IJPSR (2021), Volume 12, Issue 8 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 11 May 2020; received in revised form, 15 April 2021; accepted, 19 May 2021; published 01 August 2021

ANTI-EPILEPTIC ACTIVITY OF INDIAN MEDICINAL PLANTS - A REVIEW

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Keywords:

Epilepsy, Incidences survey, Anti-epileptic herbs, Animal models *etc*.

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ABSTRACT: In global debates, traditional herbal medicines are getting a lot of attention, especially in the treatment of Epilepsy. This deadly disease is estimated to affect around 50 million people around the world. This neurological disorder is believed to be due to excessive electric discharge in the brain and the release of neurotransmitter substances. Antiepileptic drugs are useful but are expensive and have limited supply. Above all, one has to compromise with low efficacy and bear adverse side effects too. This review provides numerous evidences which emphasize on the importance of over thirty herbal medicinal plants and their extracts in the treatment and prevention of epilepsy-related complications. These plants are *Vitex negundo, Adansoniadigitata, Abutilon indicum, Allium cepa, Annona senegalenesis, Acormuscalamus, Aegle marmelos, Biophytum sensitivum, Butea monosperm, Canna indica, Datura metal, Cocos nucifera, Citrus colocynthis, Acalypha fruitcosa, Carissa edulis, Commiphora wightti, Clerodendrum infortunatum, Desmodium triflorum, Citrus sinesis, Lobelia nicotinaefolia, Viola tricolor, Leucascephalotes, Phyllanthusamarus, Plectranthusbarbatus, Ocimum sanctum, Nepetabractaeta, Nardostachys jatamansi, Mahua longifolia, Milicia excels, Catharanthus roseus*. Reduction in increased Glutathione (GSH), Mylondialdehyde (MDA) and lipid peroxidation are some of the mechanisms of action of these medicinal plants observed in Pentylenetetrazole (PTZ), Maximal electroshocks (MES), Isoniazid (INH), Strychnine, Lithium-pilocarpine induced epilepsy. Promising results are shown in animal models for these potential herbal remedies. Rigorous research methodology combined with clinical studies will definitely lead to significant advancement in the treatment of epilepsy using traditional herbal medicines.

INTRODUCTION: Epilepsy is a neurological disorder characterized by excessive electrical discharge in brain, which causes seizures [1]. Epilepsy is a disease that affects about 40 million people worldwide. Epilepsy is a condition, which causes seizures to occur. It is one of the most common chronic diseases affecting human beings. It is a neuropsychological disorder that occurs due to over-discharge of neurotrans substance [2].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.12(8).4060-72

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.12(8).4060-72

About 70-80% of epileptic patients are able to be commonly treated with modern anticonvulsant drugs that prevent from or lessen the number of seizure attacks [3]. According to WHO, Epilepsy is the second most basic neurological disorder after stroke, affecting at least 50 million people worldwide and approximately 40% of them are women.

Epilepsy shows a spreading rate in 1-2% of the total population. Epilepsy is one of the most common chronic and progressive diseases of human beings. Seizure is a pathological body condition described by stomach, violent and uncontrolled spasmodic contraction and relaxations of the voluntary muscles. Spasms are also associated with this disease [4].

The prevalence of epilepsy is 0.7% in India. In developed countries, epilepsy responds to treatment in up to 70% of patients. In developing countries 75% of the patient does not receive the treatment due to unavailability of the drugs and there is a high rate of mortality. In recent years, the medicinal properties of plants have been examined in the light of scientific developments throughout the world, because of their potent pharmacological activities, low toxicity and economic viability [5]. Epidemiological investigations show that mental disorder is more common among individuals with epilepsy than in general population.

The existence of comorbid psychiatric disorder significantly affects the treatment of epilepsy. Among the mental comorbidities in epilepsy, anxiety disorders are highly frequent and have a deep effect on the quality of life of epilepsy patients. Anxiety is characterized as a feeling of worry, uncertainty or tension stemming from the anticipation of imagined or unreal threat. Anxiety affects one eighth population worldwide and has become a significant research region in the field of psychopharmacology. There is an unpredictable relationship between anxiety and epilepsy. Anxiety occurs as a response to diagnose of epilepsy and tension as a response to social and family stigma because of epilepsy. There is needed to come up with the drug therapy useful in the treatment of epilepsy as well as anxiety, which will improve quality of life in epileptic patients [6].

The World Health Organization (WHO) has announced 2001 as the year for psychological health in acknowledgment of the burden that psychological and brain disorders present on people and families influenced by them. In neurosciences, the last ten years of the 20th century is called "decade of the brain. Epilepsy is among the disorders that are strongly associated with significant mental and social consequences for everyday living. There is no doubt that epilepsy belongs to the most encountered neurological conditions since the disease influences around 1% of the population. Epilepsy is one of the most well-known neurological disorders with revealed pervasiveness of 6-8 per 100000, frequency of 30-50 per 100,000 every year and cumulative incidence of 3%. It requires prolonged and sometimes life-long drug therapy. The prevalence of epilepsy in development countries is typically higher than in developed countries. However, the problem of side effects has also not been circumvented totally and around 30% of the patients keep on having seizures with current antiepileptic drugs treatment.

Medicinal plants utilized in standard medicine for the treatment of 'epilepsy has been experimentally appeared to have encouraging results in animal models for screening for anticonvulsant activity. Herbal medication is as yet the basis of around 75-80% of the total population, essentially in the developing countries, for essential health care because of better social worthiness, better similarity with the human body and lesser effects. Worldwide appraisals show that 80% of around 4 billion population cannot manage with the results of the western pharmaceutical industry and need to rely on the use of standard medications which are essentially derived from plant material. Taking into account the extraordinary dependence on conventional medicinal plants for treatment of disease and the potential for drug discovery, it gets relevant to search for able, effective and moderately safe plant medicines [7].

