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# Evaluation of Anti-Depressant Activity of Leaf Extract of *Dalbergia Sissoo*

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## ABSTRACT

*Dalbergia sissoo* (family: Fabaceae) is an Asian deciduous rosewood tree. It is the state tree of Punjab state (India) called as Shisham used for antipyretic, emesis, ulcers, leucoderma, stomach troubles and skin disease, memory enhancer etc. The aim of this study is to evaluate the antidepressant activity of ethanolic leaf extracts of *Dalbergia sissoo* in mice. The animals were divided into five groups of 6 each. Group I was considered as normal control, II as Standard control (Imipramine), III, IV and V was treated group (ethanolic leaf extracts of *Dalbergia sissoo* 300, 450 and 600 mg/kg respectively). The animals were acclimatized for behavioral tests like Tail suspension test and Forced swim Test**.** In behavioral model of depression Tail suspension test and Forced swim Test, ethanolic leaf extracts of *Dalbergia sissoo* decreased the immobility time significantly and increase in the first latency in dose dependent manner. The findings in the behavioral model of depression showed significant effect was due to the monoamine theory of depression.

**Keywords:** *Dalbergia sissoo*, ethanolic leaf extracts of *Dalbergia sissoo*, Tail suspension test, Forced swim Test, Imipranine.

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# INTRODUCTION

Depression is among the most prevalent forms of psychiatric disorders and a leading cause for morbidity and mortality.[1] It is a serious disorder in today's society, with estimates of lifetime prevalence as high as 21% of the general population in many countries.[2]

It is a major cause of disability, and causes death both by suicide and due to raised rates of physical disorders.[3] Depression is a state of low mood and aversion to activity that can affect a person's thoughts, behavior, feelings and physical wellbeing.[4] Depressed people may feel sad, anxious empty, hopeless, helpless, worthless, irritable or restless. Depressive disorders are a huge public-health problem.[5] Depression, a highly debilitating and widely distributed illness in the general population, is ranked by the WHO as one of the most burdensome diseases of society, with a lifetime incidence of 15–25%. [6, 7, 8, 9] Though a certain degree of stress may be beneficial, prolonged exposure to chronic stress can lead to depression.[10, 11]

The pharmacological treatment of depression currently available include tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin–noradrenergic reuptake inhibitors (SNRIs), and other atypical antidepressant drugs such as monoamine oxidase inhibitors (MAOIs).[7] However, the efficacy of these antidepressants is often inconsistent and many of them frequently produce side-effects.[12] Hence there remains a pressing need for new effective and better-tolerated antidepressants.

In view of this, *Dalbergia sissoo* Roxb. has been selected based on its use in traditional systems of medicine for augmenting neurological health and was reported to be brain tonic, [13] which appear to offer very promising outcomes for antidepressant. A number of natural compounds are being used as brain tonic to help restore debilitated conditions. Since plants produce significant amount of antioxidants, they represent a potential source of new compounds with antioxidant activity.

The extract of *Dalbergia* species was reported to be brain tonic [13] and also possess antioxidant activity, [14] however there is no scientific data available on the antidepressant activity of title plant in animals. Hence the present study has planned with aim to determine the antidepressant activity of Indian rosewood leaf extract in experimental animal models.

# MATERIALS AND METHOD

### Drugs and chemicals

Imipramine (Reliance formulation Pvt. Ltd, Ahmedabad); Dimethyl sulphoxide (S. D. Fine Chemicals Ltd, Mumbai); Ethanol. All other chemicals and reagents are of laboratory grade.

**Plant material and extraction**

The fresh leaves of *Dalbergia sissoo Roxb*, were collected from Gandhi Krishi Vignan Kendra (GKVK) Karnataka, India in the month of July 2014. The plant was identified and authenticated by Mr. KP Sreenath, taxonomist Department Botany, Bangalore University, India.

The collected fresh leaves were shade dried or tray dried for two weeks and then grinded to a fine powder. In the continuous hot extraction method, the plant leaves powder was extracted in ethanol for 3 days at temperature of 78- 80°C. The mixture was subsequently filtered and concentrated under reduced pressure at 40°C in rotary flush evaporator. The extract yield was 26% w/w. [15] The extract was stored in desiccator.

