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Assessment of Anti-epileptic Activity of *Salvia officinalis* Linn. In Experimental Animal Models: A *In-vivo* Evidences**Payal P. Gaikwad¹, Pooja P. Gaikwad^{2*}, Rahul N. Patil^{3*}, Shweta H. Zalte⁴, Nilam S. Sanas⁵, Jyoti E. Sonawane⁶, Priti A. Kothawade⁷**¹ Department of Pharmaceutical Quality Assurance, Siddhi College of Pharmacy, Chikhali, Pune, Maharashtra, INDIA- 411062^{2*} Department of Pharmacology, Dhanaji Shelke College of Pharmacy, Vakhari, Daund, Pune, Maharashtra, INDIA- 412203^{3*,7} Department of Pharmacology, MET's Institute of D. Pharmacy, BKC, Adgaon, Nashik, Maharashtra, INDIA- 422003⁴ Department of Pharma. Chemistry, Matoshri College of Pharmacy, MES, Eklahare, Nashik, Maharashtra, INDIA- 422105⁵ Department of Pharmacology, Rajgad Dnyanpeeth's College of Pharmacy, Bhore, Pune, Maharashtra, INDIA- 412206⁶ Department of Pharma. Chemistry, SGSSPM'S Dnyanvilas College of Pharmacy, Dudulgaon, Pune, Maharashtra, India- 412105.**Email: pooja.g8045@gmail.com, patilrahul4254@gmail.com****Article Information**

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ABSTRACT**Background:** Considering the prevalence of epilepsy and the problems *Salvia officinalis* Linn., associated with currently available anti-epileptic drugs like side effects, resistance, safety issues and high cost, herbal medicines with fewer complications could be very appropriate alternative. Therefore, the present study was examined for the anti-epileptic activity of ethanolic extract of *Salvia officinalis* Linn. stem.**Material and Methods:** Earlier studies suggested that Phyto-constituents like flavonoid, alkaloid and tannins shows anti-epileptic activity and comprehensive literature revealed that *Salvia officinalis* is rich in flavonoids like chlorogenic acid, ellagic acid, quercetin, rosmarinic acid, as well as the several volatile components such as borneol, cineole, camphor, and thujone, alkaloids, tannins, polyphenol, saponins etc. Anti-epileptic activity of *Salvia officinalis* Linn stem in mice was evaluated using Pentylentetrazole (PTZ) induced seizures, Strychnine induced convulsion and Picrotoxin induced convulsion GABA estimation method.**Result:** The ethanolic extract at 100 mg/kg, 200 mg/kg and 400 mg/kg possess dose dependent anticonvulsant activity as it reduced the duration of seizures produced by and latency of seizures produced by PTZ, Strychnine, and Picrotoxin. The amount of GABA estimation which is most likely to be involved in seizure activity was increased in mice brain and the anti-epileptic activity of ethanolic extract of *Salvia officinalis* Linn. stem is justified.

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INTRODUCTION

Epilepsy is a most common and widespread serious neurological disease, affects around 70 million people worldwide and can profoundly affect many aspects of quality of life. At the molecular level in the epilepsy, there is an imbalance between inhibitory GABA-mediated and excitatory Glutamate-mediated neurotransmission.¹ The brain functions with the help of millions of neurons that transmits and receives signals. When the normal transmission pattern of signals in brain is disturbed seizures may occur that disturb the consciousness, tonic colonic jerks in body limbs, salivation, abnormal body structures which are normalized within a short period of the time when the impulse in brain are auto-normalized.²

Seizures can vary widely in their clinical presentation, depending on site, extent and mode of propagation of the paroxysmal discharge and hence now looked at as spectrum of clinically different varieties rather than a single disease. Epileptic seizures often cause transient impairment of consciousness, leaving the individual at risk of bodily harm and often interfering with education and employment.³

