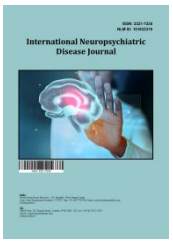

International Neuropsychiatric Disease Journal

Volume 18, Issue 3, Page 36-52, 2022; Article no.INDJ.94753
ISSN: 2321-7235, NLM ID: 101632319

Anticonvulsant Activity of Some Medicinal Plants: A Review

Felix Keneolisa Asogwa [a*], Ugwu Obiora Celestine [a] and Ali Ibeabuchi Jude [b]

[a] Department of Pharmacology, Enugu State University of Science and Technology Agbani, Enugu State, Nigeria.
[b] Department of Pharmaceutical Chemistry, Enugu State University of Science and Technology Agbani, Enugu State, Nigeria.

Authors' contributions

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

Article Information

DOI: 10.9734/INDJ/2022/v18i3355

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/94753

Review Article

Received: 14/10/2022
Accepted: 21/12/2022
Published: 24/12/2022

ABSTRACT

Epilepsy is a central nervous system (neurological) disorder characterized by a bizarre feelings, sensations, and behaviors. Muscle spasms, convulsions, and loss of consciousness occasionally from epileptic seizures. Neuronal dependent on neurotransmitters in the central nervous system. In this review, we discussed epilepsy and its therapies, placing particular emphasis on some medicinal plants and their mechanism of action. The majority of herbal remedies that are both tested for anticonvulsant activity and utilized in ethno medicine to treat epilepsy were reported. The findings demonstrate that active components extracted from medicinal plants can prevent and treat neuronal disorder.

Keywords: Transmitter; excitotoxic neuronal plasticity; seizure; neurosyphilis.

**Corresponding author: E-mail: felix.asogwaken@esut.edu.ng;*

1. INTRODUCTION

Epilepsy is a brain disorder that result from intense, improperly coordinated, confined, or broadly dispersed electrical discharges from neurons [1]. An epileptic seizure is a period of aberrant neuronal discharge that manifests clinically as alterations in sensory perception, motor coordination, mood, or autonomic function [2]. Numerous factors, including congenital, developmental, or inherited ones, can result in epileptic seizure disorders. Most seizures are spontaneous, without prior warning, short-lived (a few minutes or even seconds), and terminate on their own [3]. In various human communities, epileptic seizures are regarded as the most prevalent neurologic symptoms, and they continue to be the most prevalent neurological disorder affecting people of all ages. About fifty million people worldwide suffer from epilepsy, a chronic noninfectious brain disorder (Lozano et al., 2020) [4]. According to reports, epilepsy affects 1/125 of the population in Nigeria, which indicates that it is a significant burden [5]. Periodic seizures, which are defined by fleeting episodes of uncontrollable movement involving either a section of the body or the full body, are what make this medical disorder distinct. Sometimes they accompany loss of awareness and control of the bowels or the bladder (WHO, 2019). There are two primary categories of seizures: focused or partial seizures and generalized seizures. One area of the brain, referred to as the seizure's "focus," is the only one affected by focal seizures. Focal seizures can affect a large portion of one hemisphere or just a small portion of a lobe, but generalized seizures happen when seizure activity is widespread in both the left and right hemispheres of the brain, and the affected person falls unconscious, albeit briefly except in myoclonic seizures [6]. High-frequency action potential bursts and excessive synchronization of a neuronal population are two concurrent characteristics that mark the beginning of seizures [7]. Extracellular Ca++ causes an inflow of Na+, the opening of voltage-dependent Na+ channels, the formation of recurrent action potentials, and the bursting activity that arises from the neuronal membrane's comparatively protracted depolarization. Depending on the type of cell, the gamma-aminobutyric acid (GABA) receptors and Cl influx or K+ efflux mediate the hyperpolarizing potential [8]. GABA is a specific kind of inhibitory neurotransmitter in the brain that effectively stops the brain from delivering messages [2]. In some cases, GABA interneurons may paradoxically promote particular types of epileptic discharges. Effective anticonvulsants are those that boost synaptic GABA by inhibiting its breakdown or reuptake. These include benzodiazepines, which enhance GABA binding to the GABA receptor and increase the frequency of chloride channel openings [9,2,10]. Seizures can be brought on by several GABA production inhibitors, such as thiosemicarbazide, 4-deoxypyridoxine, isoniazid, and L-allyglycine [11]. The two main kinds of receptors, $GABA_A$ and $GABA_B$, are involved in the interactions between GABA, the main inhibitory neurotransmitter. While $GABA_B$ receptors are located presynaptically and can consequently influence synaptic release, $GABA_A$ receptors are positioned postsynaptically. In the adult brain, $GABA_A$ receptors are permeable to Cl-ions; Cl-influx activation hyperpolarizes the membrane and suppresses action potentials. Barbiturates and benzodiazepines are $GABA_A$ receptor agonists, and as a result, they reduce seizure activity. Because of their presynaptic position, $GABA_B$ receptors are associated to second messenger systems but not Cl^- channels, and thus attenuate transmitter release [12]. A kind of amino acid called glutamate serves as the brain's main excitatory neurotransmitter. Under normal circumstances, glutamate produced from synapses is taken up by astrocytes and quickly transformed by glutamine synthetase into the non-excitotoxic amino acid glutamine [13]. Epileptic seizures are mediated by the metabotropic glutamate receptor and the ionotropic N-methyl-D-aspartate (NMDA), α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid / kainate, and others [2]. In chronic epilepsy models, excitatory glutamatergic pathways have a role in both long-term adaptive neuronal plasticity associated to epileptogenesis and acute, transitory, provoked seizures. The excitatory effects of glutamate increase sodium and calcium conductance via activating ligand-gated ion channels (NMDA and non-NMDA receptors) [2]. Glutamate and aspartate are more easily reabsorbed after synaptic release, these effect is enhanced by the neuronal excitatory amino acid carrier 1 (EAAC1) and glial glutamate transporters. Reduced glutamate transporter activity may be consistent with increased excitatory activity [14].

2. ETIOLOGY OF EPILEPSY

Despite the fact that the frequency of symptomatic epilepsy gradually increases with age, idiopathic epilepsy continues to be the most

prevalent in all age groups [15]. In Nigeria, between 55 and 60 percent of epilepsy cases are considered to be idiopathic [16]. In other regions of the world, approximately 30% of seizure patients have a diagnosable neurological or systemic illness, with the remaining patients having either idiopathic or cryptogenic epilepsy.

Genetics: Recent research from several studies revealed that 20% of epilepsy sufferers, especially in adolescents, have genetic variants of the condition [17]. There is little data on the genetic epidemiology of epilepsy among Nigerians, but there have been instances of tuberous sclerosis in Nigerians who have the condition [18].

