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Research Article

An Investigation of Antiepiletic Activity of Plant Extracts in Experimental Animals

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Abstract

The current study is done on plant extracts as antiepileptic medication in ayurvedic formulation. The convulsions are induced by electro shock therapy or picrotoxin, strychnine/brucine. After induction of convulsion the plant extract is administered as standard group, control group and simple group of six albino rats and the results are screened and analyzed with standard drug comparision. Pre-treatment of MEIR (methanolic extract of *Ipomoea reniformis*) for 15days at the dose of 200 and 400 milligram per kilogram body weight was used to evaluate antiepileptic activity. The antiepileptic activity was studied against seizures induced by Maximum electro shock (MES) in rats, Isoniazid (INH) and Pentylenetetrazol (PTZ) in mice.. In pre-treatment studies of antiepileptic activity, MEIR significantly ($p<0.01$) reduced the tonic hind limb extensor phase in MES model at 400milligram per kilogram body weight, while in INH, PTZ models at the dose of 200 and 400 milligram per kilogram body weight MEIRsignificantly ($p<0.01$) delayed the onset of clonic and tonic convulsions. The results of the Pr (+) study suggest that the MEIR possess antiepileptic activity in rats and mice. The results of each activites are compared with standard medicament and evaluated.

Keywords: *Ipomoea reniformis*, maximal electroshok, isoniazid, pentylenetetazol, convulsions, antiepileptic activity

1. INTRODUCTION

Epilepsy comes from the word Epilambian means to seize. The disease is found from old time and the cause was considered as supernatural and treatment is considered as magic[1]. The extra neuronal discharge is released in the brain that causes seizures. Convulsions can be produced in laboratory animals and the medicines that treat these convulsions are known as anti-convulsant. The epilepsy may be idiopathic or sympatomatic in nature. Idiopathic epilepsy is caused by unknown resons while sympatomatic may be due to accidental brain injury or brain hemorrhage or other organic syndrome causes epilepsy[2].

The epilepsy can be created in laboratory experminatal animals like rat, mice, rabit, dog with two methods. First method is maximal electroshock threshold technique in which electricshock of fixed voltage is given to the laboratory experimental animals and animal goes to convulsion due to extra neuronal discharge. The second method is chemically induced convulsion in which medicament is administered to the laboratory expermimental animal that causes central nerous system excitation due to GABAergic block and cause extra neurone discharge that produce convulsions in experimental animals. The medicaments are strychnine, metrazole, bicuculline and other analeptic medicaments[3].

The animal is treated with different antiepileptic medicine to prevent convulsion in experimental rats. The epilepsy may be classified in partial and general epeilepsy. The partial epilepsy may be local-focal or simple type in which patient is in consciousness and one part or hemisphere of body is effected while in complex patial seizures both hemispheres are affected and patient goes to unconsciousness. The general type epilepsy is divided in absences that may be typical and atypical. The atypical seizures or absences are found in children and known as petimal epilepsy. Other epilepsies are tonic, clonic, myoclonic and generalized or tonic-clonic epilepsy in which patient goes to unconsciousness and this type of epilepsy is known as grandmal epilepsy and found in adults and elderly patients. There are unkown incidents in this period like patient runs and aura is generated that is stired and one type of activity is done with the patient like beating of tongue or jerking of arms and leges with tremors. When

patient comes to in conciousnes he does not know about these activities done by hime during seizures or absences[4].

2. MATERIALS AND METHODS

METHODOLOGY

Extraction of *Ipomoea reniformis*

This collected material was washed two times and then dried over night. This is then crushed and powdered and passed from sieve no 22 for unique particle size. This was then packed in column with n-hexane to remove fatty material and collected after 48 hours. Then it was packed in soxlet apparatus with methyl alcohol solvent to extract the active constituent from the material and the extract was washed to remove the methanol solvent and dried to make powder and for application. The clear solution was collected in siphon tube for further use[5].

Quality control and Screening of constituents

This process was performedagain and again till it gives fixed weight. Total ash % was determined by consideration with weight of initialpowder of plant material. Can be calculated as Total ash (% w/w) = (Wt. of ash/ sample Wt.) × 100 Acidinsoluble ash 2 gm of dried powder was added in pre weighed crucible of silica and burned at high temp lessthan 4500C until free from carbon. It was determined by cooling the silica dish in desiccator and weighted.The same process was repeated till constant weight was obtained[6]. The ash obtained was mixed in 25 milliliter 2MHCl and boiled upto 7 min. Then not soluble content had been added in a silica crucibles. Again hot water addedand filtered, then burned and cooled in a desiccator, weight was taken. The percentage was determined byconsidering initial weight of plant material.

