

# INTERNATIONAL JOURNAL OF UNIVERSAL PHARMACY AND BIO SCIENCES

Pharmaceutical Sciences

Research Article.....!!!

Received: 30-05-2013; Accepted: 03-06-2013

## EVALUATION OF ANTIDEPRESSANT ACTIVITY OF *BOSWELLIA SERRATA* IN SWISS ALBINO MICE BY FORCED SWIM TEST

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### ABSTRACT

#### KEYWORDS:

Antidepressant,  
*Boswellia serrata*, Forced  
Swim Test..

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**Objective:** To evaluate the antidepressant activity of *Boswellia serrata* and compare with imipramine in Swiss albino mice by Forced Swim Test model. **Methodology:** 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 using Forced Swim Test (FST) after 60 minutes of drug administration. Duration of immobility was noted for six minutes for each mouse in all groups. **Results:** 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 time in Forced Swim Test model compared to the control group ( $p < 0.05$ ). **Conclusion:** Present study shown *Boswellia serrata* has significant antidepressant activity at the dose of 100mg/kg in acute models of depression.

## INTRODUCTION:

Major depressive disorder (MDD) is a mental disorder common in psychiatry wherein patient presents with one of two major symptoms, constant sadness or anhedonia accompanied by secondary symptoms like feelings of worthlessness, difficulty in concentrating, changes in diet, and sleep patterns, for at least period of two weeks [1]. It is a relapsing, remitting illness having greater than 40% rate of recurrence over a period of two-year [2]. It must be distinguished from normal grief, sadness, disappointment, and dysphoria or demoralization associated with medical illness and from bipolar disorder in which depression alters with hypomania or mania. The MDD is often undiagnosed and frequently undertreated [3].

Depression often co-exists with other illnesses like anxiety disorders, including panic-agoraphobia syndrome, generalized anxiety disorder, posttraumatic stress disorder, and obsessive-compulsive disorder. Alcohol and other substance abuse or dependence may also present with depression.

Depression results from a combination of multiple etiologic factors genetic, biochemical, psychodynamic, and socio-environmental. The children of a depressed person are at a higher risk for depression. Monozygotic twins have a higher concordance rate (46%) than dizygotic siblings (20%) [4]. Decrease in the levels of neurotransmitters like nor-epinephrine and serotonin in the brain is the most important biochemical change causing MDD. Crucial life events, particularly the death or loss of a loved one or an emotional trauma can precede the onset of depression.

Various drugs are available for the treatment of depression. They include monoamine oxidase inhibitors, selective and non selective monoamine reuptake inhibitors and selective serotonin reuptake inhibitors. These medications work by normalizing the levels of neurotransmitters, notably serotonin and nor-epinephrine. Approximately 60 to 70% of depressed patients respond to conventional antidepressants, if it is given in a sufficient dose for 6–8 weeks. But there is no ideal antidepressant; with rapid onset of action, moderate half-life, a low side-effect profile, minimal interaction with other drugs, and safety in overdose [5]. More over conventional antidepressant drugs have unusual side effects. The medical need for newer, better-tolerated and more efficacious treatments remains high.

*Boswellia serrata* is a tree of moderate height, which grows mainly in hilly areas of India. The therapeutic value of dried resinous gum (guggulu) from *Boswellia serrata*, has been known since long time. *Boswellia* gum has been mentioned in the ancient Ayurvedic texts- Sushruta Samhita and Charaka Samhita [6]. Gum resin possess good anti-inflammatory, anti-arthritic and analgesic activity [7]. So the present study was carried out to elucidate the antidepressant activity of *Boswellia serrata* in Swiss albino mice.

**Materials and methods:**

**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.

**Drugs:** *Boswellia serrata* was purchased from Natural Remedies, Bangalore, Karnataka, India. The doses of *Boswellia serrata* were used on the basis of previous studies [8]. 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.

**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 Forced Swim Test (FST) 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.

**Forced swim test (FST):** Porsolt et al. developed the Forced Swimming model to evaluate antidepressant activity [9]. The model used in the present experiment is similar to the original method described. The animals were forced to swim in a plastic cylinder measuring 30 X 30 cm containing water to a depth of 20 cm at room temperature. After an initial two minutes of vigorous activity, each animal assumed a typical immobile posture. The mouse was considered immobile when it remained floating in the water without struggling, making only minimum movements of its limbs necessary to keep its head just above the water level. Total duration of immobility was recorded during next 4 minutes of total 6 minutes duration. The differences in the immobility period were noted after administering drugs in all the group of animals. Each animal was used only once.

