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PHYTOCHEMICAL SCREENING AND EVALUATION OF ANTICONVULSANT ACTIVITY OF ARECA CATECHUE SEEDS EXTRACT

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Abstract:
The conventional antiepileptic drugs (AED) have contributed significantly in the management of epilepsy. The areca nut (Areca catechu L. from the Palmaceae family) is a tropical fruit, which is also called betel nut and is widely distributed in different parts of the world. The preliminary Phytochemical studies were done in the Methanolic extract of Areca catechue leaves, the result suggest that presence of Alkaloids, Carbohydrate, flavonoids, Steroids, phenolic compounds and tannins. Methanolic extract of Areca catechue possesses anxiolytic and anticonvulsant effects and these findings collaborate with the ethnomedicinal uses of this plant. The isolation of active chemicals from this plant might serve as lead compounds for the synthesis of drugs which could be used in the management of these nervous disorders.

Key words: *Anticonvulsant activity, Areca catechue, Seeds extract, phytochemical screening*

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INTRODUCTION:

Epilepsy is a heterogeneous symptom complex, a chronic disorder characterized by recurrent seizures affecting approximately 1% of the world's population and second most common neurological disorder after stroke.[1] Seizure is defined as abnormal, disordered discharges of brain nerve cells resulting in a temporary disturbance of sensory, motor or mental function.[2] The incidence rate is estimated from 40 to 60/1,000,000 population/year.[3] Approximately 5% of general population experience at least one seizure, excluding febrile seizures.[4]

The conventional antiepileptic drugs (AED) have contributed significantly in the management of epilepsy. About 60-70% of patients with epilepsy achieve control of their seizures with the use of AEDs. However, in nearly one-third of epileptic patients, the seizure control is not achieved even with continued use of AEDs.[5] Moreover, these AEDs are associated with dose-related side effects, chronic toxicity as well as teratogenicity.[6] As such, there is an increased need to discover drugs which are effective in refractory epilepsy having lesser adverse effects. Medicinal plants offer important sources of new chemical substances with therapeutic benefits besides being safe, easily available, effective, and economical.[7]

The areca nut (Areca catechu L. from the Palmaceae family) is a tropical fruit, which is also called betel nut and is widely distributed in different parts of the world. As one of the major tropical crops, more than 223,800 metric tons of areca fruit were produced in Hainan province of China in 2013. About 90% of the areca harvest is available as commercial preparations which are produced on a large scale [8]. The processing involves husking fruits, removing embryos, and drying nuts in the sun or with artificial heat or sometimes smoking. The dried product is graded according to harvest, color, shape, and size. Nuts may first be boiled to reduce tannin content of nuts, and then dried [9]. The seeds of areca nut account for 45% of the total weight of fruit. However, they are discarded during the process of producing the betel quid chewing (BQC) and/or areca nut chewing (ANC). In Hainan and Hunan provinces, the annual yield of areca seeds is above 100,710 metric tons, which leads to much wastage and a serious environmental problem. Therefore, a new commercial industry for the areca nut to reutilize the waste is emerging. For more economical and efficient utilization, the characteristics and composition of the commercial product needs to be scientifically studied. The areca nut contains many nutritional and functional components with different bioactivities. Since the 4th century A.D., humans have consumed the areca nut as food and medicine. Now, it is estimated that over 600 million individuals consume areca nut world-wide. In India, areca nut has been described as a therapeutic agent in old scripts, such as Vagbhata (4th century) and Bhavamista (13th century). It was recommended for the treatment of many diseases, such as leucoderma, leprosy, anaemia, and obesity. In China, it has been used as a vermifuge to eliminate intestinal worms since the 6th century and is still employed in some areas [10]. In Philippines, the flowers are sometimes added to salads. Various medicinal preparations use the nuts, husks, young shoots, buds, leaves, or roots. These pharmacology activities are attributed to abundant phenolic compounds in the areca nuts.

In recent year there has been a tremendous increase in demand for herbal drugs due to its safety, efficacy and better therapeutic results and also due to its economic pricing as compared to synthetic or allopathic drugs, which have several therapeutic complications.Very less pharmacological studies have been carried out on the leaves of *Areca catechue*. Hence, I have decided to choose *Areca catechue* on which detailed studies on Preliminary Phytochemical and Pharmacological actions on CNS is done.

MATERIALS AND METHODS:

Collection of specimens:

The species for the proposed study that is leaves of *Areca catechue* has carefully collected from Hydrerabad, Telangana.

Shade drying:

After collection, seeds of *Areca catechue* were washed thoroughly with water to remove the dirt particles and any other foreign material adheres to seeds. Then after, the seeds were wiped off with cotton cloth and transferred to newspaper and evenly spreader on to paper.The *Areca catechue* seeds were subjected to shade drying to treat fungus until complete dryness of seeds. Then the dried seeds were powdered by mixer grinder until to get coarse powder, which was used for further detailed studies, extraction with solvent and phytochemical studies.

