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Review Article

Nanotechnology Based Drug Delivery Systems for Antiepileptic Drugs: Advances, Challenges, and Future Perspectives

Khaznah Mohammed Alrashed[1], Reham Taresh Ghazwani[1], Manar Ali Alharbi[1], Shatha Mohammed Alshammari[1], Nawal Mezel Alshammari[1], Ashfaq Ahmad[2,*]

[1]Pharm. D. Program, College of Pharmacy, University of Hafr Al Batin, Hafr Al Batin, SAUDI ARABIA.
[2]Department of Pharmacy Practice, College of Pharmacy, University of Hafr Al Batin, Hafr Al Batin, SAUDI ARABIA.

ABSTRACT

Epilepsy is one of the most debilitating neurological diseases in the world. Epilepsy is defined by an imbalance between inhibitory and excitatory neurotransmission in the brain. The epilepsy pathognomic feature is aberrant central nervous system electrical activity causing all types of seizures. It is logical that bilateral cerebral hemispheres are involved in generalized seizures and a unilateral involvement is responsible for partial seizures. Although these medications might improve the mood, associated neuropsychiatric disorders, improve the seizures epileptogenic discharges and improve both behavior and cognition, they can worsen some coexistent neuropsychological disorders or cause de novo cognitive or behavioral disorders. Antiepileptic Drugs (AEDs) face several challenges from development by pharmaceutical companies to clinical use by patients. Traditional AED treatment routes often fail to achieve effective brain concentrations without incurring systemic side effects. Nanocarrier platforms such as liposomes, polymeric nanoparticles, nanoemulsions, solid lipid nanoparticles, and magnetic nanoparticles are being explored to enhance CNS delivery and reduce off-target risk. Nanotechnology based delivery systems offer attractive strategies to overcome this limitation. This review discusses the various technologies used to prepare these nanoformulations and evaluates their potential applications in drug delivery.

Keywords: Antiepileptic drugs, Drug interactions, Epilepsy, Nanoformulation, Nanotechnology.

Correspondence:
Dr. Ashfaq Ahmad
Department of Pharmacy Practice, College of Pharmacy, University of Hafr Al Batin, Hafr Al Batin-39524, SAUDI ARABIA.
Email: ashfaqa@uhb.edu.sa

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INTRODUCTION

Epilepsy is a chronic neurological disorder that affects more than 50 million people worldwide, with an estimated five million new cases diagnosed year. Low-income nations have a substantially greater incidence than wealthier areas. Epilepsy is one of the most debilitating neurological diseases in the world. Epilepsy is defined by an imbalance between inhibitory and excitatory neurotransmission in the brain (Jenrow and Elisevich, 2019). Gamma Amino Butyric Acid (GABA), the primary inhibitory neurotransmitter, is often less effective (Gulias-Cañizo *et al.*, 2021), whereas excitatory neurotransmitters such as glutamate and aspartate increase. The N-Methyl-D-Aspartate (NMDA) receptors to be activated by the excitatory chemicals increasing not only sodium influx and neuronal hyperexcitability but also excessive synchronized neurone activation and seizures.

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Figure 1 shows key mechanisms contributing to epileptogenesis, including ion channel disorders, GABA inhibitory and glutamate excitatory neurotransmission, compromised Blood-Brain Barrier (BBB) integrity, inflammation, and neuronal networks seizure spread as the main collective mechanisms of neuronal hyperexcitability and repeated seizures (Figure was redrawn by using the concept in the literature by using GPT-5.6 Luna).

The epilepsy pathognomic feature is aberrant central nervous system electrical activity causing all types of seizures. It is logical that bilateral cerebral hemispheres are involved in generalized seizures and a unilateral involvement is responsible for partial seizures. Localized foci can be detected by Functional Magnetic Resonance Imaging (fMRI) and Electroencephalogram (EEG). The Antiepileptic Medications (AEDs) should be administered into the brain in adequate amounts to reduce frequency and intensity of fits with the least possible side effects if any (Jabir *et al.*, 2015). Although these medications might improve the mood, associated neuropsychiatric disorders, improve the seizures epileptogenic discharges & improve both behavior and cognition, they can worsen some coexistent neuropsychological disorders or cause de novo cognitive or behavioral disorders. These adverse

drug events are related to new drugs, polypharmacy, high doses with high serum levels (Witt and Helmstaedter, 2017).

