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Anticonvulsant Activity of Root Extracts of *Valeriana Jatamansii* Linn in Experimental Rats

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ABSTRACT- *Valeriana jatamansii* Linn (Valerianaceae) is a medicinal herb used in the traditional health care system of Uttarakhand (India). The present study reports the anticonvulsant activities in the aqueous and ethanolic extracts of the roots of *V. jatamansii* on the rats, induced both chemically and electrically. The models chosen for the activity were Maximal Electroshock (MES) and Pentylenetetrazole (PTZ) induced convulsions in rats. The test dose studied was 400 and 600 mg/kg body weight orally of the extracts. Acute toxicity studies show that the extracts were non-toxic up to the recommended dose 2000 mg/kg body weights orally as per OECD guideline no 423. In PTZ induced seizures, the onset of clonic convulsions was studied while in the MES model, reduction in the mean duration of the extensor phase was noted. Both the extracts showed anticonvulsant activities against MES and PTZ animal models.

Key Words: Anticonvulsant activity, MES, PTZ, Herbal drug.

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INTRODUCTION

Epilepsy has been a serious disorder that accounts for about 1% of the world's burden of diseases. Various synthetic antiepileptic drugs are available, but their effectiveness varies with the entire range of populations. They also possess drug interactions and side effects. The conventional antiepileptic drugs (AED) are effective in approximately 50% of the patients.[1] The side effects with these drugs commonly include: chronic toxicity, teratogenicity, adverse effects on cognition and behavior among others.[2]

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This may be one of the reasons that most of the scientific researches are inclined towards herbal medicines. Recently, medicinal plants are believed to be an important source of new chemical substances with potential therapeutic effects and have been used in the discovery and development of new drugs.[3] Different types of human epilepsies have been characterized based on the classification of the International League against epilepsy (ILAE). According to this classification, epilepsy has been divided into partial and generalized symptomatic and unclassified epilepsy. An imbalance between excitatory and inhibitory neurotransmitters is responsible for seizures. At the neuronal level, seizures often occur when glutaminergic excitatory neurotransmitters overrides gamma amino butyric mediated inhibition.[4] The most popular and widely used animal seizure models are traditional PTZ and MES tests. Prevention of seizures induced by PTZ in laboratory animals is the most commonly used preliminary screening

test for characterizing potential anticonvulsant drugs. The MES test is considered to be the predictor of likely therapeutic efficacy against generalized tonic clonic seizure. [5] Generally compounds with anticonvulsant activity in petit mal are effective in PTZ induced seizure model. The MES model is used to identify compounds which prevent seizure spread.[6] *V. jatamansi* Jones syn. *V. wallichii* popularly known as Indian Valerian (Mushkibala in Hindi/Kashmiri, Sugandhawal or Tagara in Sanskrit) belongs to family Valerianaceae.[7] Native to a wide expanse of central Asia, its range in the Himalayas extends from Kashmir all the way to Bhutan. It is commonly seen in the open, moist forests, in spring in the Himalayas at elevations between 4,000 and 10,000 feet, growing from rhizomes. Its deep coral colored flowers occur from March to May.

Diagnostic features

Valerian is Perennial herb with tufted stem and long fibrous roots, descending from aromatic rhizomes. Basal leaves, ovate heart shaped, long stalked toothed. Stem leaves are few, small and entire. Flowers are small, white or pink.

Uses: Root extract of *V. jatamansii* also exhibits larvicidal and adulticidal activity against different mosquito species. [8] The root of *V. jatamansii* is a source of effective antileishmanial agent. [9] Roots are acrid and bitter, which are used as carminative, laxative and are also used for curing blood diseases, burning sensation, cholera, skin disease, throat troubles, and ulcers. [10]

The aqueous and methanolic extracts of rhizomes possess anti-inflammatory activity. This could be attributed to the high amount of flavonoids and tannins in the plant. [11]

Valerian is most commonly used for sleep disorders, especially the inability to sleep (insomnia). Use of water extracts of *V. Jatamansii* Jones enhances the sedative and hypnotic effect in mice. [12]

MATERIAL AND METHODS

The roots were collected from field areas of Srinagar Garhwal, Uttarakhand, India. It was identified and authenticated by Dr Sarita Garg, NISCAIR, Delhi as *V. Jatamansii*. The voucher specimen was deposited at the herbarium.

