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Anticonvulsant Activity of Methanolic Extract of *Jasminum grandflorum* Linn in Experimental Animals

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ABSTRACT

Maximal electroshock seizures (MES) and pentylenetetarazole (PTZ) induced seizures in albino mice were used to study anticonvulsant activity of methanol flower extract of *Jasminum grandflorum* Linn. The methanolic flower extract of *Jasminum grandflorum* Linn was administered orally in graded doses (100, 200 and 400 mg/kg) in both the experimental models and the effects were compared with diphenylhydantoin in MES method and Sodium valproate in PTZ induced seizures method as standard control respectively. *Jasminum grandflorum* Linn (100, 200 and 400 mg/kg) show significant activity reduced the tonic extensor convulsion induced by maximum electroshock-induced convulsions. It significantly increased the onset of convulsion in seizure induced by pentylenetetrazole (80 mg/kg i.p.). The data obtained suggest that *Jasminum grandflorum* Linn have mild to moderate anticonvulsant property and may be due to involvement of GABA. Further experimentation is needed to explore the mechanism of this herb as anticonvulsant agent.

Keywords: anticonvulsant activity, methanol extract, *Jasminum grandflorum* Linn, pentylenetetrazole.

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INTRODUCTION

The word ‘epilepsy’ is derived from the ancient Greek word Epilēpsía means "to seize”. It is a neurological disorder characterized by recurrent unprovoked seizure. This is generally Due to excessive neuronal discharge in the brain. Epilepsy is a common chronic neurological disorder, characterized by recurrent unprovoked seizures [1]. Incidence of epilepsy in developed countries is approximately 50 per 100,000 while that of developing country is 100 per 100,000 [2]. It has been observed that the presently available antiepileptic drugs are unable to control seizures effectively in as many as 25% of the patients [3]. The conventional antiepileptic agents like phenytoin, carbamazeipine and sodium valporate carry with them several serious side effects notably neurotoxicity [4]. As majority of antiepileptic drugs are consumed life long, concomitant administration of other drugs predisposes to the risk of drug interaction. However, newer antiepileptics like gabapentin, vigabatrin, lamotrigine, etc are used supplemental to the conventional agents [5]. Thus, it is necessary to investigate for an antiepileptic agent that is highly efficacious as well as safe in items of drug related toxicity. The aim of treating an epileptic is not only to abolish the occurrence of seizures but also to lead a self sustained life.

Jasminum grandiflorum Linn (Oleaceae) is commonly known as Jasmine. It is a well known glabrous twining shrub widely grown in gardens throughout India. Its leaves are mostly ternate or pinnate; the flowers, usually white with a tubular, five- or eight cleft calyx, a cylindrical corolla-tube, with a spreading limb and two stamens enclosed in the corolla-tube. The flower is acrid, bitter with a sharp taste. It is useful in treating diseases of the mouth and teeth, especially for toothache [6]. The leaves of Jasminum grandiflorum is used in folk medicine for treating ulcerative stomatitis, toothache, skin diseases, ulcers, wounds, corms and also as gargles. The plant is reported to possess spasmolytic, anti-inflammatory, Anti-microbial [7], antioxidant, anti-ulcer, cyto-protective, chemo preventive, wound healing [8] and anti-acne activities [9]. Since there is no report on anticonvulsant activity of flowers of Jasminum grandiflorum Linn, so the present study was undertaken to investigate anticonvulsant activity of methanolic flower extract of Jasminum grandiflorum Linn.

MATERIALS AND METHODS

Plant material

The plant was identified, authenticated by an expert (botanist) and collected from the local area of Dehradun, Uttarakhand, India.

Preparation of the extract

The fresh flowers of Jasminum grandiflorum were shade dried and powdered. The powder was macerated for 24 hrs in methanol. Then it was subjected to percolation using methanol as solvent. The menstrum collected was again shade dried and viscous extract

suspended in 1% gum acacia for the present anticonvulsant study. The total yield of the extract was 9%.

Phytochemical screening

Qualitative tests for the presence of plant secondary metabolites such as Alkaloids, tannins, flavonoid, steroid, glycoside, terpenes, resins and salicylic acid were carried out on the flower powdered using standard procedures [10, 11].