The neuropsychological side effect profiles of the various antiepileptic medications might differ in both qualitative (i.e., the profile and number of affected domains) and quantitative (the amount of affection ways whereas the previously described effects are more general) (Table 1). AEDs most commonly impact the cognitive domain of executive processes and attention (Witt and Helmstaedter, 2017) as shown in Table 1. Language, memory, and other higher brain functions can also deteriorate due to drug use, but it's crucial to keep in mind these impairments typically coexist with are mediated by executive function impairments (e.g. a seemingly verbal comprehension deficit as the consequences of a reduced working memory capacity. Thus, the main and therapeutically important concern is how to get over these negative cognitive consequences of AEDs.

Table 1 showed that the new AEDs have more positive effect on cognitive function than older agents like topiramate, which has been related to negative cognitive and behavioral outcomes (Table 2).

Challenges of Antiepileptic Drugs

Antiepileptic Drugs (AEDs) face several challenges from development by pharmaceutical companies to clinical use by patients.

Challenges in Drug Development and Accessibility

High Attrition Rates and Safety Failures

The development of new AEDs is both expensive and dangerous. Even after completing Phase 1a clinical trials, the chances of successful development and regulatory approval are fewer than 10% (Lalonde *et al.*, 2007). Despite enormous investment, numerous AEDs have failed to meet safety and efficacy standards, forcing withdrawal from the market due to high toxicity. Drugs that have been removed include phethenylate for hepatic necrosis, benzchlor-propamide for long-term animal toxicity, and aminoglutethimide for a high risk of goiter (Pryles *et al.*, 1952).

Post-Marketing Restrictions and Toxicity

Certain medications may still have substantial side effects after approval, limiting their therapeutic utility. For example, felbamate's use is severely limited because post-marketing surveillance revealed that it is associated with hepatic failure and aplastic anemia. Similarly, the possibility of permanent visual field impairments limits the use of vigabatrin (Pennell *et al.*, 1995; Wallace, 2001).

Economic Barriers to Access

Aside from safety concerns, the high cost of newly developed AEDs creates a significant barrier to treatment adherence. Many patients, especially in developing nations, cannot afford these newer medications due to the requirement for lifetime therapy, which results in a substantial gap in global health equality (Wahab, 2010).

Neuropsychiatric Side Effects of Antiepileptic Drugs (AEDs)

Antiepileptic Medications (AEDs) primarily alter neuronal function in the brain, which is why the majority of their adverse effects occur in the central nervous system. Sedation, lethargy, dizziness, decreased coordination (such as ataxia, dysarthria, and diplopia), tremors, cognitive deficits, mood abnormalities, behavioral changes, and sexual dysfunctions such as diminished libido and impotence are all common side effects (Perucca, 2011). The common adverse AED events include some Psychiatric and Behavioral Side Effects (PBSEs) that may be either negligible or so grave up to severe depression and suicide attempts that makes the quality of his life worse more than the seizures themselves (Cavanna *et al.*, 2010; Mula and Monaco, 2009; Weintraub *et al.*, 2007).

Risk Factors

A person's or their family's history of psychiatric problems enhances the likelihood of having neuropsychiatric side effects, implying a genetic risk (Weintraub *et al.*, 2007). Younger individuals tend to have more behavioral issues, whereas teenagers frequently have mood-related symptoms (Guilfoyle *et al.*, 2018). Other key concerns include utilising excessive doses of AEDs, increasing doses too quickly, taking numerous drugs at the same time, and taking medications known to be risky, such as levetiracetam, zonisamide, phenobarbital, topiramate, vigabatrin, and perampanel (French *et al.*, 2004). If a patient has previously experienced psychiatric side effects with a similar medicine, they are more likely to have them again (Chen *et al.*, 2018). Long term use of medicines such as carbamazepine, phenobarbital, or phenytoin might cause folate insufficiency, increasing the risk of mood disorders (Fröscher *et al.*, 1995).

Negative Neuropsychiatric Effects

Some patients may experience symptoms like irritability, anger, depression, anxiety, hyperactivity, apathy, social withdrawal, impulsivity, and rarely, psychosis. These symptoms are difficult to detect since they match those of prevalent psychiatric diseases. Specific drugs have been linked to specific symptoms: for example, levetiracetam can cause agitation and mood swings (Chen *et al.*, 2017; Weintraub *et al.*, 2007); topiramate can cause difficulty finding words and slow thinking (Eddy *et al.*, 2011); and valproate can worsen behavior at high doses or when hyperactivity is present. Barbiturates and benzodiazepines frequently produce drowsiness and cognitive impairment (Perucca and Gilliam, 2012). Vigabatrin, zonisamide, and perampanel are all associated with an increased risk of behavioral disorders (Chen *et al.*, 2017).