PRELIMINARY PHYTOCHEMICAL ANALYSIS

Extraction of *Areca catechue* leaves:

Methanol extract:

About 250gm of air-dried powdered material was taken in 3000ml soxhlet apparatus and extracted with petroleum ether until green colour disappear. At the end of the day the powder was taken out and dried. After drying it was again packed and extracted by using Methanol (S.D. Fine Chemicals Ltd. Mumbai, India) as solvent, till colour disappeared. The temperature was maintained at 55ºC-65ºC.After that

extract was concentrated by distillation and solvent was recovered. The final solution was evaporated to dryness. The colour, consistency and yield of Methanolic extract were noted.

Table: 1 Nature of extract of *Areca catechue*

S.No.	Name of extract	Colour	Consistency	Yield% W/W
1.	Methanolic extract	Greenish black	Sticky mass	7

CHEMICAL TESTS:

Test for carbohydrates:

PHARMACOLOGICAL EVALUATION

ACUTE ORAL TOXICITY STUDY

The procedure was followed by using OECD guidelines 423 (Acute toxic class method). The acute toxic class method is a step wise procedure with 3 animals of single sex per step. Depending on the mortality and / or moribund status of the animals, on average 2-4 steps may be necessary to allow judgment on the acute toxicity of the test animals while allowing for acceptable data based scientific conclusion.

The method uses defined doses (5, 50, 300, 2000mg/kg body weight) and the results allow a substance to be ranked and classified according to the Globally Harmonized System (GHS) for the classification of chemical which cause acute toxicity.

ANIMALS:

Female albino mice of 20-30 gm of body weight obtain from Animal House, Department of Pharmacology.Animals were kept in standard animal house condition. Prior to use, the mice were housed in polypropylene cages in group of six animals under natural light-dark cycle. They were provided with commercial food pallets and tap water *ad libitum*. Cleaning and sanitation work was done on alternate days. Paddy husk was provided as bedding material. All the observations were made at room temperaturein a noiseless diffusely illuminated room. The cages were maintained clean and all experiments were conducted between 8 am to 3 pm.

PROCEDURE:

Twelve animals Albino mice, (25-30gm) were selected for studies.

Most of the crude extracts possess LD_{50}, value more than 2000mg/kg of the body weight of the animal used. Dose volume was administered 0.1ml/100gm body weight to the animal by oral route.

After giving the dose toxic signs were observed within 3-4 hours. Body weight of the animals before and after administration, onset of toxicity and signs of toxicity like changes in the skin and fur, eyes and mucous membrane and also respiratory, circulatory, autonomic and central nervous systems activities, motor activity and behavior pattern, sign of tremors, convulsion, salivation, diarrhea, lethargy and sleep and coma was also to be noted, if any, was observed. The animal toxic or death was observed upto 14 days.

OBSERVATION

Acute toxicity studies and evaluation of datas are studied as per the guideline of OECD (423). No toxicity or dth was observed for these given dose levels, in selected andtreated animals. So the LD_{50} of the Methanolic extract of leaves of *Areca catechue* was greater than 2000mg/kg (LD_{50}>2000mg/kg). Hence the biological dose was fixed at three levels, 125,250 and 500mg/kg body weight for the extract.

EVALUATION OF ANXIOLYTIC AND ANTICONVULSANTACTIVITY

Animals:

Albino mice of either sex 20-30 gm of body weight obtain from Animal House, Department of Pharmacology. Animals were kept in standard animal house condition. Prior to use, the mice were housed in polypropylene cages in group of six animals under natural light-dark cycle. They were provided with commercial food pallets and tap water *ad libitum*. Cleaning and sanitation work was done on alternate days. Paddy husk was provided as bedding material. All the observations were made at room temperature in anoiseless diffusely illuminated room. The cages were maintained clean and all experiments were conducted between 8 am to 3 pm.

Drugs and Chemicals:

- Diazepam (Calmpose Inj. Ranbaxy, India)
- Pentylenetetrazole (Sigma, USA)
- Methanol extra pure (S.D fine chemicals, Mumbai).

Experimental Design:

Animals are divided into 5 groups, each group containing 6 mice.

- Group I: Normal control mice fed with vehicle only.

- Group II: Mice treated with Diazepam 5mg/kg
- Group III: Mice treated with 125 mg/kg Methanolic extract of Areca catechue
- Group IV: Mice treated with 250 mg/kg Methanolic extract of Syzygium aquem
- Group V: Mice treated with 500 mg/kg Methanolic extract of Areca catechue

EVALUATION OF ANXIOLYTIC ACTIVITY

Elevated Plus Maze (EPM) Test.

The EPM test is the most frequently employed model for the assessment of the anxiolytic activity of novel substances (R.G.Liser 1987). The elevated plus maze apparatus consisted of two perpendicular open arms (50 X 10 cm) and two perpendicular enclosed arms (50 X 10 X 40 cm). The entire maze was constructed ofwood and elevated 50 cm above floor. The maze was placed inside a light (25 lx) and sound attenuated room.

The animals were divided into five groups, each group comprised six mice. Different groups were treated with distilled water (10 mL/kg), diazepam (5 mg/kg), and Methanolic Extract of *Areca catechue* at doses of 125, 250, and 500 mg/kg, BW. Thirty minutes later, the rat was placed in the center platform of the maze facing the enclosed arm and was observed for 10 min. The parameters assessed were the time spent in open and enclosed arms and numbers of open and enclosed arms entries. All tests were taped by using a video camera and every precaution wastaken to ensure that no external stimuli could evoke anxiety in the mice. After each test, the maze was carefully cleaned up with a wet tissue paper (70% ethanol solution) to eliminate the interference of the olfactory cues on the next rat (Peng.W.H *et al.*,2000).

