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Anti-Epileptic Activity Of Casticin Phytoconstituent From Vitex Negundo On Validated Animal Model

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Abstract

The objective of this research is to explore the potential antiepileptic effects of a methanolic extract of vitex negundo leaf on seizures in mice that were induced by lithium pilocarpine, maximum electroshock (MES), strychnine, picrotoxin, and pentylenetetrazole. Specifically, the study will focus on the effects of the extract on seizures caused by these substances. The extract was able to prevent convulsions that were brought on by MES, and it was also able to help normal medications work more effectively against convulsions that were brought on by other chemicals. In a manner that is dependent on the quantity of flavanoids that are present, the flavanoids that are contained in the methanolic extract of vitex negundo have the potential to disrupt the gabanergic process and block Na+ channels. Based on the preliminary data, it seems that the methanolic extract of vitex negundo has the potential to be used as a therapeutic resource for the treatment of epilepsy.

Keywords: *Vitex negundo, methanolic extract, MES, electroclinical, animal models, ect.*

Intorduction

Epilepsy, a complex neurological disorder characterized by recurrent seizures, represents a significant global health burden affecting millions of individuals across all age groups. This introduction provides an overview of epilepsy, encompassing its epidemiology, etiology, clinical manifestations, impact on patients' lives, current treatment modalities, and ongoing research efforts[1]. Seizures, the hallmark feature of epilepsy, result from abnormal and excessive neuronal activity in the brain, leading to temporary disturbances in behavior, consciousness, sensation, or motor function. Seizures manifest in various forms, ranging from brief episodes of staring or altered consciousness to convulsive movements and loss of consciousness. The diverse clinical manifestations of seizures underscore the heterogeneous nature of epilepsy, with different seizure types and syndromes reflecting underlying differences in the brain's structure and function[2]. Epilepsy exerts a profound impact on the lives of affected individuals, extending beyond the seizures themselves to encompass various physical, psychological, social, and economic challenges. Living with epilepsy entails navigating uncertainties regarding seizure control, managing medication side effects, coping with stigma and discrimination, and

addressing limitations in employment, education, and social participation[3]. While AEDs are effective in achieving seizure remission in the majority of patients, approximately one-third of individuals with epilepsy experience inadequate seizure control or intolerable side effects, highlighting the need for alternative therapeutic strategies[4]. Despite the availability of various treatment modalities, a significant proportion of individuals with epilepsy continue to experience seizures and face challenges in achieving optimal seizure control and quality of life. Furthermore, the psychosocial impact of epilepsy, including stigma, discrimination, and socioeconomic disparities, remains a pervasive issue that warrants attention.[5]

In conclusion, epilepsy is much prone and complex neuronal disorder found by repeated seizures, diverse clinical manifestations, & significant psychosocial consequences. Despite advances in diagnosis and treatment, epilepsy remains a challenging condition that requires holistic and individualized management approaches.[6] Ongoing research efforts hold promise for advancing our understanding of epilepsy, identifying new therapeutic targets, and improving outcomes for individuals living with this condition. By raising awareness, promoting education, fostering collaboration, and advocating for the needs of individuals with epilepsy, we can strive towards a future where epilepsy is better understood, effectively treated, and destigmatized.

1. Introduction of Epilepsy

The term "epilepsy" is used to describe a group of disorders that are characterized by bouts of seizures that occur repeatedly.[7] Epilepsy encompasses each and every one of these individual problems. One of the symptoms that is linked to a wide range of illnesses is the occurrence of a significant number of seizures. The neuronal activity in the brain that causes this kind of seizure is not only abnormal, but it is also triggered by activity. This sort of seizure is cause by both of these factors. These seizures are the result of this action, which is accountable for them. When it comes to giving epilepsy a classification, there are a few main factors that are applied. These features include, in addition to the electroclinical parameters, the type of seizure, the etiology, the age at which the seizures first manifested, and any other characteristics that may be present.[8-10] The epilepsy classification system is underpinned by this collection of traits, which acts as the foundation. Throughout the course of this conversation, we will discuss the fundamental classifications of epilepsy, as well as the clinical symptoms that are associated with each of these classifications, the underlying causes of epilepsy, and the challenges that are associated with the management of epilepsy showing in Fig.no.1