Water soluble ash Powder was taken and 2 gm powder was added in previously weighed crucible of silicaand it was then kept at high temperature not more than 4500C until it became free from carbon. It was determined by cooling the silica crucible in desiccator and weighted. The same process was repeated untilconstant weight was identified. The ash thus obtained was further boiled water was collected by filtration insilica plate and washed. The content was burned for few minutes at high temp. but not more than 4500C.

It was then heated at hightemperature not more than 4500C until it became free from carbon. It was determined by cooling the silicacrucible in desiccator and weighted. The same process was repeated till constant weight was identified. Theash obtained was mixed with 1 milliliter H2SO4, heated until release of white colored fumes finished, Furtherignited at 8000 ± 250C till all black particles get disappeared[7]. The heating was done away from direct air.The silica crucible was cooled. Again few drops of H2SO4 were added and ignited again. This process wasdone repeatedly to get constant weight. 2) Determination-Extractive values Water-soluble extractive valueMethod: 5 gm plant material powder was weighed was added in closed flask and kept for maceration in chloroform water (100 milliliter) then for 18 hours kept aside and filter. The percentage was determined byconsidering initial weight of plant material. Calculations: If twenty five milliliter aqueous filtrate produces X g of PPt, Then 100 milliliter of filtrate will give 4X g of residue, So 5 gm of powdered plant material contains 4X g of water soluble residue,So water soluble extractive value will be 80X. Alcohol-soluble extractive value: Method: Accurately weighed5 gm of powdered plant material was mixed with 95% ethanol (100 milliliter) in a closed vessel. It was maceratedfor 24 hours with occasional shaking for initial six hrs. Kept aside for 18 hours and filtered carefully to avoidevaporation of ethanol. Filtrate (25 milliliter) was evaporated in pre weighed porcelain dish, weight wascalculated. The percentage of alcohol soluble extractive value was determined by considering initial weightof powdered plant material stem. Calculations: 25 milliliter of alcohol filtrate possess about A g of residue, So 100milliliter of filtrate contains 4A gm of residue. Then this 100milliliter filtrate was prepared from 5 gm of powdered plantmaterial. So 5 gm of powdered plant material contains 4A gm of residue. And percentage of extractive valuewill be 80A gm of alcohol (90%) soluble residue Extractive Value (% w/w) = [(Wt. of residue ×100) / (25×sample wt.)] × 100 3) Determination of Crude fibre %w/w of crude fiber= (Wt. of dried residue - wt. ofincinerated residue)*100 Wt. of dried Sample 4) Determination of Volatile oil content Wt. of volatile oilcollected 5) Determination of swelling index According to the experiment protocol for each specific plant material, itis determined by adding water or a swelling agent (1 g) (whole, cut or pulverized). 6) Determination offoaming index Foaming index= = the volume of the decoction used for preparing the dilution Where foaming- 1 cm is observed. 7) LOD: The shallow glass-stopper weighing bottle was dried and weighed. 2g crudedrug was added in the bottle and closed, the weight was taken and crude drug was spread evenly to aheight not more than 10mm. Then the bottle was kept in the oven for drying keeping open without stopper. Again weighed loss on drying was calculated in percent w/w (Indian pharmacopoeia 1996)[8]. LOD=Loss in wt./sample wt. *100

Experiments to Examination of Antiepileptic Activity

1. Effectiveness of *Ipomoea reniformis* pre-treatment on Maximal electro shock induced convulsions:

Rationale and Purpose

This electro shock assaying in rats had been utilized particularly as an generation of stimulis for medicaments that have been useful in grandmal convulsion. The extensions of tonic hind limb have been generated by maximal lectroshok that has been treated with anti-convulsant medicaments and with other antiepileptic medicaments. In MES- convulsions electro shock is applied through the ear electrodes. The Maximal Electroshock convulsion have been given in five phases[9].

(a) Tone flextion

(b) Tone extenssor

(c) Clone seizures

(d) Stuporness

(e) Recoveriness / deathing

A medicament is being called to have antiepileptic action if this decreases or removes their extenssor phase of Maximal Electroshock seizures[10].

Figure 1: Convulsometer

Table 1:- Experimental design 1

Group (n=6)	Dose along with treatment	Observation
I	MES control (0.5% weight by volume SCMC l milliliter/100 g, peroral) +MES	Tonic extension of the hind limbs
II	Phenytoin (90 milligram per kilogram, intraperitonial) + MES	
III	*Ipomoea reniformis* (200 milligram per kilogram, peroral) + MES	
IV	*Ipomoea reniformis* (400 milligram per kilogram, peroral) + MES	

