

Evaluation of Antiepileptic Potential and Muscle Relaxant Activity of *Solanum Lycopersicum* Leaves in Rodents

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Abstract: Epilepsy is a collection of diverse disorders that together affect approximately 1% of the general population. It is a paroxysmal behavioural spell generally caused by an excessive disorderly discharge of cortical nerve cells of the brain and can range from clinically undetectable (electrographic seizures) to convulsions. Epilepsy is usually controlled, but not cured, with medication. **Method and materials:** In the present study plant *Solanum lycopersicum* with a CNS activity, antiepileptic activity and muscle relaxant properties was selected and a herbal extract was prepared in ethanolic medium. *Solanum lycopersicum* (tomato) belongs to the family of nightshades or Solanaceae or nightshade family. *Solanum lycopersicum* was evaluated for its antiepileptic activity against pentylenetetrazole (PTZ), isoniazid (INH) induced chemical convulsions in mice. PTZ and INH were injected at the dose of 60 and 300 mg/kg, i.p. The mice treated with *Solanum lycopersicum* (400 mg/kg) showed significant protection (60%) as compare to vehicle treated PTZ injected mice. **Result:** All the drugs were given orally. 200 and 400 mg/kg of EESL significantly reduced the time spent by the animals on revolving rod when compared to control ($P < 0.05$). There was dose dependent increase in muscle relaxation, maximum with 400 mg/kg. In conclusion it is observed that *Solanum lycopersicum* has muscle relaxant and antiepileptic activity.

Keywords: *Solanum Lycopersicum* leaves, Diazepam, Pentylenetetrazole, Isoniazid etc

1. Introduction

Epilepsy:- Epilepsy is non an illness. It's a symptoms an under brain neurons disorder. It's the word "Epilepsy" is derived from a Greek word "a condition of giving overcome, seized, or attacked". The word "Epilepsy" It means nothing all than a tendency to have seizure. The brain maintain and remote all of us action, movements, feelings, thinking, and feelings. It is the hub of memory to controls the body function of the heart and lungs. The cells of the brain do with, comminuting by electrical transmitters. An abnormal electrical discharge from a cell group occurs, resulting in a seizure. Brain cells use chemicals to generate electrical discharge and each brain cells excites or block new brain cells through its releases. The Epilepsy is the oldest cerebral disorder. It was described over 2,000 years ago in world it can be discover in the Bible. Seizure can cause many, including brain injuries, poisoning, headache or a stroke, and this variables ar'nt limited to many age group, gender or ethnicity and either are not epilepsy. Epilepsy can strike anyone at any age Before 10 years of age, 50 percent of all instances grow.

It might be worth to assess the natural remedy possessing anticonvulsant activity against epileptic seizures. Plants like *Solanum lycopersicum* containing antiepilepsy activity has shown protection against seizures induced by maximum electroshock (MES), Pentylenetetrazol (PTZ), and Isoniazid (INH).

S.lycopersicum is a medium sized plant in the solanaceae family. The phytochemical investigation of *S.lycopersicum* signifies presence of steroidal alkaloids, steroid saponins, flavonoids, carotenoids, glycosides and fatty acid derivatives in the extract. The chief constituents of tomato leaves Naringenin, Chalconaringenin, Rutin, Kaempferol,

Quercetin, Caffieciate, Ferulic acid, Coumeric, carotene, Beta- lycopene, Esculoside A, 1.9-oxo-octadecadienoic acid.

Based on the phytochemical constituents present in *S.lycopersicum* such as steroidal alkaloid and flavonoids which is also responsible for its antiepileptic activity. However, no reports are available on the anticonvulsant effect of *S.lycopersicum*, therefore, present investigation was undertaken to evaluate the muscle relaxant potential of ethanolic extract.