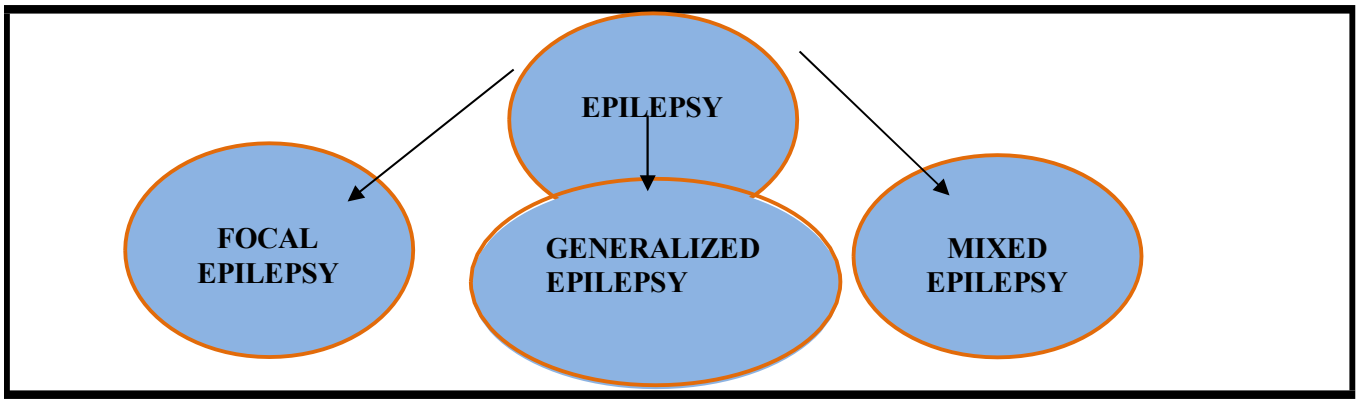


Fig.No. 1 depicted in the flow diagram in types of epilepsy

In conclusion, epilepsy encompasses a wide range of disorders that are distinguished by the occurrence of seizures for an extended period of time. The type of seizure and the electroclinical characteristics of the individual are the two primary factors that identify the two primary categories of epilepsy, which are focal epilepsy and generalized epilepsy.[11,12] When it comes to the classification, diagnosis, and treatment of epilepsy, a multidisciplinary approach is essential. It is necessary for this strategy to take into account clinical expertise,

neuroimaging investigations, information obtained from electroencephalograms, and the preferences of the healthcare provider. It is possible for medical professionals to tailor treatment strategies to the specific needs of individual patients if they have a basic awareness of the many types of epilepsy and the factors that contribute to the development of each kind.[13] Those who are living with epilepsy are able to experience an improvement in their quality of life and the opportunity to manage their seizures in the most effective manner possible.[14]

Table.1: Medications for Common Epilepsy in Children

Epilepsy Subtype	Medications Used to Treat Epilepsy
focal seizures	phenytoin, lacosamide, zonisamide, oxcarbazepine, clobazam, lamotrigine, levetiracetam, sodium valproate, and topiramate
generalised tonic clonic seizures	phenytoin, lacosamide, zonisamide, oxcarbazepine, clobazam, lamotrigine, levetiracetam, sodium valproate, and topiramate.
absence seizures	ethosuximide, lamotrigine, sodium valproate
myoclonic, tonic and atonic seizures	clobazam, clonazepam, topiramate, sodium valproate, levetiracetam, lamotrigine, and timolol
Children's spasms	prednisolone, vigabatrin, ACTH, nitrazepam
infant convulsions	topiramate, clonazepam, phenobarbitone, phenytoin, and levetiracetam

2. Advancement of herbal sources of anti-epileptic agents[16]

Herbal remedies have been utilized for centuries in the management of various health conditions, including epilepsy. While the scientific evidence supporting the efficacy of herbal treatments for epilepsy is limited compared to conventional anti-epileptic drugs, some herbal remedies have shown promise in preclinical and clinical studies. Flow diagram showing the antiepileptic drugs in herbal sources. Here are a few herbal remedies that have been explored for their potential anti-epileptic properties.

