International Journal of Farmacia (IJF)

IJF |Vol.11 | Issue 2 | Apr - Jun -2025

www.ijfjournal.com

DOI : https://doi.org/10.61096/ijf.v11.iss2.2025.44-54

ISSN: 2455-8109

Research

Evaluation of Anti-Epileptic Activity From Leaves of *Centella asiatica* In Maximal Electroshock And Isoniazid-Induced Convulsions In Wistar Rats.

Tarannum Sulthana*, M. Bhaskar[1], Rangam Chariitha[2], Musarrath Mubeen[3], Teelavath Mangilal

Smt.Sarojini Ramulamma College Of Pharmacy, Seshadrinagar, Mahabubnagar, Telangana – 509 001, India

*Author for Correspondence: Tarannum Sulthana
Email: teelavath@gmail.com

Published on: 03 May 2025

Published by:
DrSriram Publications

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Abstract

Early Tamils and Dravidians in South India are thought to have used siddha, one of India's oldest medical systems, as their primary treatment. It is the most ancient system and has many specialties that are superior to those of Ayurvedic medicine. The plant, widely recognized as Gotu Kola, Asiatic pennywort, Indian pennywort, or Spadeleaf, is a member of the Umbelliferae/Apiaceae family. It has been cultivated as a vegetable in regions such as China, Southeast Asia, India, Sri Lanka, Oceania, and Africa for centuries. In Southeast Asia, it has a traditional role in treating various ailments, including skin conditions, rheumatism, inflammation, syphilis, mental health issues, epilepsy, hysteria, dehydration, and diarrhea. In Indian medicinal practices, Centella asiatica (Gotu Kola) is valued for its memory-enhancing properties and its effectiveness in addressing skin disorders and nervous system issues. The medicinal benefits of this plant have been recognized by the inhabitants of Java and Indonesia for a long time. In China, it is referred to as Gotu Kola, and it was documented over 2000 years ago as one of the "miracle elixirs of life."The initial phytochemical analysis of the ethanolic extract of Centella asiatica revealed the presence of several phytochemical constituents, including carbohydrates, phenols, flavonoids, steroids, alkaloids, glycosides, proteins, tannins, terpenes, and saponins. However, sterols, gums, and mucilage were not detected.It can be concluded that Centella asiatica exhibits notable anti-epileptic effects in both MES and INH induced epilepsy in Wistar rats, comparable to the effects of Phenytoin and Diazepam. Additional research is required to clarify the mechanisms underlying the antiepileptic effects of Centella asiatica, particularly concerning its phytochemical components.

Keywords: Centella asiatica, Anti-epileptic activity, Maximal electroshock seizures (MES), Isoniazid-induced convulsions (INH), Wistar rats, Phytochemicals

INTRODUCTION

The World Health Organization (WHO) estimates that 50 million people worldwide suffer from epilepsy, a chronic, non-communicable brain illness. It is typified by frequent seizures, which are short bursts of uncontrollable movement that might affect the entire body (generalized) or only a portion of it. Occasionally, there is also a loss of awareness and control over bowel or bladder movements. These seizures, which can happen in various brain regions, are brought on by abrupt, excessive electrical discharges in a collection of brain cells.

From brief attentional lapses or muscular twitches to protracted convulsions, seizures can vary in intensity. Additionally, their frequency varies, ranging from fewer than one episode annually to multiple episodes daily. Remarkably, almost 80% of people with epilepsy reside in low- and middle-income nations, where it is frequently difficult to get the right care. Despite the fact that up to 70% of patients react to antiepileptic drugs, many people in developing nations do not obtain proper care because of a lack of funding and knowledge.

With a prevalence of about 1 in 200 people, epilepsy is the second most prevalent neurological condition in India. With estimations pointing to an incidence rate of 0.8%, it is most prevalent among children. Genetic predisposition, hormonal and chemical imbalances, infections, trauma, and abnormalities in the structure of the brain are all contributing causes. Although anyone of any age, gender, or race can develop epilepsy, the underlying cause of the condition is frequently unclear. The disorder is categorized as either idiopathic (when no known cause is identified) or symptomatic (when a recognized cause, such as a head injury or infection, is present).

