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Sedative and Hypnotic Activities of Ethanolic Leaves Extract of *Solanum Torvum* Sw. in Albino Mice



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ABSTRACT

The Objective was to study the sedative and hypnotic property of the ethanolic leaves extract of *Solanum torvum* Sw. in albino mice. All the animals were divided into five groups (n=5). The first group received distilled water 10ml/kg, second, third and fourth group received three doses of the extract i.e. 100mg/kg, 200mg/kg and 400mg/kg orally respectively and fifth group the standard dose of diazepam 3mg/kg intraperitoneally (i.p) and was observed in the rota rod apparatus, open field apparatus and hole board apparatus for sedative activity. For evaluation of hypnotic activity the animals were divided into five groups (n=5); first group received distilled water 10ml/kg, second, third and fourth group received three doses of the extract i.e. 100mg/kg, 200mg/kg and 400mg/kg orally respectively and fifth group the standard dose of Diazepam 3mg/kg i.p. after that phenobarbitone sodium was injected i.p at the Dose of 50mg/kg and the onset of sleep and duration of sleep was noted. All the observations were statistically analyzed with one way ANOVA and post-hoc Bonferroni's multiple comparison test. On evaluating the sedative activity in the Rota rod apparatus, hole board apparatus and open field apparatus it was seen that the ethanolic extract of *Solanum torvum* sw. showed significant results ($p < 0.05$). On evaluating the hypnotic activity the ethanolic extract of *Solanum torvum* sw. showed to increase the duration of sleep which was statistically significant but did not decrease the onset of sleep.



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INTRODUCTION:

Sedatives are a class of agents which reduce anxiety and exert a calming effect. The degree of central nervous system depression should be the minimum consistent with therapeutic efficacy. Hypnotic drugs produce drowsiness and encourage the onset and maintenance of sleep. [1]

Hypnosis should not be considered a trance like state as seen in psychiatry. Rather it resembles a natural sleep from which the person can be aroused by a strong stimulus. [2]

For centuries alcohol and opium were the only drugs available that had sedative-hypnotic effects. Chloral hydrate, a derivative of ethyl alcohol, was introduced in 1826 as the first synthetic sedative-hypnotic, and a more important drug, barbital, was synthesized in 1903. Phenobarbital became available in 1912 and was followed, during the next 20 years, by a long series of other barbiturates.[3]

Man since time immemorial has been using herbs or plant products as medicines for developing immunity or resistance against cold, coryza, joint pain, fever etc. A vast majority of our population, particularly those living in villages depend largely on herbal remedies. [4]

Historically, plants have provided a source of inspiration for novel drug compounds, as plant derived medicines have made large contribution to human health and well-being. Nearly 80% of the world population relies on traditional medicine for primary health care most of which are plant extract. Of about 300,000 plants species acclaimed worldwide, only about 5% have been investigated scientifically for their medicinal properties. [5]

Solanum torvum SW. is a prickly, tomentose, erect shrub, 1.5-3 m high, and leaves having no prickles, white bell-shaped flowers and lobed fruits seated on the calyx belonging to the family Solanaceae. It is a common plant found throughout the Indian subcontinent. In Bangladesh, it is common in dry regions and often occurs gregariously. It is locally known as tit begoon, gota begoon or hat begoon in Bengali and commonly known as turkey berry, susumber, gully-bean Thai eggplant or devil's fig. Common people of Bangladesh especially the tribes' use the fruit of *S. torvum* SW. as vegetables in their daily diet. Different parts of the plants are used as sedative, diuretic and digestive. Leaves are used as hemostatic. Extract of the fruits and leaves are said to be useful in case of liver and spleen enlargement and in the

treatment of cough. Paste of root is used to cure cracks in feet. The fume of burning seeds is inhaled for toothache. [6]

The various parts of the plant have shown to have antifungal activity, antibacterial activity, antiulcer activity, antihypertensive and metabolic correction activity, nephroprotective activity, cardioprotective activity, antidiabetic activity, analgesic and anti-inflammatory activity, anti-mitotic activity, antioxidant activity, anti-platelet activity and diuretic activity. [7- 10]