Topiramate and other older sedatives are particularly prone to cognitive and sedative adverse effects. The risk increases with cumulative drug exposure and when multiple sodium channel blockers are administered concurrently (Perucca, 2011).

Positive Psychotropic Effects

In fact, some AEDs can help individuals with mental illnesses feel happier or experience less anxiety. For example, lamotrigine can aid with depression, lessen aggression, and regulate mood, particularly in individuals taking levetiracetam (Mula *et al.*, 2003). Bipolar disorder and epilepsy can both be effectively treated with valproate and carbamazepine. Gabapentin and pregabalin may lessen generalized and social anxiety.

Cognitive Impairment

Over 3/4 of epileptic patients suffer from cognitive disorders such as deficient execution skills, memory, and attention either due to the direct effects of seizures and Interictal Epileptiform Discharges (IEDs) on the brain in addition to the adverse drug events of treatment (Novak *et al.*, 2022). The cognitive burden is a corelated to polytherapy and high treatment doses especially of the old drugs (Quon *et al.*, 2020).

Montreal Cognitive Assessment (MoCA), Mini Mental State Examination (MMSE) are used for screening, preferring the MoCA. Electroencephalography (EEG) /quantitative EEG and resting state functional Magnetic Resonance Imaging (fMRI) identify the network-level malfunction of cognitive impairment (Höller *et al.*, 2020; Montaño-Lozada *et al.*, 2021).

Management Strategies for Neuropsychiatric Adverse Effects of AEDs

As the treatment of the side effects of Antiepileptic Drugs (AEDs) is not always easy or straightforward, it requires combined approaches starting with proper selection, avoiding multiple drugs and avoiding polytherapy with carefully adjusted dose. A wise approach is to start with the lowest possible effective dose and gradually increase to get a better drug tolerance. Cognitive training and or supportive medications may be considered together with using the AEDs with education and regular assessment relying on both subjective and objective tools for early detection of any cognitive issues, particularly after changes in therapy. Folate level monitoring with phenytoin, phenobarbital, or carbamazepine can reduce the mood-related complications. The target should not be only seizure control but also improving the quality of life.

Factors Related to Pharmaceutical Formulation

Like most drugs, formulation-related factors impact not only the clinical outcomes but also the psychiatric and social well-being of patients. The half-life and plasma concentrations depend on whether immediate-release or extended-release. Switching between brand and generic drugs intentionally or accidentally causes changes in the drug bioavailability, provoking breakthrough seizures and or augmented side effects, anxiety and decreasing compliance to treatment. Interestingly, the palatability, excipients, drug form, size and or taste influence patient comfort, morale and adherence especially in vulnerable frail individuals with pre-existing mood disorders. This is why, paying attention to the drug formulation ensures not only the therapeutic efficacy but also the positive psychological impact on the patient.

The role of nanotechnology in optimising AED delivery

Epilepsy affects tens of millions globally and is characterized by unprovoked, recurrent seizures. While AEDs remain the standard treatment, their effectiveness is often constrained by biological and pharmacological barriers, such as the blood-brain barrier and systemic toxicity. Innovations in nanotechnology propose novel delivery systems that may surmount these limitations by improving drug stability and enabling targeted CNS delivery (Bennewitz and Saltzman, 2009).

Challenges in AED Delivery and Role of Nanotechnology

Traditional AED treatment routes often fail to achieve effective brain concentrations without incurring systemic side effects. Nanocarrier platforms such as liposomes, polymeric nanoparticles, nanoemulsions, solid lipid nanoparticles, and magnetic nanoparticles are being explored to enhance CNS delivery and reduce off-target risk (Jabir *et al.*, 2015). Moreover, pharmaco-resistant epilepsy, affecting many patients, is often linked to limited AED penetration across the BBB. Nanotechnology based delivery systems offer attractive strategies to overcome this limitation (Rosillo-de la *et al.*, 2014).