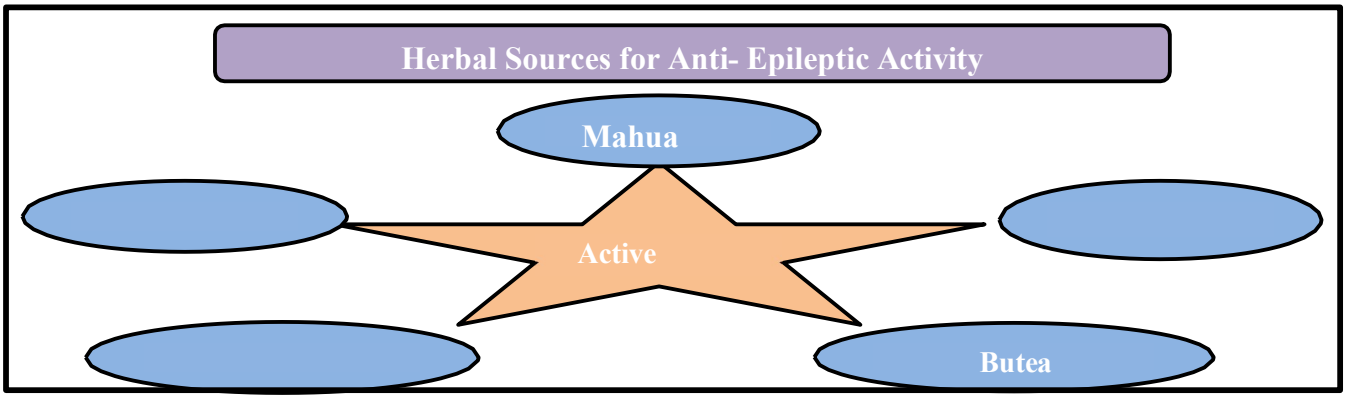


Fig.No.2 Antiepileptic Activity of Herbal Sources

3. Plant profile of Vitex Negundo

The five-leaved chaste tree, or Vitex Negundo, is a fragrant shrub or small tree that grows naturally in Southeast Asia and the Indian subcontinent. It typically grows up to 10 meters in height and has compound leaves with five lance-shaped leaflets. The flowers are small and bluish-purple in color, arranged in spikes. In traditional medicine systems like Ayurveda, different parts of Vitex negundo are used for various medicinal purposes. Its leaves, seeds, and roots are believed to have therapeutic properties and are used to treat a wide range of ailments such as fever, inflammation, respiratory disorders, skin diseases, and menstrual disorders.The plant's therapeutic qualities are due in part to the phytochemicals it contains, which include essential oils, terpenoids, alkaloids, and flavonoids.Analgesic, anti-inflammatory, antioxidant, antibacterial, antidiabetic, and immunomodulatory properties are just a few of the pharmacological actions demonstrated by scientific investigations with Vitex negundo preparations.

4. Preliminary phytochemical analysis of Vitex negundo[18,19]

Samples of plant extract were subjected to preliminary phytochemical analysis, which revealed the presence of a number of phytochemical components. These components included carbohydrates, phenols, flavonoids, steroids, alkaloids, glycosides, and saponins. Mucilage, terpenes, sterols, proteins, tannins, and gums were not present at all. Terpenes were also not present.