3. INFECTIONS

Central nervous system infections, such as bacterial and viral meningitis, encephalitis, neurosyphilis, brain abscesses, and tuberculosis, continue to be the most common cause of symptomatic epilepsy. These infections were the cause of 10% to 20% of the epilepsy cases that were documented in Africa [16]. In the tropics, where there are little medical facilities, especially in rural and suburban areas, CNS infections are the primary cause of acute seizures. There is scant evidence that local parasites frequently cause epilepsy despite the high incidence of parasitic diseases in Nigeria. Nevertheless, there are several studies from other parts of the world, particularly other developing nations, implicating parasites in the development of epilepsy [19]. In some regions of the world, cysticercosis is the most frequent cause of epilepsy because computed tomography (CT), which was developed in the 1970s and early 1980s, made it possible to diagnose it. The most prevalent manifestation of neuro cysticercosis is epilepsy, which frequently manifests as a single clinical symptom. As a result, prevalence estimates for idiopathic epilepsies in endemic locations cannot be trusted unless participants have undergone a CT scan. In contrast to her neighbors Cameroun and Togo, where cysticercosis was the leading cause of epilepsy cases, Nigeria has only seldom recorded occurrences of this infection [20,18]. It is through cardiac embolization of the brain that Trypanosoma Cruzi, the causative agent of Chaga's disease, and epilepsy are indirectly linked. Seizures are a possibility in the late stages of the African Trypanosoma infection, sleeping sickness, as well as perhaps as a follow-up in survivors [21]. One of the distinguishing features of cerebral malaria caused by Plasmodium falciparum is seizures. The most prevalent infection linked to febrile seizures in this region may be P. Vivax, the more prevalent cause of malaria in Latin America, however this is not confirmed [22].

4. TRAUMA

In Nigeria, two of the most frequent causes of epilepsy are trauma and hypoxia. Due to subpar obstetric care, these risks may act singly or in concert during pregnancy, or throughout life in instances of domestic violence, workplace violence, and auto accidents. Birth trauma can result in epilepsy after severe scalp molding and hypoxia, which then have a negative impact on the hippocampus and amygdala and induce incisura sclerosis. In Africa, it accounts for 1–2% of cases of symptomatic epilepsies [23]. The world's greatest rate of car accidents per million vehicle miles occurs in Nigeria and the East African nations, and as a result, post traumatic epilepsy is more prevalent. The occurrence of a seizure in the first week following a head injury suggests an increased likelihood of another seizure.

5. TUMORS

In Africa, 3–10% of symptomatic epilepsies are caused by cerebral tumors [24]. More occurrences of epilepsy owing to cerebral tumors are becoming visible with the introduction and installation of CT in various tertiary institutions in several African countries [18].

6. VASCULAR

Only 5% of patients with cerebral infarction have chronic seizures, which happen in 15% of individuals. Seizures can be caused by arteriovenous malformation, intracerebral hemorrhage, subdural hematoma, and inflammatory vasculitis (such as polyarteritis nodosa and lupus erythematosus) [25].

7. METABOLIC

Seizures may be caused by metabolic abnormalities, such as pyridoxine insufficiency, which is connected to elevated glutamic acid and decreased gamma aminobutyric acid (GABA) levels in the brain [26]. Alkalosis, water intoxication, hypoglycemia, hypocalcemia, hypomagnesemia, uraemia, and aminoaciduria are additional metabolic conditions that can cause epilepsy [27]. Rarely, an insulinoma that causes hypoglycemia may also cause epilepsy [28].

Table 1. Medicinal plants with anticonvulsant effect

S/N	Name of Plant	Family	Mechanism of Action	References
1	Abruss precatorius. Ethanolic extract in PTZ, MES, Picrotoxin	Fabaceae	GABAergic mechanisms, deteriorated autoregulation of glutamate release	[51]
2..	Acorus calamus Linn leaves, roots (rhizomes) Aqueous Extract	Acoraceae	Block NMDA receptors	[52]
3.	Afzelia Africana leaves. Aqueous extract in PTZ	Caesalpinioideceae		[53]
4.	Anacyclus pyrethrum roots Methanol, petroleum ether, hydro alcoholic extract	Asteraceae	Increase in GSH levels of brain, decreased MDA levels of brain, increased AChE and BChE activity in brain	[54,55]
5.	Angelica archangelica Linn. roots	Apiaceae	Block glutamatergic excitation	[56]
6.	Anisomeles malabarica	Lamiaceae	Decreased tonic hindlimb extension phase and extensor/flexion ratio in MES model	[57,58]
7.	Bunium persicum methanolic extract	Apiaceae	GABAergic mechanisms	[59,60]
8.	Centella asiatica. Leaves, methanol, hexane, chloroform, ethyl acetate, butanol	Apiaceae	Increased AChE activity, elevated levels of Ach	[61]
9.	Curcumin	Zingiberaceae	Increased brain norepinephrine level, reduced total nitrite levels of brain, reduced AChE activity	[62,63]
10.	Curcumol	Zingiberaceae	Facilitation of $GABA_A$ Rs by	[64, 65]

S/N	Name of Plant	Family	Mechanism of Action	References
	(from Rhizoma Curcumae)		curcumol in hippocampal neurons, facilitation of recombinant $GABA_A$ Rs, enhancement of phasic GABAergic inhibition by curcumol in hippocampal slices, enhancement of tonic GABAergic inhibition by curcumol in hippocampal slices	
11.	Cymbopogon winterianus Jowitt	Poaceae	GABAergic mechanisms, deteriorated autoregulation of glutamate release	[66, 67]
12.	Cyperus rotundus Linn.	Cyperaceae	Inhibit voltage-dependant Na+ channels, block glutamatergic excitation mediated by the NMDA receptor	[68, 69]
13.	Feretia apodanthera Del lyophilized aqueous extract	Rubiaceae	Decreased brain MDA levels, increased brain GSH levels, increase of AChE and BChE activity in brain	[70, 71]
14.	Ficus platyphylla methanol extract	Moracea	Affinity for undifferentiated glutamate receptors, affinity for the 3H-GABA binding assay, decrease the K+-stimulated glutamate release from rat hippocampal	[72]

S/N	Name of Plant	Family	Mechanism of Action	References
			slices	
15.	Harungana madagascariensis. Methanol extract in isoniazide induced siesure	Hypericaceae	GABAergic mechanisms	[73]
16.	Lavandula angustifolia	Lamiaceae	Modulate glutamate activation expression, reduction of the ACh-evoked release, direct interaction with the NMDA receptor complex	[74]
17.	Mentha spicata	Lamiaceae	GABAergic mechanisms	[75, 76]
18.	Nigella sativa	Ranunculaceae	Attenuate the increased NO levels resulting from pilocarpine, attenuate the decrease in hippocampal Na+, K+ ATPase activity, increase the AchE enzyme	[63, 77]
19.	Ocimum basilicum	Lamiaceae	Modulate glutamate activation expression, reduction of the ACh-evoked release, direct interaction with the NMDA receptor complex	[76]
20.	Origanum dictamnus	Rutaceae	GABAergic mechanisms	[78]
21.	Origanum vulgare	Rutaceae	GABAergic mechanisms	[79, 80]
22.	Panax ginseng root butanol extract	Araliaceae	T2 relaxation time in rat hippocampus, entorhinal cortex, piriform cortex,	[81, 82]