Salvia officinalis. Linn belonging to family Lamiaceae a medicinal herb mentioned in literature survey contains various phytochemical constituents that are been responsible for variety of pharmacological potential like anti-inflammatory, anti-diabetic, analgesic, anxiolytic and anti-diuretic. The stem of plant contains volatile components such as borneol, cineole, camphor, and thujone, polyphenol, saponins known for their therapeutic potential. The flavanoid named chlorogenic acid, ellagic acid, quercetin, rosmarinic acid present in stem of plant owing anti-epileptic potential.^{4,5}

MATERIALS AND METHODS:

Plant material collection and authentication

The stem of *Salvia officinalis* Linn. is were collected from the botanical garden of Wadgaon Sheri, Pune and authenticated by Mrs. Priyanka A. Ingle,

Scientist C, Botanical Survey of India, Koregaon Park, Pune city, Maharashtra-7.

Experimental animals, approval and maintenance:

Present study was carried out using Swiss albino mice of either sex(20-25g), procured from the National Institute of Biosciences, Dhangawadi, Tal-Bhor, Dist-Pune, were used for study. The animals were housed in animal house of college with standard laboratory conditions. They were kept in clean polypropylene cages maintained at a temperature of 25±1°C and relative humidity of 45 to 55 % under 12-hr light, 12-hr dark cycle. The animals had free access to standard pellet rodent diet (Purchased from Nutrivet Life Science Pvt Ltd., Pune Maharashtra, India) and water ad libitum. The experimental design and research plan along with animal handling and disposal procedure were approved from Institutional Animals Ethics Committee of Rajgad Dnyanpeeth's College of Pharmacy, Bhor. IAEC approval No: RDCOP/Pcol- 07/IAEC/2020-21/07 Dated 24/12/2020.

Drugs and chemicals:

Analytical grade standard chemicals were used in present study. Pentylentetrazole (PTZ), Strychnine, Picrotoxin, Ethanol, Diazepam, from Boradeomkar laboratories Ltd. GABA was obtained from Omega Laboratories, Lonand.

Drying, pulverizing and extraction of plant material:

The stems of *Salvia officinalis* Linn. were washed and shade dried for a week and coarsely powdered using a mechanical grinder. Further, plant material (100 gm) was extracted by a simple Soxhlet extraction process by 96 % ethanol (1000 ml) for 72 hours. After 72 hours of post- incubation, the extract was removed and concentrated in the Rota evaporator under vacuum condition to obtain semisolid extract and stored in refrigerator at 2°C to 4°C and utilized for further study.^{4,6}

Physical characterization and Phytochemical investigation:

In addition to authentication, the crude drug was tested for quality and purity parameters which comprises of total ash value, acid insoluble ash, water soluble ash, sulphated ash, loss on drying, alcohol and water soluble extractive value, petroleum ether extractive value and foaming index. The extract so collected was tested to find presence of various phytoconstituents viz. Alkaloids, Proteins, Glycosides, Fats and oils, Flavonoids, Steroids, Phenolic compounds and Tannins.⁷

Pharmacological study:

Assessment of Anti-epileptic potential (*In-vivo*)

Acute oral toxicity study in animal:

The acute oral toxicity study of extracts assessed conferring to Organization for Economic Cooperation and Development (OECD) guideline-423. The limit test dose of 2000 mg/kg used. All the animals housed at overnight fasting before every experiment with free excess to water. Prior to dose administration, the body weight of each animal taken and the dose calculated as per the body weight. The animals were seen for toxic effect for the first four hrs after the treatment. Further animals investigated for 14 days for any toxic effect. Behavioral changes and other parameters such as body weight, urination, food intake, water intake, respiration, constipation, changes in eye and skin colors, etc. Observed.⁸

Experimental Design:

Assessment of Anti-epileptic potential by Pentylene-tetrazole induced seizure model:

Swiss albino mice of either sex 20-25 gm will be used 6 group will be taken divided into 6 animals in each. The test and standard drug will be given orally to animals. 60 min after oral or 30 min after intraperitoneally administration of test and standard pentylenetetrazole will be injected intraperitoneally. Each animal is placed into an individual plastic cage for observation of lasting 1-hour seizures and tonic-clonic convulsion are recorded. At last, 80% of animal in the control group have to show convulsions. The number of protected animals in the treated groups will be calculated as percentage of affected animals in the control group.^{8,9}