**Preparation of *Dalbergia sissoo* leaf extracts suspension**

Weighed quantity of ethanolic leaf extract of *Dalbergia sissoo* (ELDS) was suspended in distilled water using 0.5% v/v Dimethyl sulphoxide and administered orally to mice. The suspension of extract was prepared freshly every day. The extract was administered at a constant volume of 1 ml for each animal. [13]

**Preliminary Phytochemical Investigation**

The extracts were used for preliminary phytochemical screening with a battery of chemical tests viz., Molisch's, Fehling's, Benedicts and Barfoed's test for carbohydrates; Biuret and Millon's tests for proteins; Ninhydrin's test for amino acids; Salkowski and Libermann-Burchard's reactions for steroids; Borntrager's test for anthraquinone glycosides; Foam test for saponins glycosides; Shinoda and alkaline tests for flavonoids glycosides; Dragendorff's, Mayer's, Hager's and Wagner's tests for alkaloids; and ferric chloride, Lead acetate tests for tannins and phenols. [14]

**Animals**

Swiss albino mice weighing between 18-25 g were procured from Raghavendra enterprises, Bangalore for experimental purpose. Then all the animals were acclimatized for seven days under standard husbandry conditions, i.e.; room temperature of 24 ± 10°C; relative humidity 45-55% and a 12:12h light/ dark cycle. The animals had free access to standard pellet, with water supplied *ad libitum* under strict hygienic conditions. Each experimental group had separate set of animals and care was taken to ensure that animals used for one response were not employed elsewhere. Animals were habituated to laboratory conditions for 48 hours prior to experimental protocol to minimize (if any) non-specific stress. The experimental protocols

were approved by the Institutional Animal Ethics Committee (PESCP/IAEC/03/2014, Date: 25-1-2014) and conducted according to CPCSEA guidelines, Govt. of India.

**Acute oral toxicity studies**

The acute toxicity study was performed in the laboratory and found that ELDS was not toxic up to 3000 mg/kg body weight. Acute toxicity studies were carried out on mice accordingly, alcoholic extracts at dose of 50, 100, 300, 1000, and 3000 mg/kg body weight were administered to separate groups of the mice (n=6) after overnight fasting. Subsequent to administration of ELDS, the mice observed closely for the first 3 hours for toxic manifestations like increased motor activity, salvation, clonic convulsions, coma and death. The observation is made at regular intervals for 24 hours. The animals were observed for 1 week. The dose was selected low, medium and high dose (300, 450 and 600 mg/kg) for the animal studies.

**Evaluation of Antidepressant Activity of *Dalbergia Sissoo* Leaf Extracts in Mice**

The animals were divided into following groups consisting of 6 mice in each group. (Table 1) For acute study all the animals were administered the drugs/vehicle for a period of 7 days. The animals were acclimatized one hour before for behavioral tests. 1 hour time interval between drug administration and behavioral tests were maintained.

**Table 1: Experimental design for antidepressant activity**

| Groups | Drug treatment | Dose |
|---|---|---|
| Group 1 | Vehicle (control) | (p.o) |
| Group 2 | Imipramine (Standard control) | 15mg/kg (p.o) |
| Group 3 | *D.sissoo* leaf extract | 300 (p.o.) |
| Group 4 | *D.sissoo* leaf extract | 450 (p.o.) |
| Group 5 | *D.sissoo* leaf extract | 600 (p.o) |

For chronic study a new set of animals were used. The method suggested Pemminati *et.al.* was followed with suitable modification to laboratory conditions. All the animals were administered the drugs/vehicle for a period of 28 days. Behavioral evaluation was carried out 60 minutes post drug/vehicle administration on 28$^{th}$day. The anti-depressant activity of the drug was evaluated using following experimental models of depression Tail suspension test and Forced swim test.[16]

**Tail Suspension Test (TST)**

Tail suspension test commonly employed behavioral model for screening antidepressant-like activity in mice, was first given by steru., *et.al*. Animals were moved from their housing colony to laboratory in their own cages and allowed to adapt to the laboratory conditions for

1-2 hr. Each mouse was individually suspended to the edge of a table, 50 cm above the floor, by adhesive tape placed approximately 1 cm from the tip of the tail. Each animal under test was isolated acoustically and visually from other animal during the test. The total period of immobility was recorded manually for 6 min. Animal was considered to be immobile when it didn't show any body movement, hung passively and complete any body movement, motionless. The test was conducted in a dim lighted room and each mouse is used only once in the test. [17]

**Forced Swim Test (FST)**

Forced swim test, the most frequently used behavioral model for screening antidepressant-like activity in rodents, was first proposed by Porsolt. *et.al.* Mice were individually forced to swim in open glass chamber (25 × 15 × 25cm) containing fresh water at a height of 15 cm and maintained at 26°±1°C. At this height of water, animals were not able to support themselves by touching the bottom or the side walls of the chamber with their hind-paws or tail. Water in the chamber was changed after subjecting each animal to FST because "used water" was shown to alter the behavior. Each animal showed vigorous movement during initial 2 min period of the test. The duration of immobility was manually recorded during next 4 min of the total 6 min testing period. Mice were considered to be immobile when they ceased struggling and remained floating motion less in water, making only those movements necessary to keep their head above water. Following swimming session, mice were towel dried and returned to their housing condition. [17]

**Statistical Analysis**

The values were expressed as Mean ± SEM from 6 animals. The results were subjected to statistical analysis by using one- way ANOVA followed by Dunnett's test to calculate the significance. $P<0.05$ was considered as significant.

