proven to be a clinically effective antidepressant[12].

Approximately 60 to 70% of depressed patients respond to conventional antidepressants, when taken in a sufficient dose for a period of 6–8 weeks. But there is no ideal antidepressant drug with rapid onset of action, moderate half-life, a low side-effect profile, minimal interaction with other drugs, and safety in overdose[13]. More over conventional antidepressant drugs have unwanted side effects. Hence the medical field needs newer, better-tolerated and more efficacious drugs.

Herbal medicines are still the mainstay in primary health care specially in the developing countries, because of the general belief that herbal drugs are without any adverse effects besides being economical and easily available[14,15].

Boswellia serrata is a tree of moderate height, which grows in hilly areas of India. The therapeutic value of dried resinous gum (guggulu) from *Boswellia serrata*, has been known since very long time. Boswellia gum has been mentioned in the ancient Ayurvedic texts-Sushruta Samhita and Charaka Samhita[16]. Gum resin possess good anti-inflammatory, anti-arthritic and analgesic activity[17].

So the present study was carried out to elucidate the antidepressant activity of *Boswellia serrata* in Swiss albino mice.

2. Materials and Methods:

2.1 Animals:

Institutional Animal Ethical Committee (IAEC) clearance was obtained from Yenepoya University, Mangalore, Karnataka, India before conducting the study. Healthy male Swiss albino mice of 3-4 months age, weighing 25-35 g. were included for the study. Female mice and those which are used in previous experiments were excluded from the study. The mice were inbred in the central animal house of the Department of Pharmacology, Yenepoya Medical College, Yenepoya University, Mangalore, Karnataka, India under suitable conditions of housing, temperature, ventilation and nutrition. The study was conducted in accordance with standard CPCSEA guidelines.

2.2 Drugs

Boswellia serrata was purchased from Natural Remedies, Bangalore, Karnataka, India. The doses of *Boswellia serrata* were used on the basis of previous studies[18]. Pure form of imipramine was obtained from Torrent Pharmaceutical Company, Ahmadabad, India. Normal saline (NS) was purchased from Yenepoya Medical College Pharmacy, Yenepoya University, Mangalore, Karnataka, India.

2.3 Experimental Design

A total of 30 (n=30) Swiss albino male mice were used in this study. They were divided into five groups of six mice in each. Animals were weighed and appropriate dose of drug was given to the different groups by oral route. Control group received normal saline in a dose of 10mg/kg, imipramine 10mg/kg for standard and test groups received *Boswellia serrata* in three different doses 50/kg, 100mg/kg and 200/kg orally. They were evaluated for antidepressant activity using Tail Suspension Test (TST) model after 60 minutes of oral drug administration. The experiment was conducted between 8:00 A.M. to 2:00 P.M. in Post Graduate Experimental Laboratory, Department of Pharmacology, Yenepoya Medical College, Yenepoya University, Mangalore, Karnataka, India.

2.4 Tail Suspension Test (TST)

Steru et al. developed the Tail Suspension Test to evaluate antidepressant activity[19]. The model used in the present experiment is similar to the original method described. Mice were suspended upside down on a metal rod at a height of 55 cm from the ground level with the help of an adhesive tape placed approximately 1 cm from the tip of the tail. Initially the mice tried to escape by making vigorous movements but

when unable to escape became immobile. The mouse was considered immobile when it did not show any movement of body and hanged passively.

The immobility displayed by rodents when subjected to this kind of unavoidable and inescapable stress has been hypothesized to reflect behavioral despair which in turn reflects depressive disorders in humans. The total duration of immobility was noted during six minutes period. Each animal was used only once.

2.4 Statistical Analysis

Results are presented as Mean ± SEM. One way ANOVA followed by Dunnet's multiple comparison test was used for comparison between groups. For all the tests a 'P'value of 0.05 or less was considered for statistical significance.