Table No.2 Presence of phytoconstituents presence of Vitex Negundo

S.No	Compounds	Presence/Absence
1	Carbohydrate	---
2	Flavanoids	+++
3	Saponin	+++
4	Tannin	---
5	Glycosides	+++
6	Alkaloid	+++

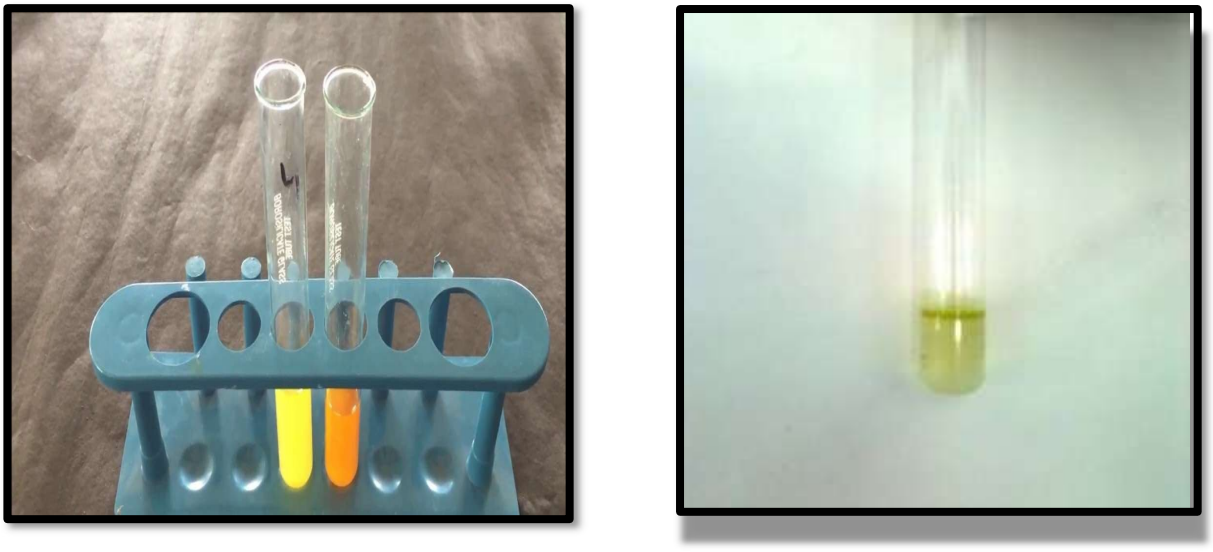
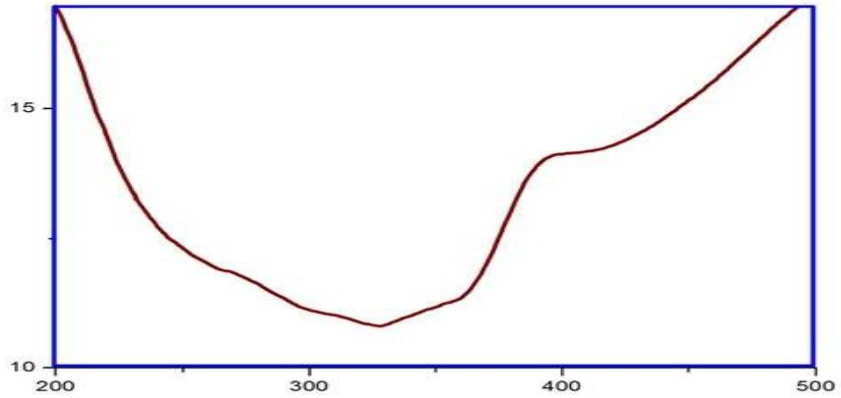


Fig.No.3 Presence of Flavonoids and Saponin

5. UV-Visible Spectroscopy analysis of Vitex negundo extracts

The UV-Vis spectrophotometer is utilized for spectroscopy involving photons in the UV-visible region. UV-Vis spectroscopy employs light within the visible range or its neighboring range. The color of the chemicals directly impacts absorption within the visible range. Molecules experience electronic transitions within these regions of the electromagnetic spectrum . In the current investigation, the UV-Vis spectral profile displayed peaks at 330 nm.

