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# ANTICONVULSANT ACTIVITY OF ETHANOLIC EXTRACT OF *SOLANUM MELONGENA LINN.* ROOTS

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## ABSTRACT

In the present study, *Solanum melongena* Linn. (Brinjal; Solanaceae), was evaluated for its antiepileptic activity against experimental seizures. The roots ethanolic extract of *Solanum melongena* protected mice against tonic convulsion induced by maximal electroshock, Pentylenetetrazole and Picrotoxin. It was found that ethanolic extract up to a dose of 300 mg/kg p.o. decreased the duration of tonic extensor phase and delayed the onset of time of jerk against maximal electroshock induced seizure and pentylenetetrazole induced seizure. In Picrotoxin induced seizure, the extract at a dose of 200 mg/kg significantly increased the onset of clonic- tonic convulsion. These findings suggest that extract of the roots of *Solanum melongena* posses anticonvulsant effect and reduce mortality. The further studies to determine the mechanism(s) and compound(s) involved in the anticonvulsant activity.

**INTRODUCTION:** *Solanum melongena* Linn., a culinary vegetable has been used in the Indian system of medicine. Various parts are useful in the treatment of inflammatory conditions, cardiac-debility, neuralgia, and ulcer in nose, cholera, antipyretic and analgesic effect of leaves in Rodents, bronchitis and asthma [1].

The plant has been studied extensively for its important chemical constituents, steroidal glycosides - melongoside A, B, E, F, G and H isolated from seed. Melongoside B identified as trillin [2]. The two steroidal saponins - melongoside L and melongoside M, and the three new saponins melongoside N, O and P, have been isolated from seeds [3]. Four new and other 4α-methylsterols in the seeds[4] have been reported. Catechol oxidase have been isolated and characterized from *Solanum melongena* [5]. Quercetin 3-0-rhamnoside and kaempferol-3-0-rutinoside were isolated from leaves. However, only few considerable pharmacological activities of this plant been studied including anti-inflammatory activity [6] and Juvenomimetic activity [7]. Dried fruit of *Solanum melongena* significantly improve signs and symptoms of asthma [8]. It has also proved to be beneficial in visual functions [9]. Flavonoids and nasunin, an anthocyanin in egg plant have been found to have antioxidant activity [10, 11]. It has also shown Hypolipidemic effect [12]. CNS, anticonvulsant and analgesic effects of an alkaloidal fraction (SM-2) from the leaves have also been studied [13].

However, there is no present work reported on the roots of *Solanum melongena*. So there is a need to explore the pharmacological properties of other part of plant.

**MATERIALS AND METHODS:**

**Plant Material:** The roots of *Solanum melongena* were obtained from a local farmer from Baruasagar, near Jhansi (U.P.). *Solanum melongena* was authenticated by Dr. Tariq Husain; scientist & Head, Biodiversity & Angiosperm Taxonomy, National Botanical Research Institute, Lucknow, India.

**Extract preparation:** The roots of *Solanum melongena* were dried in air, crushed to coarse powder and extracted with ethanol (95%) in Soxhlet apparatus and the extract was dried under vacuum. Stored at room temp and protected from direct sunlight.

**Drugs and Chemicals:** Pentylenetetrazole (PTZ) and Picrotoxin (PIC) were purchased from Himedia (Bombay). Diazepam (Torrent pharmaceuticals Ltd., Indrad) and Phenytoin (Anglo-french drugs & industries Ltd., Banglore) were obtained as gift sample. Phenytoin, Diazepam and PTZ were dissolved in normal saline (0.9% NaCl solution) were administered intraperitoneally (i.p.) in volume of 10 ml/kg. The extracts were suspended in distilled water and subjected for anticonvulsant activity using Pentylenetetrazole, Picrotoxin and MES models respectively. The extracts were administered orally (p. o.) in the volume of 10 ml/kg of mice body weight.

**Animals:** Wistar Albino mice of the either sex weighing 25-30 gm. were used throughout the studies. They were feed standard animal pellets (Amrut feeds, New Delhi) and given tap. The temperature of animal house (App. No.:-716/02/a/CPCSEA) was maintained at 22 ± $2^0$C and the animals were housed in standard cages with 12hrs light /dark cycle. The ethical guidelines for the investigation of experimental seizures in conscious animals were followed in all tests. All efforts were made to minimize animal suffering and to reduce the number of animal used [14].