Preparation of the extract

The collected roots were cleaned, shade dried, powdered and sieved. A weighed quantity of powder (500 gm) was subjected to successive hot percolation in soxhlet apparatus. Plant material was defatted by petroleum ether before extraction in ethanol. Ethanol was evaporated using a rotary evaporator under reduced pressure. The extract was concentrated under reduced pressure using rotary evaporator to obtain a dark green coloured residue.

Preliminary Phytochemical Studies

The phytochemical examination of ethanolic extracts was performed by the standard methods. [13]

Animals used

Wistar rats (150–250 gm) of either sex were obtained from the animal house of NKBR College Meerut, India. The animals were maintained in a well ventilated room with 12:12 hour light/dark cycle in polypropylene cages. All the animals were allowed for free access to water and fed with standard commercial pellete mice chaw. All the experimental procedures and protocols used were reviewed by an Institutional animal ethical committee (IAEC).

Acute toxicity studies

The acute toxicity studies of the extracts were determined in mice. The animals were fasted overnight prior to the experiment. The extracts were administered in doses 50, 300, 1000, 2000 mg/ kg b.w p.o to different groups of mice each containing 6 animals and mortality was observed after 24 hrs. The ethanolic extracts of leaves were devoid of mortality in animals at dose of 2000 mg/kg in mice p.o and hence LD_{50} was selected as cut value. Subsequent to administration of drug extracts, animals were observed closely for three hours, for any toxic manifestations, like increased motor activity, salvation, clonic convulsion, coma and death.

The animals were under further investigation up to a period of one week. It was observed that the test extracts were not mortal even at 2000mg/ kg dose. This was as per OECD guideline no 423. [14]

Maximal electro convulsive shock (MES)

Rats were divided into four groups of six animals each. The first group received vehicle control (1 ml/100 gm 2% CMC p.o), group II received the standard drug (Phenytoin, 25 mg/ kg ip), group III and IV received aqueous and ethanolic extracts of 400 and 600 mg/kg b.w, p.o respectively. The time for the extracts to reach its maximum effect was determined 60 min after oral administration. The response of the anticonvulsant effect was the abolition of hind limb extensor phase. [15]

Pentylene tetrazole (PTZ) induced convulsions

Rats were divided into four groups of six animals each. The first group received vehicle control (1 ml/100 gm 2% CMC p.o), group II received standard drug (Diazepam, 4 mg/ kg ip), group III and IV received aqueous and ethanolic extracts of 400 and 600 mg/kg bw, p.o. After 30 min of the dosage of standard and test extracts, PTZ (90 mg/kg b.w s.c) was given and response for the time of onset of seizures (tonic clonic convulsions) and their duration were recorded. [16,17]

STATISTICAL ANALYSIS

The data were expressed as mean±standard error mean (SEM). The significance of differences among groups was assessed using one way analysis of variance (ANOVA). The test followed by Dunnet's test and P value less than 0.05 were considered significant. [18]

RESULTS AND DISCUSSION

Phytochemical Screening

Ethanolic and aqueous extracts reveals the presence of Alkaloids.

Assessment of anticonvulsant activity by MES

In MES model, the duration of tonic extension of hind limb is used as an end point i.e. the protective action. The result of anticonvulsant effects of plant against MES induced convulsion is shown in Table 1. The data show that the extract reduced the hind limb extension in a dose dependent manner. Ethanolic extracts of *V. jatamansii* (EVJ) 400 and 600 mg/kg decreased the duration of hind limb extensor in 10.15±0.128 and 8.45±0.295 sec respectively, while the aqueous extracts of *V. jatamansii* (AVJ) showed the above said responses in 11±0.288 and 9.8±0.83 sec, which was significant as compared to control 15.9±0.217 sec. Fig 1 makes the picture clearer.