Procedure

Rats had been categoriezed into 4 grps of 6 rats everyone. Grp 1 administered 0.6 percent weight by volume SCMC l milliliter/100 g, peritonial. and known as MES controlling whereas Grp 2 administered standard medicine Phenytoin 90 milligram per kilogram, intraperitonial, Grp III and IV given MEIR (200 and 400 milligram per kilogram , peroral) respectively for 15 days. On the15th day, an hour after the administration of 0.5% weight by volume SCMC l milliliter/100 g, peroral in Grp I, two along with four hundred milligram per kilogram of MEIR in Grp 3 and 4 respectively and 30min after the administration of Phenytoin in Grp 2, Maximal Electroshock convulsions had been induced by electro convulse meter. A 155 milli Ampere current had been passed tran sauricular for 0.2 seconds in albino rats. The intensity of current had been generated completely tone expansion of their legs in controlling grp. Different stages of seizures, for examples. tone expansion (Tonic Phase, stupor and death because of seizures, had been timed out. The duration of tonic hind limb extension was noted[11].

2. Effect of *Ipomoea reniformis* on Isoniazid induced convulsionsPurpose and rationale

INH may induce seizures in patient with epileptic diseases and disorders. This medicament is known to be Gama Amino Butyric Acid synthetic inhibitor. Clonefull seizure, tonic convulsions had been generated into mice, that had been anta gonized by anti anxiety medicines.

Talbe 2:- Experimental design 2

Grp (n=6)	Dose along with treatment	Observation
I	INH control (0.5% weight by volume SCMC l milliliter/100 g, peroral) + Isoniazid (300 milligram per kilogram, intraperitonial)	Occurrence of tonic-clonicseizure
II	Diazepam (5 milligram per kilogram, intraperitonial) + INH(300 milligram per kilogram, intraperitonial)	
III	*Ipomoea reniformis* (200 milligram per kilogram,peroral) + INH (300 milligram per kilogram, intraperitonial)	
IV	*Ipomoea reniformis* (400 milligram per kilogram, peroral) +INH (300 milligram per kilogram, intraperitonial)	

Procedure

Mice had been categorized into 4 Grps of 6 mice everyone. Grp 1 had been given 0.55 pcent weight by volume SCMC l milliliter/100 g, peroral and also known as INH controlling, Grp 2 administered standard medicine Diazepam 6 milligram per kilogram, intraperitonial, Grp 3 and 4 administered MEIR (200 along 400 milligram per kilogram peroral) continually for 15 days. On the 15th day, an hour after the administration of 0.5% weight by volume SCMC l milliliter/100 g, peroral in Grp 1, 200 along with 400 milligram per kilogram of MEIR in Grp 3 and 4 respectively and 30 min after the administration of diazepam in Grp II, all Grps received INH 300 milligram per kilogram, intraperitonial After giving INH these mice had been replaced into isolation per-plex box, duration of further 2 hours for occurring of clonefull type convulsions, tonefull convulsion along with death had been noted. Percent of convulsions or death found into control Grp wasreceived as hundred percent. These suppress conditions of the actions in the treatment Grps is called as percent of controlling grp[12].

3. Effect of *Ipomoea reniformis* on Pentylenetetrazol (PTZ) induced convulsions Purpose and rationale

Pentylenetetrazo generated seizures show the petitmal of convulsions also that had been particularly useful as model of animal to examine anticonvulsant medicaments. Pentylenetetrazole has also capacity to inhibit conducting power of post synape $GABA_A$ receptors generated Chloride- conducting along with thus produce seizures[13].

Talbe 3:- Experimental design 3

Grp(n=6)	Dose along with treatment	Observation
I	PTZ control (0.5% weight by volume SCMC l milliliter/100 g, peroral) + PTZ (80 milligram per kilogram, intraperitonial)	
II	Diazepam (5 milligram per kilogram, intraperitonial) + PTZ (80 milligram per kilogram, intraperitonial)	Occurrence of tonic-clonic seizure
III	*Ipomoea reniformis* (200 milligram per kilogram, peroral) + PTZ (80 milligram per kilogram, intraperitonial)	
IV	*Ipomoea reniformis* (400peroral) + milligram per kilogram, PTZ (80 milligram per kilogram, intraperitonial)	

Procedure

Mice were categorized to 4 Grps of 6 animal mice each. Grp 1 obtained 0.52 percent weight by volume SCMC l milliliter/100 g, peroral also known to be PTZ controlling whereas Grp 2 given standardizd medicament Diazepam 5.5 milligram per kilogram, intraperitonial, Grp 3 and 4 obtained MEIR 200 along 400milligram per kilogram, peroral progressively for 15 days. On the15th day, an hour after the administration of 0.5% weight by volume SCMC l milliliter/100 g, peroral in Grp I, 200 along 400 milligram per kilogram of MEIR in Grp 3 and 4 respectively and 30min after the administration of diazepam in Grp II, all Grps received Pentylene tetrazole 85 milligram per kilogram, intraperitonial The mice had been kept into separated per-plex boxes, further for hour restness occurring of clone typ convulsions, tone type convulsions then deathing is obtained. This percent of convulsions or deaths obtaining in controlling Grp had been tconsidered as hundred percentage. Deppression of the actions in these treatement Grps is collected as percent of controings[14].

