

Original Article

EVALUATION OF INVOLVEMENT OF NEURO-CHEMICAL MECHANISM IN VALERIANA WALLICHII INDUCED ANTIDEPRESSANT EFFECT IN MICE

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ABSTRACT

Objective: *Valeriana (V) wallichii* DC is found among the ground flora of Himalayan regions and used as herbal medicine for CNS disorders in Indian systems of medicine. In the study, aimed to investigation of involvement of neuro-chemical-systems in *V. wallichii* induced antidepressant effects in mice.

Methods: The antidepressant activity of aqueous alcoholic extracts of *V. wallichii* was measured by using Forced Swim Test and Tail Suspension Test in mice, whereas locomotor activity was observed by Actophotometer. Involvement of adrenergic, dopaminergic and serotonergic receptors in *V. wallichii* induced antidepressant effects in mice were also observed.

Results: Sub-acute administration of *V. wallichii* in mice showed significant ($P < 0.05$) increase in the antidepressant activity similar to the Imipramine, but did not show at lower doses in FST. Whereas, pretreatment of adrenergic receptor antagonist, dopaminergic receptor antagonist and serotonin synthesis inhibitor prevented *V. wallichii* induce anti-depressant effect in mice. Lower doses of hydroalcoholic extract of *V. wallichii* did not interfering the locomotor activity in mice during the sub-acute administration, but at a higher dose significantly ($P < 0.05$) decreases the locomotor activity.

Conclusion: Hence, it is concluded that the antidepressant effect of *V. wallichii* in mice may mediate via adrenergic, dopaminergic and serotonergic systems.

Keywords: Adrenergic, Antidepressant, Dopaminergic, Serotonergic Systems and *V. wallichii*

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INTRODUCTION

Valeriana (V) wallichii DC (synonym *V. jatamansi*; family Valerianaceae), commonly called the Indian valerian, is found among the ground flora of Himalayan regions (1500-3000 m) [1, 2]. It is used as a substitute of European *V. officinalis* and also as an ingredient of many herbal medicines in Indian systems of medicine [3]. *V. wallichii* is used in the treatment of epilepsy, skin disease, hysteria, insanity, cholera, shell shock, neurosis, snake poisoning, ulcers, asthma, jaundice etc [1, 4-6]. It is also used as a stimulant, diuretic, anti-spasmodic and antioxidant [4, 7, 8]. The roots/rhizomes of the several species of *V. wallichii* are used as a sleep aid, mild sedative, neuroprotective, anticonvulsant and anti-stress activities [9-13]. Subhan *et al.*, (2009) [14] have also been reported that the terpenoid content of *V. wallichii* extracts has antidepressant response. The major active principles of *V. wallichii* are valpotriates, dihydrovaltrate, isovalerianate, 6-methylalipigenin, hesperidins and sesquiterpenoids [5, 15-17]. Thus, aimed of the study was to evaluate involvement of neurochemical receptors in *V. wallichii* induced antidepressant effects.

MATERIALS AND METHODS

Biological material

The specimens of *V. wallichii* were collected from the region of Bin Block (29.6154 °N 80.3199 °E), district Pithoragarh, Uttarakhand (India). Specimens of the plant have been identified in house and matched with the plant samples, which has cultivated in herbal garden of the Institute at field station Pithoragarh. Rhizomes/root parts of *V. wallichii* were dried at 40 °C temperature in oven to prepare fine powder with the help of mechanical grinder. The freshly prepared dried powder of plant material was subjected to overnight in 20 % ethanolic solution over a period of 48 h for cold extraction. The extract was concentrated to dryness on a rotary evaporator at 40 °C to yield a brown dry mass. The final yield was recorded 13.5% (w/w). The samples were stored in an airtight container at (-) 4 °C for further use. The sample was suspended in 5 % Tween 80 solution just before administration in mice.

Chemicals

Chemicals Ethanol and Tween 80 were purchased from E. Merck and Imipramine hydrochloride, p-Chlorophenylalanine (p-CPA), Haloperidol and Prazosin were purchased from Sigma-Aldrich USA.