**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.

**RESULTS:**

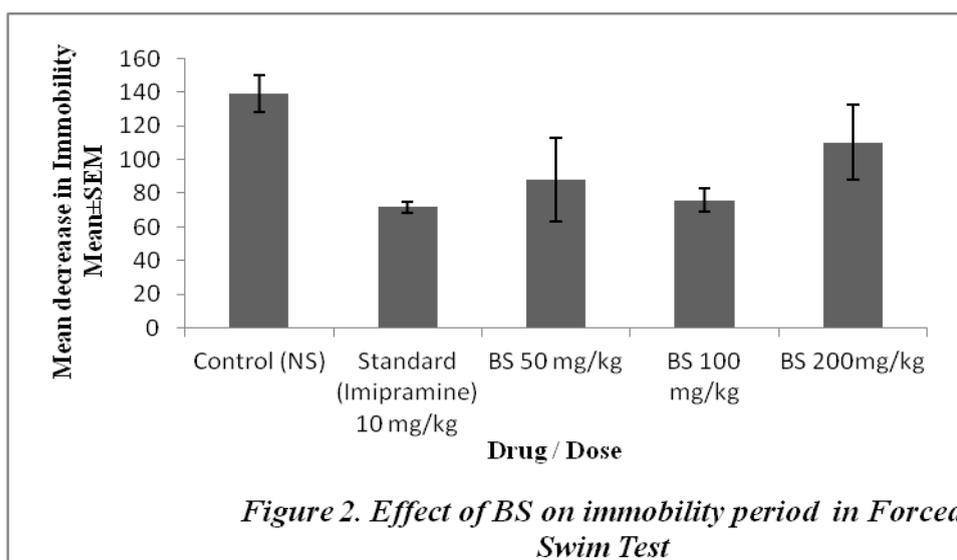
Table I: Effect of *Boswellia Serrata* on immobility period in *Forced Swim Test*

GROUP NO	DRUG/TREATMENT	NO OF ANIMALS	DOSE (Kg <sup>-1</sup> )	Immobility Time in sec (Mean+SEM)
01	Control(NS)	6	10ml	139.33±11.04
02	Standard (Imipramine)	6	10mg	71.66±3.24**
03	Boswellia Serratta	6	50mg	88.16± 24.79*
04	Boswellia Serratta	6	100mg	75.83± 6.93**
05	Boswellia Serratta	6	200mg	110.16±22.148*

Observations are Mean±S.E.M. ANOVA followed by Dunnet’s Multiple comparison test.

\*p>0.05, \*\*p<0.05, \*\*\*p<0.01.

Figure I: Bar diagram showing effect of *Boswellia Serrata* on immobility period in *Forced Swim Test*



BS-Boswellia serrata; Control- Normal Saline

**DISCUSSION:**

Recently, increased pro-inflammatory cytokines (IL-6, TNF- $\alpha$ , NF- $\kappa$ B), increased Nitric Oxide (L-arginine-NO-cGMP pathway), and increased oxidative stress are implicated in the pathogenesis of depression [10-12]. Individuals with depression display lower serum antioxidant potentials, coenzyme Q10(CoQ10), and reduced brain glutathione (GSH) levels as compared to controls [13-16]. Moreover, there a increased generation of free radicals (H<sub>2</sub>O<sub>2</sub>, O<sup>2-</sup>) in MDD individuals due to increased serum Xanthene Oxidase (XO) levels [17]. A recent post mortem study found increased XO activity in the thalamus and putamen of patients with recurrent MDD [18].

It was observed that pretreatment with amitriptyline and fluoxetine associated with increased Super Oxide Dismutase activity, and no signs of cell death were observed in the treated cells [19]. In another study, imipramine, fluvoxamine, or reboxetine inhibited Nitric Oxide (NO) production in a dose-dependent manner in an activated microglia cell culture protocol [20]. This suggests that these antidepressant drugs have additional anti-oxidant property.

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 side effects besides being economical and easily available [21-22].

Plant sources have already provided many useful drugs for mankind: Drugs like digoxin (from foxglove), quinine (from cinchona bark), and morphine (from the opium poppy) are of plant origin [23]. However, herbal medicines which can be alternative to the western medicine, need the same rigorous methods of scientific and clinical validations for the development of new effective drugs [24].

*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  $\beta$ -boswellic acid, 3-O-acetyl- $\beta$ -boswellic acid, 11-keto- $\beta$ -boswellic acid and 3-O-acetyl-11-keto- $\beta$ -boswellic acid [25]. *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 [26-33].

*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 [34]. *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) and leukotriene B4 (LTB4), which cause bronchoconstriction, chemotaxis, and increased vascular permeability [35].

As oxidative stress is the recent causative factor in depression, the present study was carried out to evaluate the antidepressant activity of *Boswellia serrata* which has anti-oxidant property. Three different doses of *Boswellia serrata* (50mg/kg, 100mg/kg and 200mg/kg) evaluated for its antidepressant activity using Forced Swim Test (FST) 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 FST compared to control group ( $P < 0.05$ ).

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.

#### **CONCLUSION:**

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*.

#### **ACKNOWLEDGEMENT:**

Authors are thankful to the entire staff of Department of Pharmacology for their valuable support in the present study.

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