The phytochemical analysis of the fruit wall and the seeds showed the presence of spirostanol glycosides, isoflavonoids, alkaloids, tannins and carbohydrates [11]. The berries also showed the presence of saponins, steroids and volatile oils also.[12]

MATERIALS AND METHODS:

Drugs and chemicals: Three concentrations of ethanolic extract of *Solanum torvum* (Swartz) SW.(EEST) was used for analyzing the sedative and hypnotic activity. The other drugs were diazepam obtained from Ranbaxy laboratories and phenobarbitone obtained from Abbott Pharmaceuticals. The vehicles used were normal saline and distilled water for administration of the chemicals and drugs.

Experimental Animals used in the Study: The sedative and hypnotic studies were carried out in healthy adult albino mice (*Mus musculus*).

Animals of either sex were included in the study. Body weights of the mice were selected between 20-30 grams. About hundred animals were used to study the sedative and hypnotic activity. Central Animal House, Assam Medical College (Registration No. 194/02/a/CPCSEA; dated 19/05/02) provided the required animals. They were housed in standard cages under normal temperature and were maintained on balanced diet (consisting of Bengal gram, wheat, maize and powdered soya bean in sufficient quantity) and water was provided *ad libitum* during the entire period of the experiment. They were housed in standard conditions with natural light and dark cycles. The study was duly permitted by the Institutional Animal Ethics Committee (IAEC), Dibrugarh University, Dibrugarh, Assam vide letter number (AEC/DU/29 dated 11.04.2014). And was conducted keeping in view with the CPCSEA (Committee for The Purpose of Control And Supervision of Experiments on Animals) guidelines.

Instruments used: The instruments used were Rota rod apparatus, open field apparatus and hole board apparatus.

ACUTE TOXICITY TEST: Acute oral toxicity tests for the ethanolic extract of the leaves of *Solanum torvum* SW was carried out as per OECD Guidelines 425 [13]. The limit test at 2000 mg/kg which required a total of 5 albino mice was used. The mice were fasted overnight prior to the experiment and their body weights measured.

A single dose of EEST (2000 mg/Kg body weight) dissolved as 1 ml/100 gm of body weight in Normal Saline was administered orally to the first animal with the help of a feeding tube. Food was withheld for further 3-4 hours. Based on its mortality or appearance of toxic signs and symptoms, the other four animals were dosed sequentially. The animals were observed individually at least once during the first 30 minutes after dosing, periodically during the first 24 hours (with special attention during the first 4 hours), and daily, thereafter, for a period of 14 days. Observations were done daily for changes in skin and fur, eyes and mucous membrane (nasal), respiratory rate, circulatory signs (heart rate and blood pressure), autonomic effects (salivation, lacrimation, perspiration, piloerection, urinary incontinence and defecation) and central nervous system changes (ptosis, drowsiness, tremors and convulsion). Body weights were determined weekly (Organization for Economic Cooperation and Development, 2008).

No sign of toxicity and mortality was recorded among the mice at the dose of 2000 mg/kg (for the extract); hence arbitrarily 100 mg/kg, 200mg/kg and 400mg/kg was selected for the study. A total of three doses were taken to see the dose dependent effect.

PREPARATION OF DRUG DOSES:

1. Vehicle: distilled water 10ml/kg was used in the control group.
2. Test drug: 100, 200 and 400mg/kg of ethanolic extract of the leaves of *Solanum torvum* was prepared with distilled water as the solvent.
3. Standard drugs: For sedative models: diazepam at the dose of 3mg/kg [14]. For hypnotic models phenobarbitone 50 mg/kg and diazepam 3mg/kg as positive control [15,16]. All the solutions were prepared with distilled water.