Individual Drugs:

***Vitex negundo*:** *Vitex negundo* is a woody fragrant shrub that belongs to the family Verbenaceae. It is bearing tri or pentafoliate leaves on quadrangular branches. Various pharmacological activities have been given to vitex negundo, for example, gastroprotective, protection against human liver cells against calcium-mediated toxicity, hepatoprotective activity. Phytochemical screening consequences of *Vitex negundo* leaf presence of flavonoids, flavones glycosides, diterpenes, triterpenes and sesqueterpenes. The methanolic extract doesn't showed significant diminished in different phase of epileptic seizure against MES induced seizures; at high dose the extract was dominant, for example it is demonstrating moderate activity that was comparable to that of Phenytoin, but in case of PTZ induced seizures the extract has indicated potentiating effect [8].

Adansonia digitata: This tree belongs to the family Malvaceae and is called as "Baobab" tree. It is the most widespread of the Adansonia species that is native to the African mainland especially in Nigeria

where it is cultivated for its medicinal values. It is used to treat antibacterial, anti-inflammatory, analgesic and antitoxin activities among others in Yoruba. The methanol extract of *Adansonia digitata* stem bark extract was capacity to important and dose-dependently raised onset of seizure and diminish seizure latency at the doses of 750 mg/kg and 1500 mg/kg body weight when compared to the normal saline-treated group. At the dose of 375 mg/kg, there was no prominent statistical rosein the mean onset of seizure as compared to control group.

The extract at all the tested doses demonstrates good percentage protection when compared to the normal saline-treated group. The good percentage protection demonstrates by this extract also suggests anticonvulsant-like activity. The pattern of activity observed with our extract was similar to that of sodium valproate, thus, the observed activity with our extract could be due to modulation of GABAergic system, although further study is recommended to investigated the exact mechanism of anticonvulsant activity of this extract [9].

***Abutilon indicum*:** *Abutilon indicum* belongs to the family Malvaceae. It is commonly known as "Thuthi". It is distributed throughout the hotter parts of India. The herb suggests very protective effect of 100 mg/kg and 400 mg/kg of AIE against identified epileptic agents. There are some suggest about anticonvulsant activity of this fatty acid and some flavonoids. So it exhibits anti-seizure action of Abutilon indicum because it is part of linoleic acid and/or flavonoid compounds present in the extracts. Thus the results of both doses of AIE, exhibited a very striking and potent antiepileptic action, it may be useful in both types of epileptic conditions like Grand mal and Petit mal epilepsy [10].

***Allium cepa*:** Allium cepa Linn. belongs to the family Alliaceae. It is commonly known as onion. It is a biennial (or) perennial herb with fragrant fleshy underground bulb; leaves are linear, hollow; flowers are many. Allium cepa L (Red Onion) is a natural plant usually utilized as a food condiment and spice in cooking. Allium cepa Linn contains antioxidants, for example, glutathione, selenium, and vitamin C. It also contains flavonoids, for example quercetin and isorhamnetin [11]. Garlic and onion metabolomes were read for antimicrobial compounds, authentication of genotypes, and Sulphur-containing compounds [12, 13, 14, 15]. The methanol extracts of bulbs of Allium cepa receive anxiolytic and anticonvulsant properties, which are possibly mediated partly *via* the facilitation of GABA transmission. Further studies on the isolation of the active constituents and exact mechanism of action are needed. GABA appears to play a significant role in the pathogenesis of several neuropsychiatric disorders. Many of the traditional agents used to treat psychiatric disorders are known to act, at least in part, by increasing GABA activity, while some of the newer agents may exert their therapeutic activity exclusively through GABAergic actions. In our present exploration, treatment with MEAC at dose levels of 200 and 400 mg/kg showed a prominent raised in whole-brain levels of GABA when compared to control. Flavonoids are known as positive modulators of GABAA receptors at low dose. Therefore, presence of flavonoids in Allium cepa is responsible for up to some extent for its anxiolytic and antiepileptic action through GABA modulation [16].

***Annona senegalenesis*:** *Annona senegalenesis* belongs to the family Annonaceae. It is commonly called a wild custard apple. It is used in the treatment of worm infestation, sleeping sickness, venereal diseases, and intestinal disorders and in blend with other herbs used for snake bites, toothache, dysentery, diarrhea, snake bites and toothache. The aqueous extract of the root of A. senegalenesis was secure at quick doses (LD50 954.9 ± 2.86 mg/kg body weight), safe drug-induced convulsion in mice, inhibited electroshock in mice, being more dominant against generalized than partial seizures and elongate drug-induced sleep in mice. It concluded that roots of A. senegalenesis had fixed anticonvulsant activity and there is an estimable pharmacological basis for worker same for this goal by the nearby people [17].

***Acorus calamus*:** *Acorus calamus* L. belongs to the family of Araceae. It is commonly called a sweet flag. It is a perennial herb, which is indigenous to central Asia, India, and the Himalayan region. It is used for the appetite and as an aid to digestion. It is also used in fever, stomach cramps, and colic.It has the property of improving memory power, intellect, flatulence, dyspepsia, helminthiasis, amenorrhea, dysmenorrheal and nephropathy.

The ethanolic *Acorus calamus* Rhizome (EEACR), when administered in a dose of 250 mg/kg and 500mg/kg, prominent reduced hind limb extension and tonic flexion of forelimbs when compared to control ($p<0.001$) in MES induced seizure model epilepsy [18].