Even while most seizures are short-lived and patients often recover quickly, 20–30% of people still have seizures even after taking medicine on a regular basis. Combination therapy with two or more antiepileptic medications (AEDs) is frequently necessary in these circumstances. Nevertheless, the effectiveness of contemporary pharmaceutical treatments is occasionally restricted, and they may come with side effects such organ damage, behavioral problems, and cognitive deterioration. As a result, alternative and complementary methods are gaining popularity, especially the usage of medicinal herbs, which have long been used for their therapeutic qualities.

Globally, herbal medicine continues to play a vital role in healthcare systems. Around 80% of people worldwide receive their primary medical care from conventional medicine, according to the WHO. Plants with antiepileptic qualities include Actaea racemosa, Piper methysticum, Hypericum perforatum, and Erythrophleum ivorense. Among these, the medicinal plant Centella asiatica, which is a member of the Apiaceae family, has drawn notice for its many pharmacological properties, such as its neuroprotective, antioxidant, and anti-inflammatory properties. Centella asiatica has long been utilized in Chinese, Siddha, and Ayurvedic medicine to treat a variety of illnesses, including epilepsy, anxiety, and skin and cognitive issues.

The current study uses two experimental models of epilepsy Maximal Electroshock Seizure (MES) and Isoniazid-induced seizures (INH) in Wistar rats to examine Centella asiatica's potential as an antiepileptic. In order to promote the use of Centella asiatica as a safer, plant-based substitute for traditional AEDs, the goal is to assess how well its ethanolic leaf extract reduces seizure activity.

PLANTPROFILE

1. Identification

Fig 1: *Centella asiatica* leaves and flowers

2. Scientific Classification
Kingdom: Plantae
Subkingdom: Tracheophytes
Super division: Angiosperms
Division: Eudicots
Class: Asterids
Order: Apiales
Family: Apiaceae
Genus: Centella
Species: C. asiatica

3. Synonyms
English: Asiatic pennywort, Gotu kola
Sanskrit: Mandukaparni
Hindi: Brahmi, Gotu kola
Tamil: Vallarai
Telugu: Saraswataku
Malayalam: Kudangal, Kudangayapala
Bengali: Thankuni

4. Distribution
Centella asiatica is native to tropical and subtropical regions of Asia. It is widely found in India, Sri Lanka, China, Indonesia, and Madagascar. The plant grows in swampy areas and thrives in wet, marshy environments, often near rivers or ponds. It is cultivated in various parts of India, including Kerala, Karnataka, Tamil Nadu, and West Bengal.

5. Cultivation Parameters
Centella asiatica prefers a warm, tropical climate with temperatures ranging between 20-30°C. It grows best in areas with an annual rainfall of 1500-2000 mm. The plant thrives in loamy or sandy soil with good organic content and pH levels between 5.5 and 6.5. It can grow in partially shaded areas and requires moderate watering.

Traditional Uses
Centella asiatica is highly valued in traditional medicine systems like Ayurveda, Siddha, and Traditional Chinese Medicine (TCM).
Ayurveda: Used as a brain tonic to enhance memory, treat anxiety, and improve cognitive function. It is also employed for skin disorders, wound healing, and as an anti-aging agent.
Siddha Medicine: Applied as a poultice for burns and wounds.
TCM: Utilized to treat digestive issues, liver diseases, and as a detoxifying agent.
Folk Medicine: Leaves are consumed fresh or as an infusion to treat urinary infections and fevers. The plant is also used for skin rejuvenation and treating varicose veins.