Potential of Nanotechnology in Reducing Neuropsychiatric Side Effects (targeted brain delivery, sustained release, and dose-sparing effects)

Treatment of patients with neurological or neuropsychiatric illness demonstrate many challenges from penetration of the drug through Blood Brain Barrier (BBB), bioavailability, efficacy and side effects. Current approach of nanoformulations and nanotechnology have helped to overcome these issues which provides targeted drug delivery by crossing BBB and reduction of side effects profile (Patra *et al.*, 2018). Penetration of the drugs into the brain faces a major problem of poor water solubility (Achar *et al.*, 2021). Benzodiazepine are one of the drugs used in epilepsy being lipophilic faces the problem of poor water solubility and heavily dependent on organic solvents, surfactant and cosolvent for solubility. Newly FDA approved benzodiazepines, Nayzilam and Voltaco, heavily rely on organic solvent which resulted in the irritation in the nasal lining (Cloyd *et al.*, 2021). Nanoformulation helped in delivery of target drug by encapsulating these

Table 1: Cognitive and Behavioral Effects of Selected Antiepileptic Drugs (AEDs).

Drug	Attention/ Executive	Memory	Language	Behavior / Mood
Lamotrigine	+ / 0	0	0	+
Lacosamide	0	0	0	0
Rufinamide	0	0	0	0
Oxcarbazepine	0 / +	0	0	+
Eslicarbazepine acetate	-	0	0	0
Levetiracetam	0	0	0	-
Pregabalin	0	-	0	+ / -
Gabapentin	0 / -	-	0	+ / -
Valproic acid	-	-	0	+
Tiagabine	0	-	0	-
Ethosuximide	-	0	0	-
Clobazam	-	0	0	+ / -
Carbamazepine	-	-	-	+
Zonisamide	-	-	-	-
Phenytoin	-	-	-	-
Phenobarbital / Primidone	-	-	-	-
Topiramate	-	-	-	-

+ positive effect, - negative effect, 0 no clear effect, AED: antiepileptic drug.

hydrophobic drugs, increasing their bioavailability and efficacy. These formulations not only allow to encapsulate these active ingredients but also helped to incorporate the excipients, binders which changes the physiochemical properties of the drugs. These nanoscale carriers, typically 1 to 1000 nanometers, are designed to encapsulate and protect therapeutic agents, enhancing their stability, solubility, bioavailability, and targeting capabilities.

Lipid based Nanosystems

Lipid based nanoparticle system provided a promising strategy for creating an optimal microenvironment at the target drug area and high biocompatibility (Patra *et al.*, 2018) and increased the dispersion and absorption of AED by encapsulating them (Balguri *et al.*, 2016). Lipid matrix around the active moiety not only shield the drug from degradation but also results in the slow release of the drug over the time and maintain the optimal rate of release (Ashfaq *et al.*, 2023; Kakkar and Kaur, 2011). This control and optimum release of the active drug prevent fluctuation in the drug concentration and minimizes the adverse effects. These minimal adverse effects due to optimal release rate make lipid based nanoformulation as superior choice when compared to conventional therapy (Ansari *et al.*, 2023; Cong *et al.*, 2024; Patel *et al.*, 2024). Such claims have been verified by recent data published where nanoformulation of berberine has significantly reduced the seizure score and provided antiseizure activity (Saha *et al.*, 2024). In another study, berberine and piperine were formulated in nanoformulation to get promising antiepileptic results (El-Nahas *et al.*, 2023). A large body of evidence supported that nanoformulations of the drugs acting on the brain and psychiatric illness provide better efficacy and targeted drug delivery (Ahmad *et al.*, 2025; El-Nahas *et al.*, 2023; Pottoo *et al.*, 2020). Lipid based nanoformulation provides the advantage of high loading dose which will optimize the slow release of the drug over the time, biocompatibility with microenvironment and high stability while leaving one grey area of economic burden due to high cost of the raw material.

Polymeric based Nanoparticles

Like the lipid base nanoformulation, polymeric based nanoformulation share the advantage of control, slow release of the drug by enhancing the drug stability and biocompatibility. One of the notable advantage of polymeric based nanoparticle over the lipid based formulation is the superior stability during the storage (Shah *et al.*, 2022). Polymers like Poly (Lactic-Co-Glycolic) Acid (PLGA) and Polyethylene Glycol (PEG) used in these formulations are highly structured and shown high resistance to degradation. Some of the drugs when used for PEGylation prevented the particle-particle interaction, reduced the particle collision and improved the colloidal stability which ultimately exhibited long term stability (Shi *et al.*, 2021; Suk *et al.*, 2016; Sur *et al.*, 2019). One of the example is diazepam-PLGA loaded in the nanoparticle lasted for 18 months (Sharma *et al.*, 2015). This delivery system is unique in the sense that it provided the loading of combined AED in one formulation (Senthilvel *et al.*, 2019). This combined formulation helped to modulate the multiple pathways involved in the seizures so nanoformulation