Table 1: Effect of extract of *Valeriana jatamansii* on MES induced seizures in rats

Treatment	Flexon	Extensor	Clonus	Stupor	Protection (%)
Control	11.51±0.246	15.95±0.2172	22.23±0.3703	31.76±0.4573	0
Standard	5.11±1.056**	3.28±1.665**	0.933±0.3252**	13.18±0.5134**	100
EVJ 400	8.467±0.167**	10.15±0.128**	13.93±0.214**	15.367±0.275**	80
EVJ 600	6.383±0.326**	8.45±0.295**	3.167±0.216**	14.05±0.203**	100
AVJ 400	9.617±0.201*	11±0.288**	20.2±0.191**	16.867±0.156**	80
AVJ 600	9±0.183**	9.883±0.83**	6.2±0.161**	16.57±0.233**	100

Values are expressed as mean±SEM of six observations. *P<0.05, **p<0.01. Comparison between Group I and Group II, Group III, Group IV. Statistical significant test for comparison was made by ANOVA, followed by Dunnet's test.
N/F= No. of animals protected/ no. of animals used.

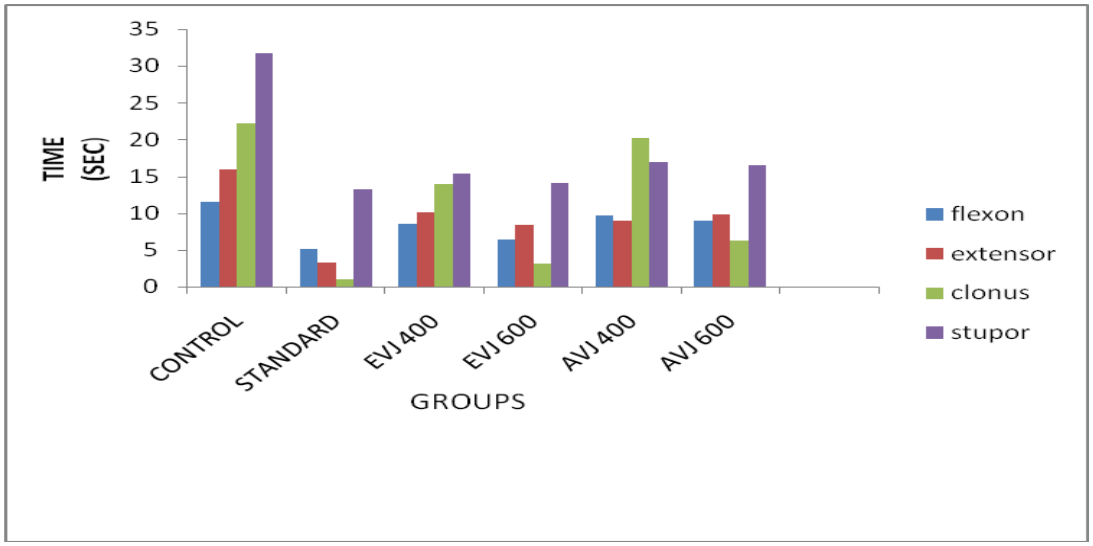

Fig. 1: Effect of extract of *Valeriana jatamansii* on MES induced seizures in rat

Assessment of anticonvulsant activity by PTZ

The anticonvulsant property of different extracts is assessed by its ability to delay the onset of myoclonic spasm and clonic convulsion. The results of anticonvulsant effects of plant against PTZ induced convulsion are shown in Table 2 and Fig 2. Ethanolic extracts of *V. jatamansii* at doses of 400 and 600 mg/kg p.o shows onset of convulsions after 402.17±2.84 sec and 512.5±4.51 sec respectively, while the aqueous extracts of *V. jatamansii* showed the above said responses in 204.5±1.89 and 220±3.15 sec, which was significant as compared to control 184.66±2.906.