Animals

Swiss albino male mice (20-25 g body weight, age 10-12 w) were selected from the Experimental Animal House of the Institute. They were kept in the polycarbonate plastic cages under standard management conditions (Temperature: 22±3 °C, Relative Humidity-50-70 %, and 12 h/12 h dark/light cycle). The animals had *ad libitum* access to food and drinking water. All procedures in the present study were carried out under strict compliance of approved directions of CPCSEA (No.1306/c/09/CPCSEA/IAEC/06), Ministry of Environment and Forest, Government of India, New Delhi. The experiments were conducted according to protocols given below.

Acute toxicity study

Fine and uniform suspension of *V. wallichii* was prepared in 5% Tween 80 solution and administered at different doses viz 30, 125, 500 and 2000 mg/kg body weight orally to different groups of mice for acute toxicity. An acute toxicity study was carried out according to the OECD Guideline (423) [18] and animals were observed for 14 d for any toxic symptoms.

Antidepressant activity by Forced Swim Test (FST)

The Forced Swim Test (FST) is the most widely used as a pharmacological model for assessing antidepressant activity [19]. The FST was conducted with some modification. Mice were individually forced to swim in an acrylic plastic water pool (25 cm height x 12 cm diameter) filled 15 cm water, maintained at 28±1 °C temperature and the total immobility time of mice was measured for assessing anti-depressant effect. Similar method was used by Brocardo *et al.* (2008) [20] and Rosa *et al.* (2008) [21] and found that classical antidepressant drugs reduces the immobility time of mice. A mouse was considered to be immobile when it remained

floating or motionless more than 7 s in the water without struggling, making only minimum movement of its limb necessary to keep its head above the water. The absence of hind leg movement was recorded as immobility by stopwatch. The mice capable of swimming for 8 s or more in three successive trials were selected for the study. The selected animals were divided into 12 different groups (n=6) to evaluate the antidepressant activity in the FST and investigate the involvement of possible neurochemical mechanism of *V. wallichii* induced antidepressant effect in mice.

Vehicle (5% Tween 80, Oral) and Imipramine (15 mg/kg, IP) were administered in group 1 (control) and 2 (positive control) of mice respectively for 21 successive d. Four doses (20, 50, 125 and 300 mg/kg) of an aqueous alcoholic extract of *V. wallichii* were given to the animals' group no 3, 4, 5 and 6 by the oral route for 21 d. All animals were tested by Forced Swim Test (FST) 30 min post administration of doses for the evaluation of antidepressant activity. Before 24 h of experiment, mice were placed in the water pool for 15 min and removed to dry in a heated enclosure (32 °C) before returning to their home cages. During experiments, animals were placed in the water pool and total duration of immobility was measured for next 5 min.

To investigate the involvement of possible adrenergic neurochemical mechanism of *V. wallichii* induced antidepressant effect in mice, 45 min post administration of adrenergic antagonist Prazosin (1 mg/kg, IP); vehicle (5% Tween 80 solution, oral) and *V. wallichii* extract (50 mg/kg, oral) were orally administered in group no 7 and 8 respectively.

While, two separate groups (Group no 9 and 10) of mice pretreated with dopaminergic antagonist Haloperidol (0.2 mg/kg, IP); 45 min post treated by vehicle (5% Tween 80 solution, oral) and *V. wallichii* extract (50 mg/kg, oral) respectively to evaluate possible involvement of dopaminergic neurochemical in *V. wallichii* induced antidepressant effect in mice.

To assess the possible involvement of serotonergic neurochemical mechanism in *V. wallichii* induced antidepressant effects; two other separate groups (Group no 11 and 12) of mice were taken. After 45 min administration of serotonin synthesis inhibitor p-CPA (100 mg/kg, IP, 4 consecutive days, once in a d), vehicle (5% Tween 80 solution) and *V. wallichii* extract (50 mg/kg) were orally administered in group no 11 and 12, respectively. Control and positive control groups of mice were administered only vehicle (5% Tween 80 solution) and *V. wallichii* extract (50 mg/kg) respectively. Thirty min post treatment; all animals were tested in the forced swimming test for the evaluation of antidepressant activity.

