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Pharmacological Review of Plants and Natural Products with Antiepileptic Effects

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This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Both recurrent and spontaneous seizures are indications of epilepsy, a disorder of the brain. Around the world, as many as sixty-five million individuals could be influenced, and 80 percent of cases are found in low-income countries. Medicinal herbs are widely utilized to treat and manage epilepsy and convulsions due to their unique healing properties. Through greater research and clinical use, medicinal plants are gaining attention on a global scale because of their potent therapeutic effects and few adverse effects. The development of innovative plant-based antiepileptic/anticonvulsant medications has drawn a lot of interest from the pharmaceutical industry. This article provides an overview of the study on medicinal plants that have been demonstrated to have antiepileptic and anticonvulsant qualities. It provides pharmacological and molecular mechanism of action data for the crude extracts and related active ingredients evaluated in preclinical research for the treatment of epilepsy and convulsions, and it works as a guide for the development of future pertinent studies in this area. Articles about ethnopharmacological and antiepileptic studies on plants or natural products from the most recent and recent years were obtained from PubMed, Web of Science, and Scopus, among other sources, using keywords related to epilepsy, medicinal plants, natural products, etc. Many plant species are commonly utilized in Asian and African countries to treat epilepsy and convulsions. It has also been discovered that natural chemicals derived from these medicinal plants may possess antiepileptic and anticonvulsant qualities. These compounds can be broadly classified as terpenoids, alkaloids, coumarins, flavonoids, and saponins. The antiepileptic capabilities of plant extracts and their active ingredients can be classified according to their ability to affect the GABAergic and glutamatergic systems, act as antioxidants, exhibit anti-neuroinflammatory characteristics, and provide neuroprotection. Additionally, we highlight the potential use of various medicinal plants as a therapeutic intervention for refractory epilepsy, as they may be able to pharmacologically reduce epilepsy and cognitive impairment. The research highlights how herbal remedies used in traditional medicine are a great source of potential candidates for antiepileptic drugs. This demonstrates and validates the antiepileptic and anticonvulsant qualities of various therapeutic herbs, which could inspire further study. To fully comprehend the ideas of metabolic processes, toxicity, clinical trials, structural optimization, and change, further research is still necessary.

Keywords: Epilepsy; anticonvulsants; seizures; natural products; plants; herbal medicine.

1. INTRODUCTION

Recurrent seizures caused by abnormal neural activity are the hallmark of epilepsy, a common chronic neurological condition [1]. “There are several nervous system syndromes caused by this third most common central nervous system (CNS) illness, which can have an impact on neurobiology, cognition, psychology, and social interactions” [2]. More than 65 million people worldwide suffer from epilepsy, with 80% of sufferers residing in developing nations. This condition severely strains families financially and contributes to socioeconomic and health issues [2]. About 10 million people in China, a developing nation, have epilepsy, and new cases are reported every year [3]. Over 10 million individuals in Africa are thought to have epilepsy, and 68.5% of them do not receive proper treatment [4]. Thus, research into the best medical care and treatment options for epilepsy will continue to be a priority and a difficult problem for various nations.

Epilepsy has long been treated mostly with medicine, surgery, nutritional therapy, acupuncture, moxibustion, etc. [5]. “Currently, medications are the most recommended option for managing and treating epilepsy among these. The global pharmaceutical industry currently offers over fifty distinct antiepileptic medications (AEDs), such as stiripentol, carbamazepine, oxcarbazepine, sodium valproate, gabapentin, lamotrigine, topiramate, levetiracetam, lacosamide, and pregabalin” [6]. However, utilizing conventional AEDs may cause negative effects in 30–40% of epileptics. In addition, about 30% of patients have medication resistance. Consequently, there is an unfulfilled demand in the management of epilepsy [7]. The main drawbacks to the clinical usage of AEDs are the side effects and increased risk of drug-drug interactions that come with using some AEDs for an extended period of time [8]. In fact, among patients on current AEDs, drug-resistant epilepsy has become more prevalent in recent years [9]. It is therefore crucial and difficult to conduct research and create innovative AEDs

with several targets and minimal adverse effects.

