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EVOLUTION OF ANTICONVULSANT DRUGS: BIRD'S EYE VIEW

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ABSTRACT: This review covers the research on the anticonvulsant properties of marketed drugs with their side effects and adverse drug reactions and the importance of medicinal plants and homeopathic medications in the treatment of epilepsy with the mechanism of actions with fewer side effects in comparison to allopathic medications that cause side effects which may be dangerous in some situations so to overcome these problem Ayurveda and homeopathy plays a major role. The new advancement in the management and cure of epilepsy with the help of several newly discovered compounds that are more advanced than the marketed drugs which are under clinical trials and have fewer side-effects than existing drugs and in coming years these compounds will be part of epileptic drugs. Development of the animal epilepsy model with the help of AI techniques to reduce the failure of the model, AI is a useful tool in drug discovery and can evaluate vast data easily and is a time-consuming technique.

INTRODUCTION:

Retrospective and Prospective Status of Epilepsy: The world scenario "Health for all" is an internationally accepted goal [1]. The impact of the rapidly transforming world is so complex that every phenomenon is entangled with the other and is impacted by its surroundings and social determinants [2]. Anticonvulsant agents are medications that show their effect on epileptic patients by preventing seizures in a particular dosage form and do not considerably affect the level of cognition. This review focuses on the effect of anticonvulsive agents on epilepsy and medicinal properties and clinical use of first, second, and third-generation antiepileptic drugs.

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The first-generation antiepileptic drugs include carbamazepine, ethosuximide, phenobarbital, phenytoin, valproate, and primidone [3]. The most commonly used second-generation antiepileptic drugs are lamotrigine, levetiracetam, vigabatrin, gabapentin, and tiagabine and the third-generation most common antiepileptic drugs are ganaxolone, lacosamide, brivaracetam, retigabine and safinamide. Anticonvulsant medications have been used to treat pain since the 1960s, just a few years after they revolutionized the treatment of epilepsy.

An Overview of Epilepsy: Throughout the Middle Ages, epilepsy was thought to be a possession by demonic spirits [4]. The simultaneous impairment of the Tri-doshic manifestation, which results in a variety of signs and symptoms, is described as the "sacred disease" of epilepsy in the Ayurvedic text. Atreya in charak Samhita Sutra (6th century B.C.), defines epilepsy as: "Paroxysmal loss of consciousness due to disturbance of memory and understanding of mind attended with convulsive

seizures" [5]. The Father of modern epileptology John Hughlings Jackson (1835-1911), for his clinical observation [6].

Any age can experience epilepsy, and anti-epileptic drugs taken consistently can successfully treat 70% of newly diagnosed cases [7]. Ranging from 4-10 people out of a thousand population have active epilepsy [8]. Since the dawn of medicine, epilepsy has been known to affect individuals of all ages, and genders [9]. About 70 million individuals worldwide suffer from epilepsy [10].

The terms seizure and epilepsy refer to related clinical conditions; epilepsy describes recurrent seizures. According to the clinical symptoms of episodes and the EEG pattern, seizures are categorized as follows: Prodrome: It is categorized by minor changes in mood, behavior, or thinking, Aura: It is the initial stage of the seizure, Ictus: It refers to the seizure episode, Postictal stage: It is an event occurs shortly after the seizure, Interictal period: It relates to the duration between episodes of seizure [11].

Social Issues of Epilepsy: A patient with epilepsy has to suffer from higher physical morbidity rates, social withdrawal, seizure-related accidents, depression, increased helplessness, poorer sexual relationships, antiepileptic drug side effects, and anxiety. Patients with an understanding of family, friends, and neighbors are less prone to loneliness, anxiety, and other problems that occur in epileptic patients as they are engaged in social activities and positive surrounding plays a major role in reducing the side effects of drugs. Many authors stated that the familial environment plays a significant role in an epileptic patient's life and has an impact on both its severity and condition, this could have a detrimental effect on the family and its functioning.

Authors including William Shakespeare, Charles Dickens, and Edgar Allen Poe have all discussed epileptic seizures [12]. Due to misunderstanding and misinformation about the real nature of this chronic condition persons with epilepsy have historically faced prejudice, stigmatization, social exclusion, and even imprisonment [13].

Rate of Epilepsy: According to WHO a large amount of the global illness burden is accounted for by epilepsy, which affects around 50 million individuals globally. Between 4 to 10 per 1000 persons are thought to be affected by epilepsy at any given moment (ongoing seizures or having treatment). Each year an estimated 5 million people receive an epilepsy diagnosis worldwide. Epilepsy is thought to be diagnosed in 49 out of every 100,000 persons annually in high-income nations. This number can go as high as 139 per 100,000 in low- and middle-income nations.

According to the World Health Organization (WHO) Fact Sheet dated June 20, 2019, 0.6% of all diseases worldwide are caused by epilepsy [14].

