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Review Article

A comprehensive overview on phytomedicines as an upcoming/emerging candidate for the management of epilepsy

Priya Kumari [1], Pravin Kumar [2]*, Mahendra Singh Ashawat [3], Palak Sharma[4]

[1] *Student, M. Pharmacy (Pharmaceutics) Laureate Institute of Pharmacy Kathog, India*

[2] *Professor, HOD (Pharmaceutics) Laureate Institute of Pharmacy Kathog, India*

[3] *Principal, Laureate Institute of Pharmacy Kathog, India*

[4] *Student, M. Pharmacy (Pharmacology) Laureate Institute of Pharmacy Kathog, India*

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*Address for Correspondence:

Dr. Pravin Kumar, Professor, HOD (Pharmaceutics) Laureate Institute of Pharmacy Kathog, India

Abstract

Background: The word "epilepsy" refers to a category of chronic CNS illnesses characterised by spontaneous occurrence of seizures, which are typically accompanied by loss of consciousness and uncontrollable shaking of the body (convulsions). Epilepsy is one of the most commonly occurring non-communicable neurological disorder that affects people of all age groups. By preventing discharge and inducing hypnosis, anticonvulsant medications are used to manage convulsions. The medication used for the therapy includes phenytoin (PHT), diazepam, valproate (VPA), levetiracetam, etc. These medications have brand-new effectiveness ranges and brand-new side effects. They also represent a significant cost increase. Herbal medicine, which has its roots in ancient civilizations, involves the use of medicinal plants to treat diseases and promote overall well-being. Although the widespread use of herbal medicine as an antiepileptic, there is little solid data supporting the effectiveness and safety of the majority of herbs. Additionally, the herbal remedy needs to pass a rigorous, evidence-based review. As herbal drugs are derived from natural sources, they are often considered safer than synthetic drugs. Therefore, there is a growing interest in exploring the potential of herbal medicine for treating neurodegenerative diseases such as Parkinson's disease. Due to their lower adverse effects, herbal medications are becoming more and more popular for the adjuvant treatment of epilepsy.

Objective: The objective of this article is to investigate whether herbal medications have potential as a treatment option for Parkinsonism, and to provide a clear understanding of the current state of research on this topic.

Keywords: Convulsion, epilepsy, herbal treatment, seizures, phytoconstituents, herbal medicine, GABA.

Introduction

Greek word "epilambanein," which meaning "to seize upon" or "to attack," is the source of the word "epilepsy." In the contemporary world, epilepsy is among the most common neurodegenerative conditions. [1] A seizure is described as an aberrant, erratic discharge of brain nerve cells that causes a momentary impairment in motor, sensory, or mental function. [2] With the right antiepileptic medications, the majority of persons with epilepsy may lead seizure-free lives. It's interesting to note that treatment-resistant seizures occur in about 30% of instances. According to reports, developing nations account for roughly 90% of epilepsy occurrences because there aren't enough antiepileptic treatments available there, they're expensive, and they have unfavourable side effects from the ones that are now on the market. [3] Although epilepsy cannot be cured, it can be managed using anticonvulsants that stop the seizures or lower their frequency. [4] AEDs are frequently used to treat a variety of conditions, including bipolar disorder, migraine, and chronic pain in addition to treating epilepsy. These medications are frequently administered for lengthy periods of time. [5] The use of herbal medicines is becoming increasingly popular among complementary and alternative treatments (CAMs). [6]

Traditional medical systems are prevalent in developing countries because up to 80% of the population depends on them for their main healthcare needs. Several plants employed in various systems of traditional medicine for the treatment of epilepsy have demonstrated activity when tested on contemporary bioassays for the detection of anticonvulsant activity, and many of these plants still need to be scientifically researched. [7] Additionally, the WHO applauds the use of herbalism with proven therapeutic efficacy and safety in various healthcare benefit programmes worldwide. [8] This review gives current information on numerous phytoconstituents that have been shown in preclinical research to have the ability to cure different types of seizures through diverse signalling pathways. Additionally, it gives a brief overview of how various anti-epileptic phytoconstituents are derived from medicinal plants that have historically been used to treat epilepsy. Regarding the status of phytoconstituents in clinical research, more details are provided. This review focuses on the pharmacology and antiepileptic potential of several phytoconstituents to present

the justification for their use as alternative therapeutic choices.