2. EPILEPTIC SEIZURE TYPES

"There are two primary categories of seizures: partial or focal seizures and generalized seizures. Only one area of the brain, also referred to as the "focus" of the seizures, is impacted by focal seizures. A focal seizure can impact a significant portion of one hemisphere or a narrow region of a lobe, but generalized seizures happen when there is widespread seizure activity in both the left and right hemispheres of the brain, resulting in temporary unconsciousness (apart from myoclonic seizures) in the affected individuals" [10].

3. FUNDAMENTAL PRINCIPLES UNDERLYING EPILEPSY

"Two factors occur simultaneously during the onset of a seizure: 1) high-frequency action potential bursts and 2) hypersynchronization of a neuronal population" [11].

"A relatively prolonged depolarization of the neuronal membrane causes bursting activity due to the influx of extracellular Ca++, which in turn causes an influx of Na+, the opening of voltage-dependent Na+ channels, and the formation of recurrent action potentials. Depending on the type of cell, either K+ efflux or Cl− influx and gamma-aminobutyric acid (GABA) receptors mediate the hyperpolarizing potential" [12]. One kind of inhibitory neurotransmitter in the brain is GABA; it essentially stops the brain from delivering messages [12].

"In some models, GABA interneurons can lead to the paradoxical facilitation of specific kinds of epileptic discharges. Anticonvulsants that boost synaptic GABA by inhibiting GABA catabolism or reuptake, such as benzodiazepines, are thought to be helpful because they enhance GABA binding to the GABA receptor and increase the frequency of chloride channel openings" [13]. "Certain GABA production inhibitors, such as thiosemicarbazide, isoniazid, 4deoxypyridoxine, and L-allyglycine, have the potential to induce seizures" [13].

The primary inhibitory neurotransmitter GABA interacts with the GABAA and GABAB subtypes of receptors. While GABAB receptors are located presynaptically and can consequently influence synaptic release, GABAA receptors are positioned postsynaptically. In adult brains, GABAA receptors are permeable to Cl- ions; Cl- inflow, when activated, hyperpolarizes the membrane and suppresses action potentials. Barbiturates and benzodiazepines are examples of GABAA receptor agonists that reduce seizure activity. Because of their presynaptic position, GABAB receptors attenuate transmitter release and are connected to second messenger systems but not Cl− channels [13].

"One class of amino acid and a key excitatory neurotransmitter in the brain is glutamate. Under normal circumstances, astrocytes absorb glutamate produced from synapses, which glutamine synthetase quickly converts to the non-excitotoxic amino acid glutamine" [14].

"Epileptic seizures are caused by the ionotropic N-methyl-D-aspartate (NMDA), a-amino-3hydroxy-5-methyl-4-isoxazole propionic acid/kainate, and metabotropic glutamate receptor-mediated pathways" [14].

"In chronic epilepsy models, excitatory glutamatergic pathways are implicated in both long-term, adaptive neuronal plasticity linked to epileptogenesis and acute, transitory, provoked seizures. In order to increase sodium and calcium conductance, glutamate excites receptors on ligand-gated ion channels (NMDA and non-NMDA receptors)" [15].

"Glutamate and aspartate reuptake following synaptic release is facilitated by neuronal (EAAC1) and glial glutamate transporters. Increased excitatory activity may be consistent with glutamate transporter down-regulation" [16].

4. BOTH OXIDATIVE STRESS AND EPILEPSY

"The oxidation of macromolecules such lipids, proteins, and nucleotides can result in cell death due to oxidative stress, which also causes cellular damage and functional disruption" [17].

"Antioxidants and oxidants' homeostatic imbalance is linked to the onset of seizures. An imbalance between the production and removal of reactive oxygen species (ROS) and reactive nitrogen species has been defined as oxidative stress" [18].

In order to perform important tasks such autophagy, cell division, chemical signaling, mitogen-activated protein kinase signaling, and death, ROS levels are comparatively well regulated. This molecule's extreme reactivity means that the ROS is strictly controlled. During epileptogenesis, ROS-induced mitochondrial dysfunction is typically observed after seizures [19].

A voltage-gated, NMDA-dependent ion channel opens during an epileptic seizure, causing a spectacular influx of calcium that raises intracellular ions and initiates metabolic cascades. ROS can be produced by high intracellular calcium levels [20]. “Certain non-enzymatic antioxidant defense mechanisms like vitamin C, vitamin E, and reduced glutathione (GSH) as well as some enzymatic ones like superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, and peroxiredoxins can scavenge ROS” [21]. In the treatment of epilepsy, antioxidant treatments that lower oxidative stress have garnered a lot of interest.