2. Material and Methods

Plant Materials

The leaf part of *Solanum lycopersicum* was collected from local garden of Lucknow Uttar Pradesh, in month of October 2018. Plants were identified and authenticated at the National Botanical Research Institute; Lucknow Uttar Pradesh. Voucher specimen No. (NBRI/CIF/259/2011) was deposited in the department of Hygia Institute of Pharmaceutical Education & Research faijullaganj, Lucknow.

Extraction

The leaves of the plant *Solanum lycopersicum* were shade dried at the room temperature (25°C) for in 10 days, finely grounded into powder form with help of an electric grinder and stored. Then powder material was extracted in ethanol via maceration process for approximately 7 days. After seven days the powder was pressed and extract is collected. The solvent was removed under decreased pressure by distillation. The residue were vacuum dried until further use. The yield of prepared extract was 87.77%.

Phytochemical Screening

Then phytochemical tests of extract were performed. In which plants extract containing alkaloids, flavonoid, glycosides, saponins, carbohydrates and steroids. In the phytochemical screening TLC, UV, IR, NMR has been performed. From the thin layer chromatography the type of constituent are present in the extract have been obtained. Five spot were detected with Rf value 0.72, 0.96, 0.23, 0.34, and 0.46 in four types of solvent system and reported Rf value of rutin was 0.79, kaempferol was 0.96, solasodine was 0.26, quercitrin was 0.30 and reported rf value of Quercetin was 0.42, which is very close to our finding. UV analysis has been performed and UV analysis of *Solanum lycopersicum* ethanolic extract shows λ_{max} at 378 nm, 32 nm and 265 nm, which is much closer to reported λ_{max} of Flavonoids (Rutin and Kaempferol), steroidal alkaloid (Solasodine).

Animals

Swiss albino male and female mice were used for the experiment, weighing 25-30gm (age 4-6 weeks) and present studies were procured from animal house of Hygia Institute of Pharmaceutical Education & Research, Lucknow, Uttar

Pradesh. The animals were kept at a temperature 25-30°C of 12 h light and dark cycle in clean polypropylene cages and a humidity of 50 to 60%. Each cage contained 5 to 6 mice of the same sex with a bedding of husk. Before the experiment began, the animals were acclimatized to the laboratory condition for one week. Food and tap water were given *ad libitum* (OECD Guidelines 423). The animals were fasted on each activity set for at least 12 hour before. All animal experiments were carried out as per CPCSEA guide line (Approval No. -1397/ac/10CPCSEA).

PTZ induced seizures in mice:- EESL at doses of 200 and 400 mg / kg b.w. in PTZ (pentylenetetrazole) caused seizures. Significantly delayed the onset of seizures ($P < 0.001$), tonic seizures ($P < 0.001$), but duration of seizures ($P > 0.05$) was not significant 1 hr prior to PTZ injection. As a comparison with the control as shown in Table 3.11, it blocked animal death and enhanced percentage safety. A 200 mg / kg b.w dose. And b.w. 400 mg / kg. Of EESL, 40% and 60% respectively protected animals from PTZ-induced seizures in mice.

Effect of EESL on Pentylenetetrazole induced seizure in mice

Group	Dose /kg	Onset of convulsion (min)	Onset of tonic convulsion (min)	Duration of convulsion (min)	Status animal alive after 30 (Min)	Status animal alive after 24 hrs	% protection
Control (N.S+ PTZ)	10ml + 60mg	6.33±0.6	8.3±0.3	20.3±0.8	5	0	0%
Diazepam + PTZ	4mg +60mg	2.3±0.3***	3.6±0.3***	15.33±0.8**	5	5	100%
Treated 1 (EESL+ PTZ)	200mg+60mg	3.6±0.4***	3.6±0.3***	19±0.5#	5	2	40%
Treated 2 (EESL+ PTZ)	400mg+60mg	2.3±0.3***	3.6±0.3***	21±0.5#	5	3	60%

Value are express as the mean±SEM; n=5, *** $P < 0.001$, ** $P < 0.05$ as compared with control statistical significance and # $P > 0.05$ as non significant was determined to by ANOVA, followed by the Dunnett's t test

400 mg/kg b.w. of EESL also blocks the convulsion in 3 mice out of 5 mice. Standard anti-epileptic drug diazepam 4 mg / kg blocks the 5 mice seizure.