Causes of Epilepsy: Epilepsy cannot be spread. Though various underlying diseases can cause epilepsy, in roughly 50% of cases throughout the world the disease's origin is still unknown. The causes of epilepsy may include structural, genetic, infectious, metabolic, immunological, and unknown causes. Due to serious head injuries; congenital abnormalities or genetic diseases with related brain malformation; birth trauma or lack of oxygen; brain damage from prenatal or perinatal causes a stroke in which the flow of oxygen to the brain is restricted; certain genetic syndromes and brain tumor may be a reason which may lead to epilepsy, stated by WHO (World Health Organisation).

People who have been diagnosed with epilepsy are 24 times more likely to die suddenly than those who do not [15]. Epileptogenesis is induced by inflammatory neuroimmune reaction [16].

Types of Seizures:

Generalised Seizures: A generalized tonic-clonic seizure, also referred to as a grand mal seizure, is characterized by a tonic phase and clonic muscular contractions. They are the seizure forms that are most feared by patients, relatives, and bystanders. Usually, they are accompanied by diminished awareness or total loss of consciousness. Motor and non-motor (absence) seizures are further classified as generalized onset seizures. The most typical type of motor seizure in epilepsy patients is a generalized tonic-clonic seizure. Bilateral cortical, subcortical, and brainstem networks are rapidly affected by generalized tonic-clonic seizures, which start within the brain. Most generalized tonic-clonic seizures have genetic epilepsy as their underlying

cause, which was formerly classified as idiopathic. In addition to genetic generalized epilepsy, structural, viral, metabolic, or immune-related diseases can cause tonic-clonic seizures as a complication of epilepsy. Acute symptomatic seizures can manifest as tonic-clonic seizures without the inherent tendency to reoccur, whereas epileptic seizures reoccur without primate provocating factors. Acute symptomatic seizures can be caused by ischemic or hemorrhagic strokes, extra-axial hemorrhage, traumatic brain injury, hypoxic-ischemic injury, acute medical illness, metabolic derangements, or substance abuse. Alcohol and narcotics, head injuries, and epilepsy are common factors in emergency room visits following seizures [17].

Myoclonic Absence Seizure: According to the National Institute of Health, myoclonic absences are defined as typical absences with abrupt start and offset that are connected to spike and wave discharge on the EEG and have specific characteristics. Clinical absence is characterized by axial hypertonia (the individual typically leans forward and elevates their shoulders and arms somewhat), jerks, and spike and wave discharges. In addition to the characteristic spike and wave discharge, axial hypertonia and rhythmic jerks may be neurophysiologic ally recorded on electromyogram and in EEG the diagnosis may go unnoticed in the absence of sufficient polygraph or film seizure. Myoclonic absence must be separated from absences that accompany other types of prominent perioral myoclonia.

Continuous Seizures: Continuous seizures cause erratic muscle moments all over the body. Status epilepticus is one of the types of continuous seizures in which the body temperature rises and muscles become fatigued. Although the body will attempt to make up for this by pumping chemicals into the blood to keep going, this only works temporarily. Status epilepticus continues for a longer period of time and affects the body system by slowing down the heart (bradycardia) and may also cause a systole due to chemical changes in the blood which occurs due to seizures and also leads to damage of muscles and soft tissues.

Focal Seizures: When a nerve cell in a specific area of the brain is affected, a focal seizure occurs. The part of the brain that is damaged determines how the patient behaves during a focal seizure. The left half of the body is managed by the right side of the brain and the left side of the body will be affected by a seizure involving the right side of the brain. The right side of the body will be affected by seizures involving the left side of the brain. Sometimes a patient is partially conscious of what is happening and aware of his or her surroundings during a focal seizure. Focal seizure leads to jerking or shaking of arms or legs on one side of the body, and movement of the eye or neck to either the left side or right side. Sometimes patients don't know about what is happening in their surroundings; they are involved in those activities that do not exist as they try to touch the objects in the air that do not exist [18].

Focal Epilepticus Seizures: It is a neurological emergency that needs to be treated right away in order to avoid serious morbidity and fatality. In the past few years, it was defined as a seizure that lasted for 30 minutes or longer and was considered to be in focal status epilepticus, as a string of seizures during which the patient's mental condition did not return to normal. Chronic conditions such as alcohol withdrawal, CNS tumors, and distant CNS disease (such as traumatic brain injury, and stroke), as well as pre-existing epilepsy with breakthrough seizures or non-compliance with anti-epileptic medications, may cause status epilepticus [19].

Over the past 20 years, tremendous progress has been made in our understanding of the epidemiology of epilepsy in Asia, but the psychosocial, cultural, economic, organizational, and political aspects still have an impact on the etiology and treatment of epilepsy [20]. There are many different types of seizures, varying degrees of severity, and a large variety of concomitant illnesses, making epilepsy a spectrum disorder [21].