provides better formulation and better efficacy which is compromised in the use of single medicine by conventional route. This polymeric based nanoparticle have been effectively utilized in the neurodegenerative disease (Cano *et al.*, 2020), neuroprotection (Szczepanowicz *et al.*, 2025) and in epilepsy when phenytoin loaded nano micelles were used (Jirofti *et al.*, 2023). Polymer loaded nanoformulation provides the advantage of good stability, scalability and customization of the drug release but left with challenges polymer toxicity and complex formulation procedure when compared to conventional dosage formulation.

Magnetic Nanoparticles

Magnetic Nanoparticle (MNP) formulation provides advantage over the other formulation in situation of delivery of the drugs directly into the central nervous system. It can be influenced from the outside magnetic environment which provided targeted drug delivery particularly in the complicated situation of status epilepticus. MNPs usually utilize iron oxide containing core like magnetite and maghemite which are stable with the surfactant and polymers. Phenobarbital was incorporated into MNPs via an aqueous microtitration method (Hemmat *et al.*, 2023) using Pluronic F-68, β-cyclodextrin, and ferrous sulfate heptahydrate. Despite a relatively large particle size (581 nm), the formulation showed immediate drug release, suggesting potential for rapid seizure control, while cyclodextrin may improve solubility and systemic stability.

This delivery system is unique from the other carrier system in the sense that target delivery of the drug to local area of the brain can be controlled by bringing magnetic field outside the body and preventing the systemic toxicity (Kong *et al.*, 2012). This magnetic delivery system becomes significant when administration of brain depressant drugs like benzodiapine and barbiturates to avoid adverse effects of respiratory depression. Iron which is one of the main agents in this nanoformulation has some darker side as well. Iron which is source of free radical can initiate oxidative stress and accumulation of the iron is another issue of this formulation (Wang *et al.*, 2024; Zorkina *et al.*, 2020). Challenges with delivery system are associated with its formulation, minimal loading dose and presence of magnetic field.

Nanotechnology Based Delivery Systems for AEDs

General Nanocarrier Strategies

Nanocarriers protect and stabilize AEDs, improving solubility and pharmacokinetics, while enabling brain targeting via surface modifications (e.g., ligands for receptor-mediated transport) and centrally accumulating the drugs in brain with minimal peripheral exposure (Chen *et al.*, 2025).

Intranasal "Nose to Brain" Delivery

It is a non-invasive approach bypassing the BBB via both the olfactory and trigeminal nerve pathways:

AEDs are shown in animals to be distributed intranasally through polymeric nanocarriers (Musumeci *et al.*, 2019).

Nanotechnology-facilitated intranasal delivery of AEDs was found to be beneficial leading to more efficacy and lower systemic exposure and toxicity (Khan and Yadav, 2024).

Nanoemulsions have a better biodistribution potential for CNS targeting.

Nose to brain nano-drug delivery methods, such as micelles, nanoemulsions, liposomes, and solid lipid nanoparticles is a newly emerging field that calls for more investigations(Nguyen & Duong, 2025).

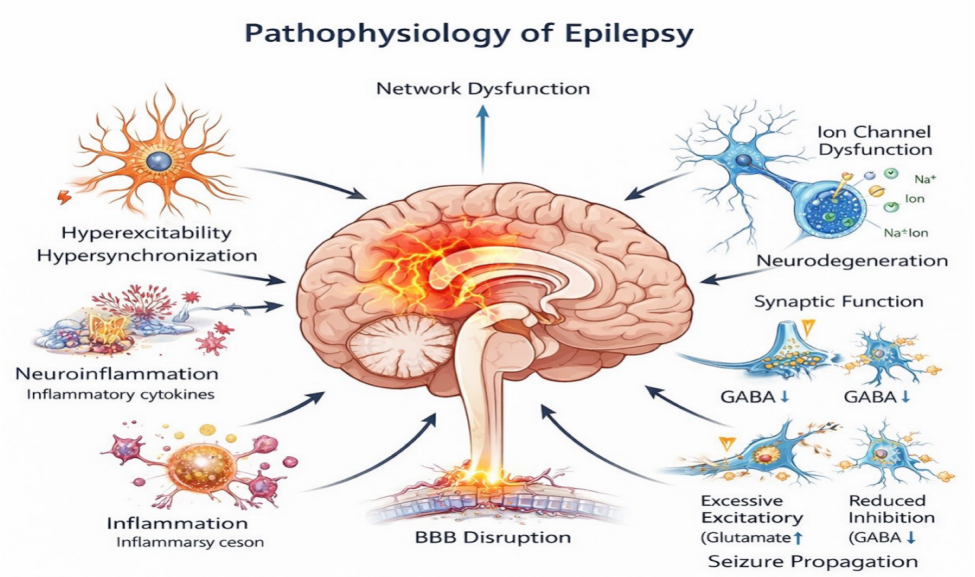


Figure 1: Involvement of different factors in the pathogenesis of Epilepsy.