Table 1: Animal grouping for treatment (Pentylenetetrazole induced)

Sr. No	Groups	Treatment received	Dose of drug
1.	Normal control	Distilled water	(1 ml/kg, P.O)
2.	Negative control	Pentylenetetrazole	(60 mg/kg, i.p)
3.	Standard	Diazepam	(5 mg/kg, i.p)
4.	Test -1	SOSE	(100 mg/kg, P.O)
5.	Test -2	SOSE	(200 mg/kg, P.O)
6.	Test -3	SOSE	(400 mg/kg, P.O)

Assessment of Anti-epileptic potential by Strychnine induced seizure model:

Swiss albino mice of either sex 20-25 gm will be used 6 group will be taken divided into 6 animals each. The test and standard drug will be given orally or intraperitoneally to animals. 1 hour later the mice will be injected with strychnine nitrate intraperitoneally. The time until occurrence of tonic extensor convulsions and death is noted during a 1-

hour period. With the dose of strychnine nitrate convulsions will be observed in 80% of the control. ED₅₀ values will be calculated using various doses taking the percentage of the controls as 100% for time response curves the interval between treatment and strychnine nitrate injection various forms 30 to 120 min.^{9,10}

Table 2: Animal grouping for treatment (Strychnine induced)

Sr. No	Groups	Treatment received	Dose of drug
1.	Normal control	Distilled water	(1 ml/kg, P.O)
2.	Negative control	Strychnine	(2 mg/kg, i.p)
3.	Standard	Diazepam	(5 mg/kg, i.p)
4.	Test -1	SOSE	(100 mg/kg, P.O)
5.	Test -2	SOSE	(200 mg/kg, P.O)
6.	Test -3	SOSE	(400 mg/kg, P.O)

Assessment of Anti-epileptic potential by Picrotoxin induced seizure model

Swiss albino mice of either sex 20-25 gm will be used. 6 group will be taken divided into 6 animal each. The test and standard drug will be given orally to animals 60 min after oral administration of test and standard drug animals are injected with 3.5 mg/kg subcutaneously picrotoxin and are

observed for the symptoms during next 30 min. Clonic convulsions, tonic seizures, death times of onset of seizures and time to death are recorded. For time response curves the animals receive the drug 30, 60 or 120 min prior to picrotoxin, picrotoxin is expressed as percent inhibition relative to vehicle control.^{9,10}

Table 3: Animal grouping for treatment (Picrotoxin induced)

Sr. No	Groups	Treatment received	Dose of drug
1.	Normal control	Distilled water	(1 ml/kg, P.O)
2.	Negative control	Picrotoxin	(3.5 mg/kg, i.p)
3.	Standard	Diazepam	(5 mg/kg, i.p)
4.	Test -1	SOSE	(100 mg/kg, p.o)
5.	Test -2	SOSE	(200 mg/kg, p.o)
6.	Test -3	SOSE	(400 mg/kg, p.o)

GABA estimation from the brain suspension of mice

The brain gamma amino butyric acid (GABA) content was estimated according to the method of Lowe. Animals were sacrificed by decapitation and brains were rapidly removed, and separated forebrain region. It was blotted, weighed and placed in 5 ml of ice-cold trichloroacetic acid (10% w/v), then homogenized and centrifuged at 10,000 rpm for 10 min at 0°C. A sample (0.1ml) of tissue extract was placed in 0.2 ml of 0.14 M ninhydrin solution in 0.5 M carbonate-bicarbonate 1 buffer (pH9.95), kept in a water bath at 60°C for 30 min, then cooled and treated with 5 ml of copper tartrate reagent (0.16% disodium carbonate, 0.03% copper sulphate and 0.0329% tartaric acid). After 10 min fluorescence at 377/455 nm in a spectrofluorometer was recorded.^{11, 12}

Statistical analysis:

Each value was expressed in a Mean ± SEM. The obtained results were analyzed by statistically using one- way ANOVA followed by Dunnett's test (n=6). Multiple comparison test, *p<0.05, **p<0.01; ***p<0.001.