SCOPE

Over 70 million people suffer worldwide today, with 80% of them residing in poorer nations, according to the WHO. At least 55% of the 3.2 million new cases that are thought to arise annually worldwide start in adolescence. About 75% of the time, seizures answers to therapy; nevertheless, some patients have subpar results because of insufficient medical supplies and appropriate care. A person with seizures is around two to three times more likely to die young. Without borders, it is the most prevalent severe brain condition in the world. Epilepsy management is a worldwide issue, and effective therapy is crucial to avoiding or at least postponing the development of permanent problems. In contrast to the synthetic drugs that are now on the market, natural remedies for these various seizure types can be found in the form of herbal medicines or medications with relatively little side effects. While professional doctors and researchers are working to find a full and permanent solution for epileptic seizures, herbal medications as therapeutic agents are a blessing in comparison to the serious adverse reactions of conventional medical treatment. Because herbal remedies have fewer side effects than conventional medicine, they have been utilized to treat a variety of illnesses. Both the treatment of epilepsy and the advancement of its consequences are thought to be aided by traditional medications. The primary goal of the planned study is to assess Centellaasiatica's positive effects, particularly its anti-epileptic properties activity by using MES and INH model.

Aim and objective

The initial phytochemical analysis of the ethanolic extract of Centella asiatica revealed the presence of several phytochemical constituents, including carbohydrates, phenols, flavonoids, steroids, alkaloids, glycosides, proteins, tannins, terpenes, and saponins. However, sterols, gums, and mucilage were not detected. It can be concluded that Centella asiatica exhibits notable anti-epileptic effects in both MES and INH induced epilepsy in Wistar rats, comparable to the effects of Phenytoin and Diazepam.

MATERIALS AND METHOD

Ethanolic extract of Centella asiatica formulation: (EECA)

Centellaasiatica's tuberous bark was gathered from the neighborhood market, cut into thin slices, and then roasted in the shade until it was a rough, fine powder. Furthermore, they were extracted.

Purification Technique:

Soxhlet's equipment was used to extract a weighed quantity of the powder with 70% ethanol over the course of five days at ambient temperature. Following the collection of the filtrates, a viscous mass was produced by evaporating them under lower pressure, leaving behind a residue with a brownish yellow hue. At 0–4°C, the extract was kept.

A percentage Yield:

5.22 percent w/w of hydro alcoholic extract was obtained, and it was stored for later use in the refrigerator.

EXPERIMENTAL ANIMALS

For this study, Wistar rats weighing between 100 and 150 grams were employed. The inbred animals were purchased from SSM College of Pharmacy's animal house in Erode. Under typical lab circumstances, they were kept in cages of three each, with a 12-hour light/dark cycle and an ambient temperature of 22±20 C. The animals were given regular pellets meal and unlimited water for a week while they acclimated to the laboratory environment. Approval from the CPCSEA IAEC's ethical committee was acquired.

Methods

The animals were split up into five groups of six each.

Normal control was **Group I**. on day 21; a MES 60 Hz alternating current with 150 mA intensity for 0.2 seconds caused a **Group II** seizure.

MES 60 Hz alternating current of 150 mA strength was used to produce **Group III** seizures 0.2 seconds after the last dose of the standard medication (Phenytoin 25 mg/kg p.o.) on day 21.

Group IV A seizure was caused by a MES 60 Hz alternating current of 150 mA strength for 0.2 seconds on the 21st day following the administration of a lower dose of EECA (200 mg/kg p. o.) for 21 days.

On the 21st day, a seizure was caused by a MES 60 Hz alternating current of 150 mA strength for 0.2 seconds (after the previous dosage) after **Group V** received a higher dose of EECA 400 mg/kg p. o. for 21 days.

WISTAR RATS WITH ISONIAZID (INH) INDUCED EPILEPSY: [56,57,83]

One of the chemically induced techniques to assess a drug's anti-epileptic action is the isoniazid model. Patients with seizure disorders may experience convulsions as a result of taking isoniazid. Considered a **GABA-synthesis inhibitor**, isoniazid is an anti-tuberculosis medication that causes epilepsy by inhibiting pyridoxal-5-phosphate-dependent Glutamic Acid Decarboxylase (GAD), which lowers the amount of Gamma-Aminobutyric Acid (GABA), a key inhibitory transmitter substance in the mammalian brain.