Open Field Test.

The study was conducted according to method previously described by Brown et al with some modifications. The apparatus was made up of plywood measuring 72 cm X 72 cm X 36 cm. One of the walls was made of transparent Perspex glass to ensure that the mouse under investigation is visible to the observer. The floor, made of cardboard, was divided into 16 equal squares (18 cm X 18 cm) with blue marker and a central square drawn with black marker. The cardboard was covered with a transparent Plexiglas. The animals were divided into five groups; each group comprised six rats. Different groups were treated with distilled water (10 mL/kg), diazepam (5 mg/kg), and Methanolic extract of *Areca catechue* at doses of 125, 250, and 500 mg/kg, BW. Thirty minutes later, each mouse was placed individually at the corner of the arena and its behavior monitored for 5 min. The number of rearings and number of square crossed by each mouse was recorded.

The apparatus was wiped between observations with 70% ethyl alcohol and allowedto dry to remove any olfactory cue.

Rota rod:

The equipment of Rotarod was used to evaluate motor coordination producedby drugs in animals. The mice were trained before the experiment to acquire the capacity to remain for 300 s on a diameter rod, rotating at 20 rpm. Two or three trials were sufficient for the animals to learn this task. Thirty mice were divided into five groups; each group comprised six rats. Different groups were treated with distilled water (10 mL/kg), diazepam (5 mg/kg), and Methanolic extract of leaves of *Areca catechue* at doses of 125, 250, and 500 mg/kg, BW. Then, the animals were placed in the four paws on the rotating bar, which is 2.5 cm in diameter and 25 cm high from the floor. The animals were observed for a period of five minutes. The difference between the fall-off time of the mice before and after treatment was considered as an index of muscle relaxation (Farkas.S *et al*., 2005).

EVALUATION OF ANTICONVULSANT ACTIVITY

Pentylenetetrazole Induced Convulsions:

Pentylenetetrazole (PTZ) induced convulsions test was performed to evaluateanticonvulsant property of drugs (Ahmadiani.A *et al*.,).Thirty male mice were divided into five groups, each group comprised six mice. Different groups were treated with distilled water (10 mL/kg), diazepam (5 mg/kg), and Methanolic extract of *Areca catechue* at doses of 125, 250, and 500 mg/kg, BW. Thirty minutes later, convulsions were induced by the intraperitoneal administration of 60 mg/kg BW of PTZ. Following the administration of PTZ, mice were placed in separate transparent plexiglass cages (25 × 15 × 10 cm) and were observed for the occurrence of seizures over a 30 min time period. Latency of convulsions (the time prior to the onset of tonic convulsions), duration of tonic convulsions, and mortality protection (percentage of deaths in 24 h) were recorded (R.S. Fischer, 1989).

Maximal Electro Shock (MES) Induced Convulsions:

The animals were divided into five groups, each group comprised six mice. Different groups were treated with distilled water (10 mL/kg), diazepam (5 mg/kg), and Methanolic extract of *Areca catechue* at doses of 125, 250, and 500 mg/kg, BW. Thirty minutes later, convulsions were induced in all the

groups of animals using electro convulsiometer. A 60 Hz alternating current of 150 mA for 2 s was delivered through the ear electrodes (Balamurukan.G.*et al.*,). The animal was observed for the occurrence of tonic hind limb extension.

Data analysis

Results of the experiments and observations were expressed as mean ± standard deviation (SD). The significance of differences between groups was determined using one-way analysis of variance (ANOVA) followed by at least one of the following post hoc tests: Dunnett's multiple comparison tests $P< 0.05$ where level of significance was considered for each test. The data is presented as mean ± S.D.

RESULTS AND DISCUSSION:

Based on literature review, the leaves of *Areca catechue* was collected, authenticated and the project was carried out. The result ofthe present study shows that the Methanol extract of *Areca catechue* seeds shows significant anticonvulsant and anxiolytic activities.

PRILIMINARY PHYTOCHEMICAL STUDIES

Table No. 2. Percentage Yield of Areca catechue

Name of extract	Yield(%w/w)
Methanol	7

The extract obtained were subjected to qualitative Phytochemical test to find out the active constituents.

Table No. 3: Qualitative Phytochemical analysis of the extract

TEST FOR PHYTOCONSTITUENTS	RESULT
Saponins	+
Alkaloids	+
Glycosides	+
Tannins and phenolic compounds	+
Carbohydrate	+
Tri Terpenoids	-
Flavonoids	+
Steroids	+

(+) - Present (-) - Absent

The preliminary Phytochemical studies were done in the Methanolic extract of *Areca catechue* leaves, the result suggest that presence of **Alkaloids, Carbohydrate, flavonoids, Steroids,** phenolic compounds and tannins.

PHARMACOLOGICAL STUDIES

ACUTE ORAL TOXICITY STUDIES

The acute oral toxicity of the Methanolic extract of *Areca catechue* was carried out as per OECD 423-guidelines (Acute toxic class method). Acute toxicity studies revealed that LD_{50}>2000mg/kg for the extract. Hence, the biological dosewas fixed at 125, 250mg and 500mg/kg body weight.