5. INFLAMMATION AND EPILEPSY

Research conducted on rodents has revealed that in the brain regions responsible for producing epileptic activity, seizures lead to an increase in inflammatory mediators [22]. Certain types of epileptic seizures have been discovered to be suppressed by direct anti-inflammatory therapies. Human epilepsy may be preceded by inflammatory processes, which may etiopathogenetically contribute to the occurrence of spontaneous seizures. Seizures brought on by chemoconvulsants or electrical stimulation cause glia to undergo a fast-onset inflammatory reaction [23].

“It has been observed that age-dependent neurological dysfunctions, including lower seizure threshold and spontaneous seizure frequency, are caused by over-expressing cytokines inside astrocytes, such as interleukin-6 (IL-6) and tumor necrosis factor-a” [24].

Toll-like receptor 4 and IL-1 receptor type I are activated by inflammatory cytokines such as IL-1b and high-mobility group box 1, respectively. Neuronal excitability can be regulated by IL-1 receptor/Toll-like receptor signaling, which can change synaptic transmission, limit the outward current of Ca2+ channels, and reduce the synthesis of GABA [25].

6. ANTIEPILEPTIC MEDICATIONS

Drug therapy, particularly anticonvulsants, is used to control the majority of epileptic seizures [26]. Anticonvulsant medications are the cornerstone of treatment for seizures, albeit different anticonvulsant pharmacological options correspond to different types of seizures and epileptic syndromes [27]. “Individuals who require treatment for newly diagnosed epilepsy can begin with traditional anticonvulsants such as carbamazepine, phenytoin, valproic acid/valproate semisodium, phenobarbital, or, more recently, gabapentin, oxcarbazepine, lamotrigine, or topiramate” [28].

A number of variables, including as age, general health, medical history, and the intensity and frequency of the seizures, influence the type of medication that is administered. Selecting the optimal course of treatment for epilepsy requires an accurate identification of its kind [28]. Medications used as traditional antiepileptics can enhance GABA action or block sodium channels. Various antiepileptic medications have several or ambiguous modes of action [29]. “Their targets include GABAA receptors, GABA transporter 1, and GABA transaminase, in addition to voltage-gated sodium channels and GABA system elements. SV2A, a2d, and voltage-gated calcium channels are other targets” [30].

“Antiepileptic medications reduce the release of excitatory glutamate, which rises in epilepsy, and GABA by blocking sodium or calcium channels” [31]. “Given that GABA has the ability to operate proconvulsively either directly or indirectly, this could be a side effect or the real mechanism of action of several antiepileptic medications” [32].

Since treating epilepsy is a long-term process and involves gradually stopping medication for approximately six months, it is necessary to look for newer drugs with fewer or no side effects and predictable pharmacological actions [32]. The majority of currently used drugs have unpleasant side effects.

One useful resource for discovering novel structural forms of AEDs is the kingdom of plants. In fact, traditional medicine has a lengthy history and a wealth of real-world expertise treating epilepsy. There is historical evidence that plants have been used medicinally to treat epilepsy [33]. Specifically, medicinal plants are frequently seen as a gentle and secure substitute for chemical AEDs in the treatment of epilepsy,

and herbal medicine has been utilized extensively around the world as an adjunctive or alternative therapy for the condition [34]. Epilepsy had no specific term in ancient Chinese medicine [35]. Patients with "horse epilepsy," "cow epilepsy," "dog epilepsy," "sheep epilepsy," "snake epilepsy," and so on were included in the "Prescriptions of Fifty-two Diseases" and "Qianjin Yaofang" according to their unusual stance, posture, and seizure sounds. Epilepsy is referred to as "Dian," "Xian," "Dian Kuang," "Yangjiao Feng," "Zao Kuang," and convulsions in Traditional Chinese Medicine (TCM) [2]. Several treatment modalities, including herbal medicine, acupuncture therapy, moxibustion therapy, tuina, emotional adjustment therapy, etc., have been evolved over thousands of years of TCM culture [2]. Two millennia ago, Huangdi's Classic of Medicine had the first documentation of the application of medicinal herbs to the treatment of epilepsy. Thousands of years of clinical practice have yielded a wealth of important expertise, and on the basis of TCM ideas, numerous traditional prescriptions with verified effects have been developed. A few of these historically documented herbal remedies are still in use today. Currently, over 20 Chinese patent medications consisting of herbs are available for use in clinical settings [2].