3. RESULTS AND DISCUSSION

A) Maximal electroshock induced convulsions

Table 2 and Figure 9 illustrate the effect of *MEIR* pre-treatment (15 days) at different dose levels (200 and 400 milligram per kilogram, peroral) in Grp III and IV respectively, Phenytoin (90 milligram per kilogram, intraperitonial) in Grp II and MES control (Sodium Carboxy Methyl Cellulose (SCMC) l milliliter/100 g, peroral) against MES induced convulsions. The duration of hind limb extension and onset of stupor for the MES control Grp was 24.00±1.155 s and 98.33±7.098 s after an electric shock (150 mA current was delivered transauricularly for 0.2 sec in MES control rats). The animals pre-treated with *MEIR* 200 milligram per kilogram, peroral, showed increase in the extensor phase of convulsions and significantly ($p<0.05$) reduced stupor phase as compared to MES control animals. But, higher dose of *MEIR* (400 milligram per kilogram, peroral) significantly ($p<0.01$) reduced the hind limb extensor phase and decrease in stupor phase of convulsion as compared to MES control animals. Standard antiepileptic drug Phenytoin (90 milligram per kilogram, intraperitonial) pre-treatment completely abolished the hind limb extensor phase and produced significant reduction in stupor phase of convulsion.

B) Isoniazid induced convulsions

Effect on onset of convulsion: The effect of *MEIR* pre-treatment (15 days) on mice at the dose levels (200 and 400 milligram per kilogram, peroral) in Grp III and IV respectively, Diazepam (5 milligram per kilogram, intraperitonial) in Grp II and INH control (SCMC l milliliter/100 g, peroral) against INH induced convulsions are Pr (+)ed in the **Table 3 and Figure 10**. The onset of clonic and tonic actions induced by INH in the INH control mice was found to be 1380 ± 34.64, 1990 ± 71.69 respectively. The mice pre-treated with *MEIR* at the dose of 200 milligram per kilogram, peroral inGrp III and IV, Diazepam (5 milligram per kilogram, intraperitonial) in Grp II and PTZ control delayed the onset of convulsion as well as tonic action compared to INH control mice but was found to be statistically non-significant. However the higher dose of *MEIR* (400 milligram per kilogram, peroral), exhibited significant ($p<0.01$) effect as compared to INH control mice. The pre-treatment of rats with diazepam (5 milligram per kilogram, intraperitonial) significantly ($p<0.001$) delayed the onset of clonic convulsions as well as tonic actions compared to INH control mice.

Percentage protection against mortality: The pre-treatment of animals with *MEIR* 200 and 400 milligram per kilogram, peroral, had shown 50% and 83.33% of protection respectively compared to the 0.00% protection of INH control Grp. Standard antiepileptic drug Diazepam (5 milligram per kilogram, intraperitonial) had shown 100% protection.

C) Pentylenetetrazol induced convulsions

Effect on onset of convulsion: **Table 4 and Figure 11** Pr (+)s the effect of *MEIR* pre- treatment (15 days) on animals at the dose levels (200 and 400 milligram per kilogram, peroral) in Grp III and IV, Diazepam (5 milligram per kilogram, intraperitonial) in Grp II and PTZ control (SCMC l milliliter/100 g, peroral) against PTZ induced convulsions. The onset of clonic and tonic actions induced by PTZ in the PTZ control animals was found to be 180 ± 20.66, 250 ± 42.19 respectively. Pre-treatment of animals with *MEIR* at the dose of 200 milligram per kilogram, peroral, delayed the onset of clonic convulsion and significantly ($p<0.05$) delayed the tonic convulsion compared to PTZ control Grp. However the higher dose of *MEIR* (400 milligram per kilogram, peroral,) exhibited significant ($p<0.01$) effect as compared to PTZ control. Absence of convulsions was observed in animals treated with standard antiepileptic drug Diazepam (5 milligram per kilogram, intraperitonial).

Percentage protection against mortality: The pre-treatment of animals with *MEIR* 200 and 400 milligram per kilogram, peroral, had shown 33.33% and 100.00% of protection respectivelycompared to the 0.00% protection of PTZ control Grp animals. Standard anti-epileptic drug Diazepam (5 milligram per kilogram, intraperitonial) had shown 100% protection.