GROUPING OF ANIMALS: The animals are grouped as follows:

Table 1: Grouping of animals for Sedative activity:

Group	Number of animals	Treatment
Group A (control)	5	10ml/kg distilled water
Group B (test drug)	5	EEST 100mg/kg
Group C (test drug)	5	EEST 200mg/kg
Group D (test drug)	5	EEST 400mg/kg
Group E (standard)	5	Diazepam 3mg/kg

Table 2: Grouping of animals for Hypnotic activity

Group	Number of animals	Treatment with phenobarbitone 50mg/kg i.p
Group A (control)	5	10ml/kg distilled water
Group B (test drug)	5	EEST 100mg/kg
Group C (test drug)	5	EEST 200mg/kg
Group D (test drug)	5	EEST 400mg/kg
Group E (positive control)	5	Diazepam 3mg/kg.

EXPERIMENTAL PROCEDURES:

(A) SEDATIVE ACTIVITY:

1. **ROTA ROD TEST:** The rota rod test is used to look at the effect of a drug on the motor coordination of the animal. As sedation causes loss of motor coordination this test can be used to evaluate the sedative activity of the drug [17]. The animals are appropriately weighed and selected. A total of five mice were selected in each group. The apparatus was turned on at the speed of 25 rotations per minute. Animals were placed one by one in the rod and the fall off time is recorded i.e. when the mouse falls off from the rod. A normal mouse usually falls off within 3-5 minutes. The fall off time was recorded. For all the test groups EEST was administered at doses of 100mg/kg, 200mg/kg and 400mg/kg per orally. Diazepam (standard) 3mg/kg was injected intraperitoneally the standard group [18,19]. The fall off time is again

recorded one hour after oral drug administration and thirty minutes after i.p.[19] The percentage decrease in fall off time was then compared.

Percentage decrease in fall off time = $\frac{\text{time before drug} - \text{time after drug}}{\text{time before drug}}$. [18]

2) **OPEN FIELD TEST:** The open field test is a measure of the locomotor activity of the animals. The number of lines crossed it means the number of grid lines crossed with all the four paws; rearings which mean the frequency with which the mice stood on their hind legs; assisted rearing means the frequency of rearings with support to the wall are measured. The apparatus consist of a box of 60x60x30 cm with 16 squares each of 15x15 cm [19,20,21]. For all the test groups EEST was administered at doses of 100mg/kg, 200mg/kg and 400mg/kg per orally. Diazepam (standard) 3mg/kg was injected intraperitoneally to the standard group. After one hour of the drug administration orally and thirty minutes i.p. the animals were placed in the box and the number of lines crossed, number of rearings and number of assisted rearings were noted [18, 19, 21].

3) **HOLE BOARD TEST:** The hole board apparatus is a simple method to measure the responses of mice to novel environment [22]. The number of head pokes is a measure of its exploratory activity [15].

The apparatus consist of a wooden box (40x40x25cm) with sixteen holes (each of diameter 3cm) evenly distributed at the base of the box. The apparatus will be elevated at the height of 25cm [21]. The animals are appropriately weighed and selected. A total of five mice were selected in each group. For all the test groups EEST was administered at doses of 100mg/kg, 200mg/kg and 400mg/kg per orally. Diazepam (standard) 3mg/kg was injected intraperitoneally to the standard group. After duration of one hour of oral administration of the extract and thirty minutes after i.p. administration of the standard drug the number of head pokes and the time duration of head dipping during the five (5) minutes was recorded. [18, 19, 22]

B) HYPNOTIC ACTIVITY: Barbiturates induce sleep in man and animals by depressing the central nervous system. The onset of sleep is recognized by loss of righting reflex and the recovery is easily detected by their gain in righting reflex [18]. All the animals were weighed and numbered. For all the test groups EEST was administered at doses of 100mg/kg, 200mg/kg and 400mg/kg per orally. Diazepam was taken as a positive control at the dose of

3mg/kg i.p [59]. One hour after oral drug administration and thirty minutes after i.p. dosage phenobarbitone was injected intraperitoneally (i.p) to all the five groups. [15,19]The data were statistically analyzed by using one way analysis of variance (ANOVA) followed by Bonferroni's multiple comparison tests, using graph pad prism software.