Additionally, in many African and South American nations, as well as Japan, Korea, Australia, India, and Mexico, herbal remedies are widely utilized in traditional medicine as an infusion or decoction for epileptic patients [36]. To cure convulsions, traditional medical healers suggest taking the leaves, roots, bark, and/or other plant materials orally or bathing in them [37]. The infusion of Margaritaria discoidea (Baill.) G.L. Webster, Dalbergia boehmii Taub., and D. nitidula Welwex Baker, Lannea discolor (Sond.) Engl., and Catunaregam spinosa (Thunb.) Tirveng, are frequently used to treat convulsions in Africa [37].

Many substances derived from medicinal plants have demonstrated strong antiepileptic efficacy throughout the past five years. For instance, results from human and animal trials have confirmed the antiepileptic/anticonvulsant properties of cannabidiol (CBD) from the genus Cannabis, and medicinal cannabis enriched with CBD has been used clinically as an adjuvant therapy for the treatment of refractory epilepsy in children and [38]. The China Food and Drug Administration (CFDA) has authorized asarone, the active component of Acorus tatarinowii Schott, for use in the treatment of grand mal epilepsy. Asarone is produced into capsule form [39].

Nevertheless, there is a dearth of reviews that concentrate mostly on pharmacological screening and investigating the mechanisms of specific isolates and crude extracts [2]. Moreover, research on the anti-epileptic qualities of medicinal herbs and botanicals has increased throughout the previous five years. The improved use of these medical herbs may be hampered by the continued lack of knowledge regarding phytoconstituents and medicinal plants, as well as their toxicities and uses throughout the past five years [40]. As a result, we provide a thorough overview of a few natural remedies and medicinal plants in this review, emphasizing their ethnomedicinal applications, phytoconstituents, pharmacology and associated mechanisms, and clinical research. In addition to offering fresh ideas for improved research and the development of new AEDs derived from plants, this review will serve as a repository of antiepileptic plants for future studies.

Uses in ethnomedicine: Many nations have utilized medicinal plants for centuries to treat epilepsy, convulsions, and other illnesses involving the central nervous system [41]. Table 1 illustrates how traditional medicine has prepared whole plants, fruits, leaves, seeds, roots, stem barks, and other parts for decoctions or other kinds of administration. Specifically, it has been observed that these plants' crude extracts can both ameliorate and decrease seizure.

Natural goods and medicinal plants that prevent epileptic seizures: Numerous medicinal plants have been shown to have antiepileptic and anticonvulsant effects through extensive in vivo study. The scientific literature primarily looks at the antiepileptic and anticonvulsant properties of crude extracts and active components that have been extracted from various medicinal species (see Table 1). Notably, several epileptic patients have attested to the antiepileptic and anticonvulsant properties of these therapeutic plants and ingredients.

Table 1. Antiepileptic medicinal plants or natural products

Plants/Natural products	Methods (induced seizures)	Mechanism of action	Reference
Ficus platyphylla methanol extract	PTZ (37.5 mg/kg) i.p. for a total of 13 convulsant injections in mice, learning performance was tested in a two-way shuttlebox	Affinity for undifferentiated glutamate receptors, affinity for the 3H-GABA binding assay, decrease the K^+-stimulated glutamate release from rat hippocampal slices	[42]
Psidium guajava (guava) leaves ethanolic extract	Delivering electroshock (50 mA) for 0.2 s through a pair of ear clip electrodes and PTZ (70 mg/kg) i.p. injection induces tonic-clonic convulsions in mice	Selectively inhibit NMDA receptor	[43]
Trachyspermum ammi (L.) methanol extract	Strychnine (4 mg/kg) i.p. injection-induced seizure in rats	Excite GABA responses mainly by stimulating human $GABA_A$ receptors and increasing the chloride ion channel opening	[44]
Zhumeria majdae essential oil and methanolic extract	PTZ (110 mg/kg) and MES models in mice	Inhibit voltage-dependent Na^+ channels, block glutamatergic excitation mediated by the NMDA receptor	[45]
Acorus calamus Linn aqueous extract	PTZ (80 mg/kg) and MES models in mice	Block NMDA receptors	[46]
Vitexin (a flavonoid)	Vitexin administered intracerebroventricularly, administered PTZ (90 mg/kg i.p.)	Vitexin is a ligand for benzodiazepine receptors, exerts anticonvulsant effects through a $GABA_A$ benzodiazepine receptor	[47]
Anisomeles malabarica (flavonoids fraction from the leaves)	MES, administrated PTZ (50 mg/kg) in rat	Decreased tonic hindlimb extension phase and extensor/flexion ratio in MES model	[48]
Angelica archangelica Linn. roots essential oil	PTZ (80 mg/kg) and MES models in mice	Block glutamatergic excitation	[49]
Cymbopogon winterianus Jowitt essential oils	Pilocarpine-induced convulsions (350 mg/kg i.p.) administrated PTZ in mice	GABAergic mechanisms, deteriorated autoregulation of glutamate release	[50]
Mentha spicata essential oils	Administrated PTZ (80 mg/kg) in mice	GABAergic mechanisms	[51]
Trichosanthes dioica Roxb fruits aqueous extract	Delivering electroshock (50 mA) for 0.2 s through a pair of ear clip electrodes, PTZ (80 mg/kg) i.p. injection	Activity against generalized tonic-clonic and cortical focal seizures	[52]