RESULTAND DISCUSSION:

Physical characterization and Phytochemical investigation:

The ethanolic extract of the *Salvia officinalis* Linn. stem were subjected to the phytochemical investigation to identify the presence of the phytochemical constituents. The preliminary phytochemical investigation of ethanolic extract of *Salvia officinalis* Linn. (SOSE) revealed the presence of flavonoids are accounted for the majority of anti-epileptic activity.

Table: 4 Effect of SOSE on PTZ induced epilepsy in mice

Group. No	Treatment	Onset of latency (sec)	Duration (sec)
1.	Normal control (1ml/kg p.o)	124 ± 1.850	281 ± 12.08
2.	PTZ (60mg/kg i.p)	147 ± 11.20	135 ± 3.733
3.	Diazepam (5mg/kg i.p)	408 ± 14.24***	60.66 ± 0.990***
4.	SOSE (100mg/kg p.o)	288 ± 14.44***	161.0 ± 1.760***
5.	SOSE (200mg/kg p.o)	345 ± 4.944***	144.3 ± 1.420***
6.	SOSE (mg/kg p.o (400mg/kg p.o)	378 ± 4.948***	138.6 ± 1.312***

Each value was expressed in a Mean ± SEM. The obtained results were analyzed by statistically using one- way ANOVA followed by Dunnett's test (n=6). Multiple comparison test, *p<0.05, **p<0.01; ***p<0.001.

Effect of SOSE on Pentylenetetrazol (PTZ) Induced Seizures:

The SOSE in selected doses 100 mg/kg, 200 mg/kg, and 400 mg/kg prevented convulsions against Pentylenetetrazol (60 mg/kg, i.p) induced convulsion in mice. The SOSE showed significantly increased latency of convulsion as well as reduced the duration of convulsion in dose dependent manner. (as describe in Table-4)

The negative control group is compared to Normal control 1 ml/kg, latency of convulsion time was (124 ± 1.850) sec. The mean of latency of convulsion in test group 1 SOSE 100 mg/kg (288 ± 14.44), SOSE 200 mg/kg (345 ± 4.944), and SOSE 400 mg/kg (378 ± 4.948) sec, and Diazepam 5mg/kg (408 ± 14.24) sec respectively which was significant when compared to negative control group in which latency of convulsion time was (147 ± 11.20) sec. The standard drug was statistically significantly increased the latency of convulsion time of the test at (408 ± 14.24) sec. The negative control group is compared to normal control 1 ml/kg, duration of convulsion time was (281 ± 12.08) sec. The mean of duration of convulsion in SOSE 100 mg/kg (161.0 ± 1.760) sec, SOSE 200 mg/kg (144.3 ± 1.420) sec, and SOSE 400 mg/kg (138.6 ± 1.312) sec and diazepam 5mg/kg (60.66 ± 0.990) sec respectively which was significant when compared to negative control group in which duration of convulsion time was (135 ± 3.733) sec.

The standard drug was statistically significant reducing the duration time of the test at 60.66 ± 0.990 seconds.

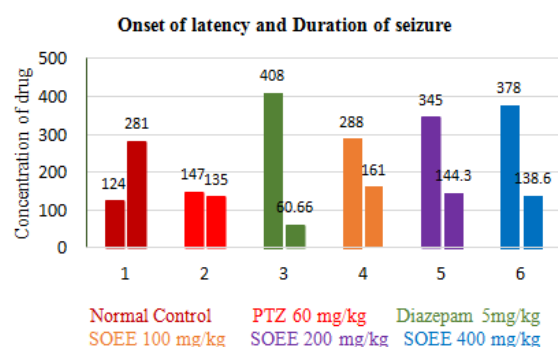


Fig. 1 Effect of SOEE on Onset of latency and Duration of

seizure by PTZ induced seizure

Effect of SOSE on Strychnine Induced Seizures

The SOSE in selected doses 100 mg/kg, 200 mg/kg, and 400 mg/kg prevented convulsions against Strychnine 2 mg/kg, i.p induced convulsion in mice. The SOSE showed significantly increased latency of convulsion as well as reduced the duration of convulsion in dose dependent manner. (As describe in Table-5)

