



Comprehensive Review on Epilepsy and the Therapeutic Potential of Indian Medicinal Plants Used in Chronic Epilepsy

Mr.Parthasarathy.B^{1*}, D.Benitojohnson¹, Thiyagheshwaran.S¹, Kaviya.G¹, Lakshana.E.V¹, Sathish.S¹,
Dr. Neelaveni Thangavel²

1.Department of Pharmacology, RVS College of Pharmaceutical Sciences, Coimbatore, Tamil Nadu, Affiliated to The Tamil Nadu Dr MGR Medical University, Guindy, Chennai - 600032, Tamil Nadu, India.

2.Department of Pharmaceutical Chemistry, RVS College of Pharmaceutical Sciences, Coimbatore, Tamil Nadu, Affiliated to The Tamil Nadu Dr MGR Medical University, Guindy, Chennai-600032, Tamil Nadu, India.

Received: 18 January 2026

Revised: 30 January 2026

Accepted: 19 February 2026

ABSTRACT:

Epilepsy is a chronic neurological disorder characterized by recurrent unprovoked seizures resulting from abnormal neuronal hyper excitability and synchronization. Despite the availability of multiple antiepileptic drugs (AEDs), nearly 30–40% of patients remain drug-resistant and long-term therapy is frequently associated with adverse effects, hepatotoxicity, cognitive impairment, and economic burden. These limitations have prompted growing interest in plant-based therapeutics as safer and more accessible alternatives. This review comprehensively summarizes the pathophysiology of epilepsy, classification of seizures, and the mechanisms and limitations of current AED therapy, and highlights the therapeutic potential of Indian medicinal plants used in chronic epilepsy management. Traditional systems such as Ayurveda and Siddha describe numerous herbs including *Bacopa monnieri*, *Withania somnifera*, *Valeriana jatamansii*, *Tinospora cordifolia*, *Centella asiatica*, and others with documented anticonvulsant, neuroprotective, antioxidant, and anxiolytic properties. Experimental evidence from MES and PTZ seizure models indicates that many phytoconstituents act through GABAergic enhancement, glutamatergic inhibition, ion channel stabilization, and reduction of oxidative stress. Emerging preclinical and limited clinical data suggest that botanical agents may serve as effective adjuncts to conventional therapy with improved safety profiles. Future directions include phytochemical isolation, standardized polyherbal formulations, and well-designed clinical trials to validate efficacy and safety. Integrative approaches combining conventional AEDs with evidence-based herbal therapies may offer improved long-term outcomes in chronic epilepsy management.

Keywords: Epilepsy, Anticonvulsant Agents, Medicinal Plants, Phytochemicals, GABAergic Mechanisms and Drug-Resistant Epilepsy

INTRODUCTION:

Epilepsy is a chronic and heterogeneous neurological disorder characterized by recurrent, unprovoked seizures resulting from abnormal, excessive, and synchronous neuronal activity in the brain. It affects millions of people worldwide and represents one of the most common long-term neurological conditions, with a global prevalence of approximately 0.5–1% and a lifetime risk of up to 3%. Seizures may arise from focal or generalized disturbances in neuronal signaling and are associated with significant physical, psychological, social, and economic burden. Advances in neuro-imaging, electrophysiology, and molecular neuroscience have improved the understanding of seizure classification and epileptic syndromes; however, effective long-term management remains a major clinical challenge.

Current management of epilepsy primarily relies on antiepileptic drugs (AEDs), which act through mechanisms such as enhancement of GABAergic inhibition, suppression of glutamatergic excitation, and stabilization of voltage-gated ion channels. Although many newer AEDs have been introduced, nearly 30–40% of patients continue to experience drug-resistant seizures. Moreover, long-term AED therapy is frequently associated with adverse effects including sedation, cognitive impairment, hepatotoxicity, endocrine disturbances, and drug–drug interactions, which negatively affect treatment adherence and quality of life. The high cost of prolonged therapy further adds to the treatment burden, especially in low- and middle-income regions.

These limitations have stimulated growing interest in alternative and complementary therapeutic approaches, particularly plant-based medicines used in traditional systems such as Ayurveda, Siddha, and other ethnomedical practices. Numerous Indian medicinal



plants have historically been used for the management of convulsive disorders and nervous system imbalances. Modern pharmacological investigations have demonstrated that many of these plants possess anticonvulsant, neuroprotective, antioxidant, and anxiolytic activities. Their bioactive phytoconstituents—including alkaloids, flavonoids, terpenoids, and saponins—are reported to modulate GABAergic transmission, regulate ion channels, reduce oxidative stress, and stabilize neuronal excitability.

In this context, a comprehensive pharmacological review of epilepsy and the therapeutic potential of Indian medicinal plants is essential to bridge traditional knowledge with modern scientific evidence and to support the development of safer and more effective adjunctive strategies for chronic epilepsy management.

TYPES OF SEIZURES:

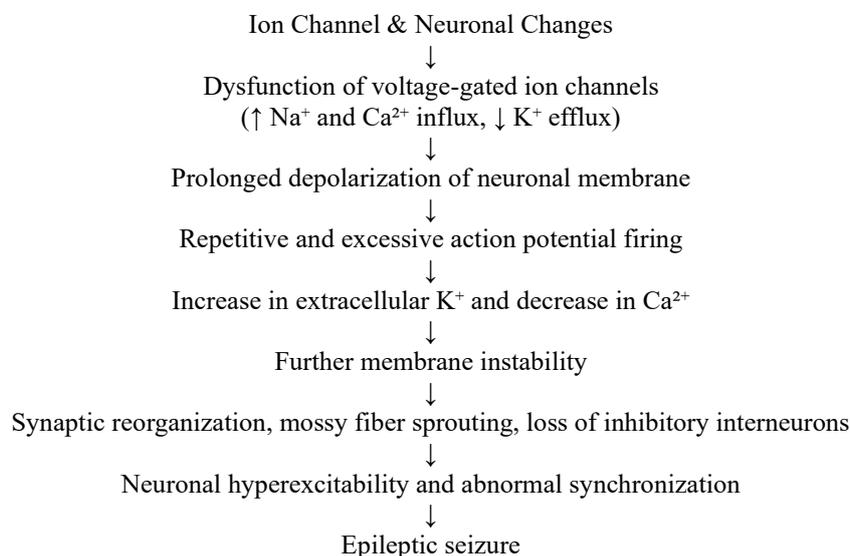
<p>1. Focal partial seizures</p> <ul style="list-style-type: none">a. Basic<ul style="list-style-type: none">i. Sensory engagementii. Independent actioniii. Psychic endeavorsiv. Jacksonian motor activityb. Complicated<ul style="list-style-type: none">i. Psychomotor or temporal lobe	<p>2. Broadly applicable</p> <ul style="list-style-type: none">i. Grand mal, or tonic-clonicii. Absence (petit mal)iii. Myocloniciv. Spasms that are infantilev. Atonic (akinetic)vi. Lennox-Gastaut syndrome (febrile seizures)
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DRAWBACKS OF AVAILABLE ANTIPILEPTIC DRUGS:

Many people are worried about the adverse effects of taking medication for epilepsy since they can negatively impact their quality of life. Many men are having erectile dysfunction after using anti-epilepsy medicine, while women with epilepsy are not able to conceive. Children's typical adverse effects include restlessness, drowsiness in class, and inattention, all of which interfere with proper brain function. As a result, some people will choose conventional drugs as a way to deal with these negative effects.

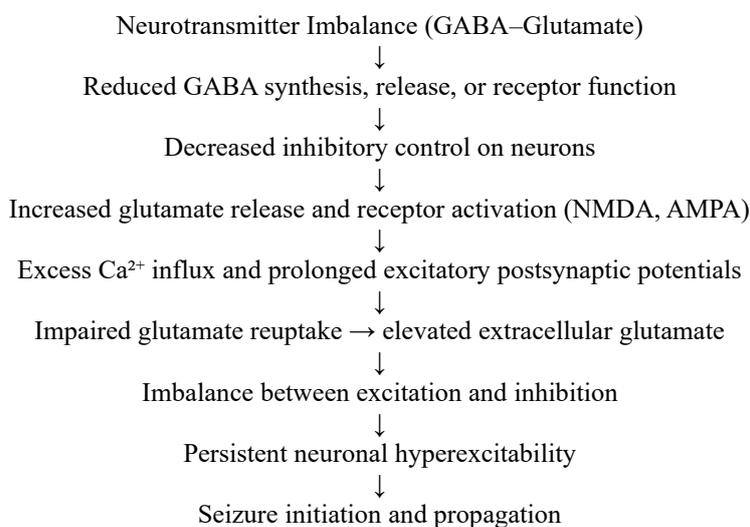
PATHOPHYSIOLOGY:

Neuronal Hyperexcitability :





Neurotransmitter Imbalance (GABA and Glutamate) :



LIMITATIONS OF CURRENT DRUG THERAPY:

Drug Resistance (30–40%):

Despite the availability of a wide range of antiepileptic drugs (AEDs), approximately 30–40% of patients continue to experience seizures and are classified as having drug-resistant or refractory epilepsy. This resistance arises due to multiple mechanisms, including altered drug targets such as ion channels and neurotransmitter receptors, increased expression of drug efflux transporters like P-glycoprotein at the blood–brain barrier, and structural and functional reorganization of epileptic neuronal networks. Genetic variations influencing drug metabolism and target sensitivity further contribute to poor therapeutic response. As a result, seizure control remains inadequate in a significant proportion of patients even after optimal monotherapy or combination therapy, highlighting a major limitation of current pharmacological management.

Side Effects (Sedation and Hepatotoxicity):

The clinical use of antiepileptic drugs is frequently limited by their adverse effect profile, which negatively impacts patient compliance and quality of life. Sedation, drowsiness, cognitive impairment, dizziness, and psychomotor slowing are among the most commonly reported central nervous system side effects, particularly with older generation AEDs. In addition, hepatotoxicity represents a serious concern with several antiepileptic agents, especially those undergoing extensive hepatic metabolism. Elevations in liver enzymes, acute liver injury, and, in rare cases, fatal hepatic failure have been reported, necessitating regular monitoring of liver function during long-term therapy. These adverse effects often require dose reduction or drug discontinuation, compromising seizure control.

Cost:

Economic burden is another important limitation of long-term antiepileptic drug therapy, particularly in low- and middle-income countries. Newer generation AEDs, although associated with improved tolerability in some cases, are often significantly more expensive than conventional drugs. The cumulative cost of lifelong medication, regular clinical follow-ups, laboratory monitoring, and management of adverse effects places a substantial financial strain on patients and healthcare systems. High treatment costs can lead to poor adherence, interrupted therapy, and increased risk of seizure recurrence.

Long-Term Dependency:

Epilepsy is a chronic neurological disorder that typically requires prolonged or lifelong pharmacotherapy. Long-term dependency on antiepileptic drugs raises concerns related to cumulative toxicity, drug–drug interactions, and declining efficacy over time. Prolonged use may also contribute to tolerance, necessitating dose escalation or polytherapy, which further increases the risk of adverse effects. Additionally, psychological dependence and reduced patient autonomy associated with continuous medication use can negatively affect social functioning and overall quality of life. These limitations emphasize the need for safer, more effective, and disease-modifying therapeutic strategies.



TRADITIONAL USE OF MEDICINAL PLANTS IN EPILEPSY:

Traditional medicine systems, particularly in developing regions, play a critical role in managing epilepsy due to limited access to modern antiepileptic drugs (AEDs), their high costs, and significant side effects. These traditional approaches are deeply rooted in cultural history and provide alternative therapeutic options for the nearly 30% of patients whose seizures do not respond to standard treatments.

Ayurveda, Siddha, and Folk Medicine Approaches:

In the Indian systems of Ayurveda and Siddha, plants like *Bacopa monnieri* (Brahmi) are traditionally used for their neuroprotective and sedative effects, with research indicating they can increase GABA levels in the brain to control seizures. *Pinus roxburghii* (Sarg.) is another significant plant used in these systems; its alcoholic extracts are employed to reduce various phases of convulsions. Folk medicine globally also relies heavily on local flora. For example, the Hausa/Fulani tribes of Northern Nigeria utilize *Securidaca longipedunculata* and *Mitragyna inermis*, both of which contain alkaloids that possess anticonvulsant properties. Additionally, *Celtis integrifolia* is used in folk traditions because it contains gamma-amino butyric acid (GABA), a deficiency of which is often linked to the onset of seizures. In Chinese medicine, *Scutellaria baicalensis* is a staple for treating epilepsy, as its active constituents, such as Baicalin, act directly on GABA-A receptors in the brain.