An Overview on the pathophysiology of epilepsy disease

Seizure disorders come in a wide variety, which is explained by the unique pathophysiology of epilepsy and seizures. The disruption of the synaptic balance between the excitatory and inhibitory (through glutamatergic signalling and GABAergic signalling) drives, which can cause seizure activity, is a typical feature of epilepsies. GABAA-receptor antagonists and glutamate-receptor (NMDA, AMPA, kainate) agonists have been shown in early pharmacologic experiments to cause seizure activity in healthy animals. It would be demonstrated by further study that interictal spikes, which are commonly observed on EEG recordings from epileptic patients, are associated with a substantial depolarization and a flurry of action potentials in individual neurons. The highly structured cortical tissue with its laminar cell layers enhances the flow of normal neuronal processing while also creating a structure that is especially prone to aberrant synchronous activity that can evolve into seizures. Excitatory synaptic activity is closely controlled by inhibitory interneurons under normal conditions; however, genetic mutation, trauma, aberrant development, or a number of other traumas compromise this regulation, causing cortical networks to become hyperexcitable.

A clinical manifestation of any of the partial seizure types can occur in around 60% of epilepsy patients who experience partial epilepsies. Partial epilepsies can have a wide range of aetiologies, such as cortical lesions, tumours, developmental malformations, or acute cortical damage brought on by trauma or stroke. As medical advancements enable people to survive more severe traumas that would have been deadly in earlier generations, trauma-induced epilepsy is growing in importance. Partial epilepsies underlying cortical abnormalities or tumour development may also be influenced by genetics.7 Generalised epilepsies, which affect about 40% of patients, typically have hereditary causes. Numerous generalised epilepsies have been linked to genetic changes in ion channels (or channelopathies), such as voltage-gated sodium channels and $GABA_A$ receptors, which inform treatment plans. [9]

Methods

The data narrated in our review were assembled from databases PubMed, google scholar until the end of journey 2023. Data consists of animal and clinical researches.

Antiepileptic property of Active phytoconstituents and herbal extract

1 American Hellebore

Cryptenamine is the standard trade name. The plant can be obtain in the US. It contains ester alkaloids that resemble steroids chemically. There are several different indications for the usage of American hellebore (Veratrum viride), including neuralgia, peritonitis, pneumonia, and seizures. American hellebore's effects on the heart can vary. Although it has been discovered that high doses can raise blood pressure, some sites recommend using it to lower these three measurements. The plant increases the degree of depolarization in heart, neuron, and muscle tissue, which increases muscle tone. This medication has a poor therapeutic index and is extremely toxic. [10]

2 Acanthus Montanus

The time it takes for isonicotinic hydrazide acid-induced convulsions to begin is prolonged by Acanthus montanus extracts, and MES (maximal electroshock)-induced convulsions are inhibited**.** However, there aren't many studies on the referenced plant's antiepileptic properties. This plant's extracts have recently been studied in numerous animal models of epilepsy. In mice given picrotoxin treatment, these plants also show notable anticonvulsant effects. [11] The pharmacological diversity of this plant is mediated by a number of different pathways. The interaction with GABAergic neurotransmission may be what causes the plant extracts to inhibit the isonicotinic hydrazide acid and pentylenetetrazol- and isonicotinic hydrazide acid-induced seizures.[12] Prolonged sodium channel inactivation is likely responsible for the protective benefits against MES-induced convulsions.[13]

3 Bacopa Monnieri (Brahmi)

B. monnieri is a recognised nootropic plant and a herbal medicine from India. often used to cure hoarseness, asthma, epilepsy, and insanity. This is a key component of formulations for medhya rasayana.[14] In an epileptic rat model, B. monniera 300 mg/kg (oral) body weight/day for 15 days reduces the severity of peripheral nervous system damage by preventing seizures.[15]

4 Betony

Folklore lists a number of diseases that betony (Stachys officinalis) may be used to treat, including anxiety, asthma, bronchitis, diarrhoea, headache, heartburn, palpitations, renal disease, roundworm, seizures, indigestion, toothaches, and wounds. It was renowned for its "magical powers" during the Middle Ages and utilised as a cure-all for a variety of illnesses. Betony is often brewed as a tea, however some herbalists advise smoking it to relieve headaches**.** A native of Europe,

northern Africa, and Siberia, a member of the mint family is betony. Tannins, which make up 15% of betony, are assumed to be the source of betony's effects. There have been reports of GI irritation (diarrhoea, nausea, and anorexia), hypotension, and hepatic dysfunction. Additionally, uterine contractions have been documented; pregnant women shouldn't use betony.[10]