When numerous synchronous low-threshold excitatory impulses occur at once, allowing for their temporal summation in the post-synaptic neurons, a hyper-excitable state can also ensue. Local changes in membrane potential caused by net positive inward ion fluxes lead to the action potential, which happens in an all-or-none manner. Normal hyperpolarization and an area of

surrounding inhibition produced by inhibitory neurons stop the spread of bursting activity. Repeated discharge cause:

- An increase in extracellular K+ tends to depolarise nearby neurons by blunting the degrees of hyperpolarizing outward K+ currents.
- Pre-synaptic terminals that have accumulated Ca++ release neurotransmitters more readily and.
- The excitatory amino acid receptor's NMDA subtype is activated by depolarization, increasing Ca++ influx and neuronal activity [22].

Visual seizures may be mistaken for migraine aura during seizures [23]. Even the presence of epilepsy may have an impact on endocrine control centers [24]. The third most frequent neurological disability in the world is epilepsy [25]. Epilepsies are different illnesses with a variety of etiologies and pathophysiologies [26].

Therapeutic Itenerary: With the invention of bromides (1856), phenobarbital (1912), and phenytoin (1938), the modern era of pharmacotherapy most likely began [27]. One of the first antiepileptic medications, phenobarbital, was created by Alfred Hauptmann (1881-1948). Phenytoin was developed by Tracy Putnam (1894-1955) and H. Houston Merritt (1902-1979), and it quickly became the standard treatment for status epilepticus, tonic-clonic seizure, and partial seizure [28].

For patients with newly diagnosed epilepsy, the first five years of treatment are important. Anti-epileptic drugs work by selectively altering the excitability of neurons to limit seizure-related firing without interfering with nonpileptic activity a variety of molecular targets [29]. Some patients also be surgical candidates. Epilepsy surgery has demonstrated excellent short-term outcomes [30]. The pathology could have been resettable based on the conventional MRI [31]. Most individuals still have intellectual impairment despite seizure control [32]. All seizures should be unstoppable by the perfect anticonvulsant drugs, without any negative side effects, Unfortunately, some patients who are treated with currently available anticonvulsant drugs not only experience uncontrollable seizure activity but also regularly experience side effects that can range in severity from mild CNS impairment to fatal a plastic anaemia or liver failure.

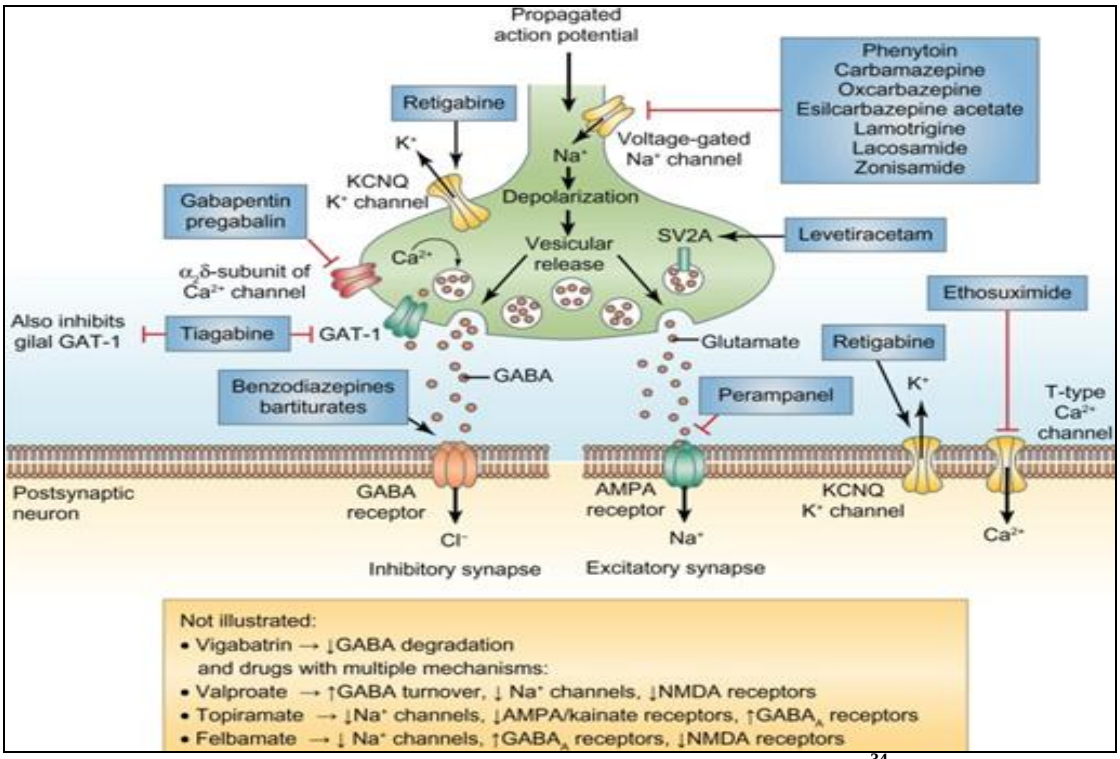


FIG. 1: MECHANISM OF ANTI-EPILEPTIC DRUGS [34]