EVALUATION OF ANXIOLYTIC ACTIVITY

Elevated plus maze:

Administration of diazepam (5mg/kg) significantly increases number of open arm entries, time spent in open arms and the number of rearings in open arm. They showed a reduction in the time spent in closed arm. Plant extracts treated mice exhibited significant increase in the number of open arm entries. The number of armentries, but decreases in time spent in closed arm as shown in the table 6.3.

Open field test:

There was significant anxiolytic activity observed with diazepam, plant extracts when compared to control. In the open field test, plant extract showed significant increase in number of rearings, number of squares crossed and number of assisted rearings during 5 min intervals of test as compared with control.

Rota rod:

Table 6.5. shows the effects of Methanolic extract of leaves of *Areca catechue*in the Rotarod test, a method used for evaluating motor coordination and presence of any muscle griping effect. It revealed that there was significantly increased grip force and fall time after administration of Methanolic extract of *Syzygium aquem* (125, 250, and 500 mg/kg) when compared to control. All the plant extract treated animals retained on the rotating rod for more than 276.35 ± 7.58 s at 500 mg/kg as shown in Table indicate the Methanolic extract of *Areca catechue* to be devoid of neurotoxicity.

Table. 4. Effect of Methanolic extract of *Areca catechue* on Elevated plus maze in mice

Group	Treatment	Dose	Time spent in open arm (s)	Entries in open arm
I	Saline	10ml/Kg	40.25±4.41	3.98±0.52
II	Diazepam	5mg/kg	239.59±3.52**	12.64±0.47**
III	Plant extract	125mg/kg	100.83±3.97	6.48±0.39
IV	Plant extract	250mg/kg	173.81±4.32*	6.53±0.42*
V	Plant extract	500mg/kg	213.92±4.80**	10.32±0.21**

The data represent the mean ±S.D (n=6) *p<0.01, **p<0.001significantly different compared to normal control and diazepam

Fig. 1. Effect of Methanolic extract of *Areca catechue* onTime Spend in Open arm in EPM Test

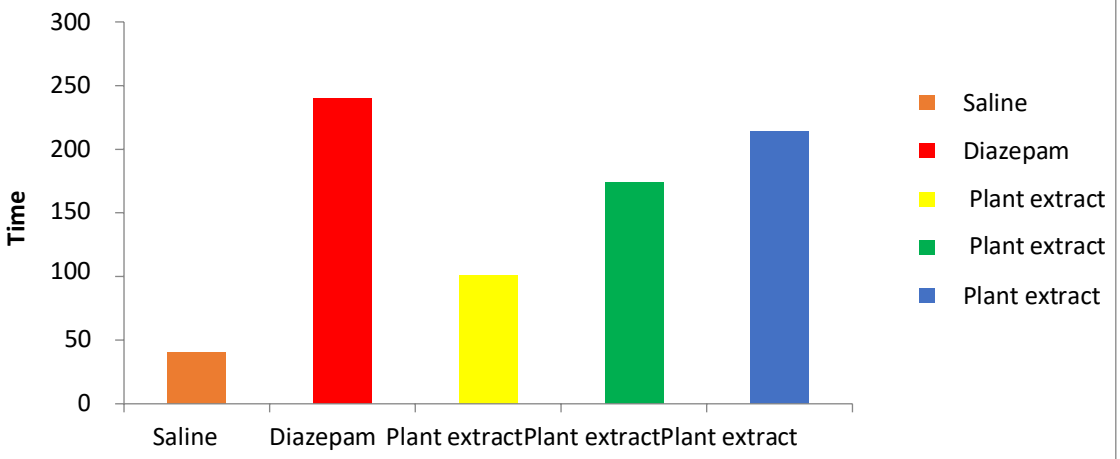


Fig. 2. Effect of Methanolic extract of *Areca catechue* on Open arm entries in EPM Test

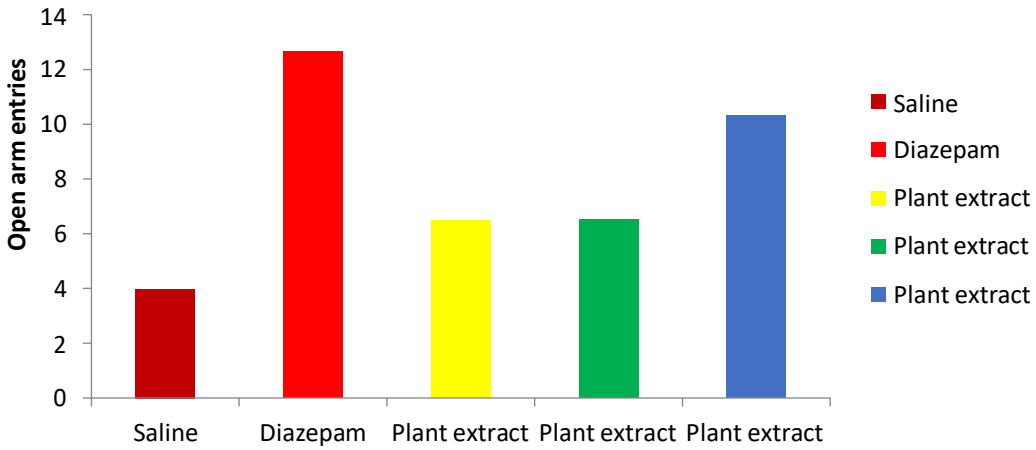


Table 5. Effect of Methanolic extract of *Areca catechue* on Open field testin mice

