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EVALUATION OF ANTI-DEPRESSANT ACTIVITY OF ETHANOL EXTRACT OF *DRYPETUS ROXBURGII*

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ABSTRACT

Depression is the leading cause of disability and the fourth leading contributor to the global burden of disease in 2000. Today, depression is already the second cause in the age category 15-44 years for both sexes combined. The present study was designed to evaluate the anti-depressant activity of ethanol extract of the leaves of *Drypetusroxburgii* belonging to family Euphorbiaceae by using actophotometer and forced swimming test (FST) in Swiss albino mice. The albino mice were treated with ethanol extract at a dose of 500mg/kg orally and behaviour was observed on actophotometer and FST. The results showed that ethanol extract at a dose of 500mg/kg of the leaves of *Drypetusroxburgii* has anti-depressant activity.

Keywords: *Drypetusroxburgii*, Forced swim test, anti-depressant, actophotometer

INTRODUCTION

The lifetime risk of depression varies from 5% to 12% in men and 10% to 25% in women. Suicide is the major consequences in most of the depressive illnesses. About 60% deaths are due to depression and related disorders ^[1]. It is characterized by emotional and physical manifestations, such as feelings of worthlessness, helplessness, hopelessness, guilt or indecision, change in appetite, change in sleep habits, loss of concentration, loss of energy, loss of interest, loss of pleasure, agitation, mental and motor slowing, and social withdrawal ^[2]. According to the World Health report, approximately 450 million people suffer from a mental or behavioural disorder. This amounts to 12.3% of the global burden of disease, and will rise to 15% by 2020 ^[3]. Depression is caused by chemical imbalances in the brain which may be due to hereditary, stressful life changes, stroke, Parkinson's disease, or multiple sclerosis, stroke, social isolation, medical conditions such as hypothyroidism (underactive thyroid), medications (such as sedatives and high blood pressure medications), cancer, major illness, or prolonged pain, and sleeping problems ^[4]. Despite the

development of new molecules for pharmacotherapy of depression, it is unfortunate that this disorder goes undiagnosed and untreated in many patients. Although the currently prescribed molecules provide some improvement in the clinical condition of patients, it is at a cost of having to bear the burden of their adverse effects.

The Indian traditional system of medicine such as, Ayurveda mentions a number of single and compound drug formulations of plant origin that are used in the treatment of psychiatric disorders. On one hand, these agents have less adverse effects, and they have been shown to be comparable in efficacy to their synthetic counterparts^[5, 6]. Synthetic antidepressants are often associated with their anticipated side effects such as dry mouth, inability in driving skills, constipation, and sexual dysfunction and majority of patients are reluctant to take this treatment.

Drypterosroxburghi is an esteemed member of Euphorbiaceae (vernacular names- English: Lucky bean tree, Hindi: Putijia, Marathi: JivanPatravanti, Kannada: AmaniPutranjiva). The plant is moderate sized evergreen tree grows up to 13 m in height. Bark is dark grey with horizontal lenticels. Leaves are simple, alternate, darkgreen, shiny, elliptic-oblong, distantly serrulate,; Flower are unisexual, Male flowers are very short pedicellate in rounded axillary clusters, female flowers 1-3 in an axil, fruits ellipsoid or rounded drupes and solitaire. *D. roxburghii*s distributed in Thailand, Nepal, Bangladesh, India (Western Ghats- in dry zones of South, Central and south Maharashtra Sahyadris), Indochina, Myanmar and SriLanka^[7]. Traditionally, *D.roxburghii*s used to treat azoospermia, diuretic, ophthalmopathy, constipation^[8] anti-inflammatory, analgesic and antipyretic^[9]. The plant is known to treat aphrodisiac, elephantiasis, eye infection, habitual abortion sterility, and laxative^[10] and it is also used for the treatment of cough, cold and fever^[11]. The plant is also used to make toys due to its soft, light and flexible woods. The toy making industries especially artisans of Nirmal toys (Andhra Pradesh) are dependent on this wood for their livelihood^[12].