Group	Treatment	Dose	After 0 minutes (in sec.)	After 30 minutes (in sec.)
Control	Normal saline	10 ml/kg	135.5±3.23	138.7±3.29
Standard	Diazepam	4 mg/kg	147±2.5*	33.6±1.7*
Treated 1	EESL - 1	200 mg/kg	85±26.23*	79.6±25.54*
Treated 2	EESL - 2	400 mg/kg	138.7±3.5*	74.3±26.33*

INH induced convulsion in mice:- EESL exhibited dose dependent significantly ($P < 0.05$ and $P < 0.01$) increased First seizure compared to INH mice control. The onset of tonic seizure ($P < 0.05$), the length of seizure ($P < 0.01$) decreased significantly. Treatment of animal with 200 mg/kg b.w. of EESL blocks convulsion in 2 mice whereas in higher dose

Effect of EESL on Iso-niazid (INH) induced seizure in mice

Muscle relaxant activity of *Solanum lycopersicum* by Rotarod:- The result obtained from the Rotarod test 0 and 30 min after treatments presented (Table 3.13). In the test, EESL (200 and 400mg/kg) In comparison with Control ($P < 0.05$), both considerably decreased the time spent by livestock on rotating rod. The conventional medication (diazepam, 4mg / kg) also had substantial impact compared to control. The result from the The rotarod test showed that the extract considerably lowered the engine coordination of the animals tested

Effects of EESL on muscles relaxant activity bythe Rotarod in mice

Group	Dose/ kg	Onset of convulsion (min)	Onset of tonic convulsion (min)	Duration of convulsion (min)	Status animal Alive after 30 (min)	Status Animal Alive after 24 (hrs)	% protection
Control (N.S+ INH)	10ml+300 mg	14±2.08	16.6±0.88	23.2±0.25	5	1	20%
Diazepam + INH	4mg++300 mg	Nil	Nil	Nil	5	5	100%
Treated 1 (EESL+ INH)	200m+300 mg	18.5±0.26*	20.4±0.29*	20.5±1.3**	5	2	40%
Treated 2 (EESL+ INH)	400m+300 mg	19.5±0.32*	20.6±0.85*	17.4±0.50**	5	3	60%

Value is expressed as mean \pm SEM ; ANOVA determined n=5, * P<0.05, ** P<0.01 compared to control statistically meaning, followed by Dunnett's t test

All values are displayed as Mean \pm SEM, n=5, * P<0.05 when ANOVA and Dunett's t test were determined compared to control statistical significance