Animals

Male mice 25 ± 2g, with three months of age, were used throughout this study. The animals were randomly housed in appropriated cages at 25 ± 2 ºC on a 12 h light/dark cycle (lights on 06:00-18:00) with free access to food and water. The protocol of study was approved by animal ethics committee of the department and the experiments were carried out as per the guidelines of CPCSEA.

Drugs

Test drug: Methanolic flower extract of Jasminum grandiflorum was used for the present study in volume 10ml/kg body weight, orally. The doses were selected by preliminary trials.

Sodium Valproate was dissolved in sterile saline and administered intraperitoneally in the dose of 50 mg/kg in volume of 10 ml/kg of body weight as a standard drug for potentiation study in PTZ induced seizures method.

Diphenylhydantoin: suspension (Parke Davis India) was given p.o in a volume of 10 ml/kg body weight in dose of 20 mg/kg used as standard drug to see the potentiation effect of test drug in MES method.

Pentylenetetrazole (Bochemzer-knoll, Ltd.) was prepared in distilled water just before use.

Acute oral Toxicity study

The acute oral toxicity study was carried out as per the guidelines set by Organization for Economic Co-operation and Development (OECD), registered under (CPCSEA), ministry of Social Justice and Empowerment, Government of India. Different doses of extract (80, 100, 120, 240, 480 and 960 mg/kg) were administered orally to groups of male mice (n = 6) and the groups were observed for 48 hr and at the end of this period mortality was recorded for each group.

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INDUCTION OF SEIZURES

Pentylenetetrazole (PTZ)-induced convulsion

In the present study (PTZ), five groups were employed and each group comprised six animals. PTZ (80 mg/kg i.p.) was used to induce clonic convulsions. Animals were divided into five groups (n = 6), control group received vehicle (10 ml/kg) and standard group was treated with Sodium Valproate (50 mg/kg, i.p.) 30 min prior to the injection of PTZ (80 mg/kg, i.p.). The remaining groups were treated with 100, 200 and 400 mg/kg of methanol extract orally. After 30 min of drug administration, the mice were treated with PTZ at a dose of 80 mg/kg (i.p.). Immediately after the injection of the convulsant, mice were individually placed in plastic boxes and observed for the time onset of clonic seizures, percent clonic seizures and deaths. The incidence of deaths was noted until 48 h after the injection of PTZ.

Group-I (pentylenetetrazole - treated control group), mice were administered with pentylenetetrazole (80 mg/kg) via intraperitoneal route.

Group-II (vehicle + PTZ-treated control group), Mice were administered with vehicle 10 ml/kg, intraperitoneal 30 min prior to the injection of Pentylenetetrazole (80 mg/kg, intraperitoneal).

Group-III (sodium valproate + PTZ-treated standard control group), mice were administered with sodium valproate 50 mg/kg, intraperitoneal 30 min prior to the injection of pentylenetetrazole.

Group-IV (low-dose extract + pentylenetetrazole treated group), mice were administered with extract 100 mg/kg, oral 60 min prior to the injection of pentylenetetrazole.

Group-V (medium-dose extract + pentylenetetrazole treated group), mice were administered with extract 200 mg/kg, oral 60 min prior to the injection of pentylenetetrazole.

Group-VI (high-dose extract + pentylenetetrazole treated group), mice were administered with extract 400 mg/kg, oral 60 min prior to the injection of pentylenetetrazole.

Maximal electroshock (MES) test

Maximal electroshock test (MES) that induces reproducible tonic convulsion characterized by tonic hind limb extension (THE) was performed (Oliveira et al., 2001). In this experiment, electroconvulsive shock (150 V, 0.2 s) was delivered through electrodes (ECT UNIT 7801- Ugo Basile) to induce tonic hind limb extension (THE). In the present study one group was employed and group comprised six animals. The group is underwent to shock and then treated with the vehicle further treatment with the extract and last with the Diphenylhydantoin.

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Statistical analysis:

The data obtained in experimental models were evaluated by one way analysis of variance (ANOVA) followed by Dunnett's test. Differences between means were considered to be statistically significant when $p < 0.05$. Data obtained from the study were statistically analyzed using one-way ANOVA. A value of $P < 0.05$ was considered to be statistically significant.

RESULTS

Preliminary Phytochemical studies

The preliminary Phytochemical screening of methanolic extract shows (Table 1) the presence of alkaloids, tannins, flavonoid, steroid, glycoside, terpenes, resins and salicylic acid were carried out on the flower powdered using standard procedures.