The negative control group is compared to Normal control (1 ml/kg), latency of convulsion time was (128 ± 1.856) sec. The mean of latency of convulsion in SOSE 100 mg/kg (291 ± 16.50) sec, SOSE 200 mg/kg (353 ± 5.948) sec, and SOSE 400 mg/kg (419 ± 6.999) sec, Diazepam 5 mg/kg (553 ± 15.24) sec, respectively which was significant

when compared to negative control group in which latency of convulsion time was (140 ± 17.8) sec.

The standard drug was statistically significantly increased the latency of convulsion time of the test at (553±15.24) sec. The negative control group is compared to normal control (1 ml/kg), duration of convulsion time was (226 ± 11.02) sec. The mean of duration of convulsion in SOSE 100 mg/kg (163 ± 1.870) sec, SOEE 200 mg/kg (149 ± 1.724) sec, SOSE 400 mg/kg (142 ± 1.432) sec and diazepam 5 mg/kg (63 ± 0.997) sec respectively which was significant when compared to negative control group in which duration of convulsion time was (171 ± 7.967) sec. The standard drug was statistically significant reducing the duration time of the test at (63 ± 0.997) sec.

Table: 5 Effect of SOSE on Strychnine induced epilepsy in mice

Group. No	Treatment	Onset of latency (sec)	Duration (sec)
1.	Normal control (1ml/kg p.o)	128 ± 1.856	226 ± 11.02
2.	Strychnine (2mg/kg i.p)	140 ± 17.8	171 ± 7.967
3.	Diazepam (5mg/kg i.p)	553 ± 15.24***	63 ± 0.997***
4.	SOSE (100mg/kg p.o)	291 ± 16.50***	163 ± 1.870***
5.	SOSE (200mg/kg p.o)	353 ± 5.948***	149 ± 1.724***
6.	SOSE (400mg/kg p.o)	419 ± 6.999***	142 ± 1.432***

Each value was expressed in a Mean ± SEM. The obtained results were analyzed by statistically using one- way ANOVA followed by Dunnett’s test (n=6). Multiple comparison test, *p<0.05, **p<0.01; ***p<0.001.

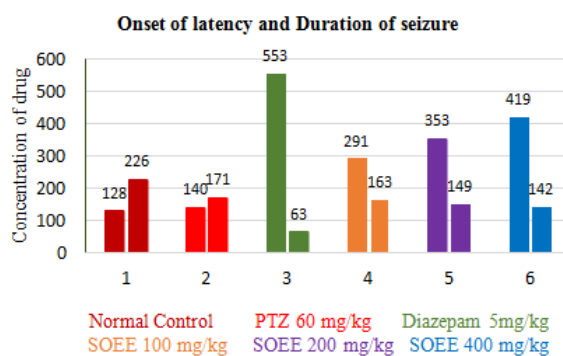


Fig. 2 Effect of SOEE on Onset of latency and Duration of seizure by STC induced seizure

Effect of SOSE on Picrotoxin Induced Seizures:

The SOSE in selected doses 100 mg/kg, 200 mg/kg, and 400 mg/kg prevented convulsions against Picrotoxin 3.5 mg/kg, i.p induced convulsion in mice. The SOSE showed significantly increased latency of convulsion as well as reduced the duration of convulsion in dose

dependent manner. (As described in Table-3)

The negative control group is compared to normal control (1 ml/kg), latency of convulsion time was (126 ± 1.750) sec. The mean of latency of convulsion in SOSE 100 mg/kg (306 ± 18.60), SOSE 200 mg/kg (340 ± 5.950), and SOSE 400 mg/kg (381±5.821) sec, diazepam 3.5 mg/kg (458 ± 13.20) sec respectively which was significant when compared to negative control group in which latency of convulsion time was (141 ± 18.9) sec.