The active form of pyridoxine, pyridoxal-5-phosphate, is an enzyme necessary for the production of GABA and a cofactor for GAD. Epilepsy is characterized by recurring seizures brought on by a drop in GABA levels.

Table 1: Wistar rats with INH-induced epilepsy fall within this group.

GROUPS	CATEGORY
Group I	Typical control: Vehicle Handled
Group II	Convulsion brought on by isoniazid (300 mg/kg intraperitoneally) is the negative control.
Group III	Isoniazid-induced convulsions (300 mg/kg i.p.) treated with the usual medication, diazepam (5 mg/kg i.p.)
Group IV	A lower dose of EECA (200 mg/kg p.o.) was used to treat convulsions brought on by isoniazid (300 mg/kg i.p.).
GroupV	higher dose of EECA (400 mg/kg p.o.) to treat convulsions brought on by isoniazid (300 mg/kg i.p.).

IN VITRO
Brain tissues from all groups were harvested post-euthanasia and homogenized in 0.1 N HCl in 80% ethanol. Samples were centrifuged, and supernatants were analyzed using High-Performance Thin-Layer Chromatography (HPTLC) for GABA estimation.

- **Mobile Phase:** n-butanol: glacial acetic acid: water (65:15:25 v/v/v)
- **Stationary Phase:** Silica gel GF254
- **Detection Reagent:** 0.2% ninhydrin in acetone
- **Scanning Wavelength:** 486 nm

GABA concentrations were quantified using standard calibration curves and expressed as ng/mg tissue.

RESULTS

PRELIMINARYPHYTOCHEMICALANALYSISOFEECA: [79, 80]
The Centella *asiatica*. Was put through the following procedures for initial phytochemical testing to determine whether phytoconstituents were present or absent.

I. The alkaloid check: Dilute chlorine dioxide was used to purify and filter the EECA. The following experiments were conducted using the filtrate.
a) Mayer's reagent (fluid of potassium mercuric iodine)
When Mayer's reagent was added to 0.5 ml of EECA, the existence of alkaloids was shown by the emergence of a cream color.
b) Dragendroff's test (Potassium Bismuth Iodide): 0.5 ml of EECA was treated with Dragendroff's reagent, and the existence of an alkaloid is indicated by the formation of a brownish-red precipitate.
c) The Hager's test (picric acid saturated solution)
Hager's analysis was performed on 0.5 ml of EECA, and the presence of alkaloids is indicated by the formation of a yellow precipitate.
d) Wagner's test (solution of iodine and potassium iodide)
Wagner's test was performed on 0.5 ml of EECA, and the existence of alkaloids is indicated by the formation of a brown precipitate.

II. Test for Carbohydrates:
a) Molisch's test:
3 milliliters of alcohol-based alpha-naphthol was included to the EECA, and then cautiously diluted sulfuric acid was injected along the test tube's walls. Carbohydrates are present when a violet color ring forms at the intersection of two liquids.
b) Fehling's test(CuSO4.7H2O+KOH+Potassium tartrates):
Fehling's solutions A and B were cooked in boiling water for a short while before being applied to the EECA. Precipitate with a reddish-brown hue suggests the presence of reducing sugars.
c) Benedict's test (CuSO4.7H2O + sodium citrate + sodium carbonate)
Benedict's test was performed on the EECA and it was then heated for a short while in boiling water. When reddish-orange precipitate forms, it means that degrading carbohydrates are present.
d) Barfoed's test (glacial acetic acid plus copper acetate)
After undergoing Barfoed's test, the EECA was heated for a short while in boiling water. The presence of sugars that are not reduced is indicated by the formation of a reddish orange solution.

III. Steroid testing
a) Liberamann-Burchard test: A tiny amount of glacial acetic acid, acetic anhydride, and concentrated sulfuric acid were applied to the EECA. The presence of steroids is indicated by the emergence of green color.