Table 1: Chemical constituents present in methanolic extract of Jasminum grandiflorum Linn flowers

Test	Methanolic extract
Carbohydrates	-
Glycosides	+
Alkaloids	+
Phytosterols	-
Flavonoids	+
Tannin	+
Saponins	-
Terpenes	+
Salicylic acid	+
Resins	+
Steroids	+

PTZ (Pentylenetetrazole) induced convulsions

The results of the anticonvulsant activity of methanolic extract of Jasminum grandiflorum on PTZ induced convulsions are shown in Table 2. The methanolic flower extract (100, 200 and 400mg/kg) of Jasminum grandiflorum Linn exhibited a significant anticonvulsant effect by increasing the latency, onset of clonic convulsion and decreases onset of tonic seizures.

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Table 2: Effect of methanolic extract of Jasminum grandiflorum Linn flowers on MES induced seizures in mice.

Treatment	Time duration (sec)			
	Tonic flexion (mean ±SEM)	Tonic extension (mean ±SEM)	Clonic stupor (mean ±SEM)	Mortality
Control	46±2.56	69±5.56	200±5.60	100
Diazepam 20mg/kg	54±7.34*	96±21.0*	381±43.8*	00
Extract 100mg/kg	42.3±6.28*	62±5.14**	218±44.6*	23.6
Extract 200mg/kg	61.2±5.17*	202±8.59**	359±46.5*	24.1
Extract 400mg/kg	66.4±5.06	221±6.90**	379±45.8*	24.00

*P < 0.05, **P< 0.001 compared with control, n = 6.

Effect on MES induced convulsions

The methanolic extract exhibited a dose dependent significant reduction in various phases of epileptic seizures on comparison with the reference standard Diphenylhydantoin 20mg/kg i.p. There was also a significant reduction in the time required for the righting reflux (recovery) in the extract treated groups (Table 3).

Table 3: Effect of methanolic extract of Jasminum grandiflorum Linn flowers on pentylenetetrazol induced seizures in mice.

Treatment	Dose mg/kg	Onset of clonic convulsions in sec (mean ±SEM)	Incidence of convulsions (%)
Control	Vehicle	148±25.18	100
Sodium Valproate	50	A	0
Methanol Extract	100	658.7±78.2*	66.2
Methanol Extract	200	793.7±25.7*	17.5
Methanol Extract	400	A	0

n = 6 in each group, *P< 0.05 when compared to the vehicle treated group. A = Absence of convulsions.

DISCUSSION

The administration of pentylenetetrazole in the present study induced Straub's tail phenomenon, followed by jerky movements of the whole body, and convulsions in pentylenetetrazole-treated control group animals along with an increase in the percentage mortality of mice. Administration of sodium valproate markedly attenuated pentylenetetrazole-induced seizure activity in mice observed in terms of onset time of Straub's tail, jerky movements of the whole body. Sodium valproate has been shown to be an effective agent in the symptoms of generalized epilepsy via blockade of voltage dependent t-type calcium channels. Thus, our results are in consonance with previous reports and sodium valproate served as a standard control in the present study. The methanolic extract of Jasminum grandiflorum inhibited in a significant manner, pentylenetetrazole-induced seizures as assessed in terms of time of appearance of Straub's tail and onset of jerky movements of whole body and convulsions. The activity of the plant may be due to the activity of present alkaloid as GABA

Potentiating effect. In conclusion, agents that have the ability of attenuating the appearance of seizures might also have anticonvulsant ability. The Jasminum grandiflorum showed a possible anticonvulsant effect in two animal models of epilepsy. It also suggests that GABAergic and serotoninergic systems may be involved. It can be concluded from the study that the anticonvulsant effects of methanolic flower extract of Jasminum grandiflorum may be via nonspecific mechanisms. However, extensive studies are needed to evaluate the precise mechanism, active principles, and remedy for convulsive disorders.

CONCLUSION

The plant Jasminum grandiflorum Linn was traditionally has large number of medicinal uses. In the present investigation, Phytochemical screening of the flower methanolic extract of Jasminum grandiflorum Linn revealed the presences of alkaloids, tannins, flavonoid, steroid, glycoside, terpenes, resins and salicylic acid. The anticonvulsant activity of the plant may be due to the activity of present alkaloid as GABA Potentiating effect.

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