The standard drug was statistically significantly increased the latency of convulsion time of the test at (458 ± 13.20) sec. The negative control group is compared to normal control (1 ml/kg), duration of convulsion time was (230 ± 15.08) sec. The mean of duration of convulsion in SOSE 100 mg/kg (165 ± 1.982) sec, SOSE 200 mg/kg (149 ± 1.724) sec, and SOSE 400 mg/kg (141 ± 1.428)sec, diazepam 3.5 mg/kg (68 ± 0.988) sec respectively which was significant when compared to negative control group in which duration of convulsion time was (176 ± 7.978) sec. The standard drug was statistically significant reducing the duration time of the test at (68 ± 0.988) sec.

Table: 6 Effect of SOSE on Picrotoxin induced epilepsy in mice

Group. No	Treatment	Onset of latency (sec)	Duration (sec)
1.	Normal control (1 ml/kg p.o)	126 ± 1.750	230 ± 15.08
2.	Picrotoxin (3.5 mg/kg i.p)	141 ± 18.9	176 ± 7.978

3.	Diazepam (5 mg/kg i.p)	458 ± 13.20***	68 ± 0.988***
4.	SOSE (100mg/kg p.o)	306 ± 18.60***	165 ± 1.982***
5.	SOSE (200 mg/kg p.o)	340 ± 5.950***	149 ± 1.724***
6.	SOSE (400 mg/kg p.o)	381 ± 5.821***	141 ± 1.428***

Each value was expressed in a Mean ± SEM. The obtained results were analyzed by statistically using one- way ANOVA followed by Dunnett’s test (n=6). Multiple comparison test, *p<0.05, **p<0.01; ***p<0.001.

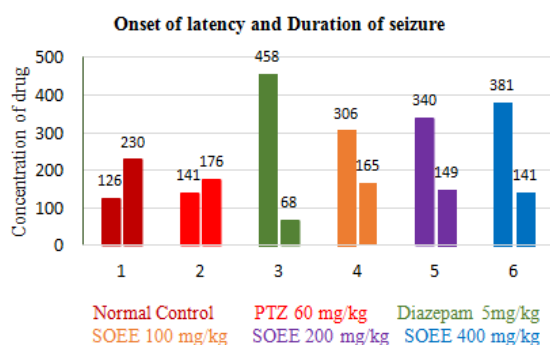


Fig.3. Effect of SOEE on Onset of latency and Duration of seizure by PCT induced seizure

Mortality and Acute oral toxicity:

No death was recorded amongst the groups of mice up to a dose of 400 mg/kg for 3 weeks. This suggests that the plant extract is relatively safe and non-toxic in mice at the doses used in this study.

Biochemical Parameter:

Effect of SOSE on GABA estimation of PTZ induced epilepsy:

The SOSE, showed significant increase in level of GABA estimation of PTZ in (SOSE 100 mg/kg), (SOSE 200 mg/kg) treatment, but highly significant increase in (SOSE 400 mg/kg) of treatment.

The mean of GABA level in brain was (0.2733 ± 0.002) sec compare negative control group with normal control group (0.2333 ± 0.009) sec. The mean of GABA level in brain was (0.2566 ± 0.00), (0.29 ± 0.003), and (0.3566 ± 0.006), (0.4833 ± 0.008), in(SOSE 100mg/kg),(SOSE 200mg/kg),(SOSE 400mg/kg) and diazepam as compare with negative control group respectively, the mean GABA level in brain in STD group (Diazepam) was significantly increased to (0.4833 ± 0.008)

Table: 7 Effect of SOSE on GABA estimation of PTZ induced epilepsy in mice

Grou p. No	Treatment	GABA (ug/ml)
1.	Normal control (1 ml/kg p.o)	0.2333 ± 0.009
2.	PTZ (60 mg/kg i.p)	0.2733 ± 0.002
3.	Diazepam (5 mg/kg i.p)	0.4833 ± 0.008***
4.	SOSE (100mg/kg p.o)	0.2566 ± 0.00***
5.	SOSE (200 mg/kg p.o)	0.29 ± 0.003***
6.	SOSE (400 mg/kg p.o)	0.3566 ± 0.006***

Each value was expressed in a Mean ± SEM. The obtained results were analyzed by statistically using one- way ANOVA followed by Dunnett’s test (n=6). Multiple comparison test, *p<0.05, **p<0.01; ***p<0.001.