Plants/Natural products	Methods (induced seizures)	Mechanism of action	Reference
	induces tonic-clonic convulsions in mice		
Lavandula angustifolia essential oils	Administrated PTZ (80 mg/kg) in mice	Modulate glutamate activation expression, reduction of the ACh-evoked release, direct interaction with the NMDA receptor complex	[53]

PTZ: Pentylentetrazole; MES: Maximal electroshock; MDA: Malondialdehyde; AChE: Acetylcholinesterase; BChE: Butyrylcholinesterase; ACh: Acetylcholine

7. DISCUSSION

Extract of Ficus platyphylla methanol: Ficus plathyphylla decoctions have long been used in Nigerian traditional medicine to treat epilepsy, and the rural communities in Northern Nigeria have long praised their effectiveness [54]. In mice given pentylenetetrazole, the study looked at how well the standardized methanol extract of Ficus platyphylla stem bark reduced the severity of seizures, cognitive deficit, and loss of neuronal cells. The extract's ability to bind to the 35 S-GTPγS, glutamate, and γ-aminobutyric acid receptors was also assessed. A total of 13 convulsant injections were administered to male CD-1 mice at an initial subeffective dose of pentylenetetrazole (PTZ, 37.5 mg/kg, i.p.), while the treatment groups also received Ficus plathyphylla (100 and 200 mg/kg) [42]. The number of saline injections given to the control animals was the same. A two-way shuttle-box test was used to gauge the animals' learning performance 24 hours after the completion of the kindling process. On day 7, following the completion of kindling, the animals were given another subeffective dose of PTZ (32.5 mg/kg, i.p.). One day following the controversial experiment, the animals were killed, and their brains were prepared for histological analysis. In PTZ-induced mice, FP reduces the severity of seizures, cognitive deficits, and loss of neural cells. The extract's constituents exhibited receptor affinity for both glutamatergic and GABAergic channels. The assay for (35) S-GTPγS binding showed no intrinsic activity at glutamatergic receptors, and there was a decrease in glutamate release. The findings supported the separation and synthesis of the physiologically active components of this medicinal plant as antiepileptic agents, as Ficus plathyphylla contains psychoactive secondary metabolites with anticonvulsant qualities [42].

Guava leaves, Psidium guajava, ethanolic extract: The anticonvulsant properties of Psidium guajava (guava leaves) ethanolic extract (200 mg/kg & 400 mg/kg) in albino mice.

Randomly selected albino mice (25-30g) of both sexes were split into 4 groups of 6 mice each: Group I (control) received 1ml of distilled water (vehicle); Group II (Standard) received 40mg/kg of valproic acid; Group III received 200mg/kg of ethanolic extract of Psidium guajava; and Group IV received 400mg/kg of ethanolic extract of Psidium guajava. [55]. Oral administration of all medications was done one hour prior to the onset of seizures. Pentylenetetrazole (PTZ) and maximal electroshock (MES) models were used to screen for anticonvulsant activity [56].