**MES-induced seizure:** Electroconvulso-meter shock, inducing Hind Limb Tonic Extension (HLTE) in 99% of the animals [15], was previously determined. The electrical stimulus (50mA; 50 Hz; 1s duration) was applied through ear clip electrode

using electroconvulsometer (Biocraft Scientific Systems Pvt. Ltd. Agra, India) for six groups of 6 mice each. In which one control were pre-treated with dist. water (10 ml/kg p.o.), one standard with Phenytoin as positive control (25 mg/kg, i.p.) and four groups pre-treated with 100, 200, 300, and 400 mg/kg, p.o. of ethanolic extract. The time of peak effect of Phenytoin as 30 min after administration was previously established [16]. The time for the extract to reach its maximum effect was determined as 60 min after oral administration. The incidence and duration of extensor tonus was noted. A complete abolition of hind limb tonic extension was considered as 100% protection [17].

**PTZ - induced seizure:** The animals were divided into six groups (n= 6). In which one control pre-treated with dist. water (10 ml/kg p.o.), one standard with PTZ as positive control (85 mg/kg i.p.) and four groups pre-treated with 100, 200, 300 and 400 mg/kg p.o. of ethanolic extract. They were all treated with PTZ at a dose of 85 mg/kg (minimal dose needed to induce convulsion) was injected i.p. to induce clonic-tonic convulsion in animals [18] immediately after the injection of PTZ. Mice were observed for 30 min to detect the onset of generalized clonic-tonic seizures and further upto 2h to detect any mortality if any [19]. Animals devoid of seizures were considered protected [20].

**Picrotoxin-induced seizures:** The animals were divided into five groups (n= 4). In which one control pre-treated with dist. water (10 ml/kg as a control), one standard with 25 mg/kg phenytoin dose was used as positive control and three groups pre-treated with 100, 200 and 300 mg/kg, p.o. of ethanolic extract. The clonic seizures were induced in male mice by the i.p. injection of 7.5 mg/kg picrotoxin (PIC) [21]. A protective effect of the extract against PIC-induced clonic seizures was recorded.

**Statistical analysis:** Results were expressed as Mean±SEM. and the data obtained were analyzed using one-way analysis of variance (ANOVA) followed by Dunnett's t-test. The level of significance was set at $P<0.05$.

## RESULTS:

### Anticonvulsant activity:

**MES-induced seizures**: The ethanolic extracts of *Solanum melongena* at a dose of 300 mg/kg exert anticonvulsant effect against MES-induced seizures. *S. melongena* significantly ($P<0.01$) decreased the duration of tonic extensor phase in MES-induced seizures. The extract showed a maximum inhibition (100% mortality) against MES-induced seizures. The observations are shown in **Table 1**.

**TABLE 1: EFFECT OF *SOLANUM MELONGENA* EXTRACT ON MES INDUCED SEIZURES IN MICE**

| Treatment | Duration of tonic extensor (sec) | Mortality D/N | % Mortality |
|---|---|---|---|
| Distilled water (10ml/kg, p.o.) | 17.25 ± 1.864 | 5/6 | 83.3 % |
| Extract (100mg/kg, p.o.) | 16.06 ± 1.607 | 2/6 | 33.3 % |
| Extract (200mg/kg, p.o.) | 12.31 ± 1.075 | 2/6 | 33.3 % |
| Extract (300mg/kg, p.o.) | 8.25 ±1.836** | 0/6 | 0 % |
| Extract (400mg/kg, p.o.) | 11.64 ± 2.523 | 4/6 | 66 .6 % |
| Phenytoin (25mg/kg, i.p.) | 3.495 ± 1.784 | 0/6 | 0 % |

Dose dependent effect of graded dose (100, 200, 300 and 400 mg/kg, p. o.) of extract on MES-induced seizures in mice.
Evaluation was made by electro- shock using ear electrode after 1hr administration of extract.
Values are expressed as mean ± S.E.M.
**P< 0.01 compared with distilled water treated group

**PTZ -induced seizures:** PTZ (85mg/kg, i.p.) induced generalized clonic tonic convulsion. This convulsion activity leads to the animal's death in 100% of case in the control group. The extract significantly ($P<0.01$) delayed the onset time of jerk at the dose of 300mg/kg. The extract at the

dose of 100, 200 and 300mg/kg did not significantly (P>0.05) increase the onset of tonic-clonic with hind limb extension phase. The increase of the latency to seizures was dose-dependent. However, the extract did dot block clonic convulsions but significantly reduces mortality. The observation are shown in **Table 2**.