Phenytoin-loaded BSA-LDH nanoparticles Intranasal injection leads to a very quick CNS targeting, better seizure control, with a higher biocompatibility in mice models (Zhang *et al.*, 2024).

Applications of Nanotechnology for AEDs

Liposomes and Solid Lipid Nanoparticles

AEDs encapsulated in liposomes may improve Central Nervous System (CNS) absorption while lower systemic peripheral toxicity. Solid Lipid Nanoparticles (SLNs) not only augment the therapeutic efficacy but also boost its bioavailability through combining the potency of solid lipids with the superior capsulation of drugs (Rai *et al.*, 2024).

Polymeric, Dendrimer and Biodegradable Nanocarriers

Biodegradable polymeric nanoparticles such as PLGA overcome the pharmacokinetic obstructing hurdles and improve seizure control through sustained release and targeted brain delivery of AEDs. Dendrimers have a better loading capacity and modify the receptor targeting as they are highly branched and customizable (Rai *et al.*, 2024).

Biodegradable Nanoparticles: Polymeric and Lipid Based

Bonilla and colleagues present very rich insights into biodegradable nanocarriers whether polymeric or lipid based not only in protecting the AEDs, enabling the controlled release, but also improving BBB penetration (Bonilla *et al.*, 2022).

Intranasal (Nose to Brain) Delivery Systems

Nanomedicine by Intranasal Route

One way to avoid the blood-brain barrier and reaching the CNS directly is intra-nasal administration of AEDs. Intranasal AEDs circumvent the BBB through the trigeminal and olfactory pathways increasing their effectiveness. Nanoparticles enhance the brain delivery and improve the patient compliance. Being noninvasive, they have a rapid onset of action and lower systemic side effects and showed an optimistic promise of intranasal nanomedicine in the treatment of epilepsy (Khan and Yadav, 2024; Musumeci *et al.*, 2019).

Real-World Intranasal Nanocarrier: Bovine Serum Albumin(BSA) coated Layered Double Hydroxide (LDHs) (BSA-LDHs) Loaded with Phenytoin

Bovine Serum Albumin (BSA) coated Layered Double Hydroxide (LDHs) nanoparticles loaded with phenytoin is a, nanoparticulate drug delivery system designed for intranasal administration, enhances the phenytoin's ability to cross the BBB for better epilepsy treatment and seizure control. By encapsulating phenytoin, it overcomes solubility, reduces systemic metabolic degradation, and minimizes side effects compared to oral phenytoin. This system was introduced in an experimental study in 2024. It quickly reached the brain, delayed the seizure onset, with much

Table 2: Differences between Antiepileptic Drug Generations.

Feature	First Generation	Second Generation	Third Generation
Era of introduction	1910s-1970s	1980s-2000s	2010 onward
Representative drugs (Johannessen *et al.*, 2010; Perucca, 2006)	Phenobarbital, Phenytoin, Carbamazepine, Valproate, Ethosuximide	Lamotrigine, Levetiracetam, Gabapentin, Topiramate, Vigabatrin	Lacosamide, Eslicarbazepine, Perampanel, Cenobamate
Mechanism specificity (Perucca, 2006)	Broad, non-selective	More targeted mechanisms	Highly selective, novel mechanisms
Enzyme induction/inhibition (Perucca, 2006)	Common and strong	Reduced	Minimal or absent
Drug-drug interactions (Perucca, 2006)	High	Moderate	Low
Therapeutic window(Jacob and Nair, 2016)	Narrow	Wider	Wider
Need for serum monitoring (Jacob and Nair, 2016)	Frequent	Occasional	Rare
Central nervous system toxicity	High	Moderate	Low
Systemic adverse effects (Jacob and Nair, 2016)	Common (hepatic, hematologic, bone)	Less frequent	Least frequent
Tolerability