Plant-Based Polyherbal Formulations:

Traditional healers frequently employ plant-based polyherbal formulations to achieve a synergistic effect that addresses multiple aspects of epilepsy simultaneously. In many regional traditions, such as those in Nigeria, healers use specific prescriptions that combine several plants; while one plant may target the core seizure activity, others are added specifically to alleviate associated symptoms like anxiety or cognitive impairment. Scientific reviews confirm that over 70% of the active phytoconstituents in these traditional plants—primarily terpenoids, alkaloids, and flavonoids—justify their use by acting on the GABAergic system. By targeting secondary systems like glutamatergic pathways and voltage-gated ion channels, these complex formulations aim to provide a more holistic stabilization of neuronal firing than single-compound treatments.

Mind-Body Balancing Therapies:

Traditional therapies often emphasize mind-body balancing to manage the psychological and cognitive comorbidities that accompany epilepsy. Many plants utilized in these systems, such as *Matricaria recutita* (Chamomile) and *Passiflora caerulea*, are prized for their dual sedative and anxiolytic effects, helping to calm the nervous system and improve general mental health alongside seizure control. *Lantana camara* is similarly used to balance mood and reduce anxiety parameters through the facilitation of GABA neurotransmission. These holistic approaches focus on more than just suppressing motor seizures; they aim to treat the whole person by addressing oxidative stress and stabilizing cognitive function through pathways like the Nrf2 and mTOR signaling systems.

Medicinal Plants Used For Chronic Epilepsy:

1. Brahmi (*Bacopa monnieri*)

- *Bacopa monnieri*, popularly known as Brahmi, is a perennial creeping herb that has been a staple of Ayurvedic medicine for centuries. Historically classified as a *Medhya Rasayana* (brain tonic), it is primarily used to enhance memory, reduce anxiety, and improve cognitive function. However, recent research has spotlighted its significant role in managing convulsive disorders.
- In experimental studies involving mice, various extracts of Brahmi were tested against Maximal Electroshock (MES) and Pentylentetrazole (PTZ) induced seizures. Findings indicate that the ethanolic extract of the stem and roots, particularly at a dose of 300 mg/kg, provides the most substantial protection. The efficacy of Brahmi is largely attributed to its unique phytochemical profile, specifically the major saponin mixture known as **Bacoside A**. Bacosides are believed to cross the blood-brain barrier and modulate neurotransmitter activity, specifically targeting GABAergic pathways and reducing oxidative stress in the brain, which are critical factors in suppressing seizure activity.

2. Tagara (*Valeriana jatamansi*)

- *Valeriana jatamansi*, or Tagara, is a medicinal herb native to the temperate Himalayan regions. In traditional practices, the roots and rhizomes are used to treat hysteria, insomnia, and nervous tension. Scientific inquiries have now confirmed that these sedative properties extend to anticonvulsant activity.



● Pharmacological evaluations using aqueous and ethanolic root extracts in rats have demonstrated that Tagara can significantly interfere with seizure progression. In the MES model, doses of 400 and 600 mg/kg were found to reduce the duration of the tonic hind limb extensor phase. In the PTZ model, the same doses delayed the onset of clonic convulsions. The safety of Tagara is well-documented, with acute toxicity studies showing no adverse effects even at doses as high as 2000 mg/kg. This high therapeutic index makes it a promising candidate for further clinical research into safer alternatives for seizure control.

3. Yashtimadhu (*Glycyrrhiza glabra*)

● Yashtimadhu, commonly known as Licorice, is valued worldwide for its roots, which contain a high concentration of glycyrrhizin and flavonoid antioxidants. While it is often associated with digestive health, its neuroprotective and anticonvulsant properties are becoming increasingly evident in laboratory research.

● Studies focusing on PTZ-induced seizures (which model petit mal or absence seizures) have shown that an aqueous extract of Yashtimadhu at 300 mg/kg significantly delays the onset of convulsions and decreases their duration. Interestingly, even lower doses between 60 and 200 mg/kg showed a marked ability to reduce seizure severity. The mechanism of action is thought to involve the modulation of calcium and sodium channels in the central nervous system, as well as the antioxidant activity of its flavonoids, which protect neurons from the oxidative damage that typically follows a seizure event.

4. Bhringaraj (*Eclipta alba*)

● Bhringaraj is a highly regarded herb in Indian folklore, often referred to as the "king of hair," but its systemic benefits are far more extensive. Systematic reviews of anti-epilepsy plants identify *Eclipta alba* as a potent neuroprotective agent.

● Unlike many conventional drugs that focus solely on suppressing electrical discharges, Bhringaraj is valued for its ability to mitigate the underlying cellular damage caused by epilepsy. It contains various coumestan derivatives and alkaloids that exhibit powerful antioxidant and anti-inflammatory effects. By reducing the "oxidative burst" in the brain—a phenomenon where seizures trigger the release of harmful free radicals—Bhringaraj helps maintain neuronal integrity. This makes it an excellent supportive herb in a holistic approach to managing chronic epilepsy, potentially reducing the long-term cognitive decline often seen in patients.

5. Haritaki (*Terminalia chebula*)

● *Terminalia chebula*, or Haritaki, is often called the "King of Medicine" in Tibet and is one of the three ingredients in the famous Ayurvedic formulation *Triphala*. Its fruit extracts have been subjected to rigorous testing to determine their effect on the central nervous system.

● Research using the ethanolic extract of Haritaki fruits (EETC) has shown significant anticonvulsant activity in albino mice. In tests involving MES, PTZ, and picrotoxin-induced seizures, Haritaki consistently reduced the duration of convulsive episodes and provided a protective barrier against tonic seizures. At doses of 200 and 500 mg/kg, it proved effective in delaying the onset of symptoms. The presence of tannins, chebulinic acid, and other phenolic compounds is believed to contribute to this activity by stabilizing neuronal membranes and enhancing the brain's natural resistance to hyper-excitability.

6. Jatamansi (*Nardostachys jatamansi*)

● *Nardostachys jatamansi*, a member of the Valerianaceae family, is traditionally prized for its sedative and neuroprotective properties. Scientific evaluation of the ethanol extract of its roots has demonstrated a significant ability to increase the seizure threshold. In the Maximal Electroshock (MES) model, Jatamansi extract was shown to decrease the extension/flexion (E/F) ratio in rats, indicating a clear anticonvulsant effect. Interestingly, research suggests that while it is highly effective against electrically induced seizures, it may be less effective against chemically induced (PTZ) models.

● When used in combination with conventional drugs like Phenytoin, Jatamansi appears to enhance the antiepileptic effect while exhibiting minimal neurotoxicity, making it a promising adjunctive therapy for reducing the dosage and subsequent side effects of synthetic AEDs.