***Aegle marmelos*:** *Aeglemarmelos* belongs to family Rutaceae. It is used in the treatment of inflammation, asthma, hypoglycemia, febrifuge, hepatitis, and analgesic. The extract of *Aegle marmelos* was administered in mice at the doses of100 and 200 mg/kg. The Extract upset hind limb tonic extensions (HLTE) affected by MES and also show protector activity in PTZ-induced seizures, at 200 mg/kg dose. MES and PTZ may be exerting their convulsant activity by preventing the action of gamma-aminobutyric acid (GABA) at GABA-A receptors. Gamma-aminobutyric acid is the major inhibitory neurotransmitter that is implicated in epilepsy. The enhancement and prevention of the neurotransmission of GABA will attenuate and raised convulsion, respectively. Diazepam a standard antiepileptic drug has been shown to exert its antiepileptic effects by enhancing GABA-mediated inhibition in the brain. It is possible that Diazepam antagonize MES and PTZ convulsions in this study by increasing GABA neurotransmission [19].

***Biophytum sensitivum*:** *Biophytum sensitivum* (L.) belongs to family Oxalidaceae. This herb has a tropical distribution. It is found in warmer parts of the world in, tropical Africa, Asia. It isused in the treatment of diabetes and phthisis, inflammatory diseases, asthma, hypoglycemic, immune-modulatory, apoptotic activity, chemo protective cellmediated immune response, hypocholestero-lemic, antitumor activity on prostaglandin biosynthesis, antibacterial activity and antioxidant activity. It is used for the prevention of prostaglandin synthesis and anti-oxidant activity; it may prevent generation of free radicals. The Extract of *B. sensitivum* was important and dose-dependently lower the period of tonic hind limb extension in both trial models and also delayed the start of tonic-clonic convulsions induced by pentylenetetrazol in mice. In this work, the dose of 200 mg/kg afforded protection to all animals. The anticonvulsant activity may be due to the presence of flavonoids and sterols in the extract. The ethanolic leaf extract of *Biophytum sensitivum* L. may be helpful in both tonic clonic and absence seizures [20].

***Butea monosperma*:** *Butea monosperma* (Lam.) belongs to the family Fabaceae. It is commonly known as Kuntze. It is used in astringent, depurate, diuretic and aphrodisiac properties. It promotes diuresis and menstrual flow. It is also used in snakebite as antivenom. The extract dose-dependently reduced the onset of pentobarbital induced sleep by raising GABA mediated synaptic inhibition either by directly activating GABA receptors or, more usually, by increasing the action of GABA on GABAA receptors. The total sleep time was able to important at the dose 300 mg/kg, indicating that the extract of Butea monosperma has a sleep potentiating properties. The protection of the extract against PTZ induced convulsion indicated that the extract interacts with GABA-ergic neurotransmission. The PTZ test is evaluated to identify anticonvulsant drugs effective against myoclonic and absence convulsions. The capability of Buteamonosperma to lower the length of tonic-clonic convulsion in the MES test exhibits its action against generalized tonic-clonic convulsions [21].

Canna Indica: *Canna indica* belongs to the family Cannaceae. It has been widely used in customary medicine for the treatment of many complaints. It was distributed in the tropics and subtropics, particularly of the western hemisphere. It is commonly cultivated in flower gardens. It is used for the treatment of malaria, as a prevention for diarrhoea and dysentery. It was also used as diaphoretic, diuretic, and in treating fever and dyspepsia [22].

The extract of *Canna indica* L. reduced the period of tonic hind leg extension in maximal electroshock-induced seizures, possibly by acting on voltage-gated Na+ channels. The latency of convulsion and lowered the seizure threshold by acting on the GABAergic system, glutaminergic mechanism, and Na+, Ca+ channels. The exact mechanism and the active principle by which these extracts put forth their action remain unclear 23.

***Datura metel*:** *Datura metel* L. Belonging to the family Solanaceae with local name “Datura”. A

perennial plant, can reach a height of 1.8m. It can be found in East Asia. It is used in traditional Bangladeshi herbal medicine. In Ayurveda medicine, seeds of D. metal are applied to treat Ulcers, Bronchitis, Skin rashes, Jaundice, and Diabetes. In Brazil, seeds are used in making tea making which serves as a sedative, and dried flowers are smoked as cigarettes [24]. The extract prevented convulsions induced by these agents may indicates that enhancement of GABA neurotransmission may be responsible for its anticonvulsant activity. The benzodiazepine-like anticonvulsants such as diazepam, which increase GABA neurotransmission act as anxiolytics at low doses and have anticonvulsant and myorelaxant or neurotoxic effects at higher doses. The ethanolic extract of *Datura metel* was exhibits important ($p<0.001$) dose-dependent protection in Swiss albino mice against MES and PTZ generated convulsions. The study showed that the leaves of Datura metel generate anticonvulsant effects through central mechanisms 25

Cocos Nucifera: *Cocos nucifera* (L.) belongs to family Arecaceae. It is popularly called coconut, coco, coco-da-Bahia, or coconut-of-the-beach. The plant is originally from Southeast Asia and the islands between the Indian and Pacific Oceans [26]. The fruits of the coconut palm are not nuts, but drupes [27]. it utilized as antiplasmodial [28], menorrhagia [29],, antiulcerogenic ,wound healing (anti-inflammatory, anti-diabetic, antimicrobial, anti-neoplastic, antioxidant, anti-parasitic, insecticidal and cell proliferation of one or more parts for example coconut water, spadix, husk fiber, oil, flowers and mesocarp of coconut fruit are documented [30, 31, 32].