S/N	Name of Plant	Family	Mechanism of Action	References
			amygdala, thalamus	
23.	Pimpinella anisum	Apiaceae	Inhibited production of dark neurons, inhibited induction of long-term potentiation in hippocampal slices	[83, 84]
24.	Piper guineen. Seeds	Piperaceae	Activity against NMDA	[85]
25.	Psidium guajava (guava) leaves ethanolic extract	Myrtaceae	Selectively inhibit NMDA receptor	[86]
26.	Rosmarinus officinalis	Lamiaceae	Elevate GABA levels in the midbrain Region	[80, 87]
27.	Soy extract	legumiaceae	Phytoestrogens of soy affect seizure Severity	[88]
28.	Trachyspermum ammi (L.) methanol extract	Apiaceae	Excite GABA responses mainly by stimulating human GABAA receptors and increasing the chloride ion channel opening	[89, 90]
29.	Trichosanthes dioica Roxb fruits aqueous extract	Cucurbitaceae	Activity against generalized tonic-clonic and cortical focal seizures	[91, 2]
30.	Turmeric methanolic extract	Zingiberaceae	Higher lipophilicity and easily cross the blood–brain barrier, suppress oxidative DNA damage and lipid peroxidation	[92, 93]
31.	Valeriana officinalis root aqueous Extract	Caprifoliaceae	Existence of adenosine ligand(s) in the valerian aqueous extract and activation of	[94, 95]

S/N	Name of Plant	Family	Mechanism of Action	References
			A1 adenosine system, binding to GABA Receptors	
32.	Withania somnifera methanolic extract	Solanaceae	Ameliorated spatial memory deficit in Ymaze	[96]
33.	Zhumeria majdae essential oil and methanolic extract	Lamiaceae	Inhibit voltage-dependent Na+ channels, block glutamatergic excitation mediated by the NMDA receptor	[96, 78]
34.	Zingiber officinale (ginger) rhizomes hydroethanolic extract	Lamiaceae	Antioxidant activity, inhibit NO production, reduce inducible nitric oxide synthase	[97, 98]
35.	Zizyphus jujuba hydroalcoholic Extract	Rhamnaceae	Increase in brain GSH, decreased brain MDA levels, increased brain AChE and BChE activity	[99, 100]

8. PATHOPHYSIOLOGY OF EPILEPSY

An overly synchronized and prolonged discharge of a set of neurons is the cause of epileptic seizures. A continuous rise in neuronal excitability is the defining characteristic of all epileptic disorders. There are many different causes of abnormal cellular discharges, including trauma, oxygen deprivation, malignancies, infections, and metabolic disturbances. However, in roughly 50% of epilepsy patients, there are no definite causes established. Some types of epilepsy, such as those brought on by neuronal migratory abnormalities and monogenic epilepsies, have underlying causes and pathophysiological mechanisms that are (partially) characterized [29,30]. There is currently little information available about a number of other kinds of epilepsy. The main neuronal migratory problems that can have hereditary or intrauterine origins are those that lead to epilepsy [31]. Different types of agyria and pachygyria are caused by abnormal neuronal migration patterns, whereas neuronal heterotopia in the subcortical white matter is caused by milder levels of neuronal migration failure [32]. Studies have shown that the microgyric cortex has higher levels of postsynaptic glutamate receptors and lower levels of gamma-aminobutyric acid ($GABA_A$) receptors, which may encourage the development of epileptogenesis [33]. Epilepsy and abnormal neural migration are two features that are frequently observed in people with tuberous sclerosis, a developmental condition inherited in an autosomal dominant manner. An X-linked dominant disease of cerebral cortical development is called periventricular heterotopia. It is known that periventricular heterotopia is caused by mutations in the filamin 1 gene, which block the movement of cerebral cortical neurons [34,35]. Females with the condition exhibit seizures, whilst males with the condition experience embryonic death. However, a male patient who had bilateral periventricular and subcortical heterotopia was recently reported, raising the possibility of a new gene involved in brain development [36,37]. Another abnormality of neuronal migration is the double cortex syndrome and X-linked lissencephaly. In contrast to more severe lissencephaly, which is prevalent in affected males, double cortex or subcortical band heterotopia frequently affects females [38, 39]. Recently, a causative mutation in the doublecortin gene was found. It has been hypothesized that doublecortin serves as an essential intracellular signaling molecule for the migration of growing neurons [40].

9. ANTICONVULSANT DRUGS

Anticonvulsants in particular are used in pharmacological therapy to manage the majority of epileptic seizures. Anticonvulsant medications are used as the mainstay of treatment for seizures, despite the fact that there are several anticonvulsant therapeutic options for distinct seizure types and epileptic disorders [41]. The conventional anticonvulsants carbamazepine, valproic acid/valproate semisodium, phenytoin, and phenobarbital, as well as more recently gabapentin, oxcarbazepine, lamotrigine, or topiramate, can be used to treat newly diagnosed epilepsy patients who require treatment [2]. The intensity and frequency of the seizures, as well as the patient's age, general health, and medical history, all affect the recommended treatment. To select the most effective treatment, an accurate identification of the epilepsy type is necessary [42,43]. Traditional antiepileptic medications may inhibit sodium channels or enhance GABA activity. Various antiepileptic medications have a variety of possibly ambiguous methods of action [44]. Their targets include $GABA_A$ receptors, GABA transporter 1, GABA transaminase, and voltage-gated calcium channels in addition to voltage-gated sodium channels and parts of the GABA system [45]. Antiepileptic medications reduce the release of excitatory glutamate, which rises in epilepsy, as well as GABA, by blocking sodium or calcium channels [46]. Given that GABA can either directly or indirectly act pro convulsively, this may be a side effect of several antiepileptic medications or perhaps their real mode of action [47]. Due to the prolonged therapy given to patients with epileptic conditions, the majority of these anticonvulsants currently in use have unpredictable pharmacological actions and undesirable side effects, such as chronic toxicity and birth defects, and yet patients continue to experience health problems [48,49]. To treat epilepsy, which is a long-term procedure, it is vital to find novel medications with minimal or no adverse effects and predictable pharmacological action. These medications are also usually tapered off gradually over a period of around six months [50]. Biochemical and biological diversity are abundant in nature. Before any other contemporary therapeutic strategy was used to treat epilepsy, numerous phytochemicals from plants have been known about and used traditionally. In effect, the present interest in

traditional medicine has sped up the development and research of numerous treatments used by different ethnic groups worldwide. Table 1 summarizes the information on the types of extracts, as well as the mechanisms of action, techniques, and references pertaining to the plants that have been studied or reported to have anticonvulsant effects in animal models.