3. Discussion

The preliminary phytochemical qualitative screening is recorded in this thesis. Through the chemical tests, ethanolic extract of *Solanum lycopersicum* leaves found to contained important phytochemicals namely, alkaloids, steroids, carbohydrates, glycosides, and flavonoids Confirming its medicinal characteristics and wed the presence of steroidal alkaloid (α -tomatine), solasodine. *Solanum lycopersicum* contains these compounds. Tomatoes comprise a range of phytochemicals, including carotenoids such as lycopene (maximum concentration of 85 percent), phytoene, phytofluene and provitamin A, carotenoid β -carotenoid, polyphenols such as quercetin, kaempferol, naringenin, neutrients such as folate vit-C, vit-E, vit-K vit-B, nitrogen, sulphur potassium calcium, iron, sugars such as aldoses, ketoses, disaccination. Due to presence of alkaloids, saponins it shows many medicinal properties such as antifungal activity anticholesterolemic activity due to α -tomatine attached to the aglycone tomatidine. α -tomatine which is an active principle of tomato leaves has been shown to be devoid of central activity. Mice provided *Solanum lycopersicum* extract at a dose of 2000 mg / kg p.o. showed no mortality in the acute toxicity assessment and all mice had no toxicity symptoms. The dose used did not appear to impact the mice's body weights and did not cause important changes in the consumptions of food and water. The rise in body weight can be due to the accumulation of fat in the body. Food and water use has shown normal metabolism in animals and this suggests that the single oral dose of *Solanum lycopersicum* has not delayed growth in animals. There were no observational changes of body during 14 days of toxicity period. Sedation was observed on the first day due to anaesthesia. There have been no modifications to the EESL after 14 days of acute toxicity research with mice Hb, TLC, lymphocytes, monocytes, platelet count, MCV, MCHC, and PCV. Granulocytes, MCH, and RBC level were found to increase. However an increase in the parameter granulocytes due to some allergic reaction or infection, reduction in RBC and MCH increase shows anaemic condition due to iron deficiency or may vitamin deficiency or may be suppression of circulating hormones. The others haematologically parameter as well as the biochemically parameter were normal. Histopathological examination of the EESL slides Hematoxyline stained and eosin revealed normal morphology in treated group. All vital organs (brain, liver, lungs, spleen, heart, and kidney) were in their normal sizes. Lungs showed thickening of wall due to weight gain of treated mice during 14 days of period of toxicity study as compared to control mice. Presence of flavonoids like kaempferol, rutin, quercetin, and quercitrin, steroids and solasodine in the *Solanum lycopersicum* have been reported. Existence of flavonoid in *S. lycopersicum* can explain many of its beneficiary effects. Flavonoids, a significant class of naturally occurring compounds, showed

CNS activities such as affinity for GABA_A receptor and anticonvulsant effects, alkaloid which is an active principle of *Solanum lycopersicum* leaves gives CNS activity. By inhibiting the activity of gamma amino butyric acid (GABA) in GABA-A receptors, PTZ may exert its seizure impacts. The significant inhibitory neurotransmitter involved in epilepsy is gamma amino butyric acid. Improving and inhibiting GABA neurotransmission will, respectively, attenuate and enhance seizures. Pentylenetetrazole may elicit seizure by inhibiting gabaergic mechanisms. Standard antiepileptic drugs, diazepam, are thought to have an effect by improving GABA-mediated brain inhibition . The current results have shown that the EESL leaves in experimental mice have significant skeletal muscle relaxing activity. In the Rota-rod sample animals at 200 and 400mg / kg p.o. handled with EESL. The effect of myorelaxant and depression on the CNS resulted in a significant decrease in muscle relaxing activity. tomato leaves are toxic, but in acute toxicity study, there was no any toxic symptom, ([http://www.rightdiagnosis.com/t/tomato_leaf_poisoning/int ro.htm#what](http://www.rightdiagnosis.com/t/tomato_leaf_poisoning/int_ro.htm#what)). There was no difference in Consumption of body weight, food and water, haematological parameter, and organ weight respectively. So we can say that at acute dose it can be used for further studies. It is found to be, flavonoids are helpful in the CNS activity thus, it can be concluded that the EESL leaves having significant anticonvulsant activity with muscle relaxant activity. But the exact mechanism which by *Solanum lycopersicum* exert its anticonvulsant activity is't determined yet and needs further investigation to elucidate the other active compounds and underlying mechanism.

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5. Conclusion

According to antiepileptic models it was confirms that dose level 400 mg/kg was more effective than dose level 200 mg/kg. So dose level 400 mg/kg shows significant epileptic activity. The ethanolic extract of *Solanum lycopersicum* was found to possess antiepileptic activity. In accordance to the present study, it has been observed that the presence of flavonoids and steroidal alkaloid which are present in the plant However, the isolated flavanoid such as rutin and quercetin and steroidal alkaloid such as solasodine may show more pronounced antiepileptic activity compared to the extract with control (vehicle) and standard drug (Diazepam). This indicates that the extract of *Solanum*

lycopersicum may be used as an effective drug for antiepileptic activity.

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