The aqueous root extract of *Cocos nucifera* L. may assess anticonvulsant activity against MES-induced seizures by affecting the voltage dependant Na+ channels or by blocking glutaminergic excitation mediated by the N-methyl- Daspartate (NMDA) receptors. Therefore, the pharmacological activity to the traditional use of this plant in the treatment of epilepsy. The parameters observed in this model are the onset of tonic convulsions and the duration of seizures. 33

***Citrullus colocynthis*:** *Citrullus colocynthis* (L.) belongs to the family Cucurbitaceae. It is commonly called bitter apple or wild gourd. It is one of the medicinal plants recommended for the treatment of seizure. This plant grows in the south, center, and east of Iran. It is used in analgesic, purgative, anti-inflammatory, antioxidant, anti-diabetic, and hypolipidemic activities. *Citrullus colocynthis* pulp extract showed a statistically prominent reduction in the seizures duration and increase in latency period of seizures induced by pentylenetetrazole in mice. This effect raised dose-dependently at doses of 10, 25, and 50 mg/kg, but reduced at the dose of 100 mg/kg, which may be due to its toxicity. The main action of the pentylenetetrazole-induced seizure is reducing g-aminobutyric acid (GABA) level in the cortex. GABA has been reported as the predominant inhibitory neurotransmitter in the central nervous system of mammals and has been implicated in convulsions. It mediates the inhibition of neuronal responsiveness and activity by enhancing the cl-conductance through the opening of the cl- channel [34].

Acalypha fruticosa: *Acalypha fruticosa* belongs to the family Euphorbiaceae. It is commonly known as “Chinnichedi” and “Birch-leaved acalypha.” It is a shrub Tribal people of different parts of the world use this plant to treat many diseases such as convulsions, cough, cold, scabies, constipation, malaria, and liver problems. It is used to treat skin diseases, wounds, stomachaches, and poisonous bites. It is also used to treat convulsions, fever, colds and swellings of the scrotum. The extract prevent convulsions in mice potent than phenobarbitone sodium. In the INH process, it delays the latency of convulsions in micein a dose-dependent fashion but failed to protect the mice against mortality. The chloroform extract demonstrated prominent and dose-dependent antiepileptic activity, which may be due to the presence of antioxidant principles like flavonoids [35].

***Carissa Edulis*:** *Carissa edulis* Vahl belongs to family Apocynaceae. It is commonly called the Arabic Natal plum. It is a spiny evergreen shrub or a small tree that may reach a height of 5 ft and an equal breadth. The plant is found in South Africa. It used as traditional medicine for different ailments for example: sickle cell anemia fever and hernia,

treatment of edema, cough, ulcer, worm infestation toothache, management of epilepsy, and cancer.

The broad spectrum of the observed anticonvulsant activity in this study might be attributed to the presence of different biologically active components in the extracts. The intraperitoneal and oral LD50 of RAF was assessed to be 2222.61 mg/kg and above 5000 mg/kg, respectively, indicating its apparent safety. The LD50 values of column fractions of RAF (S1 and S2) were evaluated to be more than 5000 mg/kg for both i.p. and p.o. routes in mice. The results of epilepsy are tremendously diverse, encompassing genetic, developmental abnormalities, traumatic, neoplastic, infective and degenerative disease processes, making it hard for a particular drug to be administered to treat this debilitating neurological dysfunction. RAF and its subfractions S1 and S2 protected the mice against PTZ-induced seizures [36].

***Commiphora wightii*:** *Commiphora wightii* (A.) belongs to family Burseraceae. It is commonly called Guggal or Guggul.38It has been utilized for over 2,500 years as a valued herb in Ayurvedic Medicine, a system of South Asian Medicine practiced in India, Bangladesh, and Pakistan [37]. It is used as an anti-inflammatory, carminative and hypoglycemic, antiseptic, astringent, sedative, stomachic, diaphoretic, diuretic, expectorant, anthelminthic, depurative, vulnerary, demulcent, aphrodisiac, liver tonic, and anti-spasmodic. Therapeutic uses of guggul are used against rheumatoid nervous diseases, hypercholesterolemia leprosy, muscle spasms arthritis, disorders, hypertension, and urinary dysfunction and as hypolipidemic and acts as anti-oxidant. *Commiphora wightii* (80mg/kg) was treated by subcutaneous route to mice. The onset of convulsion, lethality, and % protection was observed. The data's were analyzed using ANOVA followed by Dunnet‟s t-test. The outcome exhibits that 200 & 400 mg/kg of *Commiphora wightii* extract produced significant ($P<0.01$ and $P<0.001$, respectively) anticonvulsant property against Pentylenetetrazole induced convulsion in mice. 38

***Clerodendrum infortunatum*:** *Clerodendrum infortunatum* Linn. belongs to the family Verbenaceae. It is used in diarrhoea, skin disorders, venereal and scrofulous complaints, wounds, post-natal complications. Pharmacological actions include Antimicrobial, antioxidant, analgesic, anticonvulsant, and antipyretic activities.