The anticonvulsant drugs or drug combinations that best control seizure with a tolerable level of adverse effects must be selected by the treating doctors or practitioners. It is generally acknowledged that up to 50% of patients can obtain up to total seizure control, and another 25% experience significant improvement. Patients with newly diagnosed epilepsy had a higher success rate with therapy, and the kind of seizure, family history, and degree of disability.

The possibility of a seizure reoccurrence is the repercussions of ongoing seizures, and the positive and negative effects of the drug in avoiding a reoccurrence can all be taken into consideration when deciding whether to start anti-epileptic drug treatment. Depending on the seizure type or syndrome, there may be a range in the relative likelihood of reoccurrence. Patients who have congenital neurological abnormalities or epileptic form discharges on an EEG are at a significant risk (up to 90%) of reoccurrence. Additionally, patients with brain abnormalities, prior symptomatic seizures, and Todd's paralysis (a momentary, transitory paralysis following a seizure) have a higher reoccurrence risk [33].

Hyperexcitability of neurons and hypersynchrony of neuronal circuits are the two defining characteristics of seizure genesis. Antiepileptic medications may primarily function through one of three ways:

1. Lessing cell membrane's electrical excitability.
2. Increasing synaptic inhibition caused by GABA-mediated synaptic inhibition.

Algorithm for choice of antiepileptic drug (AED) among new-onset epilepsy patients as per Indian Guidelines on Epilepsy [35].

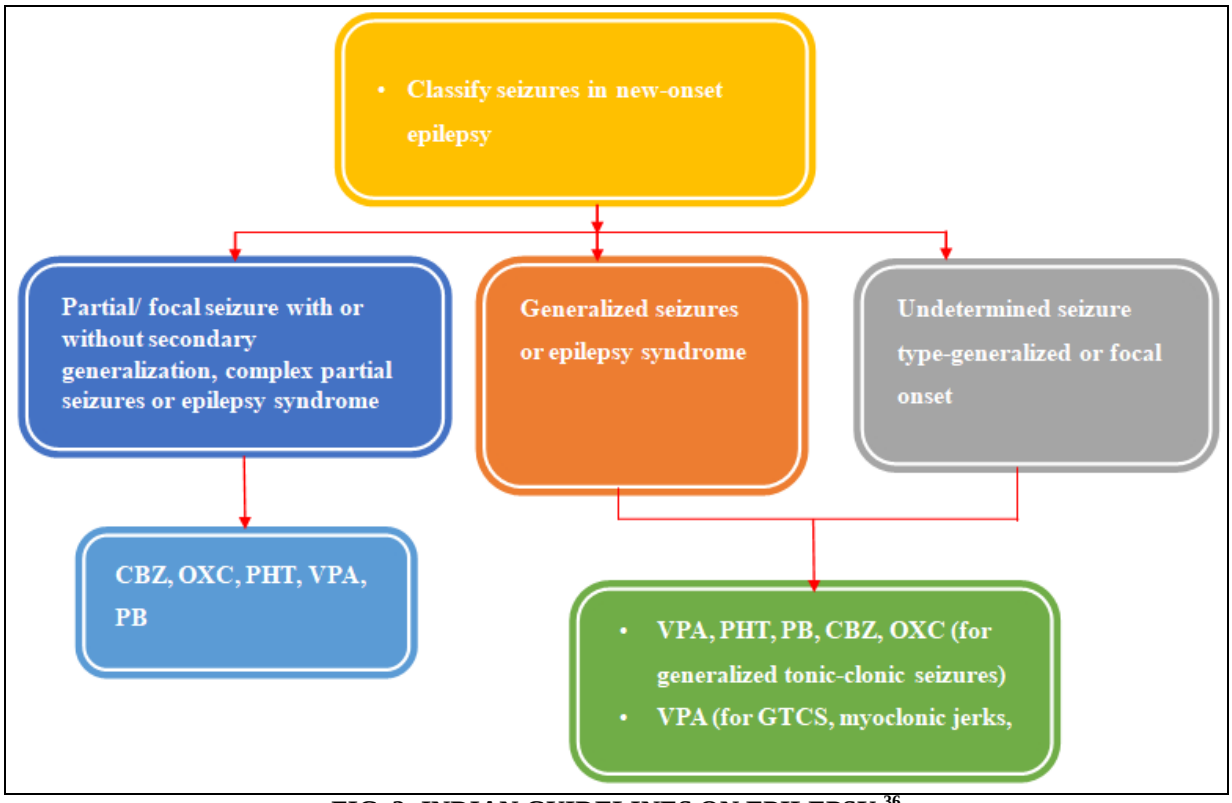


FIG. 2: INDIAN GUIDELINES ON EPILEPSY [36]