Fig.No.4 UV spectrum of plant extract of Vitex negundo



6. Chromatographic investigation by TLC Methods

To illustrate the thin layer chromatogram (TLC) that was carried out on the ethyl acetate extract of Vitex negundo that was utilized in the experiment, the figure 5.2 is presented here. After the use of a solvent phase that was composed of chloroform, ethanol, ethyl acetate, hexane, and acetic acid in the proportions of 10:2:5:1:1,

A spot with an Rf value of 0.80 was detected using the thin-layer chromatography (TLC) technique.

Fig.No.5 TLC analysis indicated the presence of a spot

7. Pharmacological Screening Tests[20,21]

7.1 Strychnine induced seizure test

Strychnine, when given intraperitoneally at a dose of 4 mg/kg, caused tonic-clonic convulsions in mice. The seizures began at 3.04 ± 0.13 seconds and all control subjects died. Compared to the control group, there was a

notable delay in the beginning of tonic-clonic convulsions when vitex negundo was administered at the same dose of 4 mg/kg (14.66 ± 0.43 seconds; $p < 0.001$). Nonetheless, the death rates of the vitex negundo-treated group and the control group were not significantly different.

7.2 Maximal electroshock seizure test

All subjects died after a 56 mA electrical shock that was given for 0.2 seconds caused the hind limbs to extend. Vitex negundo (4 mg/kg, i.p.)-treated animals, on the other hand, had no convulsions and were completely protected against death. Furthermore, there was a dose-dependent decrease in the time of hind limb extension (10.25 ± 0.41 at 4 mg/kg) after administering Vitex negundo. Furthermore, according to www.tandfonline.com, Vitex negundo medication successfully protected against mortality caused by maximal electroshock.

7.3 Pentylenetetrazole seizure test

A single intraperitoneal injection of pentylenetetrazole (75 mg/kg) was found to cause tonic-clonic convulsions in this study, with a start time of 1.79 ± 0.32 minutes, and ultimately result in a death rate of 100%. Diazepam (5 mg/kg, intraperitoneally)-administered animals failed to show no signs of convulsions and were completely protected from death. That being said,When given at different doses, Vitex negundo significantly postponed the start of tonic-clonic contractions.seizures (12.35 ± 0.95; $p < 0.05$) at 4 mg/kg, respectively. Most notably, when given Vitex The results showed that negundo (4 mg/kg) significantly reduced mortality caused by PTZ-induced convulsions by 60%, according to www.tandfonline.com.

7.4 Picrotoxin induced seizure test Exposure to picrotoxin (4 mg/kg; i.p.) instigated tonic-clonic convulsions in mice , with an onset recorded at 229.80 ± 10.20 seconds and resulting in 100% mortality within the picrotoxin-only group. Interestingly, treatment with vitex negundo at a dosage of 4 mg/kg notably postponed the initiation of tonic-clonic convulsions (1134.60 ± 14.76; $p < 0.001$) compared to the control condition.