RESULTS:

It can be seen from the table 3 that the mean fall off time for the control, In the Rota rod apparatus, the measurement of the fall off time was the standard parameter to evaluate the sedative activity 100mg/kg, 200mg/kg, 400mg/kg of EEST and diazepam 3mg/kg are 37.40±1.25, 29.00±0.31, 25.60±0.81, 14.20±0.6 and 5.00±0.45 respectively. There was a significant difference in fall off time (p<0.05) when the test groups and diazepam group are compared with the control group. As can be seen from the above table there is significant (p<0.05) decrease in fall off time when 400mg/kg is compared with 100mg/kg and 200mg/kg. The fall off time was significant (p<0.05) before and after the treatment with the extract and diazepam treated groups. The percentage decrease in time was 23% for 100mg/kg, 34% for 200mg/kg, 19% for 400mg/kg of EEST and 86% for 3mg/kg of diazepam.

Table 3: Measurement of the fall off time to evaluate the sedative activity using Rota rod apparatus

GROUPS	TREATMENT	FALL OFF TIME(sec)		Percentage decrease in time
		mean±SEM		
		Before drug	After drug	
Group A	VEHICLE/CONTROL	37.60±1.43	37.40±1.25	–
Group B	EEST 100mg/kg	38.00±0.316	29.00±0.31 ^{ad}	23
Group C	EEST 200mg/kg	38.20±0.4	25.60±0.81 ^{ad}	34
Group D	EEST 400mg/kg	38.00±0.316	14.20±0.6 ^{abcd}	19
Group E	DIAZEPAM 3mg/kg i.p.	37.80±1.530	5.00±0.45 ^{ade}	86
One Way ANOVA		P>0.05	P<0.05	

Values are expressed as MEAN ± SEM (n=5). One Way ANOVA followed by Bonferroni's Multiple Comparison test is done between the groups. ^aP<0.05 as compared with control. ^bP<0.05 as compared with group B. ^cP<0.05 as compared with group C, ^dP<0.05 Paired t test done within the groups, ^eP<0.05 as compared with groups B, C and D.

2) As seen from the table 4 the mean data for the no. of lines crossed for 100mg/kg, 200mg/kg, 400mg/kg of EEST and diazepam 3mg/kg were 56.00 ± 2.19 , 43.60 ± 2.7 , 41.60 ± 2.5 , 23.60 ± 1.25 and 12.60 ± 0.87 respectively. The $p < 0.05$ when extract and diazepam treated groups are compared with the control. It can also be seen that there is significant ($p < 0.05$) difference in reduction of number of lines crossed when 400mg/kg is compared with 100mg/kg and 200mg/kg of EEST. There is also significant decrease ($p < 0.05$) in no. of lines crossed when diazepam treated group is compared to EEST treated groups.

The mean data for the rearings are 15.80 ± 3.40 , 10.00 ± 1.05 , 9.20 ± 0.30 , 4.40 ± 0.51 and 2.00 ± 0.25 for control, 100mg/kg, 200mg/kg, 400mg/kg of EEST and diazepam 3mg/kg respectively. There was significant reduction in the number of rearings at all the three doses (100mg/kg, 200mg/kg and 400mg/kg) and diazepam as compared to the control. It can also be seen that there is significant ($p < 0.05$) difference in reduction of number of rearings when 400mg/kg is compared with 100mg/kg and 200mg/kg of EEST. The diazepam treated group also shows significant decrease ($p < 0.05$) in no. of rearings as compared to all the EEST treated groups.

The mean data for number of assisted rearings are 13.00 ± 1.22 , 8.40 ± 0.68 , 8.20 ± 0.4 , 4.60 ± 0.7 and 1.20 ± 0.20 for the control, 100mg/kg, 200mg/kg, and 400mg/kg of EEST and 3mg/kg of diazepam respectively. It can be seen that EEST (at all the three doses) and diazepam decreased the no. of assisted rearings significantly as compared to the control. It can also be seen that there is significant ($p < 0.05$) difference in reduction of number of assisted rearings when 400mg/kg is compared with 100mg/kg and 200mg/kg of EEST. The diazepam treated group also shows significant decrease ($p < 0.05$) in no. of assisted rearings as compared to all the EEST treated groups.