Antidepressant activity by Tail Suspension Test (TST)

Tail Suspension Test (TST) is simple, rapid and reliable method for screening antidepressant effect in mice. It is considered for measuring mood level assay immobility time, which indicates changes in mood. TST induced immobility in animals is reduced by a large no of clinically active and atypical antidepressant effect [22]. The TST was performed in Swiss Albino Mice weighing 20-25 g according to the method [23] with slight modifications. Mice were suspended on the edge of the table 40 cm above the floor by adhesive tape placed approximately 2 cm from the tip of the tail. The total immobility time was observed for an overall period of 6 min as described by Steru *et al.* (1985) [23]. Mice were considered immobile only when they hung passively and completely motionless. Another 72 selected mice were divided into 12 different groups (n=6) to evaluate the antidepressant activity in TST. In groups 1st and 2nd, Vehicle (5% Tween 80, oral) and Imipramine (15 mg/kg, IP) were administered for 21 successive d respectively. While, in groups no 3rd, 4th, 5th and 6th *V. wallichii* extract (20% alcohol) at dose rate 20, 50, 125 and 300 mg/kg were administered by oral route for 21 successive d respectively. In groups no 7th and 8th, Vehicle (5% Tween 80) and 50 mg/kg dose of *V. wallichii* extract (20% alcohol) were orally administered 45 min post treatment of adrenergic antagonist Prazosin (1 mg/kg, IP) respectively. In group no 9th and 10th, Vehicle (5% Tween 80) and 50 mg/kg dose of *V. wallichii* extract (20% alcoholic) was orally administered 45 min post treatment of dopaminergic antagonist Haloperidol (0.2 mg/kg, IP)

respectively. In groups no 11th and 12th, Vehicle (5% Tween 80) and 50 mg/kg dose of *V. wallichii* extract (20% alcohol) were orally administered 45 min post treatment of serotonin synthesis inhibitor p-CPA (100 mg/kg, IP, 4 consecutive d, once in a d) respectively.

After 30 min of treatment, all animals were tested by TST for the evaluation of antidepressant activity and investigate the involvement of possible neurochemical mechanism in *V. wallichii* induced antidepressant effect in mice. During experiments, duration of immobility of mice was measured for next 5 min in TST.

Locomotor activity

To evaluate the possible effects of *V. wallichii* on locomotor activity, the mice were placed in digital photoactometer (M/S Orchid Scientifics, India). Locomotor activity was measured by the interceptions in the photobeams in the instrument. Locomotor activity of mice was recorded during the next 5 min of a total 7 min test at the end of the experiment on the last day. The locomotor activity was expressed in terms of total photobeam counts (X+Y scores), 5 min per animal [24]. For locomotor activity, 36 mice were randomly divided into six different groups (n=6) for the present study.

Vehicle (5% Tween 80) and Imipramine (15 mg/kg) were administered orally for 21 successive d in the control group (Group no 1) and positive control group (Group no 2) respectively. *V. wallichii* was administered at four doses of 20, 50, 125 and 300 mg/kg body weight, orally for 21 d in four different groups (Group no 3, 4, 5 and 6) respectively. Imipramine was taken a positive control group for comparing the locomotor activity of *V. wallichii*. Thirty min after the last administration, all animals were tested in the photoactometer for their locomotor activity.

Statistical analysis

The results of the study were expressed as mean±SD. Statistical analysis of the results were done by using one way ANOVA followed by post-hoc analysis of Dunnett's 't' test for all groups compared vs. control group and Student-Newman-Keuls Test for comparing all pairs of groups. *p values<0.05 significant value vs. control group and #p values<0.05 significant value vs. VW-50 (*V. wallichii*, 50 mg/kg) treated group.

RESULTS AND DISCUSSION

Acute toxicity study

In acute toxicity studies, no significant changes in food intake, body weight, general, physical and psychological behaviour of treated animals were observed as well as there were no signs of toxicity and mortality found in oral doses of ethanolic extract of *V. wallichii* up to 2 g/kg body weight. Hence it may be categorized as non-toxic and safe.

Effect of Imipramine and *V. wallichii* on immobility time of mice

Both FST and TST tests have been used to evaluate the anti-stress, mood elevator and anti-fatigue effects of various compounds [22, 25, 26]. Both tests are quite sensitive and specific to all major classes of antidepressant drugs [22, 27]. Above induces a state of behavioral condition similar to human depression [22, 28]. Fig. 1 and 2 depicts the effect of oral doses of ethanolic extract of *V. wallichii* (20, 50, 125 and 300 mg/kg) and positive control drug Imipramine (15 mg/kg) on immobility time of mice in FST and TST. Reduction in immobility time of animals during a test, indicates neuromuscular anti-fatigue (skeletal muscle performance activity) and antidepressant effects in animals.