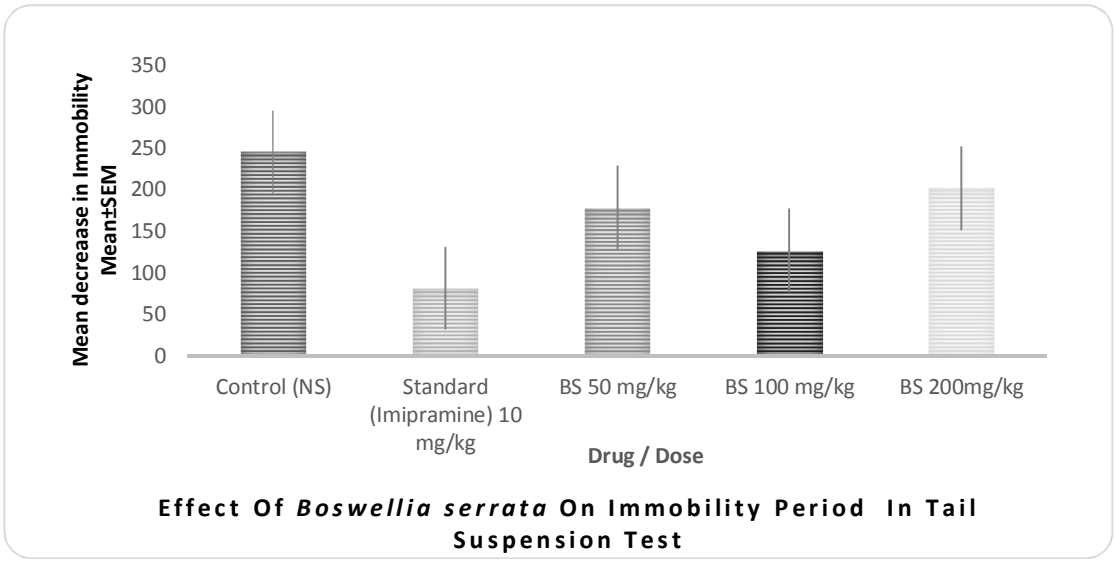
3. Tables and Figures

3.1 Table 1: Showing Effect of *Boswellia serrata* on immobility period in *Tail Suspension Test.*

GROUP NO	DRUG /TREATMENT	DOSE (Kg^{-1})	Immobility Time in sec (Mean+SEM)
01	Control(NS)	10ml	245 ± 11.26
02	Standard (Imipramine)	10mg	80.66± 13.22***
03	Boswellia Serratta	50mg	177.83± 25.62*
04	Boswellia Serratta	100mg	126± 25.16***
05	Boswellia Serratta	200mg	201.16±17.19*

Observations are Mean±S.E.M. ANOVA followed by Dunnet's Multiple comparison test. *p>0.05, **p<0.05, ***p<0.01.

3.2 Figure 1: Bar diagram showing effect of *Boswellia serrata* on immobility period in *Tail Suspension Test*.



*BS-*Boswellia serrata*; Control- Normal Saline

4. Discussion

Recently, role of cytokines in the etiogenesis of depression has been found out[20]. "Sickness behavior" as a result of an activation of the inflammatory response system shares many symptoms of depression, including fatigue, anhedonia, psychomotor retardation, and cognitive impairment. Sickness which is mediated by pro-inflammatory cytokines such as interleukin-1α, tumor necrosis factor-α, and interleukin-6, activate the Hypothalamo-Pituitary-Adrenal axis and thus impair the central serotonin system[20]. Around 30% patients receiving recombinant interferons experiences depression as adverse effect[21]. In animals, blockade of pro-inflammatory cytokine-mediated signaling process produces antidepressant-like effects[22]. The antidepressant enhancing effect of acetylsalicylic acid points to the possible clinical relevance of psychoneuroimmunology in clinical depression research[23].

Boswellia serrata, in Sanskrit is known as Gajabhakshya, implying its ingestion by elephants which being capable of carrying their weight over a long period of time, yet still outliving humans. The therapeutic value of dried resinous gum (guggulu), derived from tapping the *Boswellia* tree has been known since antiquity. Phytochemical analysis of *Boswellia serrata* has shown presence of oils and β-boswellic acid, 3-O-acetyl-β-boswellic acid, 11-keto-β- boswellic acid and 3-O-acetyl-11-keto-β-boswellic acid[24]. *Boswellia serrata* has been used in the management of wide variety of disease like cancer, inflammatory colitis, arthritis, asthma, psoriasis and as a hypolipidemic agent[25-32].

Boswellia serrata found to have anti-oxidant activity by scavenging free radicals like NO, peroxide radical, O^{2-}, OH, DPPH (1,1-diphenyl-2-picryl hydrazyl) with high reducing ability[33]. *In vitro* testing reveals Boswellic acids, in a dose-dependent manner inhibits the synthesis of proinflammatory 5-lipoxygenase products, including 5-hydroxyeicosatetraenoic acid (5-HETE) leukotriene B4 (LTB4), and also TNF-α which cause bronchoconstriction, chemotaxis, and increased vascular permeability[34,35].

As proinflammatory mediators are involved in causation of depression, the present study was carried out to evaluate the antidepressant activity of *Boswellia serrata* which significantly inhibits proinflammatory mediator release. Three different doses of *Boswellia serrata* (50mg/kg, 100mg/kg and 200mg/kg) evaluated for its antidepressant activity using Tail Suspension Test (TST) model. Immobility period for all the five different groups of mice are explained in the Table I and Figure I. *Boswellia serrata* in a dose of 100mg/kg significantly reduced immobility period in TST compared to control group ($P<0.001$). However, 50mg/kg and 200mg/kg dose of *Boswellia serrata* failed to reduce immobility period compared to control group ($p>0.05$). This shows that *Boswellia serrata* has significant antidepressant activity in a dose of 100mg/kg. Reason for non-antidepressant activity of *Boswellia serrata* at the dose of 200mg/kg needs to be evaluated.

5. Conclusions

Present study has shown *Boswellia serrata* has significant antidepressant activity in experimental animal model. Hence can be an alternative to conventional antidepressant drugs. However, further studies are required to reveal both efficacy and safety profile of *Boswellia serrata*.

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