5 Berberine

From the plant Berberis vulgaris L., berberine is an isoquinoline alkaloid. Anticonvulsant, antioxidant, anti-psychotic, and antidepressant properties are well-known uses of this substance. Berberine reduced neuronal ageing, enhanced neuronal survival, and promoted hippocampal differentiation in rat brain. The antiepileptic action of berberine has thus been compared to that of phenytoin. According to reports, berberine prevents glutamate from attaching to NMDA receptors in the brain, acting as an NMDA receptor antagonist. Berberine has not demonstrated a beneficial effect in PTZ-induced seizures, indicating that GABAergic neurotransmission is not involved in the antiepileptic mechanism of berberine.[16]

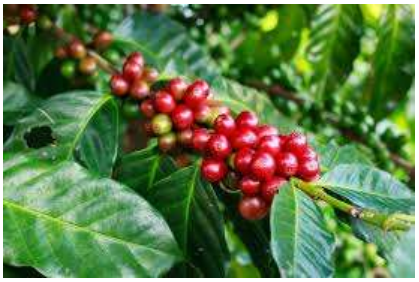
6 Chamomile

The perennial blooming plants known as German and Roman chamomile (Matricaria recutita and Chamaemelum nobile, respectively) are widely distributed and may be found growing across Europe, Africa, and Asia. It has a historical reputation for having mildly calming properties. Possible contributors to this activity include the flavonoid compound apigenin, which binds to the benzodiazepine receptor specifically and with micromolar affinity.[17] A Picrotoxin-induced seizures can be significantly reduced by chamomile (M. recutita) extracts.[18] According to recent findings from a controlled clinical research, chamomile extract may have a small amount of anxiolytic action in people with mild to moderate generalised anxiety disorder (GAD). [19]

7 Cannabis

There is historical evidence of the usage of Cannabis sativa (cannabis, marijuana), of the Cannabaceae family, to treat epilepsy. [20] Cannabis has been used medicinally for over 2700 years, and reports of its usage for epilepsy extend back to the late 19th century and mediaeval times. Cannabidiol, 9-tetrahydrocannabinol, 9-tetrahydrocannabivarin, cannabinol, and cannabidivarin are the antiepileptic components of cannabis. [21] Cannabidiol (CBD) is a functional agonist or antagonist at a variety of ion channels, neurotransmitter transporters, and 7-transmembrane receptors. [22] Using data from animal models, CBD has been demonstrated to be effective against a variety of seizure types. [23] In June 2018, the U.S. Food and Drug Administration approves that a component which do not produce any effect are found in the plant for the treatment of Lennox-Gaustaut and Dravet syndromes, two extremely uncommon epilepsy diseases. The effectiveness and safety of this medication were supported by strong clinical studies. [24,25] In the research by Craig A. Press, 43 patients (57%) reported fewer seizures, 33% reported better alertness and behaviour, 11% reported better motor and linguistic abilities, 7% reported better sleep, and 44% experienced adverse effects. In Shaun A's study, 100 patients (85%) experienced less seizures overall, with 16 patients (14%), completely seizure-free. When compared to previous exposure, side effects from cannabidiol are dramatically reduced. Additionally, reports of improved sleep (53%), alertness (71%), and mood (63%) were made. Especially, all of those who responded (93%) expressed a desire to keep using cannabidiol products once the poll was over [26] but Cannabidiol prolonged use may suppress human immune system. [21] The antiepileptic properties of cannabidiol are demonstrated by its stimulation of the action of 5HT1A receptors, glycine receptors, and the influx and efflux of intracellular calcium ions. [27]