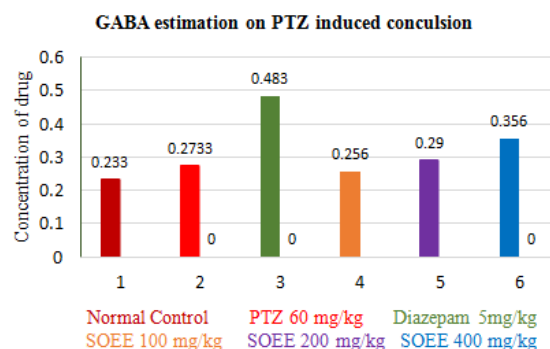


Fig. 4 Effect of SOSE on GABA estimation of PTZ induced epilepsy in mice

Effect of SOSE on GABA estimation of Strychnine induced epilepsy

The SOSE, showed significant increase in level of GABA estimation of strychnine in (SOSE 100 mg/kg), (SOSE 200 mg/kg) treatment, but highly significant increase in (SOSE 400 mg/kg) of treatment.

The mean of GABA level in brain was (0.2066 ± 0.001) sec compare negative control group with normal control group (0.1733 ± 0.002) sec. The mean of GABA level in brain was (0.2766 ± 0.157), (0.3433 ± 0.218), and (0.3866 ± 0.220), (0.4066 ± 0.004), in (SOSE 100mg/kg), (SOSE 200mg/kg),(SOSE 400mg/kg), diazepam (5 mg/kg) as compare with negative control group respectively, the mean GABA level in brain in STD group (Diazepam) was significantly increased to (0.4066 ± 0.004).

Table: 8 Effect of SOSE on GABA estimation of Strychnine induced epilepsy

Group. No	Treatment	GABA (ug/ml)
1.	Normal control (1 ml/kg p.o)	0.1733 ± 0.002
2.	Strychnine (2 mg/kg i.p)	0.2066 ± 0.001
3.	Diazepam (5 mg/kg i.p)	0.4066 ± 0.004***
4.	SOSE (100mg/kg p.o)	0.2766 ± 0.157***
5.	SOSE (200 mg/kg p.o)	0.3433 ± 0.218***
6.	SOSE (400 mg/kg p.o)	0.3866 ± 0.220***

Each value was expressed in a Mean ± SEM. The obtained results were analyzed by statistically using

one- way ANOVA followed by Dunnett's test (n=6). Multiple comparison test, *p<0.05, **p<0.01; ***p<0.001.

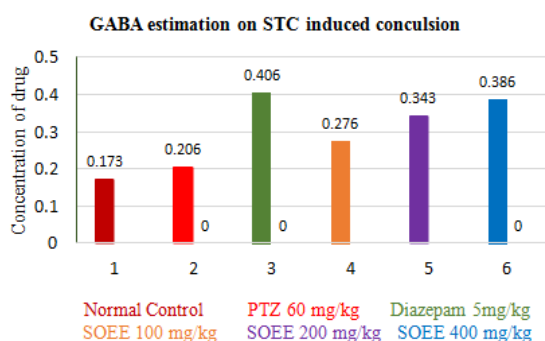


Fig. 5 Effect of SOSE on GABA estimation of Strychnine induced epilepsy

Effect of SOSE on GABA estimation of Picrotoxin induced epilepsy

The SOSE, showed significant increase in level of GABA amino acid neurotransmitter in(SOSE100mg/kg), (SOSE 200mg/kg) treatment, but highly significant increase in (SOSE 400 mg/kg) of treatment.