## RESULTS AND DISCUSSION

**Phytochemical analysis**

Phytochemical study Extract subjected for phytochemical study showed the presence of carbohydrates, proteins, amino acids, steroids, phenolic compounds, tannins, glycosides and flavonoids (Table 2).

**Table 2: Data showing qualitative chemical examinations of extract of *Dalbergia sissoo* leaves.**

| Sl.no | Tests | Alcoholic extract |
|---|---|---|
| 1 | **Carbohydrates** | |
| | Molish's test | + |
| | Benedict's test | + |
| | Fehling's test | + |
| | Barfoed's test | + |
| 2. | **Proteins** | |
| | Biuret test | + |
| | Millon's test | + |
| 3. | **Amino acids** | |
| | Ninhydrin's test | + |
| 4. | **Steroids** | |
| | Salkowski reaction | + |
| | Libermann-burchard's reaction | + |
| 5. | **Flavonois glycosides** | |
| | Shinoda test | + |
| | Alkaline test | + |
| 6. | **Anthraquinone glycosides** | |
| | Borntrager's test | + |
| 7. | **Saponin glycosides** | |
| | Foam test | + |
| 8. | **Alkaloids** | |
| | Dragendorff's test | - |
| | Mayer's test | - |
| | Hager's test | - |
| | Hager's test | - |
| | wagner's test | - |
| 9. | **Tannins and phenols** | |
| | Ferric chloride test | + |
| | Lead acetate test | + |

**(+) indicate presence while (-) stand for absence.**

**Acute toxicity studies**

The ethanolic extract did not show any signs and symptoms of toxicity and mortality up to 3000 mg/kg dose.

**Tail Suspension Test (TST)**

Tail suspension test was employed for the screening of antidepressant activity in the mice. Suspending the mice to the edge of a table for 6 mins showed changes in immobility and latency of immobility which are taken as parameters of evaluation of antidepressant activity. Administration of ELDS for 7 days in acute study at a dose of 300,450, 600 mg/kg body weight showed a significant change ($P<0.001$) compared to the control (228.83 ± 2.44) in dose dependent manner by 20.61 %, 30.15 %, 35.25 % respectively (181.66 ± 2.59, 159.83 ± 1.95,

148.16 ± 2.90 respectively) and the standard drug imipramine showed a significant decrease (P<0.0001) compared to the control 28.98 % (162.50 ± 2.32).

In chronic study the duration of immobility also moderately significant (P<0.05) in all 3 doses 300,450, 600 mg/kg by 28.79 %, 37.44 %, 56.72 % respectively (138.5 ± 2.75, 121.66 ± 2.15, 84.16 ± 3.37 respectively) compared to the control (194.5 ± 15.49) and the standard drug imipramine showed a significant decrease (P<0.01) compared to the control 39.67 % (117.33 ± 3.03). The results are shown in table 3 and Figure. 1a, 1b.

**Table 3: Effect of ELDS on immobility time in the Tail Suspension Test**

| SL NO. | Groups | Treatment | Duration of Immobility (sec) | |
|---|---|---|---|---|
| | | | Acute Study | Chronic Study |
| 1 | I | Control | 228.83 ± 2.44 (0) | 194.5 ± 15.49 (0) |
| 2 | II | Imipramine (15 mg/kg) | 162.50 ± 2.32 **** (28.98) | 117.33 ± 3.03 ** (39.67) |
| 3 | III | ELDS (300 mg/kg) | 181.66 ± 2.59 *** (20.61) | 138.5 ± 2.75 * (28.79) |
| 4 | IV | ELDS (450 mg/kg) | 159.83 ± 1.95 **** (30.15) | 121.66 ± 2.15 * (37.44) |
| 5 | V | ELDS (600 mg/kg) | 148.16 ± 2.90 **** (35.25) | 84.16 ± 3.37 ** (56.72) |

Values are expressed as MEAN± SEM. Statistical analysis is carried one way ANOVA fallowed by Dennett's test. Values in parenthesis indicate percentage change. *(P<0.05), ** (P<0.01), *** (P<0.001), **** (P<0.0001)