The ethanolic extracts of the plant were found to possess statistically prominent anticonvulsant activity ($p<0.01$) against Maximum electroshock (MES) Induced Seizures. The importance of anticonvulsant activity of EECI could be due to the saponin constituents of the leaves as has been demonstrate in previous studies; Saponin lower the period of seizures and provided protection in a dose-dependent fashion against leptazol-induced convulsions, which showed that saponin has prominent anticonvulsant effect. The anticonvulsant activity of are possibly mediated by cl- channels of GABA benzodiazepine receptor complex and by cl-channel of glycine receptor. 39

***Desmodium triflorum*:** *Desmodium triflorum* (L.) belongs to family Fabaceae. It is a perennial herb. The plant is available in all tropical countries. It is used in diarrhoea, convulsions, antispasmodic, sympathomimetic, central nervous system stimulation, curare-mimetic activity and diuretic and as a galactagogue. The ethanolic extract possessed anticonvulsant activity. EEDT dose of 400 and 800 mg/kg prominent delayed the onset of convulsion, prominent decreased the duration of convulsion. The enhancement of the GABAergic neurotransmission is reported to antagonize seizures, while the inhibition of the neuro-transmission boosts seizures. The protection of mice against PTZ-induced seizures by the standard anticonvulsant drugs, phenobarbitone and diazepam is expected since many authors have demonstrated that they describe their anticonvulsant activities by increasing GABA-mediated inhibition [40].

***Citrus sinensis*:** *Citrus sinensis* belongs to the family Rutaceae. It is commonly known as sweet orange. It was widely cultivated all over the world. Many products are being extracted from *C. sinensis* leaves, such as glycosides, flavonoids, hesperidin, Diosmin, Triterpene, lineman and ruteosides. It is used to manage neurological sickness. It also had sedative action with the methanolic extract. It is used in anti-inflammatory, antihypertensive, diuretic, and analgesic properties [41]. The genus Citrus incorporates more than 162 species belonging to the family Rutaceae [42]. The

anticonvulsant activity of hydroethanolic leaf extract of *Citrus sinensis* was more when it was given in the dose 100mg/kg than 50mg/kg. The convulsions showed by Pentylenetetrazole are valuable in identifying drugs that are powerful dominant against seizures. GABA is broadly involved in epilepsy; inhibition of GABA-ergic neurotransmission or movement has been demonstrate to promote and facilitate seizures, while enhancement of GABA-ergic neurotransmission is known to inhibit or constrict seizures. Hydroethanolic leaf extract of Citrus sinesis may perhaps be producing anticonvulsant activity by increasing level of (GABA), an inhibitory neurotransmitter in the central nervous system [41].

***Lobelia nicotianaefolia*:** L*obelia nicotianaefolia* belongs to family Campanulaceae. It is commonly called Indian tobacco, wild tobacco, asthma weed, vomit root, gag root, pulse weed, emetic herb, and bladderpod. It is also found in Deccan and Konkan at altitudes of 900-2,100 m. It is a rich source of alkaloids of the lobeline group. The plant has been recorded to contain several alkaloids, with the main alkaloid lobeline apparently observed, revealed higher concentrations [43]. Extracted lobeline (10, 20, and 30 mg/kg, i.p.) showed delayed and antagonized ($P < 0.050–0.001$) onset of PTZ-induced seizures. It also acts as antagonist of strychnine-induced seizures. The death rate was also repressed in the test group of animals. In biochemical evaluation, isolated lobe lines (5, 10, and 20 mg/kg, i.p.) demonstrate raised the brain GABA level. And at dose of 30 mg/kg, GABA level demonstrates a slight reduce in the PTZ model. Also, a biochemical analysis indicates raise GABA level in brain level at 20 mg/kg i.p. of isolated lobeline. So, it is suggested that lobeline lowers epileptic seizures by raising the GABA release supporting the GABAergic mechanism. 44

***Viola tricolor*:** *Viola tricolor* L. (*V. tricolor*) is a member of the family Violaceae. It is commonly known as wild pansy. It is utilized in the Indian Traditional medicine system to treat various skin disorders, bronchitis, anti-inflammatory, cough expectorant, and diuretic properties. Its medicinal properties is largely attributed to the presence of saponins, flavonoids, adhesives, salicylic derivatives, and carotenoids [45]. It is suggested by a study that it exhibit that V. tricolor and its ethylacetate and n-butanol fractions to obtained anticonvulsant action as confirmed by the prolongation of latency to the first GTCs induced by PTZ and lower in the incidence of HLTE induced by MES [46].

Leuca scephalotes: belonging to the family Lamiaceae. The decoction of dried aerial parts of the plant is used orally for diarrhea. It is used orally to reduce fever. It is used orally as an appetizer. It is also used orally to treat jaundice, cold and cough.47It is also called as "Dronapushpi" in Sanskrit and "Gumma" in local language [48]. *Leucascephalotes* may be required to have the same type of mechanism as diazepam in the event of the standard; it demonstrates 100% assurance and any indication of seizure. INH is used generally for the treatment and chemoprophylaxis of tuberculosis, however, can have serious effects the CNS causing seizures and comas. The INH is opinion to be an inhibition of GABA synthesis in the CNS. So diazepam treated group was exhibited upto 100% of protection of the animals. But the PLC not indicated exhibited protection of the animal, it was ineffective. Simultaneously, we found the ELC more effective than PLC. The extract may be having either by the aggravation of L-glutamate or inhibited of GABA degradation by GABA transaminase [49].

Phyllanthus amarus: *Phyllanthus amarus* belongs to the family Euphorbiaceae. This plant is widespread throughout the tropics and subtropics in sandy regions as a weed in cultivated and wastelands. Phyllanthusamarus is a generally available weed in India. Its anti-hyperglycemic, anti-nociceptive, anti-inflammatory, and anti-carcinogenic properties were attributed because of its extensive anti-oxidant activity.50, 51P. amarus may produce its anticonvulsant action when formulated in the aqueous and ethanolic extracts via non-specific mechanisms since it stops the hind limb extension induced by MES as well as delayed the latency of seizures generated by PTZ. The aqueous and ethanolic extracts of the leaves and stems of *P. amarus* (70 mg/kg, p.o) prominent ($p<0.001$) finished the hind limb extension induced by MES. The same dose, also prominent ($p<0.001$) protected the animals from PTZ induced tonic convulsions [52].