10. DISCUSSION

Epilepsy is the most common neurological disorder, after stroke affecting at least 50 million people globally [101,102]. Medicinal plants have a wider range of pharmacological effects on neurological disorders when compared to conventional synthetic antiepileptic drugs. According to ethnobotanical reports, several herbal medications have positive effects on those who are seizure prone [2,103]. One popular screening methodology for evaluating anticonvulsive drugs is the PTZ kindling model. It primarily affects the $GABA_A$ receptor's t-butyl-bicyclo-phosphorothionate/picrotoxin site. The preferred $GABA_A$ receptor chloride ionophore complex blocker is PTZ [2]. It affects numerous neurotransmitter systems, including the adenosinergic, GABAergic, and glutamatergic systems, causes convulsant effects following repeated or single intake. Significant changes in the levels of GSH, cysteine, glutathione disulfide, and protein thiols as well as protein disulfides and protein carbonyl were seen in the mouse cerebral cortex following PTZ-induced convulsions [104]. The efficacy of an anticonvulsant medicine against generalized tonic-clonic seizures is thought to be predicted by the MES seizure test, which induces tonic hind limb seizures through bilateral corneal or transauricular electrical stimulation. Some side effects from epilepsy medications are possible. The likelihood of adverse effects depends on the dosage, length of therapy, and type of medication used [48]. Higher medicine doses make side effects more likely to occur, but as the body gets used to the treatment, they usually lessen with time. Over 50% of all medications used in clinical settings globally are natural compounds and their derivatives [105]. When compared to conventional synthetic antiepileptic medicines, medicinal plants have a wider range of pharmacological effects and structural diversity.

11. CONCLUSION

From ethnobotanical reports, plant-based extracts are crucial to identifying chemical compounds for novel anticonvulsant therapy with minimal side effects and accessibility.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Chauvel P, McGonigal A. Emergence of semiology in epileptic seizures. Epilepsy & Behavior. 2014;38:94–103. Available:https://doi.org/https://doi.org/10.1016/j.yebeh.2013.12.003
2. Rabiei Z. Anticonvulsant effects of medicinal plants with emphasis on mechanisms of action. Asian Pacific Journal of Tropical Biomedicine. 2017; 7(2):166–172. Available:https://doi.org/https://doi.org/10.1016/j.apjtb.2016.11.028
3. Weinstein S. Seizures and epilepsy: An overview. Epilepsy: The Intersection of Neurosciences, Biology, Mathematics, Engineering, and Physics. 2016;65–77. Available: https://doi.org/10.1201/b10866-10
4. Suleiman M, Alade GO, Onu SO, Oladele AT. Ethnomedicinal survey and phytochemical screening of plants used to treat epilepsy by traditional healers in etche, Rivers State, Nigeria. Journal of Applied Sciences and Environmental Management. 2022;26(2):265–271. Available:https://doi.org/10.4314/jasem.v26i2.14
5. Owolabi LF, Owolabi SD, Taura AA, Alhaji ID, Ogunniyi A. Prevalence and burden of epilepsy in Nigeria: A systematic review and meta-analysis of community-based door-to-door surveys. Epilepsy & Behavior. 2019;92:226–234. Available:https://doi.org/https://doi.org/10.1016/j.yebeh.2018.12.017
6. Sinke MRT, Braun KPJ, Otte WM. White matter abnormalities at a regional and voxel level in focal and generalized epilepsy: A systematic review and meta-analysis. NeuroImage: Clinical. 2016;12:902–909. Available:https://doi.org/https://doi.org/10.1016/j.nicl.2016.10.025

7. Jiruska P, Csicsvari J, Powell AD, Fox JE, Chang WC, Vreugdenhil M, Li X, Palus M, Bujan AF, Dearden RW, Jefferys JGR. High-frequency network activity, global increase in neuronal activity, and synchrony expansion precede epileptic seizures in vitro. Journal of Neuroscience. 2010;30(16):5690–5701. Available:https://doi.org/10.1523/JNEUROSCI.0535-10.2010
8. Nawafleh S, Qaswal AB, Suleiman A, Alali O, Zayed FM, Al-Adwan MA, Bani Ali M. GABA receptors can depolarize the neuronal membrane potential via quantum tunneling of chloride ions: a quantum mathematical study. In Cells. 2022;11(7). Available:https://doi.org/10.3390/cells11071145
9. Greenfield LJ. Molecular mechanisms of antiseizure drug activity at GABAA receptors. Seizure. 2013;22(8):589–600. Available:https://doi.org/https://doi.org/10.1016/j.seizure.2013.04.015
10. Janković SM, Dješević M, Janković SV. Experimental GABA A receptor agonists and allosteric modulators for the treatment of focal epilepsy. Journal of Experimental Pharmacology. 2021;13: 235–244. Available:https://doi.org/10.2147/JEP.S242964
11. Akyuz E, Polat AK, Eroglu E, Kullu I, Angelopoulou E, Paudel YN. Revisiting the role of neurotransmitters in epilepsy: An updated review. Life Sciences. 2021;265: 118826. Available:https://doi.org/https://doi.org/10.1016/j.lfs.2020.118826
12. Alten B, Guzikowski NJ, Zurawski Z, Hamm HE, Kavalali ET. Presynaptic mechanisms underlying GABAB-receptor-mediated inhibition of spontaneous neurotransmitter release. Cell Reports. 2022;38(3):110255. Available:https://doi.org/https://doi.org/10.1016/j.celrep.2021.110255
13. Vasilev DS, Tumanova NL, Kim KK, Lavrentyeva VV, Lukomskaya NY, Zhuravin IA, Magazanik LG, Zaitsev AV. Transient morphological alterations in the hippocampus after pentylenetetrazole-induced seizures in rats. Neurochemical Research. 2018;43(8):1671–1682. Available: https://doi.org/10.1007/s11064-018-2583-y
14. Srivastava I, Vazquez-Juarez E, Lindskog M. Reducing glutamate uptake in rat hippocampal slices enhances astrocytic membrane depolarization while down-regulating CA3–CA1 synaptic response. Frontiers in Synaptic Neuroscience. 2020;12:1–11. Available:https://doi.org/10.3389/fnsyn.2020.00037
15. Sen A, Jette N, Husain M, Sander JW. Epilepsy in older people. The Lancet. 2020;395(10225):735–748. Available:https://doi.org/https://doi.org/10.1016/S0140-6736(19)33064-8
16. Olubunmi A. Epilepsy in Nigeria – A review of etiology, epidemiology and management. Benin Journal of Postgraduate Medicine. 2009;8(1). Available:https://doi.org/10.4314/bjpm.v8i1.47362
17. Laxer KD, Trinka E, Hirsch LJ, Cendes F, Langfitt J, Delanty N, Resnick T, Benbadis SR. The consequences of refractory epilepsy and its treatment. Epilepsy & Behavior. 2014;37:59–70. Available:https://doi.org/https://doi.org/10.1016/j.yebeh.2014.05.031
18. Ogunrin OA, Adeyekun A, Adudu P. Etiologies of epilepsy and health-seeking itinerary of patients with epilepsy in a resource poor setting: Analysis of 342 Nigerian Africans. Seizure. 2013;22(7):572–576. Available: https://doi.org/https://doi.org/10.1016/j.seizure.2013.04.012
19. Gourama H. Foodborne pathogens BT - food safety engineering (A. Demirci, H. Feng, & K. Krishnamurthy (eds.); Springer International Publishing. 2020;25–49. Available: https://doi.org/10.1007/978-3-030-42660-6_2
20. Siewe Fodjo JN, Remme JHF, Preux PM, Colebunders R. Meta-analysis of epilepsy prevalence in West Africa and its relationship with onchocerciasis endemicity and control. International Health. 2020;12(3):192–202. Available:https://doi.org/10.1093/inthealth/ihaa012
21. Kennedy PGE, Rodgers J. Clinical and neuropathogenetic aspects of human African trypanosomiasis. Frontiers in Immunology. 2019;10:1–11. Available:https://doi.org/10.3389/fimmu.2019.00039
22. Recht J, Siqueira AM, Monteiro WM, Herrera SM, Herrera S, Lacerda MVG. Malaria in Brazil, Colombia, Peru and