**TABLE 2: EFFECT OF *SOLANUM MELONGENA* EXTRACT ON PTZ INDUCED SEIZURES IN MICE**

| Treatment | Onset of jerk (sec) | Onset of clonic-tonic (sec) |
|---|---|---|
| Distilled water (10ml/kg, p.o.) | 83.15 ± 3.20 | 342.30 ± 28.726 |
| Extract (100mg/kg, p.o.) | 98.63 ± 10.52 | 386.30 ± 53.465# |
| Extract (200mg/kg, p.o.) | 111.03 ± 10.45 | 410.17 ± 35.346# |
| Extract (300mg/kg, p.o.) | 116.82 ± 17.97* | 471.01 ± 33.649# |
| Extract (400mg/kg, p.o.) | 127.27 ± 17.68 | 424.84 ± 31.086# |
| Diazepam (4mg/kg, i.p.) | _ | _ |

Dose dependent effect of graded dose (100, 200, 300 and 400 mg/kg, p.o.) of extract on PTZ-induced seizures in mice.
Evaluations were made by PTZ (80 mg/kg, ip) after 1hr of administration of extract.
Values are expressed as mean ± S.E.M.
*P< 0.01,
#P> 0.05 compared with distilled water treated group

**PIC-induced seizures**: PIC (7.5 mg/kg, i.p.) produced generalized clonic tonic convulsion followed by death in 50% of mice. The extract at the dose of 200 mg/kg quite significantly (P<0.05) increase the latency of clonic convulsions and quite suppress mortality. The observations are shown in **Table 3**.

**TABLE 3: EFFECT OF *SOLANUM MELONGENA* EXTRACT ON PIC INDUCED SEIZURES IN MICE**

| Treatment | Onset of clonic-tonic seizures (min) | Mortality D/N | % Mortality |
|---|---|---|---|
| Distilled water (10ml/kg, p.o.) | 10.27 ± 1.01 | 2/4 | 50% |
| Extract (100mg/kg, p.o.) | 12.71 ± 0.81 | 4/4 | 100% |
| Extract (200mg/kg, p.o.) | 14.31 ± 1.26* | 2/4 | 50% |
| Extract (300mg/kg, p.o.) | 11.93 ± 0.463 | 3/4 | 75% |
| Phenytoin (25mg/kg, i.p.) | 21.68 ± 2.192 | 0/4 | 0 % |

Dose dependent effect of graded dose (100, 200 and 300 mg/kg,po) of extract on PIC-induced seizures in mice.
Evaluations were made by Picrotoxin (7.5 mg/kg, i. P.) after 1hr of administration of extract.
Values are expressed as mean ± S.E.M.
*P< 0.05 compared with distilled water treated group

**DISCUSSION:** Currently available anticonvulsant drugs are able to efficiently control epileptic seizures in about 50% of the patients; another 25% may show improvement where as the remainder does not benefit significantly [22]. Furthermore, undesirable side effects from the drugs used clinically often render treatment difficult; so that a demand for new types of anticonvulsants exists. One of the approaches to search for new antiepileptic drugs is the investigation of naturally occurring compound,which may belong to new classes. In the present study *Solanum melongena* was evaluated for its effect on PTZ, PIC and MES-induced seizures in mice.

We observed that SM did not exhibit any protection on chemical and electric shock-induced seizures. However, the onset of generalized clonic–tonic seizures induced by PTZ, PIC and duration of extensor seizures induced by MES was delayed in pretreatment with SM, which could be due to its CNS depressant and sedative property [13]. Because the MES, PTZ and PIC test are assumed to identify anticonvulsant drugs effective against generalized to tonic–clonic partial seizures and generalized clonic seizures, respectively [23], the effect of SM in these could therefore suggest anticonvulsant efficacy against the above mentioned seizures type in man. MES–induced tonic seizures can be prevented either by drugs that inhibit voltage- dependent $Na^+$ channels, such as Phenytoin, Valproate, Felbamate and Lamotrgine or by drugs that block glutamatergic excitation mediated by the N-methy-D-aspartate (NMDA) receptor, such as Felbamate.

On the other hand drugs that reduce T-type $Ca^{++}$ current such as ethosuximide can prevent

seizures induced by PTZ[24] or by the blockade of chloride conductance associated to $GABA_A$ receptor (PIC, PTZ). Furthermore, PTZ might also induced convulsions by a direct excitatory effect of endogenous benzodiazepine substance. Drug that block glutamatergic excitation mediated by NMDA receptor, such as Felbamate have anticonvulsant activity against PTZ- induced seizures [25]. Thus, Antiepileptic drugs, like Valproate and Felbamate, which are effective in both type of seizures test, possess multiple mechanisms of action and display the broadest therapeutic utility. It seems that the multiplicity of putative mechanisms of action and the broad spectrum of anticonvulsant activity of the ethanolic extract of SM might be due to the presence of different active components in the *Solanum melongena* interacting simultaneously.

**CONCLUSION:** Results of the present study revealed that the ethanolic extract of the root of *S. melongena* possess anticonvulsant effects and reduce mortality but extract did not block tonic convulsions and clonic-tonic convulsion. It can be concluded that the present work did not include the identification of the active principle and its mechanism of action. This will be the subject of future work.

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