Table 2: Effect of extract of *V. jatamansii* on PTZ induced seizures in rats

Treatment	Onset of convulsions (sec)	Duration of convulsions (sec)	%N/F
Vehicle control	184.66±2.906	80.66±2.06	33
Diazepam	691.66±5.998	11.16±0.872	100
EVJ 400	402.17±2.84 **	24.5±1.89*	80
EVJ 600	512.5±4.51**	16.17±1.3**	100
AVJ 400	204.5±1.89**	57.5±2.2**	80
AVJ 600	220±3.15**	41.17±2.39**	100

Values are expressed as mean ± SEM of six observations.
*p<0.05; ** p<0.01. Comparison between Group I *Vs* Group II, Group III &Group IV
Statistical significant test for comparison was done by ANOVA, followed by Dunnet's test.

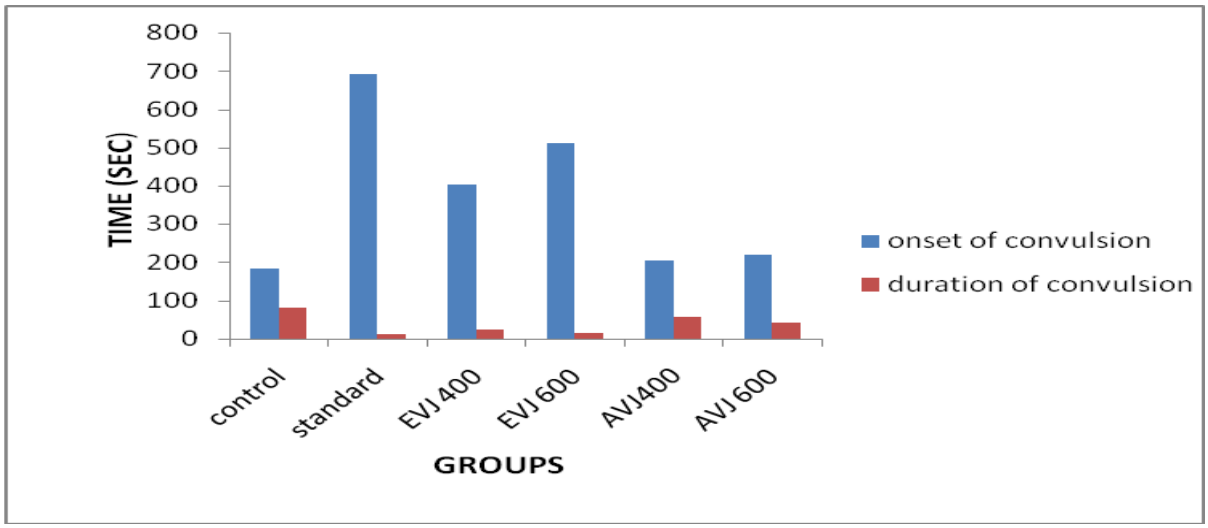

Fig. 2: Effect of extract of *V. jatamansii* on PTZ induced seizures in rats

CONCLUSIONS

In the present study anticonvulsant activity of ethanolic and aqueous root extracts of *V. jatamansii* were investigated by means of PTZ and MES models. The oral administration of the extract of *V. jatamansii* showed delayed onset of convulsions in PTZ model while reduction in tonic hind limb extension in MES model, indicating its potent anticonvulsant activity. Higher protection was observed with higher dose i.e. 600 mg/kg b.w orally. The percentage protection of ethanolic and aqueous extracts of *V. jatamansii* at a dose of 600 mg/kg orally was found to be 100% in both the chosen models. The extracts showed dose dependent protection in rats. The results demonstrated the broad and potent anticonvulsant activity in rats.

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