Table 4: Measure of locomotor activity using open field test

GROUPS	TREATMENT	No. of lines crossed	No. of rearings	No. of assisted rearings
A	VEHICLE/CONTROL	56.00 ± 2.19	15.80 ± 3.40	13.00 ± 1.22
B	EEST 100mg/kg	43.60 ± 2.7^a	10.00 ± 1.05^a	8.40 ± 0.68^a
C	EEST 200mg/kg	41.60 ± 2.5^a	9.20 ± 0.30^a	8.20 ± 0.4^a
D	EEST 400 mg/kg	23.60 ± 1.25^{abc}	4.40 ± 0.51^{abc}	4.60 ± 0.7^{abc}
E	Diazepam 3mg/kg	12.60 ± 0.87^{ad}	2.00 ± 0.25^{ad}	1.20 ± 0.20^{ad}
One Way ANOVA		$P < 0.05$	$P < 0.05$	$P < 0.05$

Values are expressed as MEAN \pm SEM (n=5). One Way ANOVA followed by Bonferroni's Multiple Comparison test is done between the groups. ^aP< 0.05 when compared with control group. ^bP<0 .05 when compared with group B. ^cP<0 .05 when compared with group C. ^dP<0.05 as compared with groups B, C and D.

As described in table 5 the mean no. of head pokes are 38.40 \pm 0.37, 25.80 \pm 0.37, 23.60 \pm 0.60, 9.00 \pm 0.27, and 4.00 \pm 0.25 for the control, 100mg/kg, 200mg/kg, 400mg/kg of EEST and 3mg/kg of diazepam respectively. EEST at all the three doses (100mg/kg, 200mg/kg and 400mg/kg) showed significant (P<.05) reduction in the number of head pokes as compared with the control. There is also significant (p<.05) difference in reduction of number of head pokes when 400mg/kg is compared with 100mg/kg and 200mg/kg of EEST. The diazepam treated group also shows significant decrease (p<.05) in no. of head pokes as compared to all the EEST treated groups.

The mean data for the duration of head pokes are 35.20 \pm 0.6, 26.80 \pm 1.25, 22.40 \pm 2.11, 10.00 \pm 0.84 and 5.00 \pm 0.25 for the control, 100mg/kg, 200mg/kg, and 400mg/kg of EEST and 3mg/kg of diazepam respectively. EEST at all the three doses (100mg/kg, 200mg/kg and 400mg/kg) showed significant (P<.05) reduction in the duration of head pokes as compared with the control. There is also significant (p<.05) difference in reduction of duration of head pokes when 400mg/kg is compared with 100mg/kg and 200mg/kg of EEST.

The diazepam treated group also shows significant decrease (p<.05) in duration of head pokes as compared to all the EEST treated groups.

Table 5 Measure of number of head pokes for exploratory activity using hole board apparatus

GROUPS	NO. OF HEAD POKES mean \pm SEM	DURATION OF HEAD POKES (min) mean \pm SEM
Group A – Vehicle /control	38.40 \pm 0.37	35.20 \pm 0.6
Group B- EEST 100 (mg/kg) p.o.	25.80 \pm 0.37 ^a	26.80 \pm 1.25 ^a
Group C- EEST 200 (mg/kg) p.o.	23.60 \pm 0.60 ^a	22.40 \pm 2.11 ^a
Group D- EEST400 (mg/kg) p.o.	9.00 \pm 0.27 ^{abc}	10.00 \pm 0.84 ^{abc}
Group E- Diazepam 3mg/kg i.p.	4.00 \pm 0.25 ^{ad}	5.00 \pm 0.25 ^{ad}
One Way ANOVA	P<0.05	P<0.05

One Way ANOVA followed by Bonferroni's Multiple Comparison test is done between the groups.^a $P < 0.05$ when compared with control group, ^b $P < 0.05$ as compared with group B, ^c $P < 0.05$ as compared with group C, ^d $P < 0.05$ as compared with groups B, C and D.