Venezuela: current challenges in malaria control and elimination. Malaria Journal. 2017;16(1):273.
Available: https://doi.org/10.1186/s12936-017-1925-6

23. Ba-Diop A, Marin B, Druet-Cabanac M, Ngoungou EB, Newton CR, Preux PM. Epidemiology, causes, and treatment of epilepsy in sub-Saharan Africa. The Lancet Neurology. 2014;13(10):1029–1044.
Available:https://doi.org/https://doi.org/10.1016/S1474-4422(14)70114-0
24. Balogun JA, Bankole OB, Okere O, Uche EO, Balogun FM, Shilong DJ, Jimoh AO, Adeolu AA. Epidemiology of brain tumors among adolescents and young adults in Nigeria. Journal of Clinical Neuroscience. 2022;96:50–55.
Available:https://doi.org/https://doi.org/10.1016/j.jocn.2021.12.019
25. Abdel Razek AAK, Alvarez H, Bagg S, Refaat S, Castillo M. Imaging spectrum of CNS vasculitis. Radiographics. 2014;34(4):873–894.
Available:https://doi.org/10.1148/rg.344135028
26. Wilson MP, Plecko B, Mills PB, Clayton PT. Disorders affecting vitamin B6 metabolism. Journal of Inherited Metabolic Disease. 2019;42(4):629–646.
Available:https://doi.org/10.1002/jimd.12060
27. Steinman B, Goilav B. Fluids and electrolytes BT - pediatric board study guide: a last minute review (O. I. Naga (ed.); Springer International Publishing. 2020;825–839.
Available: https://doi.org/10.1007/978-3-030-21267-4_24
28. Louda F, Chadli A, Elaziz S, Elghomari H, Farouqi A. Malignant insulinoma misdiagnosed and treated as epilepsy. Annales d'Endocrinologie. 2013;74(1):53–55.
Available: https://doi.org/https://doi.org/10.1016/j.ando.2012.11.002
29. Lesca G, M⊘ller RS, Rudolf G, Hirsch E, Hjalgrim H, Szepetowski P. Update on the genetics of the epilepsy-aphasia spectrum and role of GRIN2A mutations. Epileptic Disorders. 2019;21:S41–S47.
30. Engelborghs S, D'hooge R, De Deyn PP. Pathophysiology of epilepsy. Acta Neurologica Belgica. 2000;100(4):201–213.
31. Stouffer MA, Golden JA, Francis F. Neuronal migration disorders: focus on the cytoskeleton and epilepsy. Neurobiology of Disease. 2016;92:18–45.
32. Verrotti A, Spalice A, Ursitti F, Papetti L, Mariani R, Castronovo A, Mastrangelo M, Iannetti P. New trends in neuronal migration disorders. European Journal of Paediatric Neurology. 2010;14(1):1–12.
33. Sarnat HB, Flores-Sarnat L. Excitatory/inhibitory synaptic ratios in polymicrogyria and down syndrome help explain epileptogenesis in malformations. Pediatric Neurology. 2021;116:41–54.
34. Ferland RJ, Batiz LF, Neal J, Lian G, Bundock E, Lu J, Hsiao YC, Diamond R, Mei D, Banham AH. Disruption of neural progenitors along the ventricular and subventricular zones in periventricular heterotopia. Human Molecular Genetics. 2009;18(3):497–516.
35. Sarkisian MR, Bartley CM, Rakic P. Trouble making the first move: interpreting arrested neuronal migration in the cerebral cortex. Trends in Neurosciences. 2008;31(2):54–61.
36. Leventer RJ, Guerrini R, Dobyns WB. Malformations of cortical development and epilepsy. Dialogues in Clinical Neuroscience; 2022.
37. Meuwissen MEC, Mancini GMS. Neurological findings in incontinentia pigmenti; a review. European Journal of Medical Genetics. 2012;55(5):323–331.
38. D'Agostino MD, Bernasconi A, Das S, Bastos A, Valerio RM, Palmini A, Costa da Costa J, Scheffer IE, Berkovic S, Guerrini R. Subcortical band heterotopia (SBH) in males: clinical, imaging and genetic findings in comparison with females. Brain. 2002;125(11):2507–2522.
39. Liu JS. Molecular genetics of neuronal migration disorders. Current Neurology and Neuroscience Reports. 2011;11(2):171–178.
40. Wu Q, Liu J, Fang A, Li R, Bai Y, Kriegstein AR, Wang X. The dynamics of neuronal migration. Cellular and Molecular Control of Neuronal Migration. 2014;25–36.
41. Perucca E, Tomson T. The pharmacological treatment of epilepsy in adults. The Lancet Neurology. 2011;10(5):446–456.
Available:https://doi.org/https://doi.org/10.1016/S1474-4422(11)70047-3

