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## ANTICONVULSANT AND SEDATIVE EFFECTS OF LEAF EXTRACT OF *SOLANUM PUBESCENS*

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**ABSTRACT:** The herbal preparation of the leaves of *Solanum pubescens* Pers (Solanaceae) is used in traditional medicine for the treatment of Epilepsy and febrile convulsions. A pilot study has confirmed the potency of the leaf of *Solanum pubescens* in the control of seizure in mice. The current study was aimed to identify the active phytochemical responsible for the activity. Results indicated that methanolic extract of *Solanum pubescens* at 300 mg/kg exhibited a significant  $P < 0.05$  delay in the latency of myoclonic spasms and tonic-clonic phase of seizure induced by PTZ, and also decreased the latency and increased the duration of phenobarbitone induced sleeping time. While the phytochemical studies showed the presence of alkaloids, resins, glycosides, carbohydrates, reducing sugar, fats and oils, flavonoids and terpenoids. The results suggested that the extract possessed anticonvulsant activity and central depressant effects which may be attributable to the flavonoids.

**INTRODUCTION:** The use of herbal preparations in the management of various forms of epilepsies is very common in many parts of the world. Epilepsy affects more than 50 million persons world wide<sup>1</sup>. Seizure is a characteristic feature in epilepsy and is associated with disordered and rhythmic high frequency discharge of impulses by a group of neurons in the brain and status epilepticus is characterized by repeated episodes of epilepsy without the patient having recovered from the previous attack<sup>2</sup>. There are many classes of anticonvulsants that are of clinical usefulness with good prognosis for controlling seizures in most patients<sup>3</sup>.

Despite this many patients have seizures that are not adequately managed by the established antiepileptic drugs<sup>4</sup>. Moreover, the high incidence of detestable adverse effects from the use of antiepileptic drugs is also a source of wide spread concern in patients who use them chronically. These and the treatment cost have made traditional herbs and herbalists very useful and indispensable in the struggle for seizure management and future antiepileptic drug development.

There is therefore the need for research into medicinal plants with possible anticonvulsant effects, based on folklore use.

## MATERIALS AND METHODS:

**Plant Introduction:** *Solanum pubescens* belong to the family solanaceae commonly called as pajarito and commonly used in India by the tribal people for the treatment of liver disorders, diarrhoeal diseases and cancer disorders<sup>5</sup>.



**Animals:** Adult albino mice (18-39g) bred in the laboratory Animal facility of the Department of Pharmacology & Toxicology, T.R.R.C.P were used in the studies. The animals were maintained under standard laboratory conditions & had free access to standard pellets and water. On transfer to the work area, animals were allowed two weeks of acclimatization before the commencement of the experiments. All animal experiments were conducted in compliance with OECD guidelines for care and use of laboratory animals and approval of the CPCSEA on the use of laboratory animals.

**Plant Material:** Fresh leaves of *Solanum pubescens* were collected from S.V University Tirupathi in the month of June 2010 and authenticated by Dr. Madhava Chetty Botanist S.V University Tirupathi and a copy of herbarium is placed in the T.R.R.C.P. The fresh leaves were shade dried, pulverized into coarse powder. The dried powdered 2.5kg was extracted with methanol using soxhlet extractor. This was evaporated using rotary evaporator at reduced pressure to obtain a yield of 35g.

**Phytochemical test:** Phytochemical tests on the extract and fractions were performed using standard procedures<sup>6</sup>.

**Pentylentetrazole (PTZ)-induced convulsion test:** Albino mice were randomly divided into five groups (n= 5/group). Group 1 (control) received the vehicle (10 ml/kg, 40% Tween 80 + DMSO (1:1) solution, p.o). Group II received the methanolic extract of *Solanum pubescens* (300 mg/kg, p.o), while group III received diazepam (Hoffman-la Roche, 2 mg/kg, i.p). Thirty minutes later, pentylentetrazole (PTZ) (sigma, 60 mg/kg, s.c) was administered to all the animals. The animals were observed for the time of onset of myoclonic spasms and tonic – clonic phases of seizures. Percentage protection of mice was also recorded in each group. Animals devoid of seizures/convulsion without subsequent death during the 60 minutes observation period were considered protected<sup>7,8,9</sup>.

**Phenobarbitone induced sleeping time:** Adult albino mice were randomly divided into 5 groups (n= 5/group). Control (group 1) animals were treated with the vehicle (10 ml/kg, 40% Tween 80 + DMSO (1:1) solution, p.o). Mice in the group II were treated with the methanolic extract of *Solanum pubescens*

(300 mg/kg, p.o.), while group III received diazepam (Hoffman-la Roche, 2 mg/kg, i.p). These treatments were carried out 30 minutes before the administration of phenobarbitone sodium (Renaudin France, 35 mg/kg, i.p)<sup>10</sup> to all the groups. Each mouse was observed for the onset (latency) of sleep and the duration of sleep using the loss of righting reflexes as the criterion for onset of sleep and the duration of sleep or hypnosis as the time the animal presented a loss of postural reflexes.