7. Mandukaparni (*Centella asiatica*)

● *Centella asiatica*, commonly known as Mandukaparni, is a well-known Medhya Rasayana used to improve brain function and mental health. The antiepileptic efficacy of its various extracts (n-hexane, chloroform, and ethyl acetate) has been studied with a focus on its impact on brain enzyme activity. Research indicates that Pentylentetrazole (PTZ)-induced epilepsy causes a significant



decrease in the activities of vital ATPases in the rat brain. Pretreatment with Mandukaparni extracts helps restore these enzyme levels toward normalcy. This restoration of ionic balance across neuronal membranes is a critical mechanism by which Mandukaparni stabilizes neuronal excitability and prevents the propagation of seizure activity.

8. Tulsi (*Ocimum sanctum*)

- Tulsi, or Holy Basil, is revered not only for its spiritual significance but also for its diverse pharmacological profile, including antioxidant and antistress properties. Recent studies have evaluated the ethanolic extract of Tulsi leaves in both electrically and chemically induced seizure models. Results show that Tulsi significantly reduces the duration of tonic hind limb extension in the MES model and delays the onset of convulsions in the PTZ model. When compared to the standard drug sodium valproate, the higher doses of Tulsi extract (specifically around 8.5 mg/kg) demonstrated potent anticonvulsant activity. The presence of volatile oils like eugenol and various flavonoids is believed to contribute to its ability to modulate the central nervous system and offer protection against neuronal damage.

9. Kapikacchu (*Mucuna pruriens*)

- Mucuna pruriens*, known as Kapikacchu, is unique for its high natural content of L-DOPA, making it a staple in the treatment of Parkinson's disease. However, its role extends to epilepsy as well. Research on the ethanolic extract of its leaves has shown significant antiepileptic activity in models of Status Epilepticus induced by pilocarpine. At a dose of 100 mg/kg, Kapikacchu was found to significantly decrease the duration of seizures and provide protection against haloperidol-induced catalepsy. These findings suggest that the herb's therapeutic effect is mediated through the dopaminergic and serotonergic systems. By enhancing these inhibitory neurotransmitter pathways, Kapikacchu helps dampen the excessive electrical discharges characteristic of epileptic seizures.

10. Apamarga (*Achyranthes aspera*)

- Apamarga is a common weed that has recently gained attention for its potential to attenuate epilepsy through the GABAergic mechanism. In scientific trials, the methanolic extract of the aerial parts of *Achyranthes aspera* (MeAA) showed significant protection in the 6-Hertz psychomotor seizure model, which is often used to identify drugs effective against drug-resistant seizures. Further studies confirmed its efficacy in both MES and PTZ models, where it significantly delayed the onset of seizures and increased brain GABA levels. The fact that its anticonvulsant effects were inhibited by flumazenil (a GABA-A receptor antagonist) strongly suggests that Apamarga works by enhancing GABAergic neurotransmission. Furthermore, the extract did not produce significant locomotor deficits, highlighting its safety as a potential neuro-active herbal treatment.

11. Ashwagandha (*Withania somnifera*)

- Withania somnifera*, commonly known as Ashwagandha or Indian Ginseng, is a premier *Rasayana* herb valued for its adaptogenic and neuroprotective properties. Scientific investigations into its alcoholic root extract have confirmed its potent anticonvulsant activity in both electrically and chemically induced seizure models. In experimental rats, Ashwagandha at a dose of 300 mg/kg demonstrated a highly significant reduction in the duration of the tonic hind limb extension phase in the Maximal Electroshock (MES) model. Furthermore, it provided substantial protection against Pentylentetrazole (PTZ)-induced seizures by delaying the onset of convulsions. These effects are believed to be mediated through the GABAergic system; withanolides, the active constituents, are thought to interact with GABA-A receptors, thereby enhancing inhibitory neurotransmission and stabilizing neuronal membranes against the hyper-excitability characteristic of epilepsy.

12. Jyotishmati (*Celastrus paniculatus*)

- Celastrus paniculatus*, known as Jyotishmati or "The Intellect Tree," is traditionally used to enhance memory and treat various neurological conditions. The seed oil and water-soluble extracts have been extensively researched for their neuropharmacological effects. Jyotishmati is recognized for its ability to protect forebrain neuronal cells from glutamate-induced toxicity and oxidative injury, which are common pathological features of seizure activity. Beyond its nootropic action, it possesses significant anticonvulsant and sedative properties. The herb acts as a potent antioxidant, scavenging free radicals that contribute to neuronal damage during prolonged seizures. By improving cognitive function while simultaneously dampening electrical instability in the brain, Jyotishmati serves as a unique dual-action therapeutic agent for patients suffering from epilepsy-related cognitive decline.



13. Kushmanda (*Benincasa hispida*)

- Kushmanda, or Ash Gourd, is specifically mentioned in Ayurvedic classics like *Yogaratanakaram* for the treatment of *Apasmara* (epilepsy). Modern clinical research has focused on the synergistic effect of Kushmandagira swarasa (the juice of the seed-containing part) when used as a medium for processing other herbs like Yashtimadhu. In Wistar albino rats, this preparation has shown a significant ability to control seizures and prevent further attacks. The juice is believed to increase the resilience of neuronal structures, allowing them to better withstand the "seizure assault." By providing a cooling effect on the nervous system and reducing metabolic stress, Kushmanda not only helps in the immediate management of convulsions but also supports the overall physical and mental development of the patient.

14. Guduchi (*Tinospora cordifolia*)

- Guduchi is a versatile climbing shrub renowned in the Indian System of Medicine for its immunomodulatory and adaptogenic benefits. A systematic review of *Tinospora* species reveals a rich phytochemical profile, including alkaloids like berberine, terpenoids, and glycosides that contribute to its diverse therapeutic applications. While widely known for treating fever and jaundice, its neuroprotective potential is significant. Guduchi acts as a potent antioxidant and anti-inflammatory agent, which is crucial in preventing the neuroinflammation that often accompanies and exacerbates epileptic conditions. Its ability to modulate the immune system and protect against hepatic stress makes it a safe and valuable supportive therapy, particularly for patients who may be experiencing liver-related side effects from conventional long-term AED use.