Observational Study on Epilepsy [37]: In seven neurology centers across India, this cross-sectional single-visit, multicentre observational study was carried out between April 2019 and January 2020. Investigators or qualified designees obtained patient data from participant interviews and medical records for the six months prior to enrolment and entered it into individual case reports forms (CRFs). The good clinical practice (GCP) guidelines of the International Conference on Harmonization (ICH), Indian regulatory norms, and the Declaration of Helsinki were all followed

during the study's execution. The Independent Ethics Committees or Institutional review boards have given their approval to the study protocol and all pertinent papers. Traditional and Natural Remedies for Cure of Epilepsy Nature is a rich source of biologically active and chemically diverse therapeutic entities. The complicated structures of natural products cannot be figured out easily by chemical synthesis. Medicinal plants play an important role in treating neurological diseases such as Alzheimer's disease, brain ischemia, reperfusion, and other degenerative diseases [38].

TABLE 1: ANTIEPILEPTIC MEDICINAL PLANTS OR COMPOUNDS OF PLANT ORIGIN [38]

S. no.	Compounds	Mechanism of action	Reference
1	*Withania somnifera* methanolic extract	Ameliorated spatial memory deficit in Y-maze	39
2	*Trichosanthes dioica* Roxb fruits aqueous extract	Activity against generalized tonic-clonic and cortical focal seizures	40
4	*Feretia apodanthera* lyophilized aqueous extract	Decreased brain MDA levels, increased brain GSH levels, an increase of AChE and BChE activity in the brain	41
5	*Nigella sativa* oil	Potent antioxidant actions	42
6	*Psidium guajava* (guava) leaves ethanolic extract	Selectively inhibit NMDA receptor	43
7	*Trachyspermum ammi* (L.) methanol extract	Excite GABA responses mainly by stimulating human GABAA receptors and increasing the chloride ion channel opening	44
8	*Zingiber officinale* (ginger) rhizomes hydroethanolic extract	Antioxidant activity, inhibits NO production, reduces inducible nitric oxide synthase	45

This table illustrates about the medicinal plants that are effective against epilepsy and their mechanism of action against epilepsy. Here few medicinal plants are mentioned but this era of plants is very vast they have several medicinal properties against epilepsy and various other diseases, and the above-mentioned plants are active against several pathways that are involved in causing seizures.

Homeopathic System of Medication: In homeopathy, Samuel Hahnemann (1755-1843) is credited as its creator. The "dynamization" concept and the "similia" principles are the two main tenets on which homeopathy is built, the first rule states that natural ingredients are made through a series of dilutions and succussions that are used in treatment and the second principle states that a chemical that disrupted the biological system at greater doses can be used at low doses to treat diseases.[46]

TABLE 2: DRUGS USED IN THE HOMEOPATHIC SYSTEM OF MEDICATION [47]

S. no.	Drugs	Conditions Where These Are Used
1	Belladonna	Convulsions in infants
2	Stramonium	Violent convulsions involving every muscle
3	Hyoscyamus	Infants' convulsions
4	Ignatia	Convulsions from fear and fright
5	Nux Vomica	Infantile convulsions from indigestion or bad temper
6	Oenanthe	Involuntary stool during convulsions
7	Lysin	Spasms and convulsions
8	Cicuta	Sudden rigidity followed by jerks and violent distortions
9	Cuprum Metallicum	Tonic and clonic spasms, convulsions, and epileptic attack
10	Silicea	epileptic attack after emotionally stressful events, or have nocturnal (night) epileptic attacks

Artificial Intelligence Techniques and Drug Design: Artificial intelligence (AI) tools could be used to optimize the time-consuming, expensive, and high-failure task of drug development. Drug discovery necessitates the examination of intricate biological systems, which in modern times involves analyzing a vast amount of data from various sources, such as genomics, metabolomic, and proteomic profiles as well as biomedical data from wearable devices. By employing AI as a helpful tactic, researchers have taken advantage of data problems in drug development to approach the issue differently. A sophisticated computational strategy for advancing scientific knowledge could be characterized as AI. AI could be a useful tool in the drug discovery process since it can evaluate

vast volumes of data, disclose hidden molecular features, and stimulate various drug candidates. One of the most common AI approaches in healthcare is Machine Learning (ML). ML uses statistical approaches to construct a model capable of generalizing concepts based on a training dataset, a process that is possible if the model learns knowledge that can subsequently be applied to new data that it has not seen before. The model's performance is evaluated using performance metrics, which enable it to select the most efficient model, resulting in a methodological advantage by offering up different alternatives and probabilities are valuable across the drug development process, including drug discovery, clinical trial design, pharmaceutical product development and management, quality control, and assurance.