D) Apomorphine induced stereotype behavior

Table 5 and Figure 12 depicts the effect of *MEIR* pre-treatment (15 days) on rats at the dose levels (200 and 400 milligram per kilogram, peroral) in Grp III and IV, Haloperidol (1 milligram per kilogram, intraperitonial) in Grp II and Apomorphine control (SCMC l milliliter/100 g, peroral) against Apomorphine induced stereotype behavior at 10 to 90 min time intervals. The intensity of stereotyped behavior in Apomorphine control Grp was accessed according to scoring system which was found to be 4 (Constant stereotyped activity maintained at one location) and 5 (Constant stereotyped activity but with bursts of licking or gnawing and biting) respectively. Rats pre-treated with 200 milligram per kilogram, peroral, dose of *MEIR* showed significant ($p<0.001$) reduction in stereotyped score at 70, 80 and 90 min intervals. Pretreatment of rats with 400 milligram per kilogram, peroral, dose of *MEIR* exhibited significant ($p<0.001$) reduction in stereotyped score at 60, 70, 80 and 90 min intervals. Standard antipsychotic drug HAL (1 milligram per kilogram, intraperitonial), blocked stereotyped behavior at 30 to 90 min time intervals.

E) Pilocarpine induced purposeless chewing

The effect of *MEIR* pre-treatment (15 days) on rats at the dose levels 200 and 400 milligram per kilogram, peroral in Grp III and IV respectively, Scopolamine (1 milligram per kilogram, intraperitonial) in Grp II and Pilocarpine control (0.5% weight by volume SCMC l milliliter/100 g, peroral) against Pilocarpine induced purposeless chewing is Pr (+)ed in the **Table 6 and Figure 13**. Pilocarpine induced purposeless chewing in Pilocarpine control rats which was found to be 780.0 ± 12.59 chewing's in 30 min duration. Pre-treatment of rats with *MEIR* 200 and 400 milligram per kilogram, peroral, significantly and dose dependently decreased the number of chewing ($p<0.01$) as compared to Pilocarpine control rats. Scopolamine (standard drug) reduced significantly ($p<0.001$) the number of chewing's in Grp II rats when compared to Pilocarpine controlrats.

F) Apomorphine induce climbing behavior

Table 7 and Figure 14 illustrates the outcome of *MEIR* pre-treatment (15 days) on mice at the dose levels (200 and 400 milligram per kilogram, peroral) in Grp III and IV, Haloperidol (0.1 milligram per kilogram, intraperitonial) in Grp II and Apomorphine control (0.5% weight by volume SCMC l milliliter/100 g, peroral)against Apomorphine induced climbing behavior at 10 to 30 min time intervals. The intensity of climbing behavior in Apomorphine control Grp was accessed according to scoring system which was found to be 1 (forefeet holding the vertical bars) and 2 (four feet holding the bars) respectively. Pre-treatment of animals with 200 milligram per kilogram, peroral, dose of *MEIR* showed significant reduction in climbing score at 20 ($p<0.05$) and 30 ($p<0.001$) min time intervals. Pre-treatment of animals with 400 milligram per kilogram, peroral, dose of *MEIR* had also showed significant reduction in climbing score at 20 ($p<0.01$) and 30 ($p<0.001$) min intervals. Standard antipsychotic drug HAL (0.1 milligram per kilogram, intraperitonial) blocked the climbing behavior in mice.

TABLES AND FIGURES, PRE-TREATMENT DOSE STUDY

Table 4: Effect of MEIR on MES induced convulsions in rats.

Grps	Treatment	Various phases of convulsions (Sec)		
Dose (milligram/kilogram) by peroral		Extension	Stupor	Recovery/ Death
I	M.E.S. Control	25.00 ± 1.435	97.78 ± 6.945	Recovery
II	Phenytoin (90 mg)	Nil	41.00 ± 7.924	Recovery
III	MEIR (200 mg)peroral	30.68 ± 3.68	67.00 ± 8.27	Recovery
IV	MEIR (400 mg) peroral	15.00 ± 0.87	55.16 ± 6.123	Recovery

Values have been given in mean ± standard error mean (n=6)

Grp I = Maximal Electroshok control (0.5% weight/vol sodium carboxymethyl cellulose 1 milliliter per 100 gram peroral + electric shock)

Grp II = Phenytoin (90 milligram per kilogram orally + electric shock)

Grp III = Methanolic extract of Ipomoea reniformis (200 milligram per kilogram by orally + electric shock)

Grp IV = Methanolic extract of Ipomoea reniformis (400 milligram per kilogram by orally + electric shock)