42. NJ S, MSP S, ST G. EEG-based classification of normal and seizure types using relaxed local neighbour difference pattern and artificial neural network. Knowledge-Based Systems. 2022;249: 108508.
Available:https://doi.org/https://doi.org/10.1016/j.knosys.2022.108508
43. An S, Kang C, Lee HW. Artificial intelligence and computational approaches for epilepsy. Journal of Epilepsy Research. 2020;10(1):8–17.
Available:https://doi.org/10.14581/jer.20003
44. Kobayashi K, Endoh F, Ohmori I, Akiyama T. Action of antiepileptic drugs on neurons. Brain and Development. 2020;42(1):2–5.
Available:https://doi.org/https://doi.org/10.1016/j.braindev.2019.07.006
45. Rogawski MA, Löscher W, Rho JM. Mechanisms of action of Antiseizure Drugs and the Ketogenic diet. Cold Spring Harbor Perspectives in Medicine. 2016; 6(5):28.
Available:https://doi.org/10.1101/cshperspect.a022780
46. Lasoń W, Chlebicka M, Rejdak K. Research advances in basic mechanisms of seizures and antiepileptic drug action. Pharmacological Reports. 2013;65(4):787–801.
Available:https://doi.org/https://doi.org/10.1016/S1734-1140(13)71060-0
47. Wang Y, Chen Z. An update for epilepsy research and antiepileptic drug development: Toward precise circuit therapy. Pharmacology & Therapeutics. 2019;201:77–93.
Available:https://doi.org/https://doi.org/10.1016/j.pharmthera.2019.05.010
48. Perucca P, Gilliam FG. Adverse effects of antiepileptic drugs. The Lancet Neurology. 2012;11(9):792–802.
Available:https://doi.org/https://doi.org/10.1016/S1474-4422(12)70153-9
49. Charalambous M, Shivapour SK, Brodbelt DC, Volk HA. Antiepileptic drugs' tolerability and safety – a systematic review and meta-analysis of adverse effects in dogs. BMC Veterinary Research. 2016;12(1):79.
Available:https://doi.org/10.1186/s12917-016-0703-y
50. Vicens C, Bejarano F, Sempere E, Mateu C, Fiol F, Socias I, Aragonès E, Palop V, Beltran JL, Piñol JL, Lera G, Folch S, Mengual M, Basora J, Esteva M, Llobera J, Roca M, Gili M, Leiva A. Comparative efficacy of two interventions to discontinue long-term benzodiazepine use: cluster randomised controlled trial in primary care. British Journal of Psychiatry. 2014;204(6): 471–479.
Available:https://doi.org/DOI:10.1192/bjp.bp.113.134650
51. Amtul Z. Nature's medicines to treat epileptic seizures. Studies in Natural Products Chemistry. 2018;56:129–150.
52. Imam H, Riaz Z, Azhar M, Sofi G, Hussain A. Sweet flag (Acorus calamus Linn.): An incredible medicinal herb. International Journal of Green Pharmacy. 2013;7(4): 288–296.
Available:https://doi.org/10.4103/0973-8258.122053
53. Chipiti T, Viljoen AM, Cordero-Maldonado ML, Veale CGL, Van Heerden FR, Sandasi M, Chen W, Crawford AD, Enslin GM. Anti-seizure activity of African medicinal plants: The identification of bioactive alkaloids from the stem bark of Rauvolfia caffra using an in vivo zebrafish model. Journal of Ethnopharmacology. 2021;279:114282.
54. Manouze H, Bouchatta O, Bennis M, Sokar Z, Ba-M'hamed S. Anticonvulsive and neuroprotective effects of aqueous and methanolic extracts of Anacyclus pyrethrum root in kainic acid-induced-status epilepticus in mice. Epilepsy Research. 2019;158:106225.
Available:https://doi.org/https://doi.org/10.1016/j.eplepsyres.2019.106225
55. Pahuja M, Mehla J, Reeta KH, Joshi S, Gupta YK. Root extract of Anacyclus pyrethrum ameliorates seizures, seizure-induced oxidative stress and cognitive impairment in experimental animals. Epilepsy Research. 2012;98(2):157–165.
Available:https://doi.org/https://doi.org/10.1016/j.eplepsyres.2011.09.006
56. Khan AU, Akram M, Daniyal M, Akhter N, Riaz M, Akhtar N, Shariati MA, Anjum F, Khan SG, Parveen A, Ahmad S. Awareness and current knowledge of epilepsy. Metabolic Brain Disease. 2020;35(1):45–63.
Available:https://doi.org/10.1007/s11011-019-00494-1
57. Choudhary N, Bijjem KRV, Kalia AN. Antiepileptic potential of flavonoids fraction from the leaves of Anisomeles malabarica. Journal of Ethnopharmacology. 2011; 135(2):238–242.