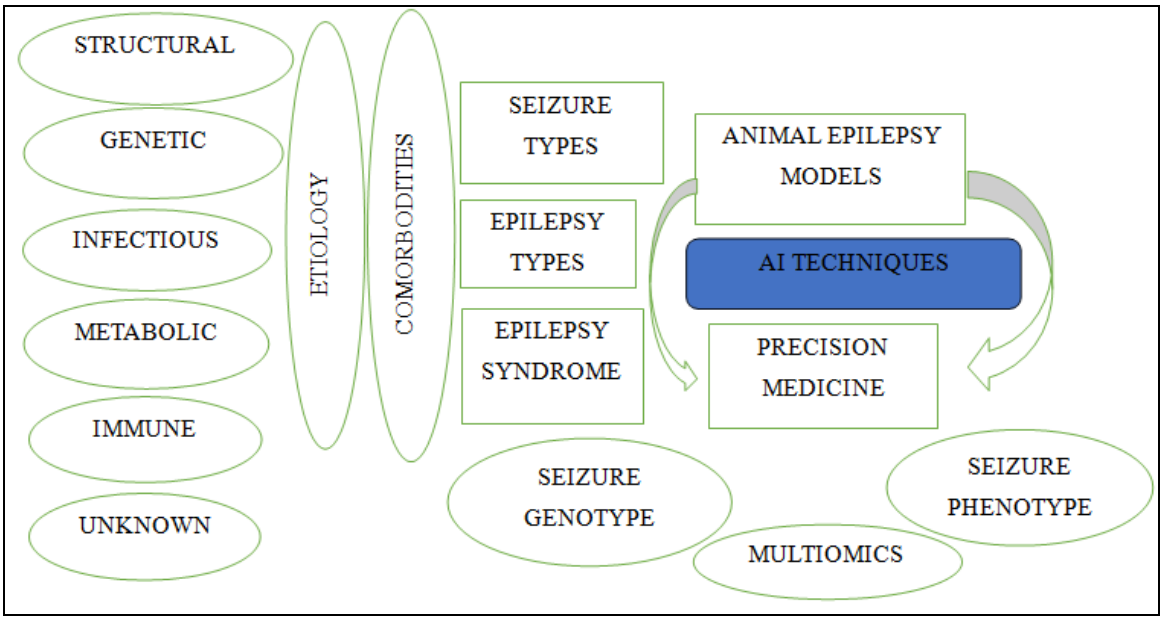


FIG. 3: SCHEFFER *ET AL* INFORMED IN THE ABOVE-DRAWN FIGURE ABOUT AED (ANTI-EPILEPTIC DRUGS) ICAAI APPROACHES. KINDLING MODELS, SCPTZ, AND MES [48]

Recent Advances in Anticonvulsant Drugs: The biggest impediment to Anti-epileptic drug development is our incomplete knowledge of the mechanisms of AED resistance, which prevents mechanism-driven drug development. Epileptic disorders have heterogeneous pathophysiological mechanisms, coupled with the almost certain multi-factorial nature of resistance, making it improbable that a single drug could eradicate refractory epilepsy. Since the discovery of phenytoin in 1938, the development of new AEDs has relied on testing in animals. Animal models based on electrically or chemically induced seizures in rodents have been crucial for discovering all the new AEDs since phenytoin [49, 50]. The effectiveness of a drug in the maximal electroshock model is thought to predict the efficacy of a compound against generalized tonic-clonic seizures, whereas protection against metrazole-induced seizures and against spontaneous seizures in genetic epilepsy models [51, 52]. Research on the mechanisms of seizure generation and propagation has identified new targets for potential AEDs. Currently, available AEDs inhibit excessive neuronal firingby blocking voltage-gated sodium channels. The serendipitous discovery of the AEDs has been a characteristic feature of antiepileptic drug discovery. Conventional use of the established models leads to a range of similar-acting drugs. Newer models are required to bring out the diversity of the anticonvulsant potential of the drugs.