Group	Treatment	Dose	Number of squares crossed	Number of rearing
I	Saline	10ml/kg	40.3±2.1	10.1±1.4
II	Diazepam	5mg/kg	29.5±3.6**	8.2±1.8**
III	Plant extract	125mg/kg	22.9±2.4	5.4±2.3
IV	Plant extract	250mg/kg	24.7±3.2*	7.3±3.5*
V	Plant extract	500mg/kg	26.4±2.8**	9.3±1.2**

The data represent the mean ±S.D (n=6) *p<0.01, **p<0.001 significantlydifferent compared to normal control and diazepam.

Fig. 3. Effect of Methanolic extract of *Areca catechue* on Open field test in mise

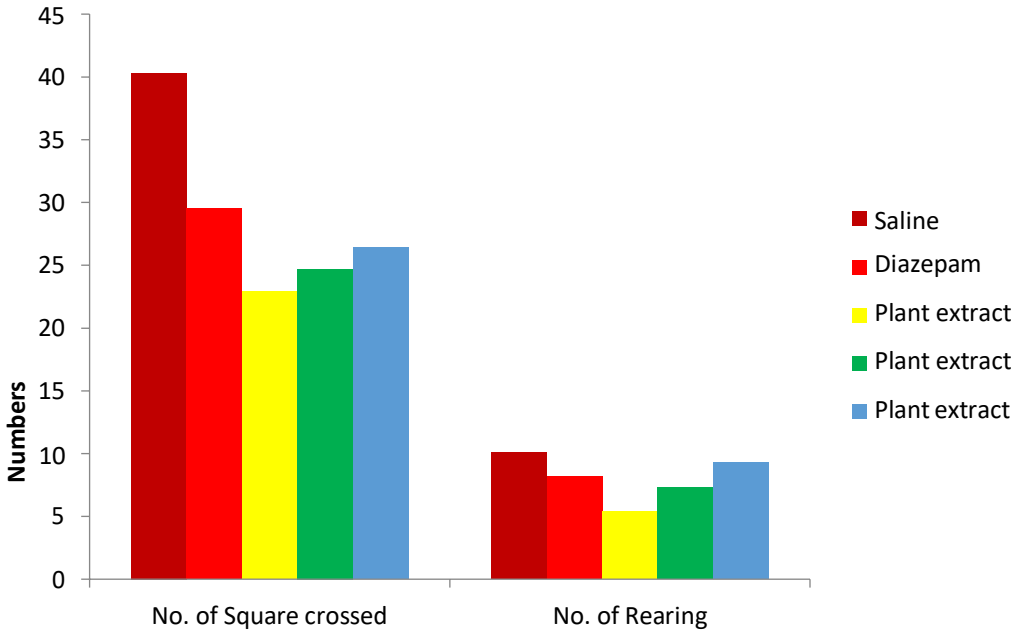
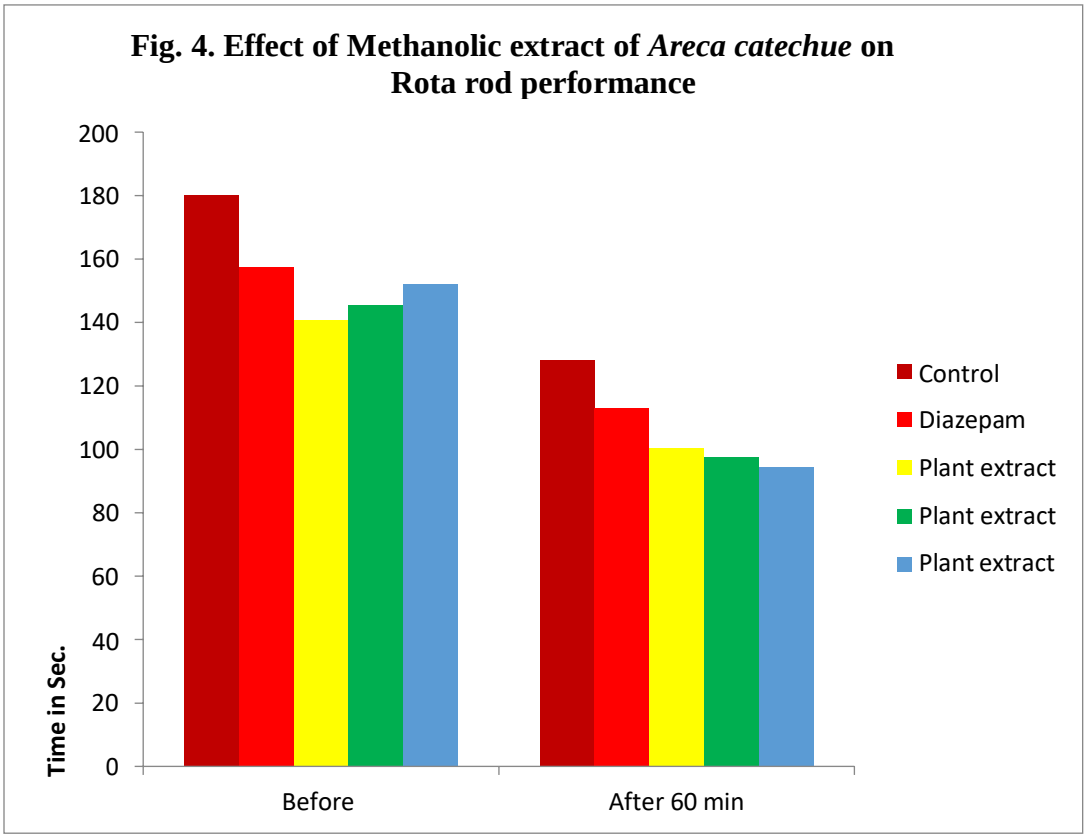