IV. Protein testing
a) Biuret's test: A solution of sodium hydroxide and copper sulphate was applied to the EECA. The presence of proteins is indicated by the emergence of violet color.
b) Millon's test: Millon's reagent was applied to the EECA. Proteins are indicated by the appearance of a pink color.

V. Examine Tannins
A 10% lead acetate solution was used to treat the EECA. The presence of tannins is shown by the formation of white precipitate.
c) An aqueous bromine solution was used to treat the EECA. The presence of tannins is shown by the formation of white precipitate.

VI. Phenol Test:
a) A neutral ferric chloride solution was used to treat the EECA. Phenols are indicated by the look of violet.
b) A solution of 10% sodium chloride was used to treat the EECA. Phenols are indicated by the appearance of a cream color.

VII. Flavonoid Test:
a) 10% v/v sulfuric acid was used to hydrolyze 5 ml of EECA solution, which was then cooled. It is then separated into three parts in three different test tubes after being extracted using diethyl ether. In the first, second, and third test tubes, one milliliter each of diluted sodium carbonate, 0.1N sodium hydroxide, and strong ammonia solution were introduced. The presence of flavonoids was indicated by the formation of a yellow color in each test tube.
b) Shinoda's test: After dissolving the EECA in alcohol, a piece of magnesium is added, and then powerful hydrochloric acid is poured dropwise along the test tube's walls. For a few minutes, it is heated in a bath of boiling water. The presence of flavonoids is indicated by the emergence of magenta color.

VIII. Gum and Mucilage Test: After treating the EECA with 25 milliliters of 100% alcohol, the mixture was filtered. The swelling characteristics of the filtrate were investigated.

IX. Glycoside Test: After dissolving the EECA in glacial acetic acid and adding a few drops of ferric chloride solution, strong sulfuric acid was added. The presence of glycosides is shown by the creation of a crimson ring at the junction of the two liquids.

X. Saponin Test: In a test tube, 1 ml of EECA was diluted with 20 ml of distilled water and thoroughly shaken. Saponins are present when foam forms in the upper portion of the test tube.

XI. Terpene Test: After treating the EECA with tin and thionyl chloride, a pink color suggests the presence of terpenes.

XII. Sterol test: After treating the EECA with a 5% potassium hydroxide solution, the presence of sterols is indicated by the emergence of a pink color.

82 Acute toxicity tests were conducted on Centellaasiatica's tuberous barks, and the results showed that they were safe. p. o. Therefore, 200 mg/kg p.o. (low dose) and 400 mg/kg p.o. (high dose) were chosen for the investigation.

IN VIVO Techniques
• **Method 1:** Wistar rats were given maximal electroshock (MES) to produce epilepsy.
• **Method 2:** Epilepsy in Wistar rats caused by isoniazid (INH)

TESTING TECHNIQUE: I [56, 57, 86] WISTAR RATS WITH MAXIMAL ELECTROSHOCK (MES) INDUED EPILEPSY

One physical technique for assessing a drug's anti-epileptic action is the MES model. While anti-absence seizure medications cannot be examined, this technique is utilized for screening medications that are helpful for regional and widespread tonic-clonic (grandmal) convulsions. This technique is frequently applied to rats or mice. For 0.2 seconds, a stimulating device with retinal or ear electrodes that delivers a steady current of 50 mA for mice and 150 mA for rats at a frequency of 50–60 Hz is used. After an electrical shock is applied, the animals are watched for two minutes. Tonic limb bending, tonic limb consequently, and a variable short clonic interval are the phases that the seizure goes through. The inhibition of tonic hind limb extension is a marker of the effectiveness of novel antiepileptic medications.

Preliminary Phytochemical analysis of Ethanolic extract of *Centella asiatica*. (EEca)

The initial phytochemical analysis of the ethanolic extract of Centella asiatica revealed the presence of several phytochemical constituents, including carbohydrates, phenols, flavonoids, steroids, alkaloids, glycosides, proteins, tannins, terpenes, and saponins. However, sterols, gums, and mucilage were not detected.