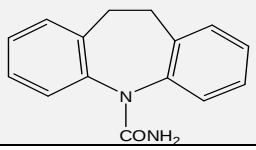
Recent Progress on New Anti-epileptic Drugs: The author Belete, Tafere Mulaw, explained about the "recent progress in the development of New Antiepileptic Drugs with novel target'' which is illustrated according to their mechanism of action and clinical trial phases of compound , the first compound is Fenfluramine which is a serotonin releaser and activate 5-HDT, 5-HT2A and 5-HT2C receptors and is in phase 3 of clinical trial, Ganaxolone directly activates and allosterically modulates GABAA receptor at GABAA receptor containing a subunit (phase2), ICA-

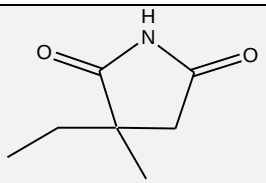
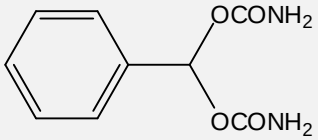
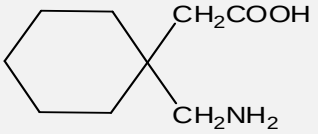
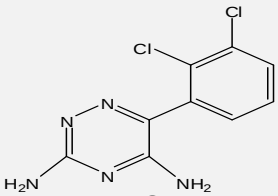
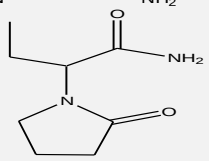
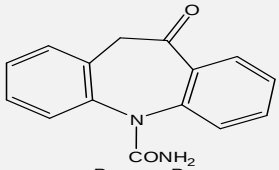
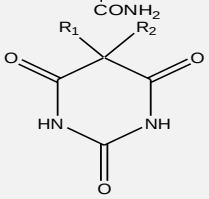
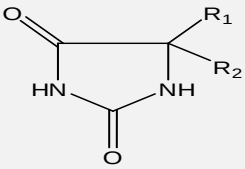
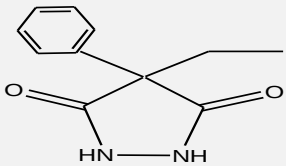
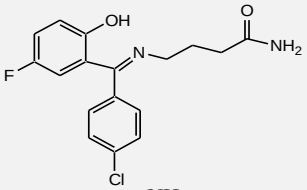
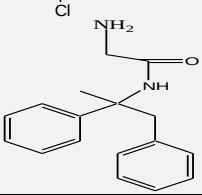
105665(PF04895162) is aselective KCNQ2/Q3 channel activator (phase2), compound VX-765 is a Selectable and reversible inhibitor of interleukin converting enzyme which is in a clinical phase 2, Cenobamate (TAK-935) is a voltage gated sodium channels, a positive allosteric modulator of GABAA receptor (phase 2), Tonabersat is a Selective neuronal gap junction inhibitor (phase 1), NAX 810-2 is a selective Gal-R2 agonist, Soticlestat (TAK-935) is a Cholesterol 24-hydroxylase inhibitor (1b/2a phase), XEN1101KCNQ/Kv7 is a potassium channel opener (phase 2), Talampanel is a non-competitive AMPA receptor antagonist (phase 2), Safinamide is a sodium channel blocker and MAO-B inhibitor (phase 3), Seletracetam and Levetiracetam analogue with increased potency synaptic vesicle protein 2A; presynaptic calcium channels inhibition (phase2) [53]. Most of the presently used AEDs were discovered by screening without a rationale as to the mechanism of action [54]. Antiepileptic drugs (AEDs) are the mainstay for the treatment of epilepsy, and although their number has expanded exponentially, current principles governing drug therapy are in many ways similar to those established a century ago [55]. AED choice is determined by seizure type, adverse-effect profile, and patient-specific features, including age, sex, and co-morbidities [56]. The patient received phenobarbital for treatment of super refractory status epilepticus in the year 2015 to 2020 and the patient received successful treatment [57].

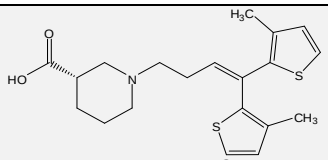
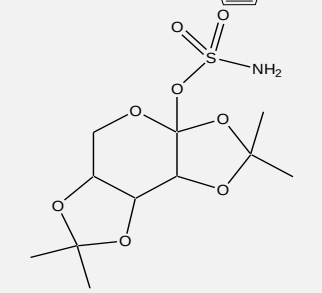
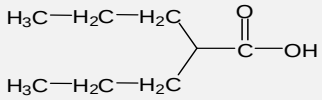
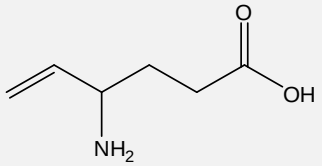
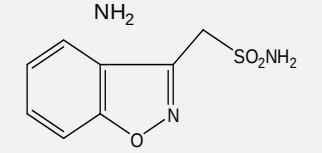
TABLE 3: CURRENT DEVELOPMENTAL STATUS OF NEW DRUGS FOR THE TREATMENT OF EPILEPSY. SOURCE [58]