As illustrated in table 6 the mean data's for the onset of sleep are 9.20 ± 0.37 , 9.40 ± 0.40 , 9.60 ± 0.40 , 9.20 ± 0.37 and 4.00 ± 0.27 for the control, 100mg/kg, 200mg/kg, 400mg/kg of EEST and 3mg/kg of diazepam respectively. There is no significant decrease in the latency in onset of sleep in all the three doses (100mg/kg, 200mg/kg and 400mg/kg) as compared to the control. But the diazepam treated group shows a significant ($p < 0.05$) reduction in the onset of sleep as compared with control.

As seen from the table 5 the mean data for the duration of sleep for the control, 100mg/kg, 200mg/kg, 400mg/kg of EEST and 3mg/kg of diazepam are 33.20 ± 2.3 , 44.00 ± 2.1 , 52.00 ± 2.5 , 82.80 ± 2.5 and 118.00 ± 2.6 respectively. EEST at all three doses (100mg/kg, 200mg/kg and 400mg/kg) significantly increase ($p < 0.05$) the duration of sleep as compared to the control. It also shows significant ($p < 0.05$) increase in the duration of sleep when 400mg/kg of EEST is compared with 100mg/kg and 200mg/kg. The diazepam treated group also shows significant increase ($p < 0.05$) in duration of sleep as compared to all the EEST treated groups.

Table 6 Measure of Onset of Sleep and Duration of Sleep for Evaluation of Hypnotic Activity

GROUPS	Treatment	Onset of sleep mean \pm SEM (min)	Duration of sleep mean \pm SEM(min)
A	Vehicle/CONTROL	9.20 ± 0.37	33.20 ± 2.3
B	EEST 100mg/kg	9.40 ± 0.40	44.00 ± 2.1^b
C	EEST 200mg/kg	9.60 ± 0.40	52.00 ± 2.5^b
D	EEST 400mg/kg	9.20 ± 0.37	82.80 ± 2.5^{bcd}
E	DIAZEPAM 3mg/kg	4.00 ± 0.27^a	118.00 ± 2.6^{bc}
One way ANOVA		$P < 0.05$	$P < 0.05$

Values are expressed as MEAN \pm SEM (n=5). One Way ANOVA followed by Bonferroni's Multiple Comparison test is done between the groups.^a $P < 0.05$ when compared with control, ^b $P < 0.05$ when compared with control, ^c $P < 0.05$ when compared with group B, ^d $P < 0.05$ when compared with group C, ^e $P < 0.05$ as compared with groups B, C and D.

Thus from the results as illustrated above in all the tables it was seen that EEST has got significant sedative and hypnotic activities as compared to the control group and has also shown dose dependent activity; but the standard drug diazepam has got better action in both.

DISCUSSION:

The purpose of the present study was to evaluate the sedative effect of ethanolic extract of leaves of *Solanum torvum* SW on diazepam induced sedation in mice in standard exploratory neurobehavioral models and to elucidate their probable mechanism of action. The present study also aimed at evaluating the hypnotic action on Phenobarbital induced sleeping time in albino mice. In this study to evaluate the sedative action of the extract a total of 25 albino mice were selected to undergo neurobehavioral experiment with diazepam at the dose of 3mg/kg on the rota rod apparatus, open field apparatus and hole board apparatus. Three arbitrary doses of the extract at 100mg/kg, 200mg/kg and 400mg/kg were selected. This was done to look for the dose dependent action of the extract and to compare the effects of the standard sedative dose of diazepam.

In the rota rod apparatus the measurement of the fall off time was the standard parameter to evaluate the sedative activity. It was seen that there was a significant decrease in the fall of time as compared with all the three doses of the extract and the control group. There was a significant difference in fall off time ($p < 0.05$) when the test groups and diazepam group are compared with the control group. As can be seen there was significant ($p < 0.05$) decrease in fall off time when 400mg/kg was compared with 100mg/kg and 200mg/kg. So, it could be seen that the extract has got dose dependant activity.