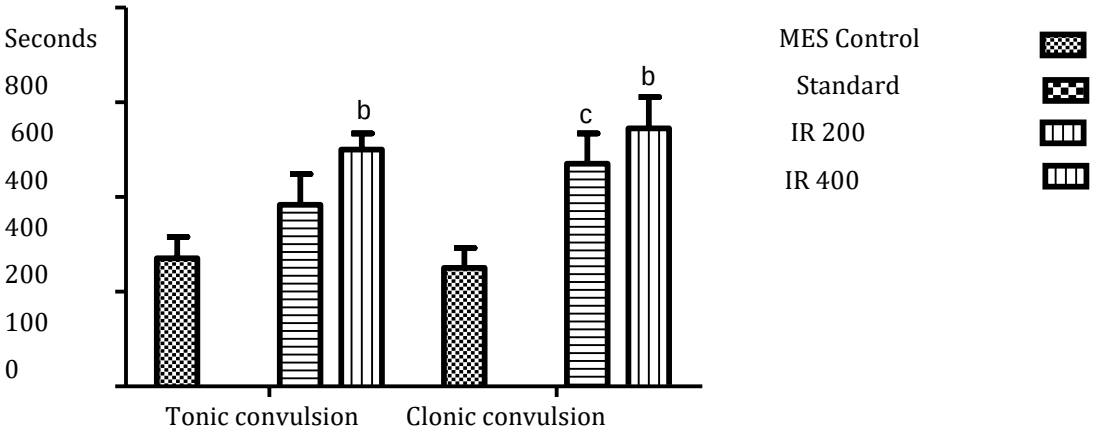

Figure 2: Effect of MEIR on MES induced convulsions in rats

Values are expressed in mean ± standard error mean; rePr (+)s different phases of convulsions in seconds (where n=6).

*Phenytoin had complete blocked the hind limb or leg extensor phase. A = $p < 0.001$, b = $p < 0.01$, c = $p < 0.05$; compared with M.E.S. control Grp.

Statistical analysis has done by one way A.N.O.V.A. followed by Tukey's experiment.

Table 5: Effect of MEIR on INH induced convulsions in MICE.

Grps	Treatment	Various phases of convulsions (Sec)				Protection against mortility %
Dose (milligram/kilogram) by peroral		onset of tonic action in sec	onset of clonic action in sec	Reco-very	Death time & number	
I	INH Control (1milliliter/100 g)	1442 ± 38.13	1978 ± 67.94	0/6	56.68±1.165	0.00
II	Diazepam (5 mg / kg)	3087 ± 387.4	3540 ± 165.4	6/6	Nil	100.00
III	MEIR (200 mg)peroral	2034 ±65.43	2234 ± 187.5	3/6	97±7.897 (3)	50.00
IV	MEIR (400 mg) peroral	2813 ± 45.87	2787 ± 67.13	5/6	124.0 (1)	84.13

Values have been given in mean ± standard error mean (n=6)

Grp I = Isoniazid control (0.5% weight/vol sodium carboxymethyl cellulose 1 milliliter per 100 gram peroral + Isoniazid)

Grp II = Diazepam (5 milligram per kilogram intraperitonial + Isoniazid)

Grp III = Methanolic extract of Ipomoea reniformis (200 milligram per kilogram by orally + Isoniazid)

Grp IV = Methanolic extract of Ipomoea reniformis (400 milligram per kilogram by orally + Isoniazid)

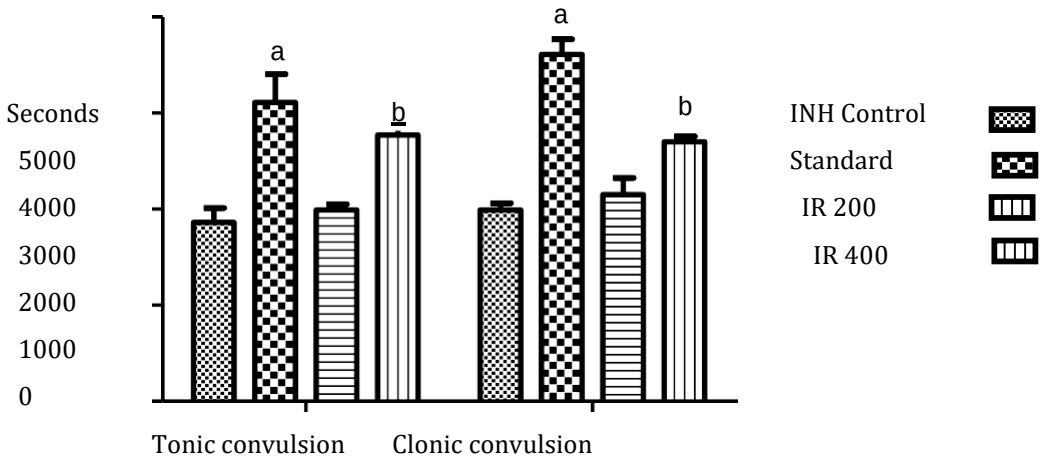

Figure 3: Effect of MEIR on INH induced convulsions in Mice

Values are expressed in mean ± standard error mean; rePr (+)s different phases of convulsions in seconds (where n=6).

*Phenytoin had complete blocked the hind limb or leg extensor phase. A = $p < 0.001$, b = $p < 0.01$, c = $p < 0.05$; compared with INH. control Grp.