S. no.	Name of intervention	Sponsor	Therapeutic target	Condition	Clinical development phase
1	Muscimol	National Institute of Neurological Disorders and Stroke (NINDS)	GABAA receptor	Epilepsy	Phase 1
2	Bumetanide	–	NKCC1 inhibition	Neonatal seizures	Phase 1
3	BGG492 (Selurampanel)	Novartis Pharmaceuticals	AMPA/kainite receptor antagonism	Refractory partial seizures	Phase 2
4	Ganaxolone	Marinus Pharmaceuticals	Positive allosteric modulator of GABAA receptors	Uncontrolled partial epilepsy; catamenial epilepsy	Phase 2
5	Buspirone	NINDS	5-HT1A receptor partial agonist	Localized epilepsy	Phase 2
6	YKP3089	SK Life Sciences	Sodium channel modulation, ↑ GABA release	Resistant partial onset seizures	Phase 2
7	PRX-00023	NINDS	5-HT receptors	TLE; partial epilepsy	Phase 2
8	GWP42003-P (Cannabidiol)	GW Research Ltd. INSYS Therapeutics Inc.	–	Dravet syndrome Lennox Gastaut syndrome Myoclonic epilepsy	Phase 2 Phase 3
9	Verapamil	Beverly S. Wical, Gillette Children's Specialty Healthcare	Calcium channel modulation	Dravet syndrome	Phase 2

TABLE 4: MECHANISMS OF ACTIONS OF ANTI-EPILEPTIC AGENTS [59]

Anti-epileptic agent	Chemical Structure	Mechanism(s) of action
Benzodiazepines		Enhances GABA action, Reduces sustained repetitive firing
Carbamazepine		Blocks voltage-dependent Na+ channels, Limitation of sustained repetitive firing

Ethosuximide		Reducing T-type Ca++ currents, Blocking synchronized thalamic firing
Felbamate		Inhibition of glutamatergic neurotransmission (reduces NMDA action, blocks glycine-site on, NMDA receptor), GABA potentiation, Blocks voltage-dependent Na+ channels, Blocks L-type Ca++ channels
Gabapentin		GABA analog but does not bind to GABA receptors, increases synaptic GABA: activation of Glutamic Acid Decarboxylase, may block amino acid transporter, Binds to voltage-dependent Ca++ channels / E reduced intra neuronal-- concentration of Ca++, Possibly: inactivation of Na+ channels
Lamotrigine		Reduces glutamate release, Inhibits voltage-activated Ca++ currents, blocks voltage-dependent Na+ channels
Levetiracetam		Unknown mechanism of action increases seizure threshold and inhibits seizure spread in kindled rats
Oxcarbazepine		Inhibition of voltage-dependent Na+ channels Inhibition of voltage-activated Ca++ currents
Phenobarbital		Enhances GABA action, reduces sustained repetitive firing, Reduces voltage-dependent Ca++ currents
Phenytoin		Blocks voltage-gated Na+ channels, Reduces Ca++ currents
Primidone		Reduces sustained repetitive firing - blocks voltage-dependent Na+ currents
Progabide		GABA agonist at A and B sites
Remacemide		NMDA receptor antagonist, Inactivation of Na+ channels

Tiagabine		Neuronal and glial GABA-uptake inhibitor
Topiramate		Na+ channel block, Reduction of L-type Ca++ currents Potentiation of GABA at the GABA(A) receptor: enhancement of Cl- flux, Inhibition of glutamatergic neurotransmission: weak block of AMPA/kainite receptors, Inhibition of carbonic anhydrase, Increases CNS GABA levels by increased synthesis and reduced catabolism
Valproate		Blocks T-type Ca++ currents, Enhances Na+ channel inactivation
Vigabatrin		GABA-Transaminase inhibitor, Inhibits GABA uptake
Zonisamide		Blocks Na+ channels Blocks T-type Ca++ channels, Enhance GABA action, Inhibition of carbonic anhydrase

CONCLUSION: The current review updated knowledge of currently available AEDs and offers insight into novel chemical entities that have demonstrated antiepileptic action. Antiepileptic pharmaceuticals are a crucial component of both general neurology and the care of epileptic patients.

They include both well-known classics and recently created medications. With the exception of a small percentage of individuals who are thought to have intractable epilepsy, epilepsy is typically treatable with these medications, in contrast to several other neurologic illnesses. Additionally, these medications are crucial in the management of numerous other neurologic and psychiatric problems. Some medicinal plants play a vital role in treating neurologic diseases with no adverse effects.

This schematic article also discussed recent developments on the time-consuming, expensive, and high-failure test of drug development could be optimized with the help of artificial intelligence, examining complex biological systems calls for the development of new drugs, which in the current day requires the analysis of a large quantity of data from many sources. Researchers have made use of data issues in drug development to address the problem differently by using AI as a helpful strategy.

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