The locomotor activity of the mice is examined in the open field test. It is seen that mice in a novel environment tends to explore the environment and as a result increase their movements. On the other hand mice tend to avoid the bright and open spaces that tend to evoke fear and anxiety which is expressed by rearings, grooming, defecation, and locomotion and so on. The inhibition of this ambulatory behaviour by any drug or extract shows that the drug has got sedative or central nervous system depressant property [22].

In the open field apparatus it was seen that there was significant ($p < 0.05$) reduction in the no. of lines crossed when extract and diazepam treated groups are compared with the control. It could also be seen that there was significant ($p < 0.05$) difference in reduction of number of lines crossed when 400mg/kg was compared with 100mg/kg and 200mg/kg of EEST.

There was significant reduction in the number of rearings at all the three doses (100mg/kg, 200mg/kg and 400mg/kg) and diazepam as compared to the control. It could be seen that there was significant ($p < .05$) difference in reduction of number of rearings when 400mg/kg is compared with 100mg/kg and 200mg/kg of EEST.

It was seen that EEST (at all the three doses) and diazepam decreased the number of assisted rearings significantly as compared to the control. It was also seen that there was significant ($p < .05$) difference in reduction of number of assisted rearings when 400mg/kg was compared with 100mg/kg and 200mg/kg of EEST. The diazepam treated group also showed significant decrease ($p < .05$) in no. of assisted rearings as compared to all the EEST treated groups.

Thus it can be said that the EEST has got significant effect in reducing the locomotor activity in the open field test and has shown a dose dependent activity at all the three doses of the extract.

The hole board apparatus is a simple method to measure the responses of animals in a novel environment. [22]

In the hole board apparatus, EEST at all the three doses (100mg/kg, 200mg/kg and 400mg/kg) showed significant ($p < .05$) reduction in the number of head pokes as compared with the control. There was also significant ($p < .05$) difference in reduction of number of head pokes when 400mg/kg was compared with 100mg/kg and 200mg/kg of EEST. Also, EEST at all the three doses (100mg/kg, 200mg/kg and 400mg/kg) showed significant ($p < .05$) reduction in the duration of head pokes as compared with the control. There was also significant ($p < .05$) difference in reduction of duration of head pokes when 400mg/kg was compared with 100mg/kg and 200mg/kg of EEST. Thus it could be seen that EEST has got significant reduction in the exploratory activity as compared with the control and has also shown dose dependent activity.

On assessing the hypnotic activity with Phenobarbital induced sleeping time in mice it was seen that the extract showed significant increase in sleep duration at 100mg/kg, 200mg/kg and 400mg/kg doses as compared with the vehicle group, this was in accordance with the study carried out by Moh et al where there was a significant increase in sleep time in Phenobarbital induce sleep in mice [23]. But regarding the onset of sleep it was seen that the Ethanolic extract of the leaves of *Solanum torvum* SW. did not show any significant difference in the three doses.

Diazepam which belongs to the benzodiazepine group is central nervous system depressants used in the management of sleep disorders such as insomnia. Benzodiazepines have a binding site on GABA receptor type-ionophore complex (GABA_A). They decrease activity, moderate excitement and calm the recipient. Substances like diazepam (the standard drug used in this study) reduce onset of and increase duration of barbiturate-induced sleep and reduce exploratory activity possessing potentials as sedative and hypnotic. Diazepam is a very well-known anxiolytic benzodiazepine which produces not only anxiolytic-like effect, but also important sedative action. The inhibitory action of GABA consists in the opening of chloride channels to allow hyperpolarization of the membrane, leading to CNS depression and resulting in sedative and hypnotic activity. Glutamate and GABA are quantitatively the most important excitatory and inhibitory neurotransmitters, respectively, in the mammalian brain. Thus, receptors for these two neurotransmitters are regarded as the important targets for psychotropic drugs. In the test of pentobarbital-induced sleeping in mice, the potentiated effect of hydroalcoholic extract of *Asperugo procumbens* was represented. It not only prolonged the sleeping time, but also decreased the latency of falling asleep and increased the sleep onset. Since the effect of barbiturates on the CNS involves activating of the inhibitory GABAergic system. [24]