Available:https://doi.org/https://doi.org/10.1016/j.jep.2011.02.019

58. Ramalingam R, Nath AR, Madhavi BB, Nagulu M, Balasubramaniam A. Free radical scavenging and antiepileptic activity of Leucas lanata. Journal of Pharmacy Research. 2013;6(3):368–372. Available:https://doi.org/https://doi.org/10.1016/j.jopr.2013.03.011
59. Mandegary A, Arab-Nozari M, Ramiar H, Sharififar F. Anticonvulsant activity of the essential oil and methanolic extract of Bunium persicum (Boiss). B. Fedtsch. Journal of Ethnopharmacology. 2012;140(2):447–451. Available:https://doi.org/https://doi.org/10.1016/j.jep.2012.01.024
60. Bansal S, Sharma K, Gautam V, Lone AA, Malhotra EV, Kumar S, Singh R. A comprehensive review of bunium persicum: a valuable medicinal spice. Food Reviews International. 2021;1–20. Available:https://doi.org/10.1080/87559129.2021.1929305
61. Visweswari G, Prasad KS, Chetan PS, Lokanatha V, Rajendra W. Evaluation of the anticonvulsant effect of Centella asiatica (gotu kola) in pentylenetetrazol-induced seizures with respect to cholinergic neurotransmission. Epilepsy & Behavior. 2010;17(3):332–335. Available:https://doi.org/https://doi.org/10.1016/j.yebeh.2010.01.002
62. Kaur H, Bal A, Sandhir R. Curcumin supplementation improves mitochondrial and behavioral deficits in experimental model of chronic epilepsy. Pharmacology Biochemistry and Behavior. 2014;125:55–64. Available:https://doi.org/https://doi.org/10.1016/j.pbb.2014.08.001
63. Noor NA, Aboul Ezz HS, Faraag AR, Khadrawy YA. Evaluation of the antiepileptic effect of curcumin and Nigella sativa oil in the pilocarpine model of epilepsy in comparison with valproate. Epilepsy & Behavior. 2012;24(2):199–206. Available:https://doi.org/https://doi.org/10.1016/j.yebeh.2012.03.026
64. Hashem S, Nisar S, Sageena G, Macha MA, Yadav SK, Krishnankutty R, Uddin S, Haris M, Bhat AA. Therapeutic effects of curcumol in several diseases; an overview. Nutrition and Cancer. 2021;73(2):181–195. Available:https://doi.org/10.1080/01635581.2020.1749676
65. Ding J, Wang JJ, Huang C, Wang L, Deng S, Xu TL, Ge WH, Li WG, Li F. Curcumol from Rhizoma Curcumae suppresses epileptic seizure by facilitation of GABA(A) receptors. Neuropharmacology. 2014;81:244–255. Available:https://doi.org/https://doi.org/10.1016/j.neuropharm.2014.02.009
66. Haerussana ANEM, Chairunnisa HF. Essential oil constituents and pharmacognostic evaluation of java citronella (*Cymbopogon winterianus*) stem from Bandung, West Java, Indonesia. Open Access Macedonian Journal of Medical Sciences. 2022;10(A):1338–1346. Available:https://doi.org/10.3889/oamjms.2022.9546
67. Quintans-Júnior LJ, Souza TT, Leite BS, Lessa NMN, Bonjardim LR, Santos MRV, Alves PB, Blank AF, Antoniolli AR. Phythochemical screening and anticonvulsant activity of Cymbopogon winterianus Jowitt (Poaceae) leaf essential oil in rodents. Phytomedicine. 2008;15(8):619–624 Available:https://doi.org/https://doi.org/10.1016/j.phymed.2007.09.018
68. Peerzada AM, Ali HH, Naeem M, Latif M, Bukhari AH, Tanveer A. Cyperus rotundus L.: Traditional uses, phytochemistry, and pharmacological activities. Journal of Ethnopharmacology. 2015;174:540–560. Available:https://doi.org/https://doi.org/10.1016/j.jep.2015.08.012
69. Al-Snafi PDAE. A review on Cyperus rotundus A potential medicinal plant. IOSR Journal of Pharmacy (IOSRPHR). 2016;06(07):32–48. Available:https://doi.org/10.9790/3013-06723248
70. Taiwe GS, Moto FCO, Ayissi ERM, Ngoupaye GT, Njapdounke JSK, Nkantchoua GCN, Kouemou N, Omam JPO, Kandeda AK, Pale S, Pahaye D, Ngo Bum E. Effects of a lyophilized aqueous extract of Feretia apodanthera Del. (Rubiaceae) on pentylenetetrazole-induced kindling, oxidative stress, and cognitive impairment in mice. Epilepsy & Behavior. 2015;43:100–108. Available:https://doi.org/https://doi.org/10.1016/j.yebeh.2014.11.022
71. Hassanzadeh M, Sharifi N, Mahernia S, Rahimi N, Dehpour AR, Amanlou M. Effects of onopordia, a novel isolated compound from Onopordon acanthium, on pentylenetetrazole-induced seizures in

mice: Possible involvement of nitric oxide pathway. Journal of Traditional and Complementary Medicine. 2021;11(1):22–26.
Available:https://doi.org/https://doi.org/10.1016/j.jtcme.2019.11.005

72. Chindo BA, Schröder H, Becker A. Methanol extract of Ficus platyphylla ameliorates seizure severity, cognitive deficit and neuronal cell loss in pentylenetetrazole-kindled mice. Phytomedicine. 2015;22(1):86–93.
Available:https://doi.org/https://doi.org/10.1016/j.phymed.2014.10.005
73. Obiora U, Ibeabuchi A, Keneolisa F, Raymond O, Samuel N. Anticonvulsant activity of methanol extract of harungana madagascariensis leaf on mice model of isoniazid-induced siezure. 2022;24(8): 34–41.
Available:https://doi.org/10.9734/JAMPS/2022/v24i8572
74. Patil SM, Al-Mutairi KA, Firdose N, Ramu R, Martiz RM, Ashwini P. Pharmacoinformatics based screening discovers swertianolin from Lavandula angustifolia as a novel neuromodulator targeting epilepsy, depression, and anxiety. South African Journal of Botany. 2022;149:712–730.
75. Mahboubi M. Mentha spicata L. essential oil, phytochemistry and its effectiveness in flatulence. Journal of Traditional and Complementary Medicine. 2021;11(2):75–81.
Available:https://doi.org/https://doi.org/10.1016/j.jtcme.2017.08.011
76. Koutroumanidou E, Kimbaris A, Kortsaris A, Bezirtzoglou E, Polissiou M, Charalabopoulos K, Pagonopoulou O. Increased seizure latency and decreased severity of pentylenetetrazol-induced seizures in mice after essential oil administration. Epilepsy Research and Treatment. 2013;1–6.
Available:https://doi.org/10.1155/2013/532657
77. Aboul Ezz HS, Khadrawy YA, Noor NA. The neuroprotective effect of curcumin and nigella sativa oil against oxidative stress in the pilocarpine model of epilepsy: a comparison with valproate. Neurochemical Research. 2011;36(11):2195–2204.
Available:https://doi.org/10.1007/s11064-011-0544-9
78. da Fonsêca DV, da Silva Maia Bezerra Filho C, Lima TC, de Almeida RN, de Sousa DP. Anticonvulsant essential oils and their relationship with oxidative stress in epilepsy. In Biomolecules. 2019;9(12).
Available:https://doi.org/10.3390/biom9120835
79. Martins N, Barros L, Santos-Buelga C, Henriques M, Silva S, Ferreira ICFR. Decoction, infusion and hydroalcoholic extract of Origanum vulgare L.: Different performances regarding bioactivity and phenolic compounds. Food Chemistry. 2014;158:73–80.
Available:https://doi.org/https://doi.org/10.1016/j.foodchem.2014.02.099
80. Bahr TA, Rodriguez D, Beaumont C, Allred K. The effects of various essential oils on epilepsy and acute seizure: a systematic review. Evidence-Based Complementary and Alternative Medicine. 2019;6216745.
Available:https://doi.org/10.1155/2019/6216745
81. Suleymanova E, Gulyaev M, Chepurnova N. Ginseng extract attenuates early MRI changes after status epilepticus and decreases subsequent reduction of hippocampal volume in the rat brain. Epilepsy Research. 2014;108(2):223–231.
Available:https://doi.org/https://doi.org/10.1016/j.eplepsyres.2013.11.018
82. Mohd Sairazi NS, Sirajudeen KNS, Asari MA, Muzaimi M, Mummedy S, Sulaiman SA. Kainic acid-induced excitotoxicity experimental model: protective merits of natural products and plant extracts. Evidence-Based Complementary and Alternative Medicine. 2015;972623.
Available:https://doi.org/10.1155/2015/972623
83. Shojaii A, Abdollahi Fard M. Review of pharmacological properties and chemical constituents of pimpinella anisum . ISRN Pharmaceutics. 2012;1–8.
Available:https://doi.org/10.5402/2012/510795
84. Karimzadeh F, Hosseini M, Mangeng D, Alavi H, Hassanzadeh GR, Bayat M, Jafarian M, Kazemi H, Gorji A. Anticonvulsant and neuroprotective effects of Pimpinella anisum in rat brain. BMC Complementary and Alternative Medicine. 2012;12(1):76.
Available:https://doi.org/10.1186/1472-6882-12-76
85. PF Guine R, J Goncalves F. Chemistry and health effects of bioactive compounds in selected culinary aromatic herbs.