Statistical analysis has done by one way A.N.O.V.A. followed by Tukey's experiment.

Table 6: Effect of MEIR on PTZ induced convulsions in MICE**.**

Grps	**Treatment**	**Various phases of convulsions (Sec)**				**Protection against mortility %**
Dose (milligram/kilogram) by peroral		**onset of tonic action in sec**	**onset of clonic action in sec**	**Reco-very**	**Death time & number**	
I	PTZ Control (1milliliter/100 g)	187 ± 21.13	250 ± 43.34	0/6	6.687±0.2098	0.00
II	Diazepam (5 mg / kg)	AC	AC	6/6	Nil	100.00
III	MEIR (200 mg)peroral	384 ±56.47	471 ± 65.57	2/6	7±1.956 (4)	33.33
IV	MEIR (400 mg) peroral	500 ± 35.17	546 ± 67.13	5/6	Nil	100.00

Values have been given in mean ± standard error mean (n=6)

Grp I = Pentylene tetrazole PTZ control (0.5% weight/vol sodium carboxymethyl cellulose 1 milliliter per 100 gram peroral + PTZ)

Grp II = Diazepam (5 milligram per kilogram intraperitonial + PTZ)

Grp III = Methanolic extract of Ipomoea reniformis (200 milligram per kilogram by orally + pentylene tetrazole)

Grp IV = Methanolic extract of Ipomoea reniformis (400 milligram per kilogram by orally + pentylene tetrazole)

The methyl alcohol extract of plant Ipomoea reniformis in dosage of 200 mg and 400 mg was administered to pentylene induced convulsions in rate. The conrol Grp is given to pentylene tetrazole or PTZ. The standard Grp is treated with diazepam 5 mg per 100 g mice and rats. These all are compared.

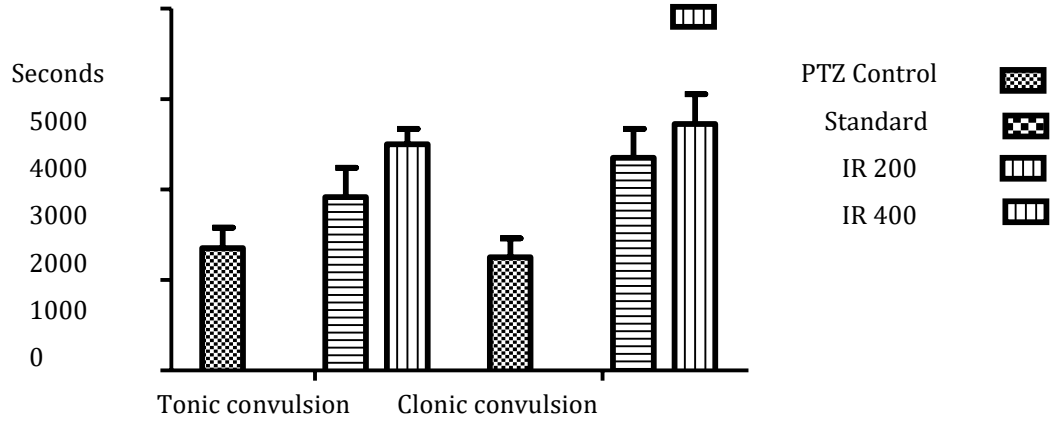

Figure 4: Effect of MEIR on PTZ induced convulsions in Mice

Values are expressed in mean ± standard error mean; rePr (+)s different phases of convulsions in seconds (where n=6).

*Phenytoin had complete blocked the hind limb or leg extensor phase. A = $p < 0.001$, b = $p < 0.01$, c = $p < 0.05$; compared with Pentylene tetrazole PTZ control Grp. Statistical analysis has done by one way A.N.O.V.A. followed by Tukey's experiment.

Convulsions are induced in rats and mice with different standard drugs. There are two method of convulsion induction. First method is maximal electroshock threshold convulsions in which voltage of current in fixed quatity is given to the rats and the animal show convulsion and then the methanolic extract of plant was given orally or perorally to the patients.

Second method of convulsion induction is chemical procedure in which medicament is administered orally or intraperitonial to mice and rats. The medicaments are central nervous stimulant in nature. The medicaments that are administered to animal are strychnine, Isoniazid, picrotoxin, pentylene tetrazole and bicuculline. These are administered by different routs. Doses are calculated according to weight of animals. There are four Grps of rats and mice prepare and every Grp has six animal. The Grps are standard, control and experimenting Grps. Two methanolic extracts of Ipomoeia were prepared in dosage of 200 and 400 mg. these are administered to rats and mices. These results were tabulated and the bar graph is produce for analysis. ANOVA or one way analysis of variance is utilized for calculated of the results. As above mentioned three control Grps are parepared by inducing convulsion with maximal electroshock, isoniazid and pentylene tetrazole.