Barbiturates appear to act primarily at the GABA BZD receptor complex and increases the Gabanergic transmission by increasing the lifetime of chloride channel complex. at higher doses it has got depressant action on the on calcium dependent neurotransmitter release and inhibition of the sodium and potassium channels which is a possible cause for showing the hypnotic property. [25]

Earlier reports on the chemical constituents of the plants and their pharmacology suggest that plants containing flavonoids, saponins and tannins possess activity against many CNS disorders. Phytochemical tests of *Fagonia cretica* Linn revealed the presence of saponin and flavonoid. It may possible that the mechanism of anxiolytic action of *Fagonia cretica* could be due to the binding of any of these phytochemicals to the GABA_A-BZD complex. In support of this, it has been found that flavones bind with highaffinity BZD site of the GABA_A receptor. [26]

Another study carried out by Al Mamoon showed that plant with similar chemical constituent like mine showed a significant decrease in locomotor activity. [27]

Albizzia julibrissin flowers are used as sedatives in oriental traditional medicine. The phytochemical study of this plant led to the isolation of two flavonol glycosides, quercetin and isoquercitrin. These compounds were observed to increase pentobarbital-induced sleeping time in a dose-dependent manner in mice. It was reported by Marder et al., (2003) that the flavonoid 2S (-)-hesperidin isolated from *Valeriana officinalis* has sedative and sleep enhancing properties whereas 6-methylapigenin also isolated from *Valeriana officinalis* exhibited ability to increase the sleep enhancing properties of hesperidin. The phytochemical screening of *Myricaria elegans* Royle (Tamaricaceae) led to the isolation of six terpenes from the chloroform fraction (Eleganene-A, eleganene –B, Corsolic acid, Betulin, Ursolic acid and Erythrodiol). These compounds were suggested by the researchers to be responsible for the mild sedative activity of the plant. [28]

In a study carried out by Jiang G on the semen of *Ziziphus jujuba* it was seen that flavonoids, saponins and polysaccharides has got significant effect in reducing the locomotor activity in mice. It was also observed that these ingredients have significant sleep inducing and maintenance property in barbiturate induced sleeping time in mice. [29]

In a study done by Ramapalli et al on the sedative activity on *Allium cepa* it was proposed that flavonoids and saponins were the phytochemical responsible for the sedative and hypnotic activity. [30]

Other studies have shown that the alkaloids, flavonoids, saponins and tannins may have sedative and hypnotic properties. [31,32]

As can be seen from the above studies that flavonoids and saponins were found to have sedative and hypnotic property and as preliminary phytochemical analysis of my plant reveals the presence of flavonoids and saponins, it can be said that the potential sedative and hypnotic activity of my plant is probably due to the presence of these phytochemical.

CONCLUSION:

The Ethanolic extract of the leaves of *Solanum torvum* on experimental models produced significant muscle relaxation, showed significant decrease in exploratory behaviour and locomotor activity which are definite signs of sedation. The extract also showed significant hypnotic action by prolonging the phenobarbitone induced sleeping time. Both the sedative

and hypnotic activities of the extract are dose related. The efficacy of the extract was compared with the standard sedative and hypnotic drug diazepam.

Solanum torvum was used in traditional medicine as digestive, diuretic, haemostatic, analgesic, anti-inflammatory, sedative hypnotic and cough remedies etc. Some phytochemical constituents present in *Solanum torvum* like flavonoids, saponins, terpenes, tannins etc. were found to be responsible for the medicinal property of the plant. However, there is need for evaluation of the molecular and biochemical basis of sedative and hypnotic action of *Solanum torvum* on other animals and human that may provide definite data for its safety, efficacy, cost and therapeutic use. So more emphasis should be laid upon development of more purified products from *Solanum torvum* so that it may be proved as a safe and effective sedative and hypnotic drug.

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