Table.6. Effect of Methanolic extract of *Areca catechue* leaves on Rota rodperformance

Group	Treatment	Dose	Experimental mean time(10min) (s)	
			Before	After 60 min
I	Control	10ml/kg	180.21±9.1	128.10±7.6
II	Diazepam	5mg/kg	157.61±6.9**	112.90±6.3
III	Plant extract	125mg/kg	140.82±5.7	100.39±7.2
IV	Plant extract	250mg/kg	145.41±3.6*	97.46±5.9
V	Plant extract	500mg/kg	152.13±5.8**	94.53±6.5

The data represent the mean ±S.D (n=6) *p<0.01, **P<0.001 significantly differentcompared to normal control and diazepam.



EVALUATION OF ANTICONVULSANT ACTIVITY

PTZ Induced Convulsion:

Pentylenetetrazole produced tonic seizures in the entire animals used. A dose of 125 mg/kg of Methanolic extract of leaves of *Areca catechue* protected 33.33% of the animals against seizures and did not affect the onset (latency) of seizures to any significant extent. Methanolic extract of leaves of *Areca catechue* at the dose of 250 and 500 mg/kg protected 50.0% and 100% of the mice against seizures and increased the latency of the seizures.

Maximal Electro Shock Model:

Maximal electroshock produced hind limb tonic extension (HLTE) in all the animals. The vehicle treated mice showed tonic hind limb extension for duration of12.88 ± 0.35 s. Administration of Methanolic extraction of leaves of *Areca catechue* (125–500 mg/kg) showed a dose dependent increase in the delay of the onset time of seizures induced by maximal electroshock induced convulsion and also decreased duration of tonic hind limb extension.

Table 7. Effect of Methanolic extract of leaves of *Areca catechue* on PTZinduzed convulsions in mice

Group	Treatment	Latency of Tonic convulsion (s)	Duration of Tonic convulsions (s)	Mortality (% death)	% Protection
I	Control	100.20±3.34	446.10±5.19	6/6(100)	0.0
II	Diazepam (5mg/kg)	478.34±6.07**	126.69±1.93**	0/6(0.0)	100
III	Plant extract (125mg/kg)	141.43±1.98	216.29±1.23	4/6(66.66)	33.33
IV	Plant extract (250mg/kg)	298.16±4.45*	189.19±1.72*	3/6(50.00)	50.0
V	Plant extract (500mg/kg)	416.42±6.14**	137.11±2.61**	0/6(0.0)	100

The data represents the mean S.D ± (n=6) *p<0.1, **p<0.001significantly differentcompared to normal control and diazepam.

Fig. 5. Effect of Methanolic extract of *Areca catechue* onPTZ induced convulsions in mice