8 Caffeine



The most popular CNS stimulant is caffeine (1,3,7-trimethylxanthine), and it is used to treat a variety of conditions. [28] It is found in eight kinds of plants that are frequently used as food and supplements, along with its methylxanthine cousins theophylline and theobromine. [29] Caffeine reduces tiredness and improves alertness, quickness of thought, information processing, arousal, and motor activity. [28] These include cola or kola (Cola acuminata and Cola nitida), mate (Ilex paraguariensis), guarana (Paulinia cupana), coffee (Coffea arabica and Coffea robusta), tea (Camellia sinensis), chocolate (Theobroma cacao), and cocoa powder. [29] Around 300 mg are typically consumed daily on average around the globe, primarily in the form of coffee, tea, soft drinks, and energy beverages. Caffeine content in a standard 200 mL cup of coffee is around 74 mg. [30,31] Caffeine is a mixed competitive adenosine A1 and A2A receptor antagonist with a chemical structure that is comparable to adenosine. Through regulating GABA-A receptors, caffeine alters the response to gamma-aminobutyric acid (GABA), a significant inhibitory neurotransmitter. [32,33] Caffeine has a "pepping" impact by increasing the release of dopamine, glutamate, and inhibiting GABA. [34,35]

9 Delplunium Denudatum

Delphinium denudatum Wall. (Ranunculaceae) is a native plant used as a medicine that is commonly known to as "Jadwar" as medicinal herb in the subcontinent**.** It is a plant that grows between 40 and 80 cm tall and is obtain in Himalayan area, from Pakistan to Kashmir and northwestern India. [36] It is employed for the management of epilepsy in the conventional Unani (Greco-Arabic) medical care system now practised in the subcontinent. [37] furthermore it is frequently used as a substitute and tonic, as well as in the treatment of syphilis, rheumatism, bites from snakes, toothaches, and aconite poisoning. [38] Aqueous fraction (AF) displayed dose-dependent anticonvulsant effect against seizures brought on by PTZ and BIC as well as significantly enhanced anticonvulsant activity against the hind limb tonic extension phase (HLTE) of maximum electroshock (MEST). [39]

10 Ephedra

Ephedra is one of the more alarming substances that is often consumed worldwide. Ephedra agents are often discovered in weight-loss treatments but are not typically included on ingredient lists. [40] Many ephedra species, such as Ephedra sinica, which are frequently known to by the Chinese name ma hua, contain the stimulant substance ephedrine. [41] 1.25% of ephedrine is found in ephedra sinica, along with other related alkaloids such pseudoephedrine, methylephedrine, and norpseudoephedrine. [40] Ephedra dosages more than 32 mg per day increase the risk of hemorrhagic stroke by 3.59 times. [41] Ephedrine acts as an agonist at the α1, β1, and β2 receptors, which mediates its stimulant and sympathomimetic actions . [42]

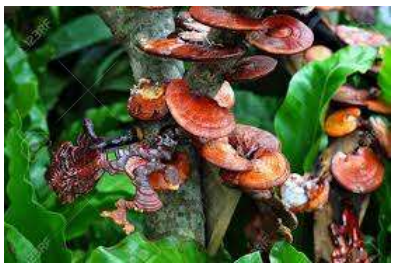
11 Ficus plathyphylla

Ficus platyphylla Del.-Holl, a member of the Moraceae -family, primarily exists in the savannah regions of the West African coast. The plant has long been used to treat mental problems, depression, epilepsy, pain, and inflammation in Nigerian traditional medicine, and the Hausa people of northern Nigeria highly respect the efficacy of the therapy. [43] The extract contains tannins, flavonoids, and saponins, which have hallucinogenic properties. The extract has anti-seizure effects in models of seizures brought on by pentylenetetrazol and strychnine, but it is ineffective in treating seizures brought on by sonicotinic hydrazide acid, aminophylline, and mescaline. With the exception of MES-induced seizures, the extracts dramatically increased the delay in involuntary muscle jerk and all other types of seizures. Additionally, the extract can lessen neuronal cell death and enhance learning impairment in the hippocampus's cornu ammonis 1 and cornu ammonis 3 areas. [44] The ability of the extract to block T-type Ca2+ currents, prevent glutamatergic neurotransmission mediated by the NMDA receptor, obstruct with postsynaptic inhibition mediated by glycine an important inhibitory transmitter to motor neurons and interneurons in the spinal cord scavenge free radicals (such as reactive oxygen and nitrogen species), and have harmony for GABAergic and glutamatergic receptors are some potential mechanisms of the extract's antiepileptic activity. [45,46]