***Plectranthus barbatus*:** *Plectranthus barbatus* Andr. Belonging to family Lamiaceae. It is a perennial shrub that is grown in Africa and is used as a traditional medicine to heal different disorders. It is used to treat digestive, respiratory, circulatory, nervous disorders, infections, gastritis, intestinal spasms, nausea, stomach ache, and as a purgative. It used in respiratory disorders include the relief of colds, cough, and bronchitis, and in the circulatory system, uses include my algia, angina, and hypertension. The aqueous-alcoholic formulation of leaves of *Plectranthus barbatus* shows anticonvulsant activity against both strychnine and pilocarpine-induced seizures. The mechanism of strychnine-induced seizures is hypothesized to engage direct antagonism of strychnine sensitive glycine receptors not only in main brain areas but also in the spinal cord and brainstem, thus abrogating spinal reflexes and causing motor activity, elevated muscle tone, visual and auditory perception, tonic convulsions, hyperactivity of sensory and death through respiratory or spinal paralysis or by cardiac arrest. The result revealed that strychnine-induced seizures are partly inhibited by P. barbatus treatment [53].

***Ocimum sanctum*:** *Ocimum sanctum* belongs to the family Lamiaceae. It is commonly called holy basil or tulsi means "one i.e. comparable". *Ocimum sanctum*, because of its medicinal properties has great importance in Indian traditional medicine and Ayurveda.54Tulsi help with the body's internal physiologic balance and protection of the body from toxin-induced damage [55]. It is used in analgesic, anti-cancer, anti-asthmatic, anti-diabetic, anti-fertility, hepatoprotective, hypotensive, hypo-lipidemic, anti-inflammatory, anti-oxidant, immune modulatory and anti-stress properties.

The treatment with OS extracts (4.25 and 8.5 mg/kg) in rats prominent decreased THLE in the MES-induced seizure model. MES-induced seizures are finished by the drugs that block voltage-gated Na^+ channels, for example: phenytoin and carbamazepine or by the drugs that block N-methyl-D-aspartate receptors such as felbamate. Protection of OS extract against THLE suggests that the drug investigated the ability to inhibit or finish the spread of seizures within the brain, indicating the presence of an anticonvulsant compound in the extract[56].

TABLE 1: LIST OF HERBAL DRUGS USED IN EPILEPSY ACTIVITY

S. no	Biological Name/Family	Common Name	Part	Extract/Dose	Standard Dose	Model	Animals
1	*Vitex negundo* (Verbenaceae)	Horseshoe vitex	Leaf	Methanolic 200 & 400 mg/kg,b.wt.	Phenytoin sodium 20mg/kg, b.wt.	MES	Albino mice (n=24)
2	*Adansonia digitata* L. (Malvaceae)	Baobab	Bark Stem	Methanolic 1500, 750 &375mg/kg,b.wt.	Sodium valproate 200mg/kg,b.wt.	PTZ	Wister rat (n=25)
3	*Abutilion indicum* (Malvaceae)	Thuthi	Leaf	Aqueous and Ethanolic 100 & 400mg/kg,p.o.	Diazepam 2mg/kg,p.o.	MES	Wister rat (n=36)
4	*Allium cepa* L. (Alliaceae)	Onion	Bulb	Methanolic 200&400 mg/kg,p.o.	Diazepam 2mg/kg,i.p.	PTZ	Albino mice (n=24)
5	*Annona senegalenesis* (Annonaceae)	Wild custard apple	Root	Aqueous 50,100,200.400,800&100mg/kg,b.wt	Phenobarbitone sodium 35mg/kg,i.p.	PTZ	Albino mice (n=40)
6	*Acorus calamus* (Araceae)	Vacha	Rhizome	Ethanolic 250 & 500 mg/kg,p.o.	Phenytoin sodium 50mg/kg.p.o.	MES PTZ	Albino mice (n=48)
7	*Aegle marmelos* (Rutaceae)	Bael	Leaves	Ethanolic 100 & 200 mg/kg,p.o.	Diazepam 4mg/kg,p.o.	MES PTZ	Albino mice (n=40)
8	*Biophytum sensitivum* (Oxalidaceae)	Little tree plant	Leaf	Ethanolic 50,100 & 200mg/kg,p.o.	Phenytoin 25mg/kg,i.p.	MES PTZ	Albino mice (n=30)
9	*Butea*	Flame of	Stem	Methanolic	Pentobarbitol	Pentobarbit	Albino