15. Kantakari (*Solanum xanthocarpum*)

- *Solanum xanthocarpum*, or Kantakari, is a prickly herb whose phytochemical profile includes alkaloids like solasodine, flavonoids, and glycosides. While it is traditionally highlighted for its efficacy in respiratory disorders, systematic reviews have unveiled its broader therapeutic benefits, including antioxidant and antimicrobial properties. In the context of neurological health, the plant's bioactive compounds help mitigate oxidative stress within the central nervous system. The presence of steroidal saponins and alkaloids suggests a potential for stabilizing cell membranes. Research into its fruit and total plant extracts indicates that it can offer neuroprotective benefits, helping to shield brain tissues from the biochemical imbalances triggered during convulsive episodes.

16. Shankpushpi (*Convolvulus pluricaulis*)

- Shankpushpi is celebrated in Ayurveda as a premier *Medhya Rasayana*, primarily used to enhance memory and reduce mental fatigue. Scientific evaluation has demonstrated its significant role as a co-therapeutic agent in seizure management. Specifically, research using animal models has shown that an aqueous extract of *Convolvulus pluricaulis* possesses potent anticonvulsant activity against Strychnine-induced convulsions. When co-administered with standard drugs like Phenytoin sodium, Shankpushpi significantly enhances the anticonvulsant effect compared to the drug alone. This synergy suggests that Shankpushpi not only provides independent neuroprotective benefits but can also serve as an adjunct to modern therapies, potentially allowing for lower doses of synthetic AEDs and reducing their associated toxicity.

17. Vacha (*Acorus calamus*)

- Vacha, or Sweet Flag, is widely documented for its effectiveness in treating epilepsy, insomnia, and memory loss. A critical aspect of its traditional use is *Shodhana* (purification), and modern comparative studies have validated this classical processing. In Maximal Electroshock (MES) seizure models, both raw and classically processed Vacha rhizomes demonstrated significant anticonvulsant activity by reducing the duration of the tonic extensor phase. Interestingly, the *Shodhita* (processed) Vacha showed superior efficacy in shortening the recovery period and stupor phase compared to the raw form. This confirms that traditional processing techniques in Ayurveda are not merely ritualistic but are scientifically sound methods to enhance the pharmacological potency of the herb.

18. Sarpagandha (*Rauwolfia serpentina*)

- Historically famous for the discovery of reserpine, Sarpagandha occupies a complex position in anticonvulsant research. While reserpine itself is a potent CNS depressant, research indicates it does not always protect against convulsions; in some experimental models, it can actually lower the seizure threshold. However, historical pharmacological studies have noted that other alkaloids within the *Rauwolfia* complex can modulate the effects of anti-epileptic drugs like phenytoin. Sarpagandha's primary value in epilepsy management often lies in its profound sedative and antihypertensive properties, which help manage the severe agitation and high blood pressure that can accompany certain types of convulsive disorders, provided it is used under strict therapeutic guidance to avoid threshold-lowering effects.



19. Neem (*Azadirachta indica*)

• Neem is a versatile medicinal plant whose leaves and seeds contain a high density of bioactive limonoids and flavonoids. Systematic reviews of medicinal plants used in regions like Ethiopia and India highlight Neem's role in central nervous system disorders. While widely known for its antimicrobial properties, Neem extracts have shown significant antioxidant activity that protects neuronal cells from oxidative stress. In the context of epilepsy, this antioxidant capacity is vital for mitigating the secondary brain damage caused by the massive release of free radicals during a seizure. By protecting the blood-brain barrier and reducing neuroinflammation, Neem serves as a systemic support agent in the holistic management of chronic epilepsy.

20. Dashmool (Group of 10 Roots)

• Dashmool is a powerful polyherbal combination comprising five "great roots" (Bilva, Agnimantha, Shyonaka, Gambhari, and Patala) and five "small roots" (including Kantakari and Gokshura). This group is the gold standard in Ayurveda for treating *Vata* disorders, under which epilepsy is often categorized. Dashmool is frequently used as a base decoction for many anticonvulsant formulations. Its primary strength lies in its profound anti-inflammatory and analgesic properties. By normalizing the "movement" of nerve impulses and reducing systemic inflammation, Dashmool helps stabilize the internal environment of the nervous system. Clinical and experimental observations suggest that its balanced composition provides a synergistic effect that no single root can achieve, offering a broad-spectrum approach to neurological stability and recovery.

MECHANISM OF ACTION:

1. Enhancement of GABAergic Transmission

Enhancing GABAergic inhibition is a primary strategy for suppressing neuronal hyperexcitability.

- Receptor Modulation: Benzodiazepines and barbiturates bind to specific sites on the GABA-A receptor complex, increasing the frequency or duration of chloride channel opening. This leads to an influx of chloride ions, causing neuronal hyperpolarization.
- Inhibition of GABA Metabolism: Drugs like vigabatrin irreversibly inhibit GABA-aminotransferase, the enzyme responsible for degrading GABA, thereby increasing its synaptic concentration.
- Inhibition of GABA Reuptake: Tiagabine blocks the GAT-1 transporter, preventing the reuptake of GABA into neurons and glial cells, which prolongs its inhibitory effect.

2. Inhibition of Excitatory Neurotransmission

Reducing the activity of excitatory neurotransmitters, primarily glutamate, prevents seizure initiation and propagation.

- NMDA Receptor Antagonism: Certain agents block the NMDA (N-methyl-D-aspartate) receptor, which is responsible for slow excitatory postsynaptic potentials and calcium influx.
- AMPA/Kainate Receptor Blockade: Drugs can also target non-NMDA receptors (AMPA and kainate) to inhibit fast excitatory neurotransmission.
- Reduced Glutamate Release: Some AEDs, such as lamotrigine, may decrease the presynaptic release of glutamate by stabilizing sodium channels.

3. Reduction of Oxidative Stress

While the specific term "reduction of oxidative stress" is not a primary heading for *established* AED mechanisms in these papers, it is a known secondary neuroprotective effect.

- Prevention of Excitotoxicity: By inhibiting excessive glutamate activity and calcium influx, AEDs indirectly reduce the production of reactive oxygen species (ROS) and free radicals that cause neuronal damage during prolonged seizures.



4. Ion Channel Stabilization

Stabilizing ion channels regulates the intrinsic excitability of neurons and prevents high-frequency repetitive firing.