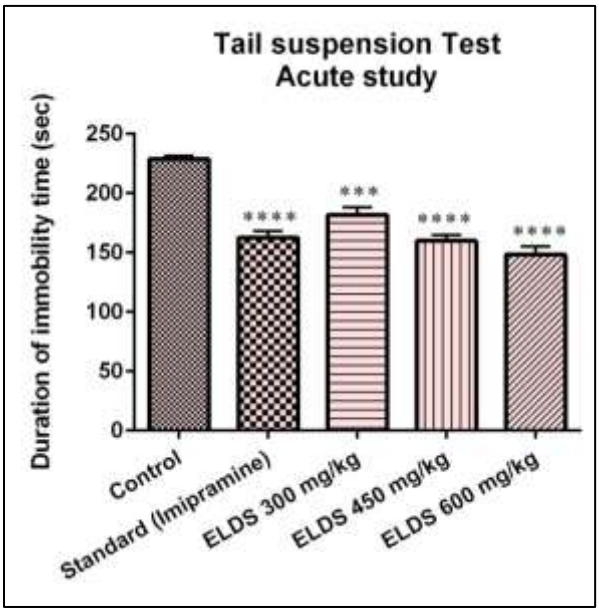


**Figure 1a: Acute Study TST**

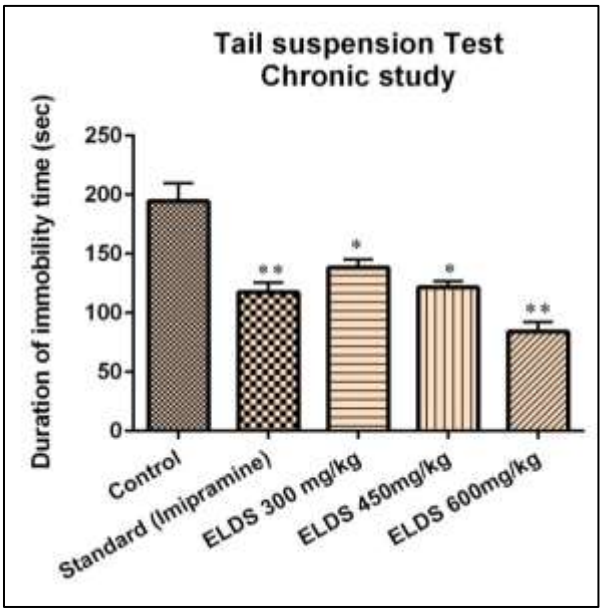


**Figure 1b: Chronic study TST**

**Figure1: Effect of ELDS on immobility time in the Tail Suspension Test**

Each bar represents the Mean ± SEM (n = 06).

Statistical analysis is carried one way ANOVA fallowed by Dennett's test.

* (P<0.05), ** (P<0.01), *** (P<0.001), **** (P<0.0001)

A significant (P<0.001) increase in the dose-dependently increased the latency to the first immobility was seen with the ELDS in all the tested doses 300,450, 600 mg/kg in dose dependent manner (57.00 ± 2.81, 88.66 ± 2.52, 121.33 ± 2.75 respectively) as compared to the control (28.33 ± 3.69) in acute study ($7^{th}$ day).

A significant (P<0.001) increase in the dose-dependently increased the latency to the first immobility was seen in all the tested doses of ELDS 300,450, 600 mg/kg in dose dependent manner (60.17 ± 2.85, 96.66 ± 1.54, 134.50 ± 3.17 respectively) as compared to the control (31.83 ± 3.74) and the standard drug imipramine (58.50 ± 1.89) showed significant (P<0.001) increase in the latency to the first immobility in chronic study ($28^{th}$ day).

The results are shown in table 4 and Figure 2a, 2b.