12 Ginseng

In China, Korea, and the United States, ginseng is among the most often utilised herbal remedies for treating illnesses. Many of ginseng's pharmacological benefits, such as its anti-inflammatory and neuroprotective properties, have been demonstrated to be significantly influenced by ginsenosides, according to certain research. [47-49] Usually, the terms "Asian ginseng" and "American ginseng" (Panax ginseng and Panax quinquefolius, respectively) refer to two plant species. [50] A group of compounds known as the ginsenosides are the primary active ingredients in ginseng. [51] Chronic ginseng extract administration to rats did not cause any harmful effects, although high dosage therapy (more than 150 mg/kg) enhanced the death rate following status epilepticus brought on by pilocarpine. [48] Inhibiting NMDA-dependent and status epilepticus-induced Ca2+ influx as well as L-type Ca2+ channels in hippocampus neurons is one of ginsenosides' neuroprotective mechanisms, according to certain research. [47,52,53]

13 Ganoderma lucidium



Traditional Chinese medicine frequently uses the herb Ganoderma lucidum to treat illnesses. A study group's researches have shown that Ganoderma lucidum spore possesses antiepileptic capabilities both in vivo and in vitro. [54-57] Its spore reduces the expression of NF-B and N-Cadherin in the brains of epileptic rats and increases the expression of neurotrophin-4 in hippocampal neurons. [54] The findings of the present investigation suggest that the antiepileptic effects of Ganoderma lucidum spore may also be a result of Ca2+ accumulation suppression in epileptic hippocampal nerve cells and subsequent CaMK II expression enhancement. [58]

14 Ginkgo

Ginkgo biloba is one of the most popular herbs and has frequently been among the top five sellers for many years. [59-61] this plant is used by patients and prescribers to cure a number of ailments, such as Alzheimer's disease, dementia, memory loss, and loss peripheral circulation. [62] This plant contains a number of chemical compounds that are physiologically active, including substances that cause seizure activity and substances that reduce seizure activity. [63-65] Terpene lactones and flavonoid glycosides are thought to be the active ingredients in ginkgo.Ginkgo is known to improve cholinergic transmission, but its precise mode of action for its promnestic effects has not yet been resolved . [66-68] Some ginkgo components, particularly bilobalide, may have neuroprotective and seizure-preventing quality. [69,70] According to one electrophysiological research, ginkgo extract makes people's alpha (α) activity rise while their delta (δ) and theta (θ) activity falls. [71]

15 Harpagophytum procumbens

Traditional South African medicine frequently employs H. procumbens DC (Pedaliaceae). The experimental animal model employed has shown that H. procumbens aqueous root extract has anticonvulsant properties. It is likely that the herb might be utilised to treat both petit mal and grand mal forms of epilepsy given the plant's extract's success in the experimental convulsion paradigm that was employed. In convulsions brought on by PCT and PTZ, in which the reference drug they used is phenobarbitone (PBT, 20 mg/kg i.p), The plant's extract seems to work a little better. [72]

16 Kava

In the South Pacific, kava (Piper methysticum) is frequently used ceremonially, but its usage as a popular anxiolytic has grown as well. Several putative neuromodulatory effect pathways have been proposed by limited investigations. Kava is a potent inhibitor of L-type Ca2 channels and a negligible blocker of Na channels. Gamma-aminobutyric acid transmission and early K outward current are both increased by kava. An impact on serotonin 1A has been identified. [73] They may attach to the inactive Na1 channel and keep it from activating, according to a theory. Kavain inhibits L-type Ca21 channels at micromolar doses, drastically lowering the release of endogenous glutamate thereafter. [74] Kava must be avoided by those who are nursing during pregnancy, those who are under 12 years old, those who have renal illness, neutropenia, and thrombocytopenia.