- **Sodium Channel Inactivation:** Many common AEDs, including phenytoin and carbamazepine, bind to voltage-gated sodium channels in their inactive state. This slows the recovery of the channels, limiting the neuron's ability to fire rapid, sustained action potentials.
- **Calcium Channel Blockade: T-type Channels:** Drugs like ethosuximide reduce low-threshold (T-type) calcium currents in thalamic neurons, which is the specific mechanism for treating absence seizures.
 - **High-Voltage Activated Channels:** Other drugs may block L-type or P/Q-type calcium channels to reduce neurotransmitter release.
- **Potassium Channel Modulation:** Opening potassium channels helps repolarize the membrane and maintain a stable resting potential, though this is a less common target for traditional AEDs.

PRECLINICAL AND CLINICAL EVIDENCE:

1. Animal Models (MES and PTZ)

Preclinical research has historically relied on acute seizure models to identify and validate antiepileptic drugs (AEDs). The Maximal Electroshock (MES) test is the gold standard for identifying compounds effective against generalized tonic-clonic seizures, as it induces a seizure pattern through electrical stimulation that mimics human grand mal epilepsy. Complementing this is the Subcutaneous Pentylentetrazol (scPTZ) test, which is primarily used to identify therapies for absence seizures by utilizing a chemical convulsant to lower the seizure threshold. While these models successfully defined the antiepileptic activity of most AEDs introduced since 1993, they are increasingly viewed as limited because they primarily identify symptomatic treatments rather than disease-modifying ones. Consequently, current research is shifting toward more complex in vivo kindling models and genetic models—such as Thorase-deficient mice—to better understand the molecular pathophysiology of acquired and refractory epilepsy.

2. Human Trials (Brahmi, Ashwagandha, and Botanicals)

Clinical evidence suggests a growing interest in using plant-derived nutraceuticals as adjunctive therapies for epilepsy, driven by the fact that nearly 40% of patients remain refractory to conventional drugs. While traditional systems of medicine emphasize plants like Brahmi (*Bacopa monnieri*) and Ashwagandha (*Withania somnifera*), preclinical studies show they often work by potentiating GABAergic inhibitory activity and providing neuroprotection through the modulation of the Keap1/Nrf2 pathway. Clinical meta-analyses of conventional AED trials (such as those for Levetiracetam and Vigabatrin) show significant efficacy in reducing seizure frequency, but they often come with high dropout rates. In contrast, botanical products like Apigenin and EGCG are being investigated in human trials for their ability to target multiple pathways—including oxidative stress and neuroinflammation—offering a more holistic neuroprotective profile that traditional single-target drugs may lack.

3. Safety and Toxicity Data

The safety profiles of epilepsy treatments reveal a stark contrast between synthetic AEDs and botanical alternatives. Meta-analyses of pivotal clinical trials for drugs such as Topiramate, Tiagabine, and Zonisamide demonstrate that patients are significantly more likely to discontinue treatment due to adverse events (AEs) compared to placebo groups. These side effects often involve CNS depression, cognitive impairment, and somnolence, which are particularly prevalent in drugs that target glutamate receptors like the AMPA or NMDA receptors. Conversely, herbal medicines are generally better tolerated and exhibit fewer side effects in preclinical and early clinical observations. However, toxicity is not absent in natural products; for instance, certain plant-derived glutamate agonists can induce status epilepticus and neuronal degeneration. Therefore, while botanicals offer a promising safety margin, rigorous clinical monitoring remains essential to prevent potential neurotoxicity and drug-herbal interactions.

FUTURE PERSPECTIVES:

The future of epilepsy management using natural products focuses on rigorous scientific validation, targeted chemical research, and the development of standardized, integrated treatment models.



Need for clinical validation:

Methodological Rigor: Future clinical trials for herbal therapies must move beyond anecdotal reports and utilize standardized methodologies, including proper randomization, blinding, and the use of control groups to ensure scientific validity.

Safety and Tolerability: There is a critical need to formally evaluate natural products for safety and efficacy, particularly in patients with drug-resistant seizures who are most likely to seek alternative treatments.

Addressing Inconsistencies: Current evidence for traditional systems like Traditional Chinese Medicine (TCM) and Ayurveda is often deemed insufficient due to inadequate trial methodologies, necessitating high-quality, evidence-based studies to confirm their therapeutic potential.

Phytochemical Isolation:

Active Constituent Identification: Future research aims to isolate specific neuroactive molecules—such as alkaloids, flavonoids, and terpenoids—to understand their precise molecular mechanisms.

Mechanistic Clarity: Isolating compounds like Baicalin from *Scutellaria baicalensis* or Allicin from garlic allows researchers to study how these substances interact with specific pathways, such as the GABAergic system or the Nrf2/ARE antioxidant signaling pathway.

Bioavailability Improvements: A key future focus is improving the bioavailability of isolated phytochemicals to ensure they can effectively cross the blood-brain barrier (BBB) and reach their neural targets.

Novel Herbal Formulations

Synergistic Design: Future developments will focus on polyherbal formulations that leverage the synergy between different plants to target multiple epilepsy-related factors, such as seizures, inflammation, and oxidative stress, simultaneously.

Standardization: Transitioning from crude extracts to standardized, "natural origin" antiepileptic drugs is essential for ensuring consistent dosing and reducing the risk of proconvulsant side effects.

Cost-Effective Alternatives: There is a push to develop herbal treatments that are not only effective against drug-resistant seizures but are also low-cost and highly accessible, especially for populations in developing countries.

Integrative Medicine Approaches

Holistic Management: Future perspectives emphasize an integrative approach that treats epilepsy as a complex condition, using natural products to manage seizures while also addressing comorbidities like anxiety, depression, and cognitive decline.

Personalized Care: Moving toward a "holistic, personalized approach" rather than a purely disease-focused one may help bridge the gap between traditional whole-medical systems (like Ayurveda and TCM) and Western evidence-based practices.

Complementary Use: Natural products are increasingly viewed as complements to conventional antiepileptic drugs (AEDs), potentially helping to alleviate the side effects of standard medications and improve the overall quality of life for patients.

CONCLUSION:

Epilepsy remains a major neurological disorder worldwide, producing sustained medical, psychological, and socioeconomic impact. Despite continuous advances in neurobiology, diagnostic methods, and antiepileptic drug development, a considerable proportion of patients still experience uncontrolled seizures. Conventional antiepileptic drugs are effective in many cases, but their long-term use is frequently limited by drug resistance, adverse effects, toxicity, interaction risks, and treatment cost. These limitations highlight the ongoing need for safer, more tolerable, and mechanism-diverse therapeutic options.