DISCUSSION

The MES is a standard procedure that evaluates the experimenting materials ability to protect against Hind Limb Extension (HLE) in MES. Toman *et al*. (1914) reported that the seizure pattern in MES for all laboratory animals and man are similar except for time scale. *Ipomoea reniformis* exhibited a significant ($p<0.01$) anti-epileptic activity in MES induced seizures in a dose dependent manner in rats and showed maximum protection at 400 milligram per kilogram, peroral, which was comparable to that of standard Phenytoin (90 milligram per kilogram, intraperitonial). Phenytoin, a standard AED that suppresses HLE is effective in the therapy of generalized tonic-clonic and partial seizures. It limits the repetitive firing of action potentials and this effect is mediated by a slowing of the voltage activated sodium ion channels from recovering from inactivation. Protection against HLE in the MES predicts anticonvulsant activity of anti-epileptic drugs that prevent the spread of the epileptic seizure from an epileptic focus during seizure activity. Protection against HLE also indicates the ability of the experimenting material to inhibit or prevent seizure discharge within the brain stem substrate. Since, the *Ipomoea reniformis* showed anti-epileptic activity in the MES, it may act through any of the above-mentioned mechanisms.

The convulsant action of INH involves disruption of GABAergic neurotransmission in the CNS. INH is metabolized to hydrazine's. These cause a functional pyridoxine (vitamin B6) deficiency by inhibition of pyridoxine phosphokinase, the enzyme that converts pyridoxine to active B_6. Activated B_6 is required by Glutamic acid decarboxylase (GAD) to convert glutamic acid to GABA. Decreased levels of GABA are believed to lead to seizures. Severe lactic acidosis may develop as a result of seizure activity. So it has been reported that INH inhibits GAD, an enzyme that catalyzes the synthesis of GABA from glutamic acid. Several anti-epileptic drugs in current clinical use facilitate GABA neurotransmission by different mechanism: barbiturates, benzodiazepines and other anti-epileptics modulate the action of GABA by enhancing chloride currents in channels linked to different receptor sites. [62, 63]

The *Ipomoea reniformis* exhibited a significant anti-epileptic activity against INH induced seizure in mice. Highest anti-epileptic activity was observed at a dose of 400 milligram per kilogram, peroral, with a significant ($p<0.01$) increase in mean time of latency in onset of clonic action and tonic action. *Ipomoea reniformis* (400 milligram per kilogram, peroral), on 15days pre-treatment dose study showed 83.33% protection against mortality. Thus results are comparable to that of Diazepam (5 milligram per kilogram, intraperitonial). [56]

Pentylenetetrazol (PTZ), a selective blocker of the chloride channel coupled to the $GABA_A$ receptor complex, is the most popular chemoconvulsant used for evaluation of antiepileptic drugs (AEDs). A sufficiently high dose of PTZ can produce a continuum of seizure

activity that progress from mild myoclonic jerks to face and forelimbs clonus without loss of righting reflex (which is known as minimal clonic seizure, MCS), to clonic seizures of limbs with loss of righting reflex, to full tonic extension of both forelimbs and hind limbs (generalized tonic–clonic seizures, GTCS). [64]

The *Ipomoea reniformis* exhibited a significant anti-epileptic activity against PTZ induced seizure in rats. Highest anti-epileptic activity was observed at a dose of 400 milligram per kilogram, peroral, with a significant ($p<0.01$) increase in mean time of latency in onset of clonic action and tonic action. *Ipomoea reniformis* 400 milligram per kilogram, peroral, on 15days pre-treatment study, showed 100% protection against mortality. Thus results are comparable to that of Diazepam (5 milligram per kilogram, intraperitonial). As early as the 19th century, investigators have described the simultaneous appearance ofpsychiatric disorders as well as epileptic seizures. There is an increased incidence of interictal psychosis in patients with epilepsy.

Summary and conclusion

These results scientifically validated the traditional use of *Ipomoea reniformis* in the treatment of epilepsy and neuronal disorders

The plant was extracted with methanol in a Soxhlet apparatus. The therapeutic doses of the *Ipomoea reniformis* were selected on the basis of earlier reports.

The anti-epileptic activity of *Ipomoea reniformis* was studied against seizures induced by MES, INH, and PTZ.

In pre-treatment (15days) study of antiepileptic activity, *Ipomoea reniformis* (400 milligram per kilogram) showed significant ($p<0.01$) reduction in tonic hind limb extensor phase in MES model, while in INH and PTZ significantly ($p<0.01$) delayed the onset of clonic and tonic convulsions.

In conclusion, the Pr (+) study showed that *Ipomoea reniformis* possess anti- epileptic activity against MES, INH, and PTZ induced convulsions.

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