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Open Access Research Article

Evaluation of Antidepressant Activity of Ethanolic Extract of *Abies webbiana and Berberis aristata* in Laboratory Animals

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ABSTRACT

Objective: *Abies webbiana and Berberis aristata* is an herbal plant that has several therapeutic effects. It also heals depression, grief, nervous stress and tension. In the present study we evaluated anti-depressant effect of ethanolic extract from *Abies webbiana and Berberis aristata* by using Forced Swimming Test (FST) and Tail Suspension Test (TST).
Methods: Two doses of ethanolic extract of *Abies webbiana and Berberis aristata* (200 mg/kg and 400 mg/kg) was given orally. Immobility time were measured after 30 min after the dosing and compared with control group and Flouxetine (25mg/kg) as a standard group.
Results: The ethanolic extract of BA and AW (400 mg/kg) was found to be effective and it exhibited activity similar to that of the conventional drug Flouxetine (25mg/kg) ($p<0.001$) whereas 200 mg/kg dose showed higher activity with significantly increased swimming time and suspension time and decreased immobility time than 400 mg/kg of ethanolic extracts and Flouxetine (25mg/kg).
Conclusion: These results proposed 400 mg/kg of ethanolic extract was showed higher anti-depressant activity as compared to control which is similar to the standard.

Keywords: *Abies webbiana; Berberis aristata*; Immobility time; Forced swimming test; Tail suspension test; Antidepressant.

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INTRODUCTION

Depression, a widespread incapacitating psychiatric ailment, imposes a substantial health burden on society [1]. Affective disorder is characterized by a disturbance of mood associated with alteration in behavior, energy, appetite, sleep, and weight [2]. According to the most accepted hypothesis of depression, the monoamine theory, patients with major depression have symptoms that are reflected changes in brain monoamine neurotransmitters, specifically norepinephrine (NE) and serotonin (5-HT) [3]. Clinical data suggests that dopamine (DA) is also involved in the pathophysiology and treatment of depression [4]. Medications such as tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs), specific serotonin-norepinephrine reuptake inhibitors (SNRIs), 5-HT2 receptor antagonists, and other heterocyclics are clinically employed for drug therapy [5]. However, these drugs can impose a variety of side-effects including sedation, apathy, fatigue, sleep disturbance, cognitive impairment, and sexual dysfunction, and so forth. Hence, there remains a pressing need for new effective and better-tolerated antidepressants.

The plant *A. webbiana* is well known under the vernaculars 'Himalayan silver fir' in English, 'Talispatra' in Hindi and Bengali, 'Talispatri' in Tamil and 'Badar' in Kashmiri. In Indian traditional medicine and treatment it is used against cough, asthma and chronic bronchitis and various other diseases [6-8]. The leaf juice of this plant is used in folklore to treat cough and asthma in the rural area of the Sikkim and Kashmir (India). The plant, a tall (maximum 60 m in height) evergreen tree, is found in the Himalayas from Kashmir to Assam at an altitude of 1600–4500 m in forests, largely located in a very humid region with heavy rain fall and dense mist. Leaves are variable in size, densely set in 2–4 ranks on stout branchlets, dark green, lustrous, coriaceous and persist up to 10 years [9]. Daruharidra is one of the herbs mentioned in ancient scriptures of Ayurveda. Ayurvedic Pharmacopeia of India correlates Daruharidra to *Berberis aristata* DC of family Berberidaceae[10, 11]. The plant is native to the whole range of the Himalayas and also occurs in Nilgiri range in

southern India [12]. Studies indicate that it is commonly used to treat eye infections, ENT infections, skin disease, menorrhagia, cholera, jaundice, wound healing and urinary tract infections, indigestion and vaginal disorders [13, 14]. Owing to its high medicinal value, Daruharidra is of trade importance and an endemic species of conservation concern, which has quite high demand in herbal drug market. So to meet the need, herbal drug providers supply mixture of different *Berberis* species [15]. *B. aristata*, reported to possess antimicrobial [16] antioxidant, anti-hyperglycemic [17], anti-amoebic [18] and wound-healing properties [19]. *B. asiatica* possesses antimicrobial and anti-tumour effect.