**Statistical analysis:** Data analyzed using One Way Analysis of Variance (ANOVA, SPSS Version 16) and expressed as mean  $\pm$  SEM and comparisons was done using Dunnet's test as post-hoc. Difference between means were regarded significant at  $P < 0.05$ .

## RESULTS:

**Phytochemical constituents:** The phytochemical studies revealed the presence of carbohydrates, alkaloids, glycosides, reducing sugar, resins, flavonoids and terpenoids and the absence of tannins, saponins and acidic compounds.

### Preliminary Phytochemical screening of *Solanum pubescens* leaves

S. No.	Chemicalconstituent	Methanolicextract
1	Alkaloids	Present
2	Carbohydrates	Present
3	Glycosides	Present
4	Saponins	Present
5	Tanins	Present
6	Flavonoids	Present
7	Proteins and aminoacids	Absent

**Pentylentetrazole-induced convulsion test:** The methanolic extract of *Solanum pubescens* significantly ( $P < 0.05$ ) prolonged the onset of both myoclonic spasms (MS) and tonic-clonic phases of seizures (TCS) induced by pentylentetrazole. At 300 mg/kg, methanolic extract of *Solanum pubescens* offered 60 percent protection against seizures induced death.

**Phenobarbitone induced sleeping time:** Results indicated that methanolic extract of *Solanum pubescens* significantly ( $P < 0.05$ ) reduced the latency for the onset of sleep and potentiated the duration of sleep at all the doses tested when compared with the control.

**TABLE 1: EFFECTS OF EXTRACT AND FRACTIONS ON PENTYLENETETRAZOLE-INDUCED CONVULSION**

Treatment	Dose (mg/kg)	Onset of seizures (min.)		Percentage Protection
		Myoclonic spasms	Tonic – Clonic Phase	
Control	-	2.48 ± 0.27	6.74 ± 1.52	0 %
Diazepam	2	60.00 ± 0.00**	60.00 ± 0.00**	100 %
MESP	300	5.90 ± 1.00**	22.40 ± 2.11	60 %

Values are expressed as Mean ± SEM: Significance \*\*P<0.01, \*P<0.05 using ANOVA, post hoc Dunnet's test compared to control, n=5.

**TABLE 2: EFFECTS OF EXTRACT AND FRACTIONS ON PHENOBARBITONE-INDUCED SLEEP TIME**

Treatment	Dose (mg/kg)	Sleep Time (min)	
		Latency	Duration
Control	-	24.30±5.77	184 ± 11.54
MESP	300	19.67±1.46*	211.06±2.42**
Diazepam	2	18.45 ± 3.46	184 ± 8.66**

Values are expressed as Mean ± SEM: Significance \*P<0.05, \*\*P<0.01, ANOVA, post hoc Dunnet's test compared to control.

**DISCUSSION:** The results obtained in the study showed that the extract and fraction of *Solanum pubescens* possesses anticonvulsant and sedative activity. The extract significantly prolonged the onset of both myoclonic spasms as well as tonic-clonic phases of seizure in mice. The effect of pentylenetetrazole induced seizures is an indication of possible effectiveness of the methanolic extract of *Solanum pubescens* against absence seizures as drugs that inhibit pentylenetetrazole-induced convulsions are generally effective against absence seizures<sup>11,12</sup>.

The reduction in the latency time and prolongation of the duration of sleep is suggesting of the central depressant effects of the extract and fractions. Decrease in latency of onset and prolongation of duration of sleep by the extract and fractions is an indication of central inhibition through the stimulation of the CNS inhibitory pathways. Hence the anticonvulsant and sedative activity of the methanolic extract of *Solanum pubescens* tend to suggest a central inhibitory activity as their possible mechanism of action.

Anticonvulsant drugs such as barbiturates and benzodiazepines exhibit their effects through enhancement of gamma amino butyric acid (GABA) receptors chloride channel complex which is a GABA/ Benzodiazepine mediated inhibition pathway in the central nervous system (CNS)<sup>13</sup>.

Pentylenetetrazole induces convulsion by inhibiting the GABA<sub>A</sub> receptor-chloride channel complex<sup>14, 15</sup> and therefore agents that abolishes or tend to reduce the effects of pentylenetetrazole possibly acts through the stimulation of such receptors.

Benzodiazepines as well as certain anticonvulsants exhibit pharmacological actions through the reduction of sedation and induction of sleep by antagonizing the GABA receptor/ chloride channel complex<sup>16</sup>. The phytochemical analysis showed the presence of flavonoids in methanolic extract of *Solanum pubescens*. The Phytochemical in the methanolic extract of *Solanum pubescens* was comparable with those present in the methanol extract which has been documented<sup>17</sup>.

Flavonoids have been implicated in various pharmacological actions including anticonvulsant and CNS depressant activity<sup>18</sup>. Since flavonoids are the only Phytochemical that is found present in the active extract and fractions. This is more so since flavonoids have been accorded central inhibitory and neuromodulatory effects<sup>19</sup>.

In conclusion, the results indicated that the leaf of *Solanum pubescens* exhibited significant anticonvulsant and sedative effects that support the evidence for its folkloric use, while these neuropharmacological effects might possibly be due to the presence of flavonoids. Meanwhile further studies on the purification and structural elucidation of the active Phytochemical is ongoing.

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