Administration of Imipramine (15 mg/kg) in mice was significantly decreased the immobility time in both tests. Similarly to Imipramine, Oral administration of different dosage (50, 125 and 300 mg/kg body wt) of *V. wallichii* for 21 d in mice were showed significant (P<0.05) decrease in immobility time in both tests, but lowest doses (20 mg/kg) did not exhibit in FST as compared to control group. *V. wallichii* at the dosage 20, 50, 125 and 300 mg/kg in mice showed decreased immobility time a dose related graded manner in the FST and TST in mice, whereas the effect at the highest dose (300 mg/kg)

exhibit decreased immobility time but did not in a dose related graded manner in FST. Hence, *V. wallichii* at the dosage 20, 50, 125 and 300 mg/kg in mice showed dose dependent manner decrements the immobility time in both tests. Similarly, Subhan *et al.* (2010) [29] has reported that fluoxetine as well as methanolic and aqueous extracts of *V. wallichii* induced monophasic dose-related decrements in immobility times in FST and TST tests. While, the aqueous-ethanolic fraction induced a biphasic dose-response profile since it produced a graded effect up to 200 mg/kg but the highest dose (250 mg/kg) was inactive in the FST. The results of the present study

revealed that oral administration of ethanolic extract of *V. wallichii* (50, 125 and 300 mg/kg body weight) significantly ($P < 0.05$) enhances neuromuscular endurance and antidepressant effects in mice. Ahmad *et al.* (1998) [30] have reported that a gem-containing Unani formulation with *V. wallichii* has anti-stress activity against the physical stress of forced swimming. The present study is also well supported by Subhan *et al.* (2009) [14] who have reported that terpenoid content of *V. wallichii* extracts has antidepressant response. Hence, from the study it concluded that *V. wallichii* extracts have antidepressant effects in mice.

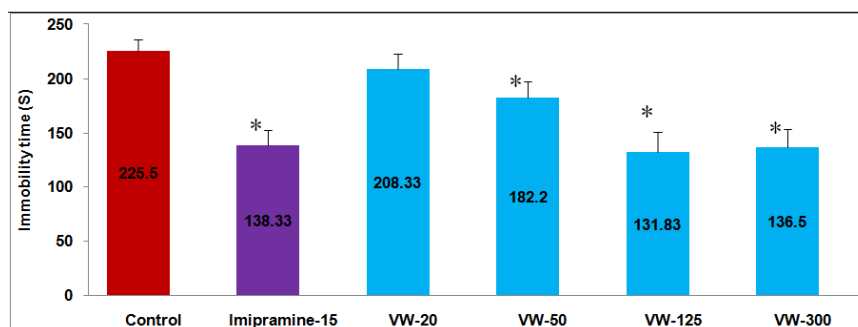


Fig. 1: Effect of *V. wallichii* and Imipramine on immobility time of mice in FST, [Values expressed in time (s) as mean \pm SD from six animals in each group at respective time-points. VW-20, VW-50, VW-125, and VW-300: *Valeriana wallichii* (20, 50, 125 and 300 mg/kg body wt.)]

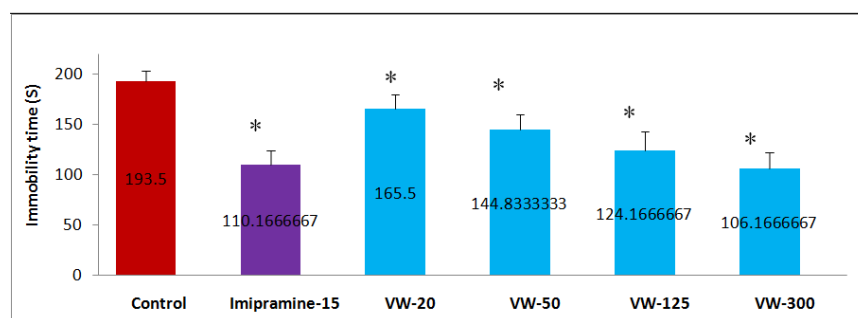


Fig. 2: Effect of *V. wallichii* and Imipramine on immobility time of mice in TST, [Values expressed in time (s) as mean \pm SD from six animals in each group at respective time-points. VW-20, VW-50, VW-125, and VW-300: *Valeriana wallichii* (20, 50, 125 and 300 mg/kg body wt.)]