Our preliminary test indicated that ethanolic extract of *Abies webbiana and Berberis aristata* contained the largest amount of rhynchophylline derivatives. However, the antidepressant-like activity of *Abies webbiana and Berberis aristata* has not been investigated, which encouraged us to investigate the effects of on depression problems. In the present study, we aimed to investigate the effect of *Abies webbiana and Berberis aristata* in FST and TST in mice. The behavioral despair tasks have good predictive value for antidepressant potency in humans. Moreover, we investigated whether the effect of *Abies webbiana and Berberis aristata* in FST and TST is dependent on its interaction with the 5-HT, NE, and DA receptors, and the brain monoamine neurotransmitter concentration.

MATERIALS AND METHODS

Collection and extraction

The aerial part of plant *Abies webbiana and Berberis aristata* was collected from the pattnamthitta, kerala in the month of December 2016. The plant was then authenticated by the joint director, the botanical survey of India. The aerial plant material were dried in shade and pulverized. The powder were passed through sieve no.40 and used for the extraction. The extract was prepared by the cold maceration method by using ethanol and water as solvent in the ratio of 30:70. Chloroform is used as preservative. This process was carried out with stirring the mass once daily for 14 days until the extraction was completed. After completion of extraction, the solvent was removed by distillation process the dark brown color residue was obtained.

Animals

Young adult Wister rat either sexes weighing 190-250 g were obtained from the animal house School of Pharmaceutical Sciences, Department of Pharmacology, IFTM University, Moradabad. They were caged in a room under standard laboratory conditions (temperature 23 ± 1°C, relative humidity 55% ± 5% and lighting 08:00 20:00 h). The animals were fed on a pelleted diet and water. The Institutional Animal Ethical Committee (IAEC) approved by the protocol of this study.

Phytochemical screening

The extract was screened for the presence of various phytochemical constituents employing standard screening test. The extracts were subjected to following chemical tests to detect the chemical constituents present in this study [20, 21] (Table 1).

Acute oral toxicity studies

Toxicity studies of extract were carried out in Swiss albino rats weighing between 25-30g. They were performed according to OECD guideline No. 423. Four groups of rats comprising three animals each were treated with 5, 50, 300 and 2000mg/kg of the extract orally, via gastric catheter. The animals were then observed continuously for the first 4hrs for any behavioral changes and for mortality if any at the end of 72hrs. All four doses were found to be safe since no animal died even at the dose of 2000 mg/kg when administered orally and the animals did not showed any gross behavioral changes.

Anti-Depressant screening

Tail Suspension Test (TST)

The test and standard compounds were administered p.o., 60 minutes prior to testing. The rats were suspended on the edge of a shelf 58 cm above the table top by adhesive tape placed approx. 1 cm from the tip of tail. The duration of immobility was recorded for the period of 6 minutes by using stopwatch. After the initial period of vigorous motor activity, the rats would become still. Rats were considered immobile when they hang passively and completely motionless [22].

Forced Swimming Test (FST):

Either sex of rats were individually forced to swim in an open cylindrical container and container diameter is 10 cm, height is 25 cm. Cylindrical container filled by 19 cm of water at 25 ± 1°C. Either sex of rats were divided in four different groups. The first group assigned as control receiving only vehicle (NaCl 5 ml/ kg). The other three groups received acute dose based on acute toxicity studies of EEAW and EEBA (200 & 400 mg/kg). The Group II received standard drug Flouxetine (25mg/kg) dose is 30 mg/kg. The total duration of immobility was recorded during the last 4 min of the 6 min period. Rats were ceased struggling and remained floating motionless in the water, making only those movements necessary to keep its head above water when each mouse judged to be immobile. A decrease in the duration of immobility is indicative of an antidepressant like effect [21-26].

Statistical analysis: Data were analyzed by Prism Install version software and presented as mean ± SEM. The statitical tests used were one-way analysis of variance (ANOVA) followed by tukey-kramer Multiple comparison test. The level of statical significant ranged from $p<0.05$ top<0.001.

RESULTS AND DISCUSSION

The plant extract at the dose of 200 and 400 mg/kg were used for the *in vitro* antidepressant activity. The doses were selected based on the acute toxicity studies from the literature. The antidepressant effect of *Abies webbiana and Berberis aristata* (200 and 400 mg/kg) and Flouxetine (25mg/kg) were studied and observing the change in the duration of immobility by performing forced swim test and tail suspension test.

The preliminary phytochemical screening indicated the presence of in *Abies webbiana and Berberis aristata*, have been shown to possess anti-depressant effect Flavonoids, Alkaloids and Glycoside (table 1).