Table 2: Preliminary Phytochemical analysis of Ethanolic extract of Tuberous barks of *Centella asiatica*

S.No	Phytochemical constituents	Presence/Absence
1	Alkaloids	*Present*
2	Carbohydrates	*absent*
3	Steroids	*Present*
4	Proteins	*Present*
5	Tannins	*Present*
6	Phenol	*Present*
7	Flavonoids	*Present*
8	Gumsand mucilage	*Absent*
9	Glycoside	*Present*
10	Saponins	*Present*
11	Terpene	*Present*
12	Sterols	*bsent*

EFFECTOFEECA ONISONIAZID(INH)INDUCEDEPILEPSYINWISTAR RATS.

Table 3: Effect of EECA on Latency in INH induced epilepsy in wistar rats.

GROUPS	LATENCY onsetepilepticseizurein sec)
GroupI	NIL
GroupII	148 ±4.79
GroupIII	105 ±2.4a****b****
GroupIV	NIL
GroupV	113±6.31a****b****

Valuesareexpressedasmean±SEMof6animals. Comparisons were made between the following:

- Group II compared with Group III, IV and V was considered asa
- Group III compared with Group IV and V was considered asb

StatisticalSignificancetestforcomparisonwasdonebyonewayANOVAfollowedby Dunnets‘t’ test. Where * ($p< 0.05$), **($p< 0.01$), *** ($p<0.001$), ****($p<0.0001$)
ns-nonsignificant.

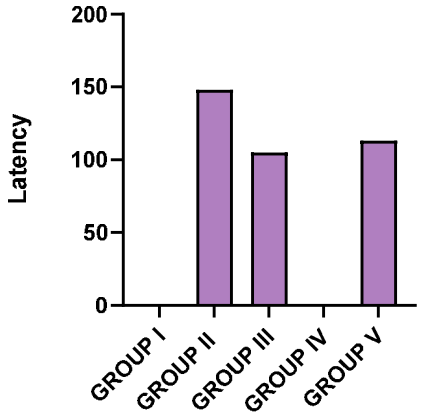

Fig 2: Effect of EECA on Latency in INH induced epilepsy in wistar rats.

Latency in INH induced epilepsy in wistar rats.

- The LatencyinGroupIIIwassignificantlydecreasedcomparedwithgroupII,IVand V ($p<0.0001$).
- The LatencyinGroupIVwassignificantlyabolishedwhencomparedwithgroupII and V ($p<0.0001$).

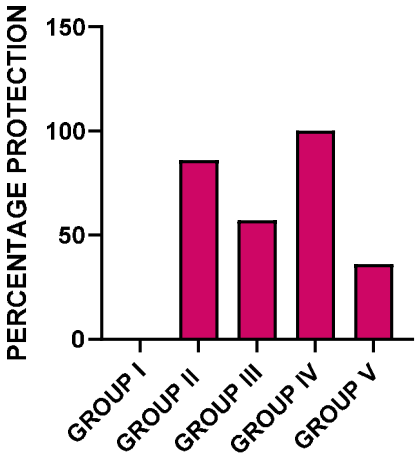

Fig 3: Effect of EECA on Percentage protection in INH induced epilepsy in wistar rats.

ThepercentageprotectioninINHinducedepilepsyinwistarrats

- ThepercentageprotectioninGroupVwassignificantlydecreasedwhen compared with group II, III and IV.
- ThepercentageprotectioninGroupIVwassignificantlyincreasedwhencompared with group II and III.

INVITRO-EFFECTOFEECAONESTIMATIONOFGABAINMESINDUCED EPILEPSY IN WISTAR RATS

Table 4: Effect of EECA on estimation of GABA in MES induced epilepsy in wistar rats

Groups	GABA(ng/mgtissue)
GroupI	416.38±1.57
GroupII	255.46±2.37a****
GroupIII	368.28±1.84a****b****
GroupIV	287.44±1.98a****b****c****
GroupV	310.57±1.48a****b****c****

Valuesareexpressedasmean±SEMof6animals. Comparisons were made between the following:

- Group I compared with Group II, III, IV and V was considered asa
- Group II compared with Group III, IV and V was considered asb
- Group III compared with Group IV and V was considered asc

StatisticalSignificancetestforcomparisonwasdonebyonewayANOVAfollowedby Dunnets't' test. Where * (p< 0.05), **(p< 0.01), *** (p<0.001), ****(p<0.0001) ns-nonsignificant.