Effect of prazosin on *V. wallichii* induced reduction in immobility time of mice

Etiology of depression is well known that abnormalities of noradrenergic, GABAergic, dopaminergic and serotonergic transmission are known to play a key role in the depression. Monoamine neurotransmitters like serotonin, dopamine, norepinephrine and

epinephrine in the central nerve system have had important roles in the regulation of mood, emotion, cognition, fatigue etc. In the study, we aimed to investigate the association of neurochemical mechanism with antidepressant effects of *V. wallichii* in mice. Fig. 3 and 4 depicts the effect of alpha-1 adrenergic antagonist prazosin (1 mg/kg, IP) alone and in combination with aqueous alcoholic extract of *V. wallichii* (50 mg/kg) on immobility time in mice during FST and TST tests.

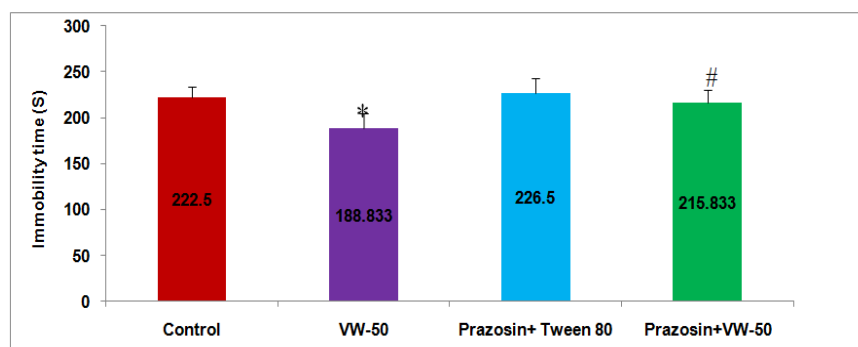


Fig. 3: Effect of prazosin on *V. wallichii* induced reduction in immobility time in FST, [Values expressed in time (s) as mean \pm SD from six animals in each group at respective time-points. VW-50: *Valeriana wallichii* (50 mg/kg body wt.)]

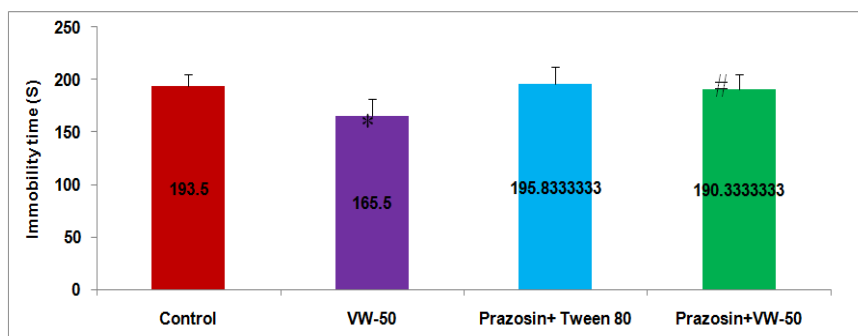


Fig. 4: Effect of prazosin on *V. wallichii* induced reduction in immobility time in TST, [Values expressed in time (s) as mean±SD from six animals in each group at respective time-points. VW-50: *Valeriana wallichii* (50 mg/kg body wt.)]

Prazosin is sympatholytic drug which acts as alpha-1 adrenergic neuron antagonist (inverse agonist) and it is used to treat high blood pressure, anxiety, stress disorder etc. Administration of aqueous alcoholic extract of *V. wallichii* (50 mg/kg) in mice were showed significant ($P < 0.05$) decrease in immobility time as compared to control group. Whereas, *V. wallichii* (50 mg/kg) induced reduction in immobility time in mice was significantly prevented by pretreatment of alpha-1 adrenergic antagonist Prazosin (1 mg/kg, IP) in FST. Similar to FST test, *V. wallichii* (50 mg/kg) induced reduction in immobility time in mice was significantly prevented by pretreatment of alpha-1 adrenergic antagonist Prazosin (1 mg/kg, IP) in TST test. While, alone treatment of Prazosin (1 mg/kg, IP) did not show significant change in immobility time in mice in both FST and TST tests. Similarly, Sah *et al.* (2011) [31] have reported that prolong the treatment of *V. wallichii* significantly increases the levels of norepinephrine in forebrain of a mouse. He has also reported that