The mean of GABA level in brain was (0.2233 ± 0.003) sec compare negative control group with normal control group (0.1966 ± 0.027) sec. The mean of GABA level in brain was (0.3366 ± 0.159), (0.3733 ± 0.219), and (0.4033 ± 0.221), (0.44 ± 0.154), in (SOSE 100 mg/kg), (SOSE 200 mg/kg), (SOSE 400 mg/kg) and diazepam (3.5 mg/kg) as compare with negative control group respectively, the mean GABA level in brain in STD group (Diazepam) was significantly increased to (0.44 ± 0.154).

Table: 9 Effect of SOSE on GABA estimation of Picrotoxin induced epilepsy

Group. No	Treatment	GABA (ug/ml)
1.	Normal control (1 ml/kg p.o)	0.1966 ± 0.027
2.	Picrotoxin (3.5 mg/kg i.p)	0.2233 ± 0.003
3.	Diazepam (5 mg/kg i.p)	0.44 ± 0.154***
4.	SOSE (100mg/kg p.o)	0.3366 ± 0.159***
5.	SOSE (200 mg/kg p.o)	0.3733 ± 0.219***
6.	SOSE (400 mg/kg p.o)	0.4033 ± 0.221***

Each value was expressed in a Mean ± SEM. The obtained results were analyzed by statistically using one- way ANOVA followed by Dunnett's test (n=6). Multiple comparison test, *p<0.05, **p<0.01; ***p<0.001.

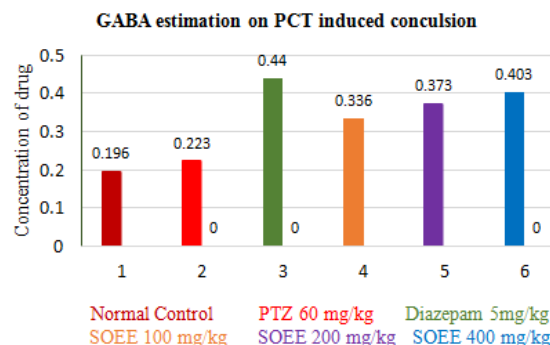


Fig. 6 Effect of SOSE on GABA estimation of Picrotoxin induced epilepsy

CONCLUSION:

Epilepsy is a most common and widespread serious neurological disease, affects around 70 million people worldwide and can profoundly affect many aspects of quality of life. The potential of *Salvia officinalis*. Linn stem extract was evaluated against epilepsy induced in mice by Pentylenetetrazole, Strychnine and Picrotoxin. The study revealed that ethanolic extracts *Salvia officinalis*. Linn possessed dose-dependent anti-epileptic properties. The biochemical examination (GABA estimation) is evidence to convince the potential of ethanolic extract of *Salvia officinalis*. Linn. These findings provide some basis to justify the common use of *Salvia officinalis*. Linn. Stem extracts in the treatment of epilepsy. However, there is a scope for further studies to explore molecular mechanism and to identify the Phyto- constituent responsible the activity.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE:

The Institutional Animal Ethics Committee authorized the study protocol, and CPCSEA approved the regulation (RDCOP/Pcol-07/IAEC/2020-21/07 Dated 24/12/2020).

CONFLICT OF INTEREST:

There is no conflict of interest, according to the authors.

ABBREVIATIONS:

PTZ: Pentylenetetrazol; **SOSE:** *Salvia officinalis*. Linn stem extract; **I.P:** Intraperitoneally; **P.O:** Per oral; **ANOVA:** Analysis of Variance; **SEM:** Standard Error Mean; **GABA:** Gamma-Aminobutyric Acid; **OECD:** Organization for Economic Co-operation and Development; **IAEC:** Institutional Animal Ethics Committee; **CPCSEA:** Committee for the purpose of Control and

Supervision on Experimental Animals.

SUMMARY

Salvia officinalis's potential as an anti-epileptic drug. Swiss Albino mice were used to test *Salvia officinalis*'s. Linn stem extract in accordance with the OECD guidelines. Critical in-vivo evaluations have demonstrated the extract's effectiveness in treating epilepsy.

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