17 Laurus Nobilis

The leaves of L. nobilis Linn (Lauraceae) have been used to treat Parkinsonism, neuralgia, and epilepsy. Pharmacological investigations have shown that eugenol and methyleugenol have analgesic, hypothermic, muscle relaxant, and anticonvulsant properties, as well as an antistress impact. Against seizures brought on by PTZ, the leaf essential oil of L. nobilis is protective. The essential oil caused drowsiness and motor impairment at anticonvulsant dosages. Additionally, several a-pinene analogues protect vulnerable rats from developing audiogenic seizure**s.** [75]

18 Magnolia grandiflora (Him-champa)

After oral administration of ethyl ether (EE) and hydroalcoholic extract (HE) of Magnolia grandiflora L. (Magnoliaceae) seeds, the extensor reflex of the maximum electric produced seizure test was eliminated in 50 and 40% of the experimental animals, respectively. They dramatically increased the amount of time spent sleeping after taking pentobarbital [76]. The ethyl ether (EE) and hydroalcoholic extract (HE) of Magnolia grandiflora L. (Magnoliaceae) seeds were examined in adult male Wistar rats. Magnolia grandiflora L. is a popular plant used in ancient Mexican therapy due to its antispasmodic and other claimed pharmacological benefits. The extensor reflex of the maximum electric induced seizure test was eliminated by EE and HE when given orally at single doses of 250 mg/kg (calculated on lipidic base) and 200 mg/kg, respectively. They considerably extended the amount of time that pentobarbital made the animals sleep, and only the ethanol extract caused hypothermia. The gait, posture, and righting tests revealed that neither extract had any neurological deficits. Despite the need for more toxicological and pharmacological information, these findings prove that the biological components of this plant may be useful in improving the condition of epileptic individuals experiencing convulsive seizures. [76.]

19 Melatonin

The widespread usage of melatonin, which is advertised as a dietary supplement, calls for debate. An expression similar to nutribiotic, which is used to describe vitamins and plants, is used to relate melatonin. A by-product of serotonin

breakdown, melatonin is typically synthesized by the pineal gland and released to the brain where it assists in sleep promotion. Melatonin has been said to have anti-seizure properties, and studies in animals point to a relationship between the hormone and seizures. Antimelatonin antibody can cause seizures in animals. [77] In rats, the removal of the pineal gland, which generates melatonin, results in seizures [78]. Rats with audiogenic convulsions experience damage to the pineal. Patients who experienced midday tonic-clonic, complex partial, or psychogenic seizures did not have any conversions in their melatonin rhythms [79]. Children who have photosensitive epilepsy have been found to have stunted melatonin levels. In epilepsy patients using more melatonin, seizure frequency has been seen to increase and decrease. The evaluation of reduced seizures related to melatonin usage may be distorted by its use as a sleep aid.

20 Nardostachys jatamansi (Jatamanasi)

N. jatamansi DC. (Valerianaceae), which is listed in Ayurveda, has roots and rhizomes that can be used to cure epilepsy, tremors, anxiety, and mental lassitude. The ethanol extract of N. jatamansi significantly raise the seizure threshold in the experimental model of generalized analeptic-clonic seizures while having very little neurotoxic effects. [80]

21 Passion Flower

Passiflora coerulea and Passiflora edulis are a few of the passionflower species that are familier for their sedative properties. For its sedative and anxiolytic properties, Native Americans used a passionflower tea. The flavonoid chrysin (5,7-dihydroxyflavone), which has a micromolar affinity for benzodiazepine receptors and works as a partial agonist there, is thought to be the substance that is active. [81,82] where Passiflora active components are not fully known. Although the majority of the evidence suggest that the real active components of passiflora may be flavonoids. [26] Studies on animals have shown that chrysin has sedative and anxiolytic properties. [82,83] The processes might involve flavonoids' second order positive regulation of GABAA receptors and the combination of GABA with other substances that facilitate its membrane penetration. [84-86] It hasn't yet undergone empirical testing on people, though. In one research, chrysin inhibited pentylenetetrazol-induced seizures in rats, while pre injection of a benzodiazepine antagonist prevented the seizures. [87]

22 Piperine

Black pepper's main bioactive component, piperine, has been used as a culinary seasoning as well as a possible therapy for a variety of illnesses, including inflammation, obesity, and various malignancies. [88] By raising the levels of GABA and glycine in the CNS in the pilocarpine experimental paradigm, it has demonstrated a modulatory impact on the GABAergic and glycine system. Studies on convulsions brought on by the L-type calcium channel agonist BAYK-8644 have found piperine as a voltage-gated sodium and calcium ion channel inhibitor. Additionally, serotoninergic and other neurotransmitter systems linked to epileptogenesis have been discovered to be regulated by piperine. Piperine blocked TRPV1 receptors in the MES and PTZ models. TRPV1 is a non-specific cation channel that has a high affinity for calcium influx and controls glutamate release. Additionally, it reduced Fos expression and coordinated neuronal activity in the hippocampal region. [89-91]