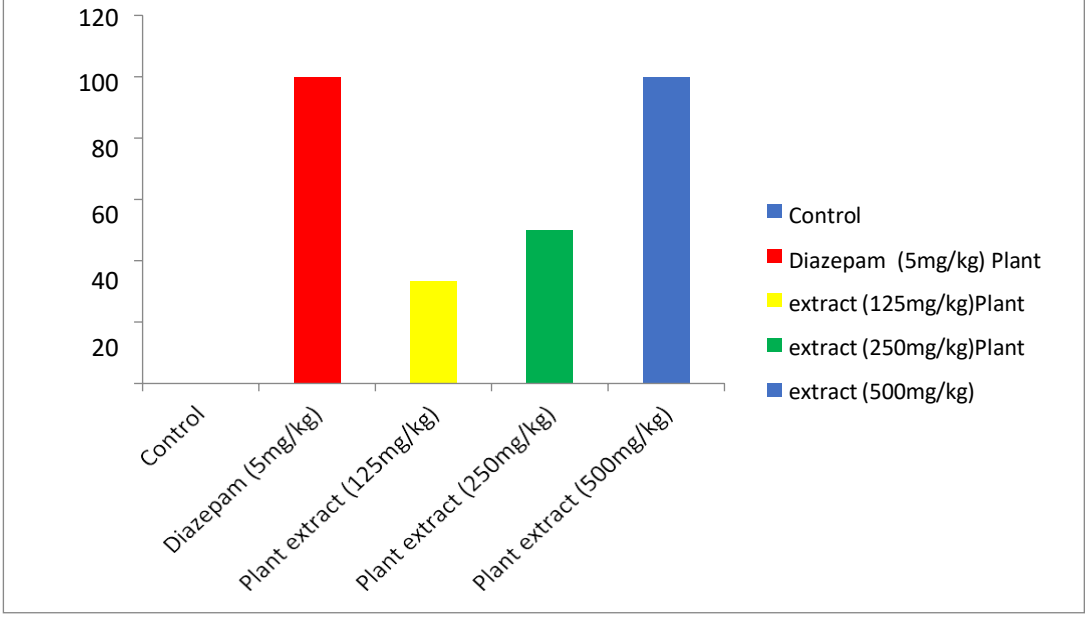
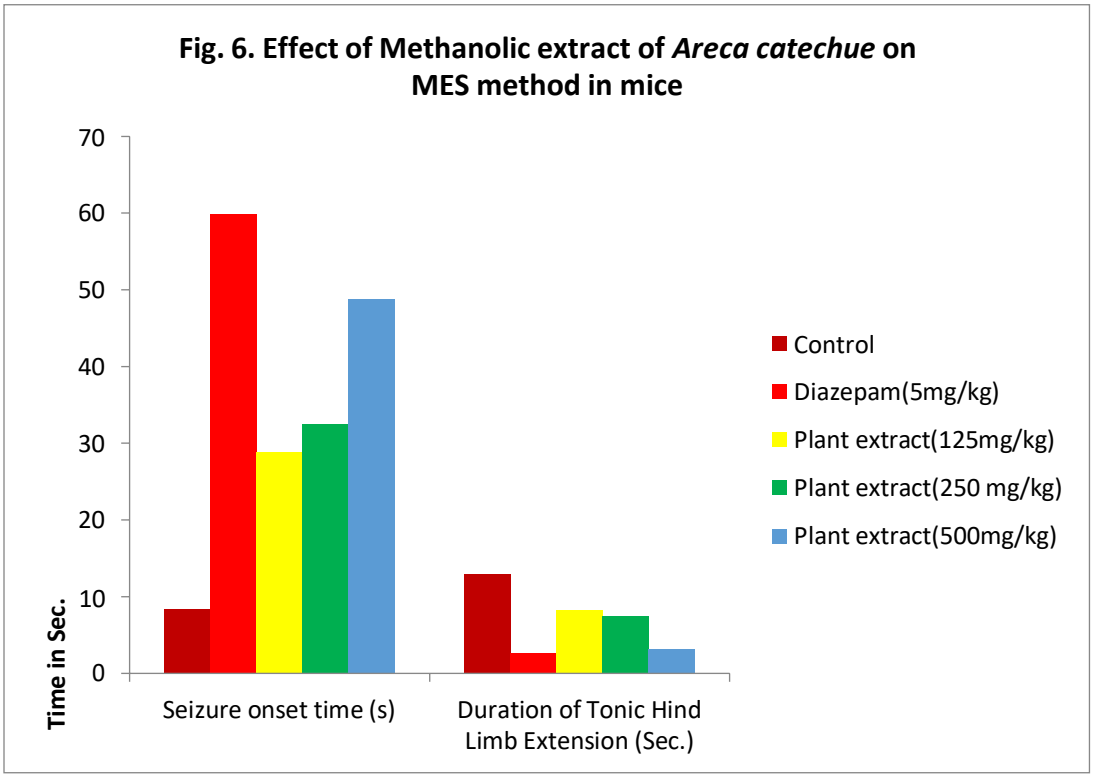


Table 8. Effect of Methanolic extract of *Areca catechue* on Tonic seizuresinduced by MES method in mice

Group	Treatment	Seizure onset time(s)	Duration of TonicHind Limb Extension (Sec.)
I	Control	8.38±1.88	12.88±0.35
II	Diazepam(5mg/kg)	59.88±1.35**	2.63±1.72**
III	Plant extract(125mg/kg)	28.81±1.10	8.28±1.19
IV	Plant extract(250 mg/kg)	32.43±1.44*	7.44±1.01*
V	Plant extract(500mg/kg)	48.84±1.25**	3.21±1.25**

The data represent the mean ±S.D (n=6) *p<0.05, **p<0.001 significantly differentcompared to normal control and diazepam.



SUMMARY AND CONCLUSION:

The seeds of *Areca catechue* has been examined to gain an insight of its Phytochemical and pharmacological behaviors.

The preliminary phytochemical investigation of Methanolic extract of leaves of Syzygium aquem showed the presence of **Carbohydrate, Alkaloids, Phytosteroids, Flavonoids, Phenolic compounds and Tannins.**

The pharmacological and acute toxicity studies of Methanolic extract was performed by following, OECD-423 guidelines (Acute toxic class method). No mortality or acute toxicity was observed upto 2000mg/kg of body weight.

Medicinal plants have served as sources of readily accessible, inexpensive, and effective medication since the earliest times known to man. Several ethnomedicinal plants have been found to possess neurobehavioral profile and serve as alternative to modern medicine. Biological evaluation and scientific validation of the ethnomedicinal plants are the need of the hour. The present study was proposed to assess anxiolytic, and anticonvulsant effects of methanolic extract of leaves of an ethnomedicinal plant, *Areca catechue*.