the antidepressant effect of essential oil (20 mg/kg) of *V. wallichii* was prevented by pretreatment of mice with l-arginine (750 mg/kg IP) and sildenafil (5 mg/kg IP) [31]. Hence, the present study revealed that *V. wallichii* induced anti-fatigue and antidepressant effects in mice is significant ($P < 0.05$) blocked when pretreated with an alpha-1 adrenergic antagonist Prazosin in TST and FST tests. However, it reveals from the study that the adrenergic neuronal system may have involved in the *V. wallichii* induced anti-fatigue and antidepressant effect in mice.

Effect of haloperidol on *V. wallichii* induced reduction in immobility time of mice

Fig. 5 and 6 depicts the effect of dopaminergic antagonist Haloperidol (0.2 mg/kg, IP) alone and in combination with aqueous alcoholic extract of *V. wallichii* (50 mg/kg) on immobility time of mice in the FST and TST.

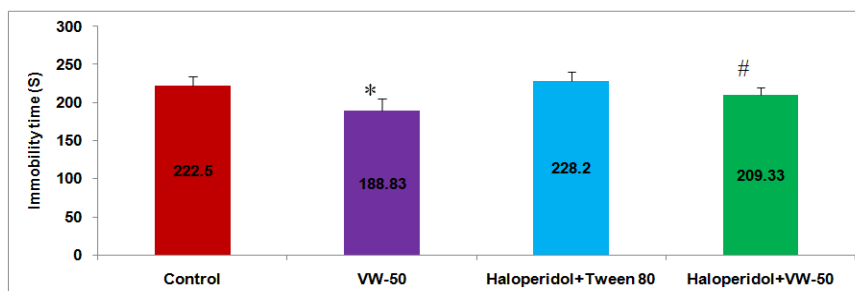


Fig. 5: Effect of haloperidol on *V. wallichii* induced reduction in immobility time in FST, [Values expressed in time (s) as mean±SD from six animals in each group at respective time-points. VW-50: *Valeriana wallichii* (50 mg/kg body wt.)]

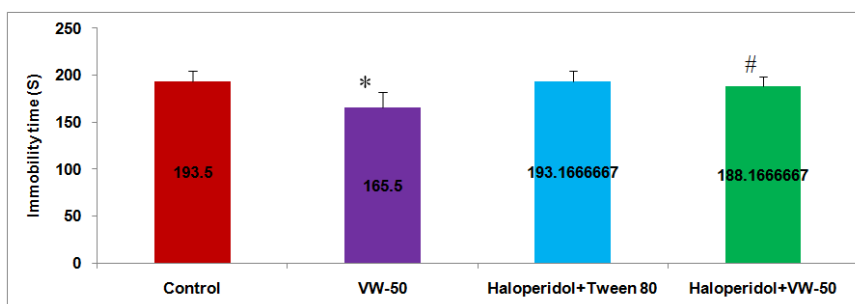


Fig. 6: Effect of haloperidol on *V. wallichii* induced reduction in immobility time in TST, [Values expressed in time (s) as mean±SD from six animals in each group at respective time-points. VW-50: *Valeriana wallichii* (50 mg/kg body wt.)]

Haloperidol is a typical antipsychotic drug which acts as non-selective D-2 dopamine receptor antagonist and it is used to treat schizophrenia, mania, psychosis etc. disorders. In FST and TST tests, *V. wallichii* (50 mg/kg) induced decrements in immobility time of mice was significantly prevented by pretreatment of D-2 dopamine non selective receptor antagonistic Haloperidol (0.2 mg/kg, IP).

Whereas, alone treatment of Haloperidol (0.2 mg/kg, IP) did not show significant change in immobility time in above both tests. Hence, the findings of the present study revealed that *V. wallichii* induced reduction in immobility time was significantly ($P < 0.05$) blocked by pretreatment of a D-2 dopamine receptor antagonistic Haloperidol. Our study is supported by Sah *et al.*, (2011) [31] who

have reported that prolong the treatment of *V. wallichii* significantly increase the levels of dopamine in forebrain of mouse. Hence, the present study revealed that *V. wallichii* induced anti-fatigue and antidepressant effects in mice are significant ($P < 0.05$) blocked when pretreated with a Haloperidol. However, in the present study concluded that the dopaminergic neuronal system may have interaction in *V. wallichii* induced anti-fatigue and antidepressant effects in mice.