Current Nutrition & Food Science. 2015; 11(2):145–164.

86. Nurhussen DHA. Antimicrobial activity of psidium guajava leaves extract against staphylococcus aureus using pure extracts. World Journal of Pharmaceutical Research. 2017;6(9):14–47. Available:https://doi.org/10.20959/wjpr20179-8210
87. Capatina L, Boiangiu RS, Dumitru G, Napoli EM, Ruberto G, Hritcu L, Todirascu-Ciornea E. Rosmarinus officinalis essential oil improves scopolamine-induced neurobehavioral changes via restoration of cholinergic function and brain antioxidant status in Zebrafish (Danio rerio). In Antioxidants. 2020;9(1). Available:https://doi.org/10.3390/antiox9010062
88. Goudarzi R, Zamanian G, Partoazar A, Dehpour A. Novel effect of Arthrocen (avocado/soy unsaponifiables) on pentylenetetrazole-induced seizure threshold in mice: Role of GABAergic pathway. Epilepsy & Behavior. 2020; 104:106500. Available:https://doi.org/https://doi.org/10.1016/j.yebeh.2019.106500
89. Khan S, Shameem I, Sahibole S, Siddiqui A. Trachyspermum ammi: ancient unani medicine for modern cure, a review of potential therapeutic applications. World Journal of Pharmaceutical Research. 2016;5(12):169–178. Available:https://doi.org/10.20959/wjpr201612-6875
90. Asif HM, Sultana S, Akhtar N. A panoramic view on phytochemical, nutritional, ethanobotanical uses and pharmacological values of Trachyspermum ammi Linn. Asian Pacific Journal of Tropical Biomedicine. 2014;4:S545–S553. Available:https://doi.org/https://doi.org/10.12980/APJTB.4.2014APJTB-2014-0242
91. Arora R, Gill NS. Phytochemical screening and antioxidant activity of trichosanthes dioica roxb. seeds. Plant Archives. 2020;20:2084–2088.
92. Orellana-Paucar AM, Serruys ASK, Afrikanova T, Maes J, De Borggraeve W, Alen J, León-Tamariz F, Wilches-Arizábala IM, Crawford AD, de Witte PAM, Esguerra CV. Anticonvulsant activity of bisabolene sesquiterpenoids of *Curcuma longa* in zebrafish and mouse seizure models. Epilepsy & Behavior. 2012;24(1): 14–22. Available:https://doi.org/https://doi.org/10.1016/j.yebeh.2012.02.020
93. Dixit P. Medicinal properties of Garlic: a review. Anusandhaan - Vigyaan Shodh Patrika. 2018;6(1). Available:https://doi.org/10.22445/avsp.v6i1.13914
94. Nouri MHK, Abad ANA. Gabaergic system role in aqueous extract of Valeriana officinalis L. root on PTZ-induced clonic seizure threshold in mice. African Journal of Pharmacy and Pharmacology. 2011;5(9):1212–1217. Available:https://doi.org/10.5897/AJPP11.241
95. Rezvani ME, Roohbakhsh A, Allahtavakoli M, Shamsizadeh A. Anticonvulsant effect of aqueous extract of *Valeriana officinalis* in amygdala-kindled rats: Possible involvement of adenosine. Journal of Ethnopharmacology. 2010;127(2):313–318. Available:https://doi.org/https://doi.org/10.1016/j.jep.2009.11.002
96. Khattak ZF, Ansari B, Jamal M, Awan AA, Sherkheli MA, ul Haq R. Anticonvulsant activity of methanolic extract of Withania cogulans in mice. Metabolic Brain Disease. 2021;36(8):2437–2443. Available:https://doi.org/10.1007/s11011-021-00850-0
97. Hosseini A, Mirazi N. Acute administration of ginger (*Zingiber officinale* rhizomes) extract on timed intravenous pentylenetetrazol infusion seizure model in mice. Epilepsy Research. 2014;108(3): 411–419. Available:https://doi.org/https://doi.org/10.1016/j.eplepsyres.2014.01.008
98. Gawel K, Kukula-Koch W, Banono NS, Nieoczym D, Targowska-Duda KM, Czernicka L, Parada-Turska J, Esguerra CV. 6-Gingerol, a major constituent of *Zingiber officinale* rhizoma, exerts anticonvulsant activity in the pentylenetetrazole-induced seizure model in larval zebrafish. In International Journal of Molecular Sciences. 2021; 22(14). Available:https://doi.org/10.3390/ijms22147745
99. Al-humaidhi AM, Abd AH, Ghazi HF. Hydro-alcoholic Extract of *Ziziphus spina christi* mice attenuates pentylenetetrazole-induced kindling in male. Systematic Reviews in Pharmacy. 2021;12(2):314–317.

100. Pahuja M, Mehla J, Reeta KH, Joshi S, Gupta YK. Hydroalcoholic extract of *Zizyphus jujuba* ameliorates seizures, oxidative stress, and cognitive impairment in experimental models of epilepsy in rats. Epilepsy & Behavior. 2011;21(4):356–363. Available:https://doi.org/https://doi.org/10.1016/j.yebeh.2011.05.013
101. Feigin VL, Abajobir AA, Abate KH, Abd-Allah F, Abdulle AM, Abera SF, Abyu GY, Ahmed MB, Aichour AN, Aichour I, Aichour MTE, Akinyemi RO, Alabed S, Al-Raddadi R, Alvis-Guzman N, Amare AT, Ansari H, Anwari P, Ärnlöv J, Vos T. Global, regional, and national burden of neurological disorders during 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. The Lancet Neurology. 2017;16(11):877–897. Available:https://doi.org/https://doi.org/10.1016/S1474-4422(17)30299-5
102. Siuly S, Zhang Y. Medical big data: neurological diseases diagnosis through medical data analysis. Data Science and Engineering. 2016;1(2):54–64.
103. Devinsky O, Marsh E, Friedman D, Thiele E, Laux L, Sullivan J, Miller I, Flamini R, Wilfong A, Filloux F. Cannabidiol in patients with treatment-resistant epilepsy: an open-label interventional trial. The Lancet Neurology. 2016;15(3):270–278.
104. Pieróg M, Socała K, Wyska E, Poleszak E, Wlaź P. Effect of ellagic acid on seizure threshold in two acute seizure tests in mice. Molecules. 2021;26(16):4841.
105. Thomford NE, Senthebane DA, Rowe A, Munro D, Seele P, Maroyi A, Dzobo K. Natural products for drug discovery in the 21st century: innovations for novel drug discovery. International Journal of Molecular Sciences. 2018;19(6):1578.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/94753