Anxiety disorders are due to involvement of GABAergic, serotonergic, involvement. The adrenergic and dopamanergic system have also been shown to play a role in anxiety. BZA have been extensively, used for the last 40 years to treat several forms of anxiety, but due to their unwanted side effects, alternative treatmentstrategies with favorable side effect profiles. Medicinal plants are a good source to find new remedies for these disorders. Despite the wide spread traditional use of *Areca catechue* for treating various disorders there are no reports of scientific evaluation of its anxiolytic and anticonvulsant activity. The present work demonstrates that the *Areca catechue* leaf extract had anxiolytic activity in mice by Elevated Plus Maze, Rotarod and Open field models.

Elevated Plus Maze is used to evaluate psychomotor performance and emotional aspects of rodents. Results showed that plant extracts treated mice exhibited significant increase in the number of open arm entries but decreases in time spent in closed arm, which reflects plants anxiolytic property.

The open field test is used to evaluate the animal emotional state. The open field model examines anxiety related behavior characterized by the normal aversion of the animal to an open area. Thus, animals removed from their acclimatized cage and placed in environment express anxiety and fear, by showing alteration in all or some parameters. Mice treated with extract showed increase in number of rearings and time spent in the center.

Rota rod test, the difference in the fall of time from the rotating rod between the vehicle and extract treated groups were taken as an index of muscle relaxation. Plant extract showed significant decrease in the locomotory score and fall of time of the mice from the rotating rod.

The results of the present laboratory animal study indicate that Methanolic extract of *Areca catechue* leaf extract possesses anticonvulsant activity. The present study demonstrated the anticonvulsant effects of the methanolic extract of *Areca catechue* in both chemically and electrically induced seizures in mice. The extract exhibited dose dependent protection in the MES and PTZ induced convulsions. Nevertheless, in unprotected animals, the extract significantly increased seizure latency and reduced seizure duration compared with the control group in all two models at all tested doses. The effect of most of antiepileptic agents is to enhance the response to GABA by facilitating the opening of GABA-activated chloride channels. GABA receptors were involved in epilepsy and their direct activation would have an antiepileptic effect.

The anticonvulsant, anxiolytic, and sedative effects of benzodiazepines like diazepam are mostly attributed to enhance the action of gamma-aminobutyric acid ($GABA_A$) (Yemitan O.K. *etal*.,2005). Actually, benzodiazepines bind to the gamma subunit of the $GABA_A$ receptor, due to which a structural modification of thereceptor results in an increase in $GABA_A$ receptor activity. Benzodiazepines do not substitute for GABA, which bind at the alpha subunit, but increase the frequency of channel opening events, which leads to an increase in chloride ion conductance and inhibition of the action potential (Muhammed.N *et al*.,and Garcia 2006). According to some researchers, the anxiolytic action of benzodiazepines may be due to the direct activation of glycine synapses in the brain (Muhammed.N *et al*., and P.Brambilla, 2013). This may explain the mechanism of action of the tested extract as well, because it is clear from the results that the effect of the extract was similarto diazepam.

Previous phytochemicals reported in the literature, various Flavonoids, glycosides, Alkaloids and triterpenoids, isolated from *Syzygium aquem* would be the effective constituents for their anxiolytic and anticonvulsant effect.

In conclusion, Methanolic extract of Areca catechue possesses anxiolytic and anticonvulsant effects and these findings collaborate with the ethnomedicinal uses of this plant. The isolation of active chemicals from this plant might serve as lead compounds for the

synthesis of drugs which could be used in the management of these nervous disorders.

REFERENCES:

1. Porter RJ, Meldrum BS. Antiseizure drugs. In: Katzung BG, Masters SB, Trevor AJ, editros. Basic and Clinical Pharmacology. 12th ed. USA: McGraw Hill; 2012. p. 403-26.
2. Saraf SA, Gupta R, Mishra A, Sharma AK, Punia RK. Advancements in traditional medicinal plants used in epilepsy. Phcog Rev. 2008; 2:229-40.
3. Deshmukh RS, Chaware VJ, Biyani KR. Alpha lipoic acid potentiates the antiseizure activity of Gabapentin in mice. Intern J Res Pharm Biomed Sci. 2012;3(3):1004-7.
4. Wahab A. Difficulties in treatment and management of epilepsy and challenges in new drug development. Pharmaceuticals (Basel). 2010;3(7):2090-2110.
5. Brodie MJ. Antiepileptic drug therapy the story so far. Seizure. 2010;19(10):650-5.
6. Swann AC. Major system toxicities and side effects of anticonvulsants. J Clin Psychiatry. 2001;62 Suppl 14:16-21.
7. Prakash P, Gupta N. Therapeutic uses of Ocimum sanctum Linn (Tulsi) with a note on eugenol and its pharmacological actions: A short review. Indian J Physiol Pharmacol. 2005;49(2):125-31.
8. McDonald S., Prenzler P.D., Antolovich M., Robards K. Phenolic content and antioxidant activity of olive extracts. Food Chem. 2001; 73:73–84.
9. Zhang C.J., Lv F.J., Tai J.X., Wang Z.N., Fu Q. Quantitative dtermination of total phenolics and tannin in areca nut and its products. Food Res. Dev. 2008; 29:119–121.
10. Dahmounea F., Spigno G., Moussia K., Remini H., Cherbal A., Madani K. Pistacia lentiscus leaves as a source of phenolic compounds: Microwave-assisted extraction optimized and compared with ultrasound-assisted and conventional solvent extraction. Ind. Crop. Prod. 2014; 61:31–40.