Effect of p-CPA on *V. wallichii* induced reduction in immobility time of mice

Fig. 7 and 8 depicts the effect of p-CPA (100 mg/kg, IP, 4 consecutive days) alone and in combination with ethanolic extract of *V. wallichii* (50 mg/kg) on immobility time of mice in the FST and TST.

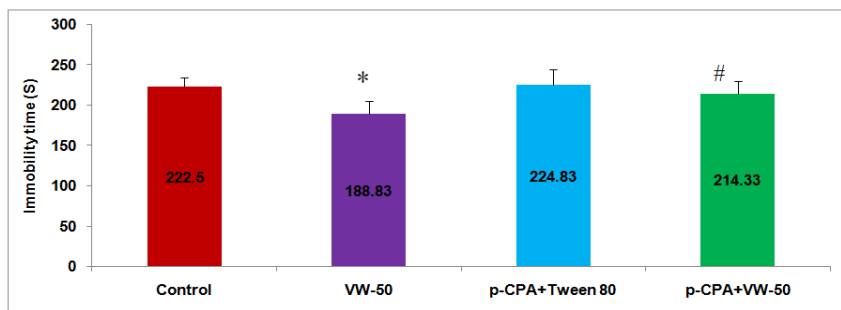


Fig. 7: Effect of p-CPA on *V. wallichii* induced reduction in immobility time in FST, [Values expressed in time (s) as mean \pm SD from six animals in each group at respective time-points. VW-50: *Valeriana wallichii* (50 mg/kg body wt.)]

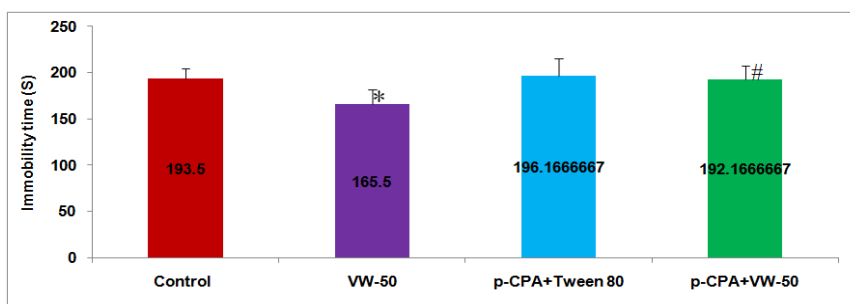


Fig. 8: Effect of p-CPA on *V. wallichii* induced reduction in immobility time in TST, [Values expressed in time (s) as mean \pm SD from six animals in each group at respective time-points. VW-50: *Valeriana wallichii* (50 mg/kg body wt.)]

p-CPA acts as irreversible and selective inhibitor of tryptophan hydroxylase enzymes, which is a rate limiting factor for biosynthesis of serotonin. *V. wallichii* (50 mg/kg) induced reduction in immobility time was significantly prevented by pretreatment of p-CPA (100 mg/kg, IP, 4 consecutive days) in FST. Similar to FST test, *V. wallichii* (50 mg/kg) induced reduction in immobility time was significantly blocked by pretreatment of p-CPA (100 mg/kg, IP, 4 consecutive d) in TST test also. While, alone treatment of p-CPA (100 mg/kg, IP) did not show significant change in immobility time in FST and TST tests. Hence, the findings of the present study revealed that the effect of *V. wallichii* on reduction in immobility time was significantly ($P < 0.05$) blocked by pretreatment of a serotonin synthesis inhibitor p-CPA in mice.

According to the results of the present study, *V. wallichii* has induced anti-fatigue and antidepressant effects in mice were prevented by

the pretreatment of alpha-1 adrenergic antagonist Prazosin, nonselective dopaminergic antagonist Haloperidol and serotonin synthesis inhibitor p-CPA in both FST and TST tests, which is indicative of involvement of adrenergic, dopaminergic and serotonergic systems in the enhancement of neuronal anti-fatigue and antidepressant effect of *V. wallichii* in mice. Hence, the results suggested that *V. wallichii* enhanced neuronal anti-fatigue and antidepressant effects through adrenergic, dopaminergic and serotonergic system.