23 Rhizoma pinelliae

It is a tuber of the araceae family's Rhizoma ternate (thumb). Many studies on the sedative/hypnotic medications tested the anticonvulsant activity. The study's findings indicated that by reducing the rate of nikethamide (NKTM)-induced convulsion mortality, ethanol fraction from Rhizoma Pinelliae Praeparatum (EFRP) may be able to alter the course of convulsive episodes, interfere with seizure threshold, and/or prevent seizure propagation and increasing the delay without increasing the convulsion latency. It offered pharmacological justifications for the use of Rhizoma Pinelliae Praeparatum in the management of CNS diseases and insomnia.[92]

24 Skullcap

The family of skullcap plants includes two species, both of which have anticonvulsant properties and are utilised as herbal medicines. Europeans and Native Americans have traditionally utilised American skullcap to treat epilepsy. [93] Skullcap is also known as helmet flower and hoodwort. The S laterifolia and S baicalensis leaves and roots, which are indigenous to temperate parts of North America, constitute the source. Skullcap is advertised as an anticonvulsant, calming agent, antihelminthic, and antibiotic in addition to its purported anti-inflammatory, anti-cholesterol, and anti-

splasticity properties. Out of the whole of American Skullcap's extracts, ten flavonoids and two phenylethanoid glycosides have been identified and purified. Flavonoids which are now present both in Baikal skullcap and American skullcap have the potential to be the primary factors which develop the anticonvulsant effects, which might be very affine for the $GABA_A$ receptor and the ability to protect the brain. [94-96]

25 Valerian

Since ancient times, the herb valerian has been used as an antiepileptic, and at one point it was regarded to prevent epilepsy, as the first line of protection. Because valerian decay over time, its chemical makeup varies widely depending on where it is cultivated and its age. It is possible to convert up to 1% of the root into isovalerate, which has a similar structural makeup to valpropate. One of the most popular sleep aids is valerian (Valeriana officinalis). [97] The terms "valerian" and "wild valerian" are synonyms for "all-heal," "Baldrian," and "cat's love." It was once employed to cure upper respiratory and stomach disorders. [98] The herb valerian itself may not be well tolerated, since it has sleepiness and an unpleasant flavour and odour alike to damp socks as adverse effects. Isovaleramide has begun clinical studies, and doses up to 2,400 mg/d seem the capacity for acceptance. [97] However, the quantity of isovalerate being studied is around 20 times. More than what would be present in a single dosage of valerian. Although valerian has a long history of use in treating epilepsy, there is no proof for this that it possesses anti-convulsant qualities. [99]

26 Zingiber Officinale Roscoe

Various countries use ginger, the real Roscoe, as a condiment often. Some of these countries also utilise it to treat ailments including colds, arthritis, migraines, hypertension, and other issues. [100-103] Different doses of ginger extract were shown to considerably lower the threshold for myoclonic seizures in recent research on anticonvulsant properties of ginger in timed iv pentylenetetrazol-induced seizure mice models ,only extremely high dosages of ginger significantly improved the threshold for generalised clonic seizures, in contrast to control groups, and forelimb tonic extension that was not related to the pentylenetetrazol intravenous duration. [104] This suggests that ginger may inhibit oxidative stress, increase intracellular cGMP levels, inhibit Cl(chloride) channels in the complex of $GABA_A$ receptors, inhibit nitric oxide synthesis and reduce inducible nitric oxide synthase in lipopolysaccharide-stimulated mouse macrophages, and inhibit nitric oxide synthase. [104-107]

Conclusion

The majority of traditional herbal products are complex mixtures of chemical elements with a variety of phytochemical and pharmacological activity, which is the main reason for this. Finding safer and more effective antiepileptic medications may be possible by using medicinal plants as a source. The information acquired in this study on a variety of herbal treatments and constituents with positive effects on epilepsy in laboratory animals will be taken into consideration in the search for prospective pharmacological interventions from conventional treatments for this condition. The pharmaceutical substances with well-defined development, associated, and therapeutic potential may be excellent candidates for more research and eventually help with therapeutic intervention.

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