Indian medicinal plants described in traditional systems such as Ayurveda and Siddha represent an important complementary resource in epilepsy management. Many botanicals reviewed — including *Bacopa monnieri*, *Withania somnifera*, *Tinospora cordifolia*, and *Centella asiatica* — demonstrate anticonvulsant and neuroprotective effects in experimental models. Their phytoconstituents act through multiple pathways such as enhancement of GABAergic inhibition, ion channel stabilization,



antioxidant action, and reduction of neuronal hyperexcitability. Such multi-target activity makes plant-based therapies particularly attractive as adjuncts to standard AED treatment, with potential added benefits on cognition and emotional well-being.

At the same time, traditional use alone is not sufficient for universal acceptance. Standardization, phytochemical profiling, dose validation, and well-designed clinical trials are essential to translate herbal evidence into reliable clinical practice. The most practical future direction is an integrative model combining modern pharmacology with validated herbal support. After all, when seizures are complex, therapy should be smart — not stubborn — and sometimes nature and neuroscience work best as teammates rather than competitors.

REFERENCE:

1. Epilepsy—definition, classification, pathophysiology, and epidemiology J Falco-Walter - Seminars in neurology, 2020 - thieme-connect.com
2. Engelborghs S, D'Hooge R, De Deyn PP. Pathophysiology of epilepsy. *Acta Neurologica Belgica*. 2000;100:201-213.
3. Czapinski P, Blaszczyk B, Czuczwar SJ. Mechanisms of action of antiepileptic drugs. *Current Topics in Medicinal Chemistry*. 2005;5:3-14.
4. Waris A, Ullah A, Asim M, Ullah R, Rajdoula MR, Bello ST, et al. Phytotherapeutic options for the treatment of epilepsy: pharmacology, targets, and mechanism of action. *Frontiers in Pharmacology*. 2024;15:1403232. doi:10.3389/fphar.2024.1403232
5. Macdonald RL, Kelly KM. Antiepileptic drug mechanisms of action. *Epilepsia*. 1995;36(Suppl 2):S2-S12.
6. Beghi E. The epidemiology of epilepsy. *Neuroepidemiology*. 2020;54:185-191. doi:10.1159/000503831
7. Kandravicius L, Ruggiero RN, Hallak JE, Garcia-Cairasco N, Leite JP. Pathophysiology of mood disorders in temporal lobe epilepsy. *Revista Brasileira de Psiquiatria*. 2012;34(Suppl 2):S233-S259
8. Lawal M, Omobayo H, Lawal K. Epilepsy: pathophysiology, clinical manifestations and treatment options. *British Journal of Neuroscience Nursing*. 2018;14(2):58-?. doi:10.12968/bjnn.2018.14.2.58
9. Mittal P, Kaushik D, Kaushik P, Gupta V, Ghaiye P, Krishan P. Therapeutic efficacy of phytochemicals as anti-epileptic - a review. *Pharmacologyonline*. 2011;1:246-271.
10. Merish S., Essakkyandian G.(2020). Role of medicinal plants in the treatment of epilepsy: a systematic review. *Journal of Research in Biomedical Sciences (JRBMS)*, 3(1), 28-36. Link: <http://biosci.in/>
11. Kaur J., Famta P., Famta M., Mehta M., Satija S., Sharma N., Vyas M., Khatik G.L., Chellappan D.K., Dua K., Khurana N.(2020) Potential Anti-epileptic Phytoconstituents: An Updated Review. *Journal of Ethnopharmacology*. DOI: <https://doi.org/10.1016/j.jep.2020.113565>
12. Rostami Mehr S., Khazaeifard F., Nakhaei B., Soltani F., Tajeri M., Merati S., Gholizadeh S.H., Abbasi-Maleki S.(2025). Medicinal plants and their derivations for epilepsy: A meta-analysis on the GABAergic system in animal models. *Phytomedicine Plus*. DOI: <https://doi.org/10.1016/j.phyplu.2025.100937>
13. Deckers C.L.P., Genton P., Sills G.J., Schmidt D. (2003). Current limitations of antiepileptic drug therapy: a conference review. *Epilepsy Research*, 53, 1-17. DOI: 10.1016/S0920-1211(02)00257-7
14. Muazu J., Kaita A.H.(2008). A review of traditional plants used in the treatment of epilepsy amongst the Hausa/Fulani tribes of Northern Nigeria. *African Journal of Traditional, Complementary and Alternative Medicines*, 5(4), 387-390.
15. Nassiri-Asl M, Saroukhani S, Zamansoltani F. Anticonvulsant effects of aqueous extract of *Glycyrrhiza glabra* root in PTZ-induced seizure in mice. *Int J Pharmacol*. 2007;3(5):432-436.
16. Srivastav N, Saklani S, Juyal V, Tiwari BK. Anticonvulsant activity of root extracts of *Valeriana jatamansi* Linn in experimental rats. *Int J Life Sci Scienti Res*. 2016;2(2):121-126.
17. Bhat SD, Ashok BK, Acharya RN, Ravishankar B. Anticonvulsant activity of raw and classically processed Vacha (*Acorus calamus* Linn.) rhizomes. *Anc Sci Life / AYU*. 2012;33(1):119-124. (journal issue inferred from page - adjust if needed)
18. Ratha KK, Mishra SS. Anticonvulsant activity of *Shankhapushpi* (*Convolvulus pluricaulis* Choisy) on strychnine induced seizure in experimental animals. *Int J Ayurvedic Med*. 2012;3(2):82-87.
19. Bianchi C. Anticonvulsant action of some anti-epileptic drugs in mice pre-treated with *Rauwolfia* alkaloids. *Br J Pharmacol*. 1956;11:141-146.
20. Raju SK, Basavanna PL, Nagesh HN, Shanbhag AD. A study on the anticonvulsant activity of *Withania somnifera* (Dunal) in albino rats. *Natl J Physiol Pharm Pharmacol*. 2017;7(1):17-22.
21. Jain NK, Anand S, Kesari P, Rani R, Kumar S, Tiwari A, et al. Unveiling the phytochemical profile and therapeutic benefits of *Solanum xanthocarpum*: A systematic review. *Pharmacogn Res*. 2025;17(2):440-451.
22. Birhan YS. Medicinal plants utilized in the management of epilepsy in Ethiopia: ethnobotany, pharmacology and phytochemistry. *Chin Med*. 2022;17:129.
23. Mishra A, Mishra AK, Tiwari OP, Jha S. Pharmacognostic, physicochemical and phytochemical investigation of *Bacopa monnieri* L. stem and its anticonvulsant potential in laboratory animals. *Int J Epilepsy*. 2015;2:9-27.