Effect of *V. wallichii* and Imipramine on locomotor activity

Fig. 9 depicts the effect of ethanolic extract of *V. wallichii* (20, 50, 125 and 300 mg/kg) and positive control drug Imipramine (15 mg/kg) on locomotor activity of mice in photoactometer.

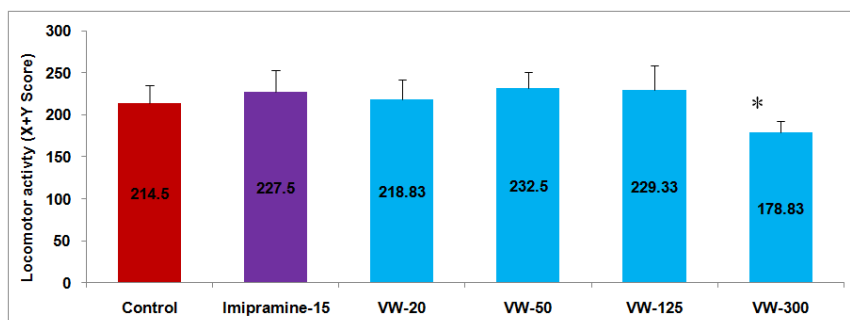


Fig. 9: Effect of *V. wallichii* and Imipramine on locomotor activity in actophotometer, [Values expressed in scores as mean \pm SD from six animals in each group at respective time-points. VW: *Valeriana wallichii*] Locomotor activity (X+Y scores) of each mouse were measured 30 min post injection time-period

In the experiment, locomotor activity of Imipramine treated animals was not significantly affected as compared to control animals. Similar to Imipramine, 20, 50 and 125 mg/kg dosage of *V. wallichii* did not alter the locomotor activity of mice significantly. Whereas, higher dose of *V. wallichii* (300 mg/kg body weight, orally) significantly ($P < 0.05$) decreased locomotor activity as compared to control and positive control (Imipramine) groups. Hence, this study reveals that Imipramine and *V. wallichii* has no effect on locomotor activity but higher dose of *V. wallichii* (300 mg/kg body wt.) has a significant effect in decreasing the locomotor activity, similar to Subhan et al. (2010) [29] they have exhibited that the highest doses of aqueous-ethanolic extract reduced locomotor activity. However, *V. wallichii* does not interfere the motor activity of mice at lower doses; while higher doses may produce other effects-like sedative or sleep enhancing in mice. One another researcher has also reported that the presence of sedative and sleep-enhancing compound flavanone glycoside 2S (-) hesperidin (HN) in *V. officinalis* and *V. wallichii* [9]. Thus, it may be concluded that the higher doses of *V. wallichii* may have sedative or sleep-enhancing-like effect in mice.

CONCLUSION

Oral administration of *V. wallichii* at dosage rate (50-300 mg/kg body weight) showed significant ($P < 0.05$) enhancement in neuronal anti-fatigue, mood elevator and antidepressant effects in mice without interfering their motor activity. While, pretreated animals with Prazosin alpha 1-adrenoreceptor antagonist, Haloperidol as nonselective D-2 dopaminergic antagonist and p-CPA as serotonin synthesis inhibitor did not show significant ($P < 0.05$) enhancement in *V. wallichii* induced anti-fatigue, mood modifying and antidepressant effects. Hence, it is concluded that the neuronal anti-fatigue, mood elevator, and antidepressant effects of *V. wallichii* may be mediated via adrenergic, dopaminergic and serotonergic systems. No significant difference was noticed in the locomotor activity of mice, which were administered with Imipramine (15 mg/kg) and *V. wallichii* (20, 50, and 125 mg/kg). While, *V. wallichii* at the higher dose (300 mg/kg) exhibited significant ($P < 0.05$) reduction in locomotor activity, which may be attributed to sedative or sleep enhancing-like effect in mice. Therefore, there is scope of more research on the effect of *V. wallichii* and involvement of specific parts of brain and receptor.

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AUTHORS CONTRIBUTIONS

Harsahay Meena: Study design, conduct experiments, data collection and analysis, and preparing manuscript. Col. V K Joshi: The manuscript was reviewed and edited. The experiment was conducted under the guidance and supervision of Dr Madhu Bala, Scientist 'G'.

CONFLICTS OF INTERESTS

No conflicts of interest

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