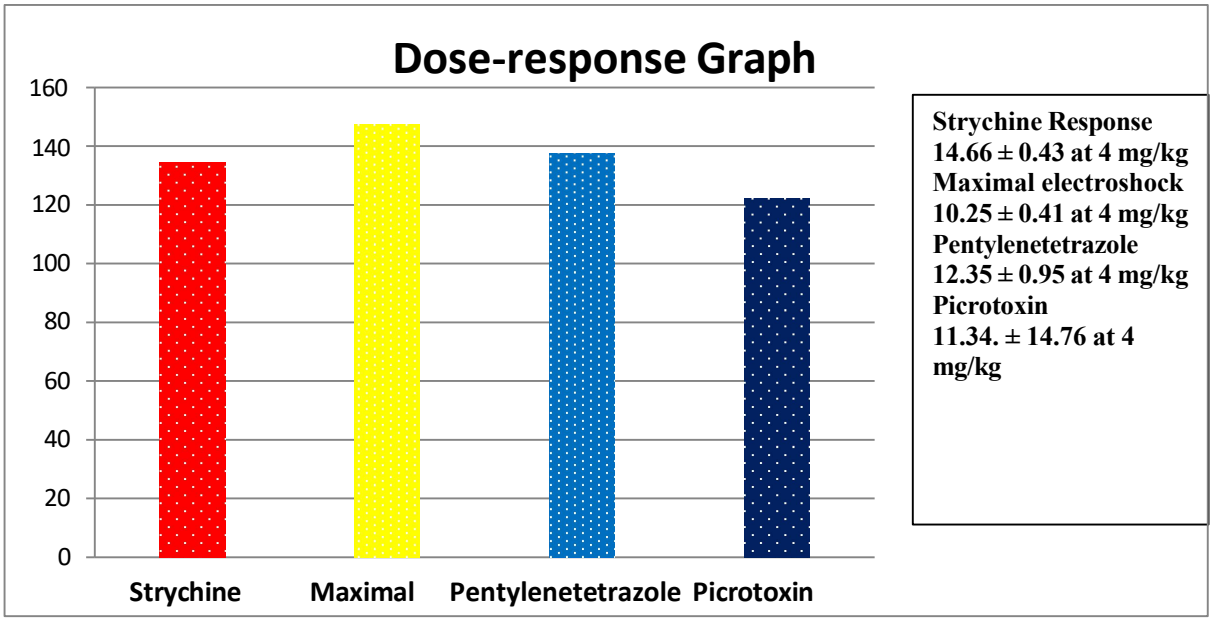


Fig.No.6 Bar graph showing the Different model and Dose response curve

Fig.No.7 Experimental photographic images showing the activity of mice after dose

Results and Discussion

To determine whether or not Vitex negundo possesses anticonvulsant effects, the research included a number of different assays. Particular absorption peaks at 330 nm were discovered by UV-Vis spectroscopy, which indicated the presence of electronic transitions inside the molecule. An ethyl acetate extract of Vitex negundo was subjected to thin layer chromatography (TLC), which revealed the existence of a distinct spot with an Rf value of 0.80. This finding may indicate the presence of specific chemicals. During the strychnine-induced seizure test, the administration of Vitex negundo resulted in a considerable delay in the beginning of convulsions when compared to the control group. However, this did not bring about any changes in fatality rates. Additionally, throughout the most severe electroshock seizure test, Vitex negundo demonstrated a dose-dependent protective effect against convulsions as well as mortality. According to the results of the pentylenetetrazole seizure test, Vitex negundo slowed down the start of convulsions and offered some degree of protection against death. To conclude, in the test of seizure induced by picrotoxin, the administration of Vitex negundo resulted in a considerable delay in the beginning of convulsions as compared to the control group. Overall, these findings suggest that Vitex negundo possesses anticonvulsant properties, as evidenced by its ability to delay the onset of convulsions in various seizure models. Further research could explore the specific compounds responsible for these effects and their mechanisms of action.

Conclusion

The future scope of research on the anti-epileptic activity of phyto-constituents from herbal plants is broad and promising. By advancing phytochemical profiling, optimizing extraction and formulation techniques, developing novel animal models, and elucidating mechanisms of action, researchers can uncover new therapeutic potentials. Clinical translation, comprehensive safety assessments, economic evaluations, and regulatory considerations will be crucial for bringing these findings to clinical practice. Engaging with the public and professionals, adhering to ethical standards, and respecting cultural contexts will ensure that research is conducted responsibly and effectively. Embracing interdisciplinary approaches, exploring synergistic effects, and focusing on rare and intractable epilepsy forms will further enhance the impact of herbal medicine in epilepsy treatment. The investigation of phyto-constituents for their anti-epileptic properties holds significant

promise, yet the research is subject to various limitations that impact its scope, reliability, and applicability. Here, we explore the limitations in depth, spanning methodological, biological, and practical constraints, and their implications for future research and clinical application.

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