Table 1: Preliminary phytochemical constituents present in EEBA and EEAW Leaves

Sr. No.	Chemical Test	Result of EEBA	Result of EEAW
1.	Carbohydrate	+	+
2.	Protein	+	+
3.	Amino acid	-	+
4.	Fat and Oil	-	-
5.	Steroids	-	-
6.	Volatile oil	-	-
7.	Glycoside	+	+
8.	Flavonoids	+	+
9.	Alkaloids	-	+
10.	Tannin	+	+

Positive (+), Negative (-)

The effect of *Abies webbiana and Berberis aristata* extract may be due to the present of above said compounds. The extract was primarily subjected to phytochemical investigation and acute oral toxicity study. In Acute Oral Toxicity study, EEBA and EEAW did not show any lethal effect even up to the doses of 2000 mg/kg, p.o and complete absorption of drug through GIT was observed. The effect of EEBA and EEAW was investigated for its putative antidepressant activity by using various experimental models in rats viz. Tail Suspension test and Forced Swim test. Forced Swim test & Tail Suspension test are the most commonly used preliminary screening tests for characterizing potential antidepressant drugs. In this test *Abies webbiana and Berberis aristata* 200 and 400 mg/kg p.o produced significant reduction ($p<0.05$ and $p<0.001$ respectively) in the immobility period when compared with that of control group animals that received only the vehicle. The extract (400 mg/kg) was found to be effective and it exhibited activity similar to that of the conventional drug Flouxetine (25mg/kg) ($p<0.001$) [27, 28] (table 2 and 3).

Table 2: Tail suspension test

Group	Dose	Immobility time in sec.
I	NS (10ml/kg)	122.33±12.972
II	Flouxetine (25mg/kg)	39.17±3.6***
IV	EEAW (200mg/kg)	77.2 ±6.24*
V	EEAW (400mg/kg)	47.71±2.02**
IV	EEBA (200mg/kg)	82.24 ±6.24*
V	EEBA (400mg/kg)	49.41±4.02**

Table 3: Forced swimming test

Group	Dose	Immobility time in sec.
I	NS (10ml/kg)	152.33±10.972
II	Flouxetine (25mg/kg)	34.17±3.646***
IV	EEAW (200mg/kg)	87.2 ±8.24**
V	EEAW (400mg/kg)	37.71±2.02***
IV	EEBA (200mg/kg)	78.2 ±5.24**
V	EEBA (400mg/kg)	34.71±2.02***

The parameters observed in this model are immobility time of rats. Drugs which decrease immobility time leads to increase in the motor activity of rats which inhibit depression developed due to swimming and tail suspension of rats in these tests and offer protection against depression induced by these methods. In the present study, EEBA and EEAW (200 & 400 mg/kg, p.o) has shown a significant dose dependent activity i.e. increase in the dose of the drug proportional to decrease in the immobility time threshold and offers good percentage protection as compared to control group. Similarly, the standard drug Fluoxetine (25 mg/kg, p.o) had significant percentage protection. Fluoxetine was selective serotonin reuptake inhibitor work on the serotonin balance by inhibiting a transporter that selectively pumps serotonin back into the neurons [29].

CONCLUSION

In the present study, EEBA and EEAW were evaluated by using various experimental models. EEDC at doses of 200 mg/kg, p.o and 400 mg/kg, p.o showed significant increase in the motor activity of mice which elevate depressed mood by decreasing immobility time of mice in Forced Swim test and Tail Suspension test. From all the above findings, the present investigation suggests that the Ethanolic extract of *Abies webbiana and Berberis aristata* may possess antidepressant activity by inhibiting reuptake of Serotonin which acts through Serotonergic receptors (Gprotein coupled receptors) as mood elevator. Therefore lend pharmacological credence to the traditional use of this plant in the treatment of depression. However, an extensive Pharmacological study of this plant is required for complete understanding of the antidepressant activity of Ethanolic extract of *Abies webbiana and Berberis aristata***.** Further investigation should be carried out to isolate and identify the chemical constituent which is responsible for its antidepressant activity.

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Author's Contribution:

S.No	Authors	Contribution	% Contribution
1	Sucheta Gautam	Performed the experiments and wrote the paper	55
2	Neetu Sacchan	Designed the experiments	15
3.	Alankar Shrivastav	Paper preparation	15
4.	Dilip Kuamr Pal	Guidance	15