Comparing the ethanol extract of Psidium guajava to the control, it was discovered that there was a dose-dependent significant antiepileptic activity. Comparing the MES test results to the control, the percentage inhibition of seizures is T2 49% and T1 – 37%. Compared to the standard drug, T2 protects against seizures in the PTZ test 83.4% of the time, while T1 only protects 50% of the time.

At a higher dose of 400 mg, the results indicated that the ethanol extract of Psidium guavajava leaves exhibited significant anticonvulsant activity [57].

In a strychnine-induced epileptic model, Trachyspermum ammi (L.) was tested using single- and multiple-dosing schedules [58]. A vehicle served as the control, di-azepam served as the standard, and Trachyspermum ammi (L.) extract served as the test in each of the three groups of twenty-one animals. Trachyspermum ammi (L.) was shown to have antiepileptic effects because there was a highly significant delay in the onset of convulsions compared to the control, and because a higher percentage of animals survived or ignored seizure than the control [59].

However, the duration of convulsions was significantly longer when both diazepam and Trachyspermum ammi (L.) were used, as compared to the control. The antiepileptic effect of the methanol extract of Trachyspermum ammi (L.) may have been enhanced by thymol [58].

In mouse models of maximum electroshock (MES) and pentylenetetrazol (PTZ), the anticonvulsant effects of Zhumeria majdae's essential oil (ZMEO) and methanolic extract (ZMME) were investigated. Mice were given different doses of ZMEO and ZMME thirty minutes prior to the onset of chemical and electrical convulsions [60]. Neurotoxicity, which includes sedation and movement toxicity, was evaluated using the Rota-rod test. Twenty-four hours after injecting different doses of ZMEO and ZMME, the mortality was measured. The findings show that ZMEO protected mice in a dose-dependent manner against tonic convulsions caused by PTZ and MES with effective doses (ED50) of 0.26 (0.13–0.39) and 0.27 (0.17–0.37) ml/kg, respectively [61]. According to the study, there is potential for further anticonvulsive research on Z. majdae essential oil [61].

In a number of oxidative stress-related disorders, vitexin has been demonstrated to have antioxidant properties that protect against lipid peroxidation, reactive oxygen species, and other oxidative damages [62]. Seizures, memory loss, cerebral ischemia, neurotoxicity, respiratory and myocardial damage, and metabolic disorders are among these illnesses. Cellular and molecular mechanisms are thought to be responsible for the protective effects. This review investigates how the antioxidant action of vitexin affects signaling pathway activation or inhibition [63].

Anisomeles malabarica leaf ethyl acetate extract (2.12% w/w) was made, and it was separated into total flavonoids fraction (AMFF) and tannins fraction (AMTF). The antiepileptic activity of these fractions was then assessed in wistar rats using the PTZ- and MES model [64]. Reference medications included diazepam and phenytoin (2 mg/kg and 25 mg/kg, i.p., respectively). Effective against both MES and PTZ-convulsions, a single dose pretreatment with AMFF (25 and 50 mg/kg, i.p.) has been found; however, it is also linked to a significant reduction in locomotor activity and motor activity performance (i.e., neurotoxic effects), which is comparable to the effects of diazepam treatment. Fascinatingly, long-term administration of AMFF at lower dosages (6.25 and 12.5 mg/kg, i.p., for one week) has also demonstrated strong antiepileptic effects without having a neurotoxic effect [65].

Accordingly, this study found that Anisomeles malabarica leaf EA extract flavonoid fraction has antiepileptic potential against both MES and PTZ convulsion models [65].

An evaluation of the effectiveness of Angelica archangelica Linn root essential oil was conducted in relation to electrical and chemically induced seizures [49]. Pentylenetetrazol and maximum electroshock were used to induce seizures in mice. To evaluate the effect of Angelica archangelica root essential oil on seizures, a comparison study was carried out between the traditional anticonvulsant drugs, diazepam and phenytoin. The maximum amount of seizures brought on by electroshock was improved, and the length of tonic convulsions was decreased by Angelica archangelica root essential oil. It also prevented death in seizures caused by pentylenetetrazol and postponed the onset of clonic convulsions [66].

8. CONCLUSION

Studies on the active components of natural products and plant-based extracts may be essential for identifying the chemical building blocks required to develop antiepileptic drugs in the future. But because of this review, we now know more about the therapeutic benefits of medicinal plants against epilepsy and the necessity of investigating this possibility in order to develop an improved antiepileptic medication with fewer adverse effects.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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