24. Visweswari G, Siva Prasad K, Lokanatha V, Rajendra W. The antiepileptic effect of *Centella asiatica* on the activities of Na⁺/K⁺, Mg²⁺ and Ca²⁺-ATPases in rat brain during pentylenetetrazol-induced epilepsy. *Indian Journal of Pharmacology*. 2010;42(2):82-86. doi:10.4103/0253-7613.65404
25. Manu G, Padmanabha ST, Chandrakantha T, Ravishankar M. Evaluation of anticonvulsant activity of ethanolic extract of leaves of *Ocimum sanctum* (Tulsi) in albino rats. *National Journal of Physiology, Pharmacy and Pharmacology*. 2017;7(7):762-766. doi:10.5455/njppp.2017.7.0308123032017
26. Bhanumathy M, Chandrasekar SB, Chandur U, Somusundaram T. Phyto-pharmacology of *Celastrus paniculatus*: An overview. *International Journal of Pharmaceutical Sciences and Drug Research*. 2010;2(3):176-181.
27. Ekstein D, Schachter SC. Natural products in epilepsy - the present situation and perspectives for the future. *Pharmaceuticals (Basel)*. 2010;3(5):1426-1445. doi:10.3390/ph3051426
28. Chaudhary A, Das R, Mehta K, Mehta DK. Indian herb *Tinospora cordifolia* and *Tinospora* species: Phytochemical and therapeutic application. *Heliyon*. 2024;10:e31229. doi:10.1016/j.heliyon.2024.e31229
29. Sivan NT, Ommen PS. Anticonvulsant activity of *Kushmandagira swarasa* and *Yashtimadhu choorna* in Wistar albino rats. *Journal of Medical Science and Clinical Research*. 2019;7(8):798-801. doi:10.18535/jmscr/v7i8.135
30. Rao VS, Rao A, Karanth KS. Anticonvulsant and neurotoxicity profile of *Nardostachys jatamansi* in rats. *Journal of Ethnopharmacology*. 2005;102(3):351-356. doi:10.1016/j.jep.2005.06.031
31. Viswanatha GL, Venkataranganna MV, Prasad NBL, Godavarthi A. *Achyranthes aspera* attenuates epilepsy in experimental animals: Possible involvement of GABAergic mechanism. *Metabolic Brain Disease*. 2017;32:1769-1782. doi:10.1007/s11011-017-9981-8
32. Champatisingh D, Sahu PK, Pal A, Nanda GS. Anticatalytic and antiepileptic activity of ethanolic extract of leaves of *Mucuna pruriens*: A study on role of dopaminergic system in epilepsy in albino rats. *Indian Journal of Pharmacology*. 2011;43(2):197-199. <https://doi.org/10.4103/0253-7613.77368>
33. Schachter SC. Botanicals and Herbs: A Traditional Approach to Treating Epilepsy. *Neurotherapeutics*. 2009;6(3):415-420.
34. Asif M. Natural Plants with Antiepileptic Activity-The Present and Future Perspectives. *The Natural Products Journal*. 2012;2(4):270-279.
35. Dey A, Nandy S, Mukherjee A, Pandey DK. Plant Natural Products as Neuroprotective Nutraceuticals: Preclinical and Clinical Studies and Future Implications. *Proceedings of the National Academy of Sciences, India Section B*. 2020.
36. Debnath J, Sharma UK, Kumar B, Chauhan NS. Anticonvulsant activity of ethanolic extract of fruits of *Terminalia chebula* on experimental animals. *International Journal of Drug Development & Research*. 2010;2(4):764-768.
37. Slater J, Chung S, Huynh L, Duh MS, Gorin B, McMicken C, Ziemann A, Joussi J. Efficacy of antiepileptic drugs in the adjunctive treatment of refractory partial-onset seizures: Meta-analysis of pivotal trials. *Epilepsy Research*. 2018;143:120-129
38. Manchishi SM. Recent Advances in Antiepileptic Herbal Medicine. *Current Neuropharmacology*. 2018;16:79-83.

How to cite this article:

Mr.Parthasarathy.B et al. *Ijppr.Human*, 2026; Vol. 32 (3): 30-43.

Conflict of Interest Statement: All authors have nothing else to disclose.

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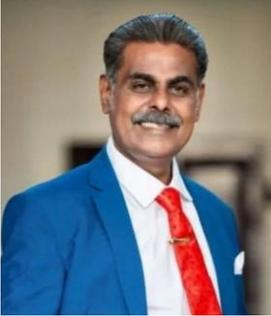


Mr. B. Parthasarathy – Corresponding Author

Assistant professor.

Department of Pharmacology, RVS College of Pharmaceutical Sciences, Coimbatore, Tamil Nadu, Affiliated to The Tamil Nadu Dr MGR Medical University, Guindy, Chennai - 600032, Tamil Nadu, India.



	<p>Dr. D. Benitojohnson Professor. Department of Pharmacology, RVS College of Pharmaceutical Sciences, Coimbatore, Tamil Nadu, Affiliated to The Tamil Nadu Dr MGR Medical University, Guindy, Chennai - 600032, Tamil Nadu, India.</p>
	<p>Thiyareshwaran .S Student. RVS College of Pharmaceutical Sciences, Coimbatore, Tamil Nadu, Affiliated to The Tamil Nadu Dr MGR Medical University, Guindy, Chennai - 600032, Tamil Nadu, India.</p>
	<p>Kaviya .G Student. RVS College of Pharmaceutical Sciences, Coimbatore, Tamil Nadu, Affiliated to The Tamil Nadu Dr MGR Medical University, Guindy, Chennai - 600032, Tamil Nadu, India.</p>
	<p>Lakshana .E.V Student. RVS College of Pharmaceutical Sciences, Coimbatore, Tamil Nadu, Affiliated to The Tamil Nadu Dr MGR Medical University, Guindy, Chennai - 600032, Tamil Nadu, India.</p>
	<p>Sathish .S Student. RVS College of Pharmaceutical Sciences, Coimbatore, Tamil Nadu, Affiliated to The Tamil Nadu Dr MGR Medical University, Guindy, Chennai - 600032, Tamil Nadu, India.</p>



Dr. Neelaveni Thangavel

Principal.

RVS College of Pharmaceutical Sciences, Coimbatore, Tamil Nadu, Affiliated to The Tamil Nadu Dr MGR Medical University, Guindy, Chennai - 600032, Tamil Nadu, India.