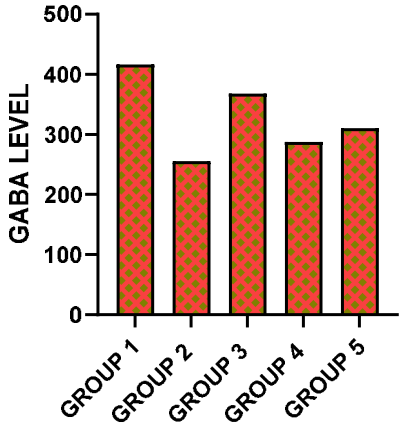

Fig 4: Effect of EECA on estimation of GABA in MES induced epilepsy in wistar rats

Estimation of GABA in MES induced epilepsy in wistar rats

- The Concentration of GABA in Group I (Vehicle Control) was significantly increased when compared with Group II, III, IV and V ($p<0.0001$).
- TheConcentrationofGABAinGroupIIwassignificantlydecreasedwhencompared with Group III, IV and V ($p<0.0001$).
- TheConcentrationofGABAinGroupIIIwassignificantlyincreasedwhencompared with Group IV and V ($p<0.0001$).

HISTOPATHOLOGICALANALYSISOFBRAININMESINDUCEDEPILEPSY IN WISTAR RATS

Table 5: Histopathological analysis of braininMES induced epilepsy in wistar rats

GROUPI	Normalcontrol	HaematoxylinandEosin-stained section shows the normalbraintissuedepictedintactcell architecturewithnormalamountof neurotransmitters
GROUPII	Negativecontrol-Convulsioninduced by MES 60 Hz alternating current of 150 mA intensity for 0.2 sec.	Haematoxylin and eosin-stained sectionshowthereislessneuron density.
GROUPIII	Convulsion induced by MES 60 Hz alternatingcurrentof150mAintensity for0.2sectreatedwithstandarddrug - Phenytoin (25mg/kg p.o.)	Haematoxylin and eosin-stained section of the brain tissue showed no significant alterations observed in this group and tissues showed a normal picture or brain cells, less proliferation and more neuronaldensityat hippocampal region
GROUPIV	Convulsion induced by MES 60 Hz alternatingcurrentof150mAintensity for 0.2 sec treated with Lower dose of EEMR (200 mg/kg p.o).	Haematoxylin and Eosin-stained sectionofthebraintissueshowedno pathological damages and cellular architecture are intact with more neuronal density compared to the MESalonetreated group.
GROUPV	Convulsion induced wistar rats by MES 60 Hz alternatingcurrent of 150 mA intensity for 0.2 sec treated with HigherdoseofEEMR(400mg/kgp.o).	Haematoxylin and Eosin stained section of the brain tissue showed increased neuron density when comparedtotheEEMR(200mg/kg/p.o)