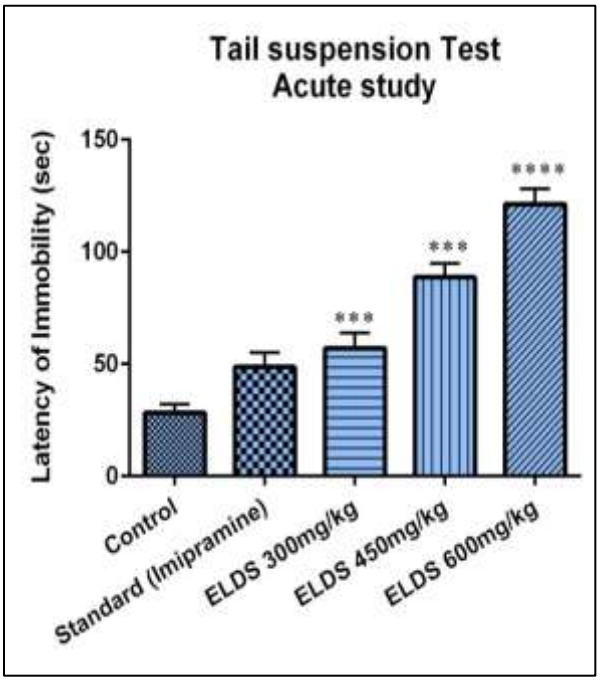


**Figure 2a: Acute Study TST**

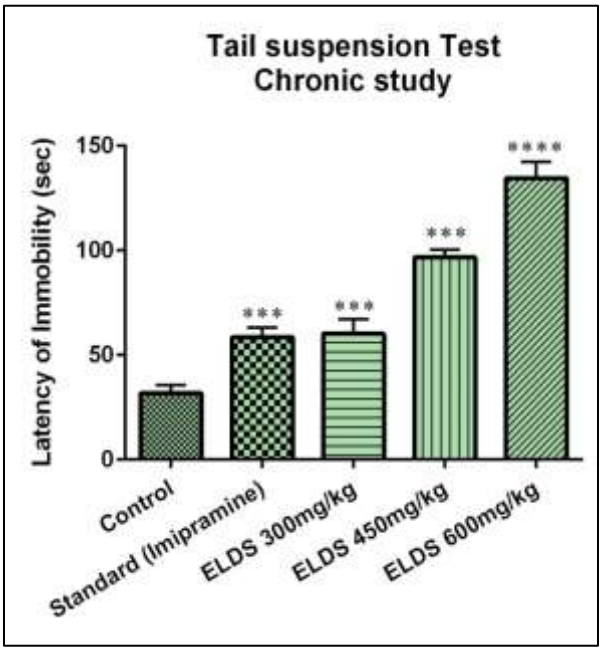


**Figure 2b: Chronic study TST**

**Figure 2: Effect of ELDS on latency of immobility time in the Tail Suspension Test**

Each bar represents the Mean ± SEM (n = 06).

Statistical analysis is carried one way ANOVA fallowed by Dennett's test.

* (P<0.05), ** (P<0.01), *** (P<0.001), **** (P<0.0001)

**Table 4: Effect of ELDS on latency of immobility time in the Tail Suspension Test**

| SL NO. | Groups | Treatment | Latency of Immobility (sec) | |
|---|---|---|---|---|
| | | | Acute Study | Chronic Study |
| 1 | I | Control | 28.33 ± 3.69 | 31.83 ± 3.74 |
| 2 | II | Imipramine (15 mg/kg) | 48.66 ± 2.67 | 58.50 ± 1.89 *** |
| 3 | III | ELDS (300 mg/kg) | 57.00 ± 2.81 *** | 60.17 ± 2.85 *** |
| 4 | IV | ELDS (450 mg/kg) | 88.66 ± 2.52 *** | 96.66 ± 1.54 *** |
| 5 | V | ELDS (600 mg/kg) | 121.33 ± 2.75 **** | 134.50 ± 3.17 **** |

Values are expressed as MEAN± SEM.

Statistical analysis is carried one way ANOVA fallowed by Dennett's test.

*** (P<0.001), **** (P<0.0001)

**Forced Swim Test (FST)**

Forced swim test, the most frequently used behavioral model for screening antidepressant-like activity in rodents. Swimming in open glass for 6 mins, the mice showed changes in immobility and latency of immobility which are taken as parameters of evaluation of antidepressant activity.

Administration of ELDS for 7 days in acute study at a dose of 600 mg/kg body weight showed a significant change (P<0.001) compared to the control (142 ± 1.96) by 21.59 % (111.33 ± 3.01) and the standard drug imipramine showed a significant increase (P<0.0001) compared to the control 21.24 % (111.83 ± 3.89).

In chronic study the duration of immobility also moderately significant (P<0.001) 600 mg/kg by 31.07 % (88 ± 2.98) compared to the control (127.66 ± 2.92) and the standard drug imipramine showed a significant increase (P<0.001) compared to the control 23.38 % (97.83 ± 1.88).

The results are shown in table 5 and Figure 3a, 3b.

**Table 5: Effect of ELDS on immobility time in the Forced swim Test**

| SL NO. | Groups | Treatment | Duration of Immobility (sec) | |
|---|---|---|---|---|
| | | | Acute Study | Chronic Study |
| 1 | I | Control | 142 ± 1.96 (0) | 127.66 ± 2.92 (0) |
| 2 | II | Imipramine (15 mg/kg) | 111.83 ± 3.89 *** (21.24) | 97.83 ± 1.88 *** (23.38) |
| 3 | III | ELDS (300 mg/kg) | 141.33 ± 2.26 (0.46) | 130 ± 1.52 (-1.82) |
| 4 | IV | ELDS (450 mg/kg) | 136.33 ± 1.68 (3.99) | 124.16 ± 1.57 (2.74) |
| 5 | V | ELDS (600 mg/kg) | 111.33 ± 3.01 *** (21.59) | 88 ± 2.98 *** (31.07) |

Values are expressed as MEAN± SEM.

Statistical analysis is carried one way ANOVA fallowed by Dennett's test.

*** (P<0.001)

Values in parenthesis indicate percentage change.

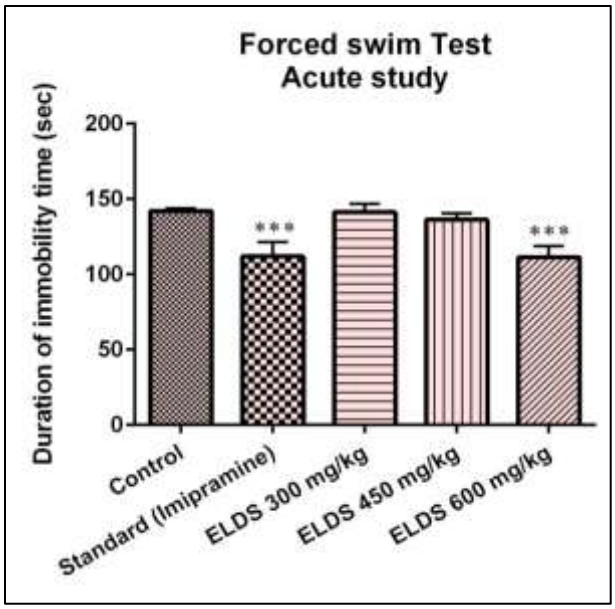


**Figure 3a: Acute Study FST**

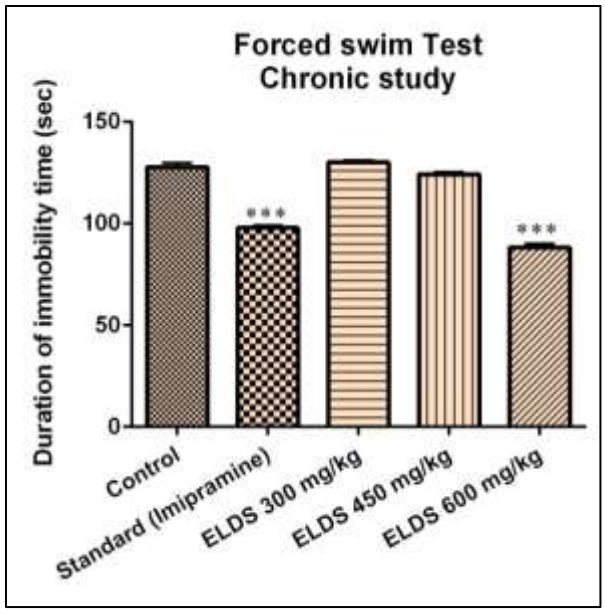


**Figure-3b: Chronic study FST**

**Figure 3: Effect of ELDS on immobility time in the Forced swim Test**

Each bar represents the Mean ± SEM (n = 06).

Statistical analysis is carried one way ANOVA fallowed by Dennett's test.

*** (P<0.001)

A significant (P<0.001) increase in the dose-dependently increased the latency to the first immobility was seen in all the tested doses of ELDS 300,450, 600 mg/kg in dose dependent manner (69.66 ± 2.40, 97.66 ± 2.95, 117.5 ± 3.80 respectively) as compared to the control (54.66 ± 3.91) and the standard drug imipramine (90.83 ± 3.16) showed significant increase (P<0.01) in acute study ($7^{th}$ day).

A significant (P<0.001) increase in the dose-dependently increased the latency to the first immobility was seen in all the tested doses of ELDS 300,450, 600 mg/kg in dose dependent manner (74.33 ± 2.04, 103.5 ± 2.47, 123.66 ± 4.55 respectively) as compared to the control (58.16 ± 3.61) and the standard drug imipramine (98.33 ± 2.83) also showed significant increase (P<0.001) in chronic study ($28^{th}$ day).

The results are shown in table 6 and Figure 4a, 4b.

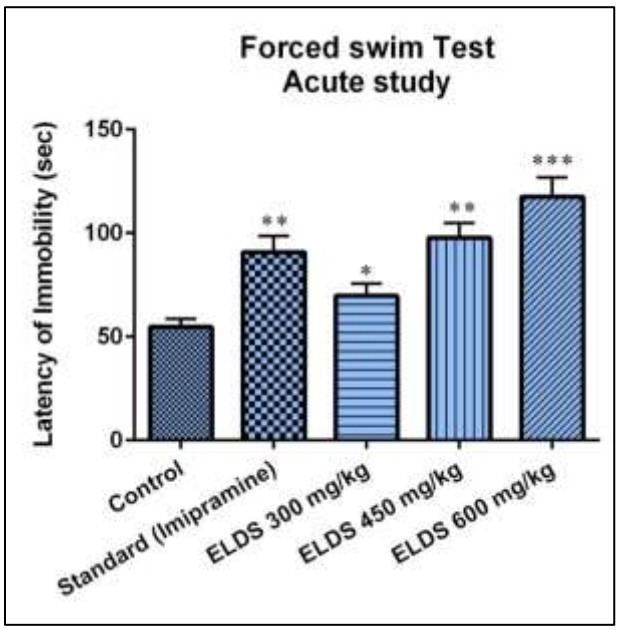


**Figure 4a: Acute Study FST**

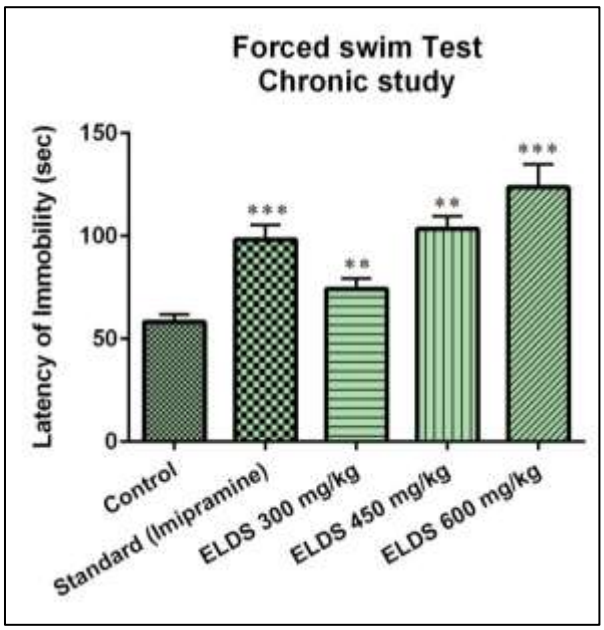


**Figure4b: Chronic study FST**

**Figure 4: Effect of ELDS on latency of immobility time in the Forced swim Test**

Each bar represents the Mean ± SEM (n = 06).

Statistical analysis is carried one way ANOVA fallowed by Dennett's test.

*(P<0.05), ** (P<0.01), *** (P<0.001)

**Table 6: Effect of ELDS on latency of immobility time in the Forced swim Test**

| SL NO. | Groups | Treatment | Latency of Immobility (sec) | |
|---|---|---|---|---|
| | | | Acute Study | Chronic Study |
| 1 | I | Control | 54.66 ± 3.91 | 58.16 ± 3.61 |
| 2 | II | Imipramine (15 mg/kg) | 90.83 ± 3.16 ** | 98.33 ± 2.83 *** |
| 3 | III | ELDS (300 mg/kg) | 69.66 ± 2.40 * | 74.33 ± 2.04 ** |
| 4 | IV | ELDS (400 mg/kg) | 97.66 ± 2.95 ** | 103.5 ± 2.47 ** |
| 5 | V | ELDS (500 mg/kg) | 117.5 ± 3.80 *** | 123.66 ± 4.55 *** |

Values are expressed as MEAN± SEM.

Statistical analysis is carried one way ANOVA fallowed by Dennett's test.

*(P<0.05), ** (P<0.01), *** (P<0.001)

Depression is a severe illness with a lifetime prevalence of between 10 and 20 %, according to large studies. Suicide is a major risk in depression, with about 15% of depressed patients commits suicide. The main behavioral changes are low mood, negative evaluation of events, helplessness, decreased energy and concentration. Our ideas about pathophysiology of depression have derived from studies on the mechanism of antidepressant and the physiological alterations seen in depression. Early theories concerning depression suggested that the condition arises when there is too little NE and 5-HT. This was consistent with the

observation that reserpine, a drug used to control blood pressure and which depleted catecholamine, led to an increased rate of depression and suicide among the patients.

Despite the widely popular use of *Dalbergia sissoo* for treating nervous disorders, there is an absence of scientific reports about the evaluation of its pharmacological effects. In this study, ELDS was examined for their antidepressant-like activity using behavioral model of depression; such as tail suspension and forced swim test.

Behavioral model is generally thought to be the most promising and valuable rodent model to study depression in animals, mimicking several human depressive symptoms. The mechanisms of action of antidepressant drugs compared to acute stress models. Therefore, in the present study antidepressant-like effects and mechanisms of chronically administered ELDS in the models were investigated. Many studies have indicated changes in behavioral and biochemical characteristics in depressed patients. On exposure to chronic stress, mice appeared to have behavioral deficits including increased immobility time. [3]

The previous reports confirmed that chronic sequential exposure to a variety of mild stressors causes a substantial decrease in the sucrose preference index (anhedonia), a core symptom of depression, and that this deficit can be effectively reversed by chronic treatment with the traditional antidepressant drug imipramine. The results of the present study also hold true to the observations (increased immobility time in Forced swimming test and Tail suspension test) made in the previous studies. [18,19]

Administration of ELDS decreased the immobility time significantly and increase in the first latency in dose dependent manner in tail suspension test. (Table 3 and 4 and Figure 1 and 2); where as in the forced swimming test, ELDS decreased the immobility time significantly and increase in the first latency in all doses. (Table 5 and 6 and Figure 3 and 4). This decrease in duration of immobility is considered to have a good predictive value in the evaluation of potential antidepressant agents.

Exact mechanisms underlying the antidepressant action cannot be concluded at the moment due to the presence of large number of phytochemicals in the ELDS. However, the antidepressant activity may be attributed to the presence of tannic acid, polyphenols and flavonoids in the extract. Tannic acid has been shown to be a non-selective inhibitor of monoamine oxidase, thereby increasing the levels of monoaminergic neurotransmitters in the brain. Another possible mechanism of action is the attenuation of oxidative stress produced during depression, by the polyphenols and tannic acid present in ELDS. [20]

Imipramine prevents reuptake of nor adrenaline and serotonin resulting in their increased availability in the synapse and therefore an increase in adrenergic and serotonergic neurotransmission [21]. Fluoxetine is selective serotonin reuptake inhibitor facilitates serotonergic neurotransmission[22]. Since catecholamine and 5-hydroxytryptamine is implicated in etiology of depression, the positive effect of these drugs in TST and FST seems to be due to increased availability of these neurotransmitters at the post synaptic receptor sites. Antidepressant activities of ELDS achieved at sub-effective level in combination with imipramine suggest involvement of ELDS extract in increasing monoamines level at post synaptic sites.

*Dalbergia sissoo* leaf extract showing anti-depressant activity can be explained by monoamine theory of depression, which states that shortage of nor-adrenaline (NA) and serotonin (5-HT; 5-Hydroxytryptamine) in the synaptic clefts is the neurobiological basis of depression. [23]

The first effective treatments for depression were primarily monoamine modulating drugs. Over the past five decades, the leading theory behind the mechanism of action of these drugs has been known as the monoamine hypothesis of depression, postulating that depressive symptoms are primarily caused by disruptions in Serotonin, nor-adrenaline and/or dopamine neurotransmission. [24] The monoamine hypothesis grew originally out of associations between the clinical effects of various drugs that cause or alleviate symptoms of depression and their known neurochemical effects on monoaminergic transmission in the brain. Initially the hypothesis was formulated in terms of nor-adrenaline, but subsequent work showed that most of the observations were equally consistent with 5-hydroxytryptamine (5-HT) being the key substance. [25, 26]

Based on the aforementioned reports and the results of the present studies, ELDS can be assumed to produce antidepressant activity by modulating the 5HT, NE and DA system in the brain. However from the past findings and present study shows that the anti-depressant activity of alcoholic extracts of *Dalbergia sissoo* attributes by maintaining the serotonin levels in the important areas of the brain.

In conclusion, ethanol leaf extract of *Dalbergia sissoo* showed significant antidepressant activities possibly by increasing monoamines level at post synaptic sites. Hence *Dalbergia sissoo* may be served as a potential resource for natural psychotherapeutic agent against stress related disorders such as depression. The antidepressant activity was enhanced at higher dose which might be due to the concentration of tannins and flavonoids present, which possess many CNS activities.

## CONCLUSION

The present study is to investigate the antidepressant like activity of alcoholic extraction of *Dalbergia sissoo* leaf in the chronic variable induced depression model in mice, the findings of the current study show that ELDS display a behavioral profile consistent with an antidepressant-like action. The findings in the behavioral model of depression, tail suspension test and forced swimming test, where ELDS (300,450 and 600 mg/kg) were able to decrease the immobility time and were able to increase the first latency in the stressed animal respectively. Therefore, the antidepressant-like effect ELDS in chronic variable stress induced depression model can be attributed to the monoamine theory of depression, by maintaining the level of serotonin in the synaptic cleft of the brain. Furthermore, the phytoconstituents of ELDS has also been reported to produce antidepressant activity by modulating the 5-HT, NE and DA system in the brain. These pharmacological actions could make ELDS a potentially valuable drug for the treatment of depression. However, the precise mechanism of action is yet to be established and further research is warranted towards studying the fractions and isolated chemical compounds for antidepressant like activities.

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