	monosperma (Fabaceae)	forest		100,200 & 300mg/kg,p.o.	45mg/kg,i.p.	ol	mice (n=30)
10	*Canna indica L.* (Cannaceae)	Edible canna	Aerial	Methanolic 100,200& 400mg/kg,p.o	Phenytoin 50mg/kg,i.p.	MES INH Strychnine	Albino mice (n=30)
11	*Datura metal* (Solanaceae)	Devil's trumpet	Leaf	Ethanolic 200 &400mg/kg,p.o.	Phenytoin 25mg/kg,i.p. Diazepam 0.5mg/kg,i.p.	MES PTZ	Albino mice (n=25)
12	*Cocos nucifera* L. (Arecaeae)	Palm tree	Root	Aqueous 50& 100mg/kg,p.o.	Phenytoin 25mg/kg,p.o.	MES PTZ	Albino mice (n=20)
13	*Citrullus colocynthis* (Curcurbitaceae)	Bitter apple	Fruit	Hydroalcholic 10,25,50&100mg/kg,i.p.	Pentylenetrazole 60mg/kg,i.p.	PTZ	Albino mice (n=36)
14	*Acalypha fruticosa* (Euphorbiaceae)	Chinnichedi	Aerial	Chloroform 30,100&300mg/kg,p.o.	Diazepam 3mg/kg,p.o.	MES PTZ	Albino mice (n=25)
15	*Carissa edulis* (Apocynaceae)	Natal plum	Root	Aqueous 150,300&600mg/kg,i.p.	Valproate 200mg/kg,i.p.	PTZ	Albino mice (n=30)
16	*Commiphora weightii* (Burseraceae)	Indian bdellium	Resin	Oleogum resin 200&400mg/kg,p.o.	Clonazepam 0.1mg/kg,i.p.	PTZ	Albino mice (n=24)
17	*Clerodendrum infortun*atum L. (Verbenaceae)	Glory bower	Leaves	Ethanolic 400,600&800mg/kg,p.o.	Phenobarbital 10mg/kg,b.wt.	MES PTZ	Albino mice (n=30)
18	*Desmodium triflorum* (Fabaceae)	Creeking tick trefoil	Leaves	Ethanolic 400&800mg/kg,p.o.	Diazepam 10mg/kg,i.p.	INH	Albino mice (n=24)
19	*Citrus senesis* (Rutaceae)	Sweet orange	Leaf	Hydroethanolic 50&100mg/kg,p.o.	Sodium valproate 150mg/kg,i.p.	PTZ	Albino mice (n=24)
20	*Lobelia nicotinaefolia* (Campanulaceae)	Tabacco	Leaf	Hydroalcholic 5,10,20&30mg/kg,i.p	Diazepam 1mg/kg,i.p.	PTZ Strychnine	Albino mice (n=36)
21.	*Viola tricolor* (Violaceae)	Johnny jump up	Leaves	Hydroalcholic 100,200&400mg/kg,i.p.	Diazepam 3mg/kg,i.p	PTZ MES	Albino mice (n=260)
22	*Leuca scephalotes* (Labitatae)	Dronpushpi	Whole plant	Ethanolic &Petroleum 20,40&60mg/kg,p.o.	Diazepam 5mg/kg,i.p	INH Strychnine	Albino mice (n=48)
23	*Phyllanthus amarus* (Euphorbiaceae)	Herbaceous plant	Leaves Stem	Aqueous&Ethanolic 70mg/kg,p.o.	Phenytoin 25mg/kg,i.p.	MES	Albino mice (n=30)
24	*Plectranthus barbatus* (Lamiaceae)	Indian coleus	Leaves	Hydroalcholic 1,10,30&100mg/kg,p.o.	Strychnine 300mg/kg,p.o.	Strychnine	Albino mice (n=40)
25	*Ocimum sanctum* (Lamiaceae)	Tulsi	Leaves	Ethanolic 1.75,4.25&8.50mg/kg,i.p.	Sodium valproate 300mg/kg,p.o.	MES PTZ	Albino mice (n=36)
26	*Nepeta bractaeta* (Lamiaceae)	Nepeta	Flower	Methanolic&Aqueous 190&560mg/kg,p.o.	Sodium valproate 15mg/kg,p.o.	ICES PTZ	Albino mice (n=36)
27	*Nardostachys*	Jatamansi	Root	Ethanolic	Sodium	PTZ	Albino

	jatamansi (Caprifoliaceae)			200&400mg/kg,i.p.	valproate 0.5mg/kg,i.p.	MES	rats (n=30)
28	*Mahua longifolia* (Sapotaceae)	Mahuwa	Wood	Aqeous 100,200&400mg/kg,p.o.	Daizepam 5.0mg/kg,i.p.	MES PTZ Lithium-pilocarpine	Albino mice (n=30)
29	*Milicia excels* (Moraceae)	Iroko tree	Leaf	Ethanolic 250,500&1000mg/kg,p.o.	Daizepam 1mg/kg,i.p.	PTZ	Albino mice (n=36)
30	*Catharanthus roseus* (Apocynaceae)	Vinca	Leaf	Petroleum ether 100,200&400mg/kg,i.p.	Daizepam 4mg/kg,i.p.	PTZ	Albino mice (n=30)

Nepeta bractaeta: *Nepeta bractaeta* is, an aromatic perennial herbaceous plant that belongs to the family Lamiaceae; it is a brightly colored shrub or sub-shrub that ranges from 30-100 cm in height. Found in western temperate Himalayas from Garhwal to Kashmir at altitudes of 1800-2400 m. It is also reported to be used in boils and abscesses, cystitis, gastritis, fever, rheumatism, cold, cough, asthma, earache, insect bites, flatulence, and characterized by unprovoked, recurring seizures that disrupt the nervous system and can cause mental and physical dysfunction. Approximately 50 million individuals suffer from this debilitating disease. *Nepeta bractaeta* extracts may have an efficient anticonvulsant activity which maybe because of the presence of certain active phytoconstituent.

The anticonvulsant activity of *Nepeta bractaeta* may involve GABAergic transmission and glutaminergic transmission or Na^+ channel blockage. The methanolic and aqueous extracts of the flowers of *Nepeta bracteata* were observed for their antiepileptic activity by raised current Electroshock seizures (ICES) test and Pentylenetetrazole (PTZ) test using Swiss albino mice. Both the extracts demonstrate prominent activity in ICES and PTZ induced convulsions in comparison to control. In ICES model, NBAE at a higher dose demonstrate 16.7%, and NBME at a higher dose demonstrate 33.3% protection against seizure, and in PTZ model, NBME at a higher dose demonstrate 33.3% protection against seizure. From the experiments performed, it can be said that Nepetabractaeta does obtain anticonvulsant property [57].