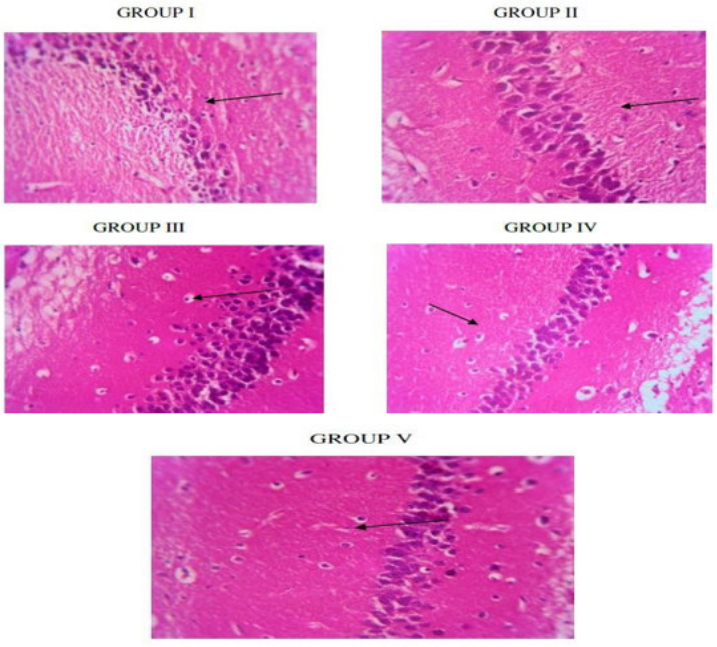

Fig 5: HistopathologyofBrainin MES induced epilepsy in wistar rats

DISCUSSIONS

The present study evaluated the anti-epileptic potential of ethanolic extract of Centella asiatica (EECA) using two established seizure models: Maximal Electroshock (MES) and Isoniazid (INH)-induced convulsions in Wistar rats. The results demonstrated a significant protective effect of EECA against seizures in both models, supporting the traditional use of C. asiatica for neurological conditions.

In the MES model, which mimics generalized tonic-clonic seizures in humans, EECA treatment for 21 days significantly reduced the duration of all major seizure phases, including flexion, extension, clonus, stupor, and recovery. A notable reduction in the hind limb extensor phase suggests that EECA can inhibit the spread of seizure activity, an effect similar to that observed with phenytoin. The MES model typically causes increased Na^+ and Ca^{2+} influx, leading to depolarization and neuronal hyperexcitability. The observed effects of EECA may be attributed to the modulation of these ion channels, potentially stabilizing neuronal membranes.

Similarly, in the INH-induced seizure model, which is used to replicate aspects of temporal lobe epilepsy and status epilepticus, EECA significantly delayed seizure onset and reduced seizure duration. INH inhibits GABA synthesis by interfering with pyridoxine metabolism, thus lowering GABA levels and triggering seizures. The ability of EECA to reduce seizure severity and increase protection percentage in this model suggests that it may enhance GABAergic neurotransmission.

Biochemical analysis revealed increased GABA levels in the brain tissue of EECA-treated groups, compared to the untreated seizure groups, particularly in the MES model. This finding supports the hypothesis that EECA may exert its anti-epileptic effects by increasing GABA synthesis or inhibiting GABA degradation, possibly through GABA transaminase inhibition.

Histopathological studies further confirmed the neuroprotective effect of EECA, showing increased neuronal density in the hippocampal regions of EECA-treated animals when compared to seizure-only groups. This indicates that the extract may mitigate neuronal damage commonly associated with recurrent seizures.

The anti-epileptic effect of Centella asiatica can also be linked to its rich phytochemical composition, particularly its flavonoids, saponins, and triterpenoids. Flavonoids are known to possess antioxidant and neuroprotective properties and have been shown in other studies to modulate GABA_A receptors. The antioxidant potential of C. asiatica may also play a role in protecting neurons from oxidative stress, a key contributor to seizure-induced neuronal injury.

While conventional antiepileptic drugs like phenytoin and diazepam are effective, their long-term use is associated with significant side effects and toxicity. In contrast, plant-based treatments like EECA offer a promising alternative due to their safety profile, cost-effectiveness, and ease of access. In conclusion, the findings from this study support the traditional use of Centella asiatica in managing epilepsy and highlight its potential as a complementary therapeutic agent. However, further studies are required to isolate specific active compounds, clarify the exact mechanisms of action, and evaluate long-term safety and efficacy through clinical trials.

CONCLUSION

In conclusion, it can be stated that Centella asiatica demonstrates significant anti-epileptic activity in both MES and INH induced epilepsy in Wistar rats, comparable to the effects of Phenytoin and Diazepam. Additional research is required to clarify the mechanisms underlying the antiepileptic effects of Centella asiatica, particularly concerning its phytochemical components.

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