A plant's medicinal value is due to the presence of some chemical substance that produces a physiological action on the Human body and therefore researchers always try to isolate these chemical substances from plants. With the same intent, Garg and Mitra^[13] had successfully isolated Roxburghonic acid, and putraflavone from the alcoholic extract of *D. roxburghii*leaves. *D. roxburghii*s acknowledged for its medicinal properties to treat neurological disorders^[14, 15, and 16]. In the present study the anti-depressant activity was assayed.

MATERIAL AND METHODS

Collection of Plant material

*D. roxburghii*was collected from the forest region of Uttarkannada taluk Sirsi, parts of Western Ghats of Karnataka and authenticated by taxonomist Dr.Rudrapa, Dean and Department of Botany S.R.N.M College, Shimoga.

Extraction and phytochemical screening

The powdered material of leaves of *Drypterosroxburghii* was collected and extracted with various solvents-petroleum ether, chloroform, ethanol and aqueous with increasing polarities by using Soxhlet apparatus. Preliminary qualitative phytochemical screening was carried out with standard procedures and confirmed for the presence of bioactive compounds like flavonoids, alkaloids, coumarins, saponins, mucilage, gums, proteins, phenols were estimated^[17-26].

Experimental Animals

Swiss Albino Mice of either sex were used for the study. The animals were kept at 27°±2°C, Relative humidity 44-56% and light and dark cycles of 10 and 14 hr, respectively, for 1 week before

and during the experiments. Animals were provided with water ad libitum and standard diet and the food was withdrawn 18-24 hr before the start of the experiment.

Acute Toxicity Study

Acute toxicity study was performed on Swiss Albino Mice the fixed dose method was adopted as per OECD (Organization for Economic Co-operation and Development) Guideline No.423 of CPCSEA^[27, 28] the animal were kept fasting for overnight providing water and libitum, after which the extracts were administered orally and observed the mortality of animals.

Anti-depressent activity

Actophotometer

The locomoter activity can be easily measured using an actophotometer which operates on photoelectric cells which are connected in circuit with a counter. When a beam of light falling on the photocell is cut off by the animal, a count is recorded^[29]. Animals were divided into three groups of six animals in each, weighing between 20 and 30g.

Group I: Control (distilled water 1 ml/kg, p.o)

Group II: Standard (Diazepam 2 mg/kg, i.p)

Group III: Test Drug (ethanol extract *D. roxburgii* 500 mg/kg, p.o)

Forced swim test

Animals were divided into three groups of six animals in each, weighing between 20 and 30g.

Group I: Control (distilled water 1 ml/ kg, p.o)

Group II: Standard (Diazepam 2 mg/ kg, i.p)

Group III: Test Drug (ethanol extract of *D. roxburgii* 500 mg/ kg, i.p)

For the FST, mice of the either sex were individually forced to swim in an open cylindrical container (diameter 10 cm, height 25 cm) containing 19 cm of water at 25°C±1°C. Treatment was given 60 minutes prior to study as described by study design all animals were forced to swim for 6 minutes and the duration of immobility was observed and measured during the final 4 minutes interval of the test. Each mouse was judged to be immobile when it ceased struggling and remained floating motionless in the water, making only those movements to keep its head above water. A decrease in the duration of immobility is indicative of an antidepressant-like effect.

Statistical analysis

The results of the study were expressed as mean ± SEM, n = 6. One way ANOVA was used to analyse and compare the data

RESULTS & DISCUSSION

RESULTS

Preliminary phytochemical screening revealed the presence of proteins, carbohydrates, saponins, glycosides, steroids, triterpenes, flavonoids, tannins and phenolic compounds.

Table: 1 Phytochemical screening summary

S. No	EXTRACT	YIELD	CONSTITUENTS
1.	Petroleum ether	05 gm	Steroids
2.	Chloroform	33 gm	Alkaloids, Triterpenoids, glycosides
3.	Ethanol	02 gm	Flavonides, alkaloids, coumarines, phenols, glycosides, saponins, tanins.
4.	Aqueous	10 gm	Gums, mucilage, protein's, carbohydrates, saponins, fatty acid

Acute toxicity Studies

Acute toxicity was evaluated on Swiss albino mice weighing between 25-30g. The fixed dose method was adopted as per OECD (Organization for Economic Co-operation and Development) Guideline No.423 of CPCSEA^{24, 25}. The therapeutic dose fixed was 500mg/kg body weight i.e., $1/10^{\text{th}}$ of the lethal dose.

Anti-depressant activity**Actophotometer**

Ethanol extract of *Drypetus roxburgii* by using actophotometer has shown anti-depressant activity.

Table: 2 Locomotors activity by using Actophotometer

S.No	GROUPS	LOCOMOTARY ACTIVITY(per 5 min)
1	Control	787.33±2.36
2	Standard-(Diazepam 2mg/kg)	1370.83±2.01***
3	Ethanol extract of <i>D.roxburgii</i> (500mg/kg)	833.50±1.26**

Note: Data was analyzed using one way ANOVA followed by pairwise comparison.

Values are expressed as mean ± S.E.M. $n=6$, *** $P < 0.001$ HS is considered as highly significant

Forced swim test

Ethanol extract of *Drypetus roxburgii* by using Forced swim test has shown anti-depressant activity.

Table: 3 Time of immobility by using forced swim test

S.No	Treatment Groups	TIME OF IMMOBILITY(in sec)
1	Control	31.33±1.15
2	Standard-Diazepam(2mg/kg)	74.33±1.23***
3	Ethanol extract of <i>D.roxburgii</i> (500mg/kg)	61.77±1.96**

One way ANOVA followed by pairwise comparison.

Values are expressed as mean ± S.E.M. $n=6$, *** $P < 0.001$ is considered as highly significant

DISCUSSION

Depression is a heterogenous mood disorder characterized with regular negative moods, decreased physical activity, feelings of helplessness, and is caused by decreased brain levels of monoamines such as noradranline, dopamine, and serotonin. Therefore, drugs restoring the reduced levels of these monoamines in the brain either by inhibiting monoamine oxidase or by inhibiting reuptake of these neurotransmitters might be fruitful in the treatment of depression that has been classified and

treated in a variety of ways. Although a number of synthetic drugs are being used as standard treatment for clinically depressed patients, they have adverse effects that can compromise the therapeutic treatment. Thus, it is worthwhile to look for antidepressants from plants with proven advantage and favorable benefits-to-risk ratio^[30]. Ethanol extract of *D.roxburgii* was selected for evaluating its antidepressant activity due to its traditional use in the treatment of neurological problems. The Actophotometer and forced swimming test is the most widely used tool for assessing anti-depressant activity pre-clinically. The widespread use of this simple model is mainly due to its ability to detect a broad spectrum of antidepressant agents. The test is based on the observation that mice following initial escape-oriented movements develop an immobile posture when placed inside an inescapable cylinder with water. The immobility is thought to reflect either a failure of persistence in escape-directed behavior (i.e., despair behavior) or the development of a passive behavior, meaning the loss of the animal's ability to cope with stressful stimuli. In the present study test sample of Ethanol leaf extract exhibited anti-depressant activity at a dose of 500 mg/kg body weight. It may be due to the presence of alkaloids, Phenols, carbohydrates, glycosides, saponins and flavonoids.

CONCLUSION

It can be concluded from the study that the anti-depressant activity of the ethanol extract of *Drypetusroxburgii* may be via non-specific mechanisms. However, extensive studies are needed to evaluate the precise mechanism(s), active principles and the safety profile of the plant as a medicinal remedy for depression disorders.

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