***Nardostachys Jatamansi*:** *Nardostachys jatamansi* belongs to the family Valerianaceae [61]. The rhizomes and roots of *Nardostachys jatamansi* (Valerianaceae), a plant indigenous to China, India, and Tibet [58]. It contains various able to bioactive chemical components, for example, monoterpenoids, sesquiterpenoids, triterpenoids, and lignans [59, 60]. It is a small, perennial, dwarf, hairy, rhizomatous, herbaceous, endangered, and most primitive species. It is used in modern medicine for a cognitive and neurological functions used. It relieves side effects such as vertigo, seizures, *etc*. in fever. It has protective activity in epilepsy, cerebral ischemia, and liver damage. It is also used in mental disorders, insomnia, hypertension, and heart disease [61].

The ethanolic formulation of *Nardostachys jatamansi* at the dose of 400 mg/kg has result edmajor anticonvulsant activity in maximal electroshock seizure (MES) model and pentylenetetrazole induced seizure model, the ethanolic liquid of *Nardostachys jatamansi* has showed important anticonvulsant action at the dose of 200 mg/kg and 400 mg/kg body weight of animal [62].

***Madhuca longifolia* (Koen.) Macb:** *Madhuca longifolia* belongs to the family Sapotaceae. It is commonly known as mahua [63]. It is developed in hot and damp atmospheres of India. There is extremely old's faith and observation of the medicinal uses of plant *M. longifolia* for the skin-related issue and radioprotective [64, 65, 66]. It is used to treat stimulant, anthelmintic, analgesic, diuretic, aphorodisiac, helminths, tonsillitis, pharyngitis, bronchitis, diabetes, rheumatism, ulcer, and antiepileptic activity. In MES-induced seizure, extract was potential to produce dose-dependent reduced the duration of hind limb extension, from which the extract at 400 mg/kg p.o. assessed

significant ($p<0.05$) antiepileptic activity as compared with disease control. In PTZ model, extract at dose 400mg/kg p.o. significantly ($p<0.05$) decreases duration of convulsion and 50% survivality. In lithium-pilocarpine induced seizures, extract dose 400 mg/kg p.o. exhibited significant ($p<0.05$) reduce in seizures as compared with disease control group. 100, 200 and 400 mg/kg p.o. dose were used during screening, from that 400 mg/kg p.o. dose exhibited potent antiepileptic activity against seizures due to occur because of imbalance of neurotransmitters in brain [63].

Milicia excela: *Milicia excelsa* belongs to the family Moraceae. It is popularly known as Iroko tree or African teak. It is used for the treatment of malaria, anemia, sexual dysfunction, rheumatism, lactation failure, mental illnesses, and convulsion. The mechanism of anticonvulsant activity, AF was used, and significant as the most active fraction, because it gave the highest percentage protection of 83.3 and 100 at the highest dose of 1000 mg/kg, p.o in PTZ and PTX-induced convulsion models respectively. Another set of mice were pretreated with flumazenil (GABAA receptor antagonist, 3.0 mg/kg, i.p.), cyproheptadine (5-HT receptor antagonist, 4 mg/kg i.p) and L-NNA (Nitric oxide synthase inhibitor, 10 mg/kg, i.p.), for 15 minutes prior to oral administration of AF (1000 mg/kg, p.o.). One hour later, the mice were given PTX (10 mg/kg, i.p.). The onset of clonic, tonic convulsion and death latency were recorded for each mouse. Animals that survived beyond 30 min were prominent protected [67].

***Catharanthus roseus*:** *Catharanthus roseus* belongs to the family Apocynaceae. It is commonly called vinca. It is an evergreen subherb or herbaceous plant growing to 1 m tall [68]. It produces over 100 various terpenoid indole alkaloids.69It is a commercial source for anti-cancer terpenoid indole alkaloids [70]. It was used as diuretic, astringent and to cure cough, wasp stings, for nose bleeding, sore throat, mouth ulcer and for bleeding gums. The roots of SW petroleum ether extract of *Catharanthus roseus* contains all the above constituents hence the anticonvulsant activity the petroleum ether extract of *Catharanthus roseus* at the dose 400 mg/kg produce a prominent decreased in the duration of extensor, clonus and stupor phase as compared to control group [68].

CONCLUSION: Traditionally, herbal medicines have been used for decades as a remedy for many diseases. In this review, 30 herbal plants are processing antiepileptic activity. The epileptic activity of plants plays an important vital in herbal medicines exhibited able anticonvulsant properties and low toxicity in the experimental model at the doses used. However, further studies still needed to be carried on an exhibit of the extract to people, and it's used in folk medications for seizure control should be including by regular assessment of the level of consciousness and blood pressure. This reviews an overview of the antiepileptic activity in traditional medicinal plants as able use for the development of new medicines used in the protection against epileptic activity. However, we can safely state that herbal medicines have enormously able to provide some remarkable drugs.

ACKNOWLEDGEMENT: The authors wish to thank the Management of Sunder Deep Pharmacy College (SDPC), Ghaziabad, for providing the necessary facilities and encouragement to complete this article.

CONFLICTS OF INTEREST: The authors declare that they have no conflict of interest.

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How to cite this article:
Bushra A, Monika S, Shalini S, Mohseen and Bushra C: Anti-epileptic activity of Indian medicinal plants - a review. Int J Pharm Sci & Res 2021; 12(8): 1000-13. doi: 10.13040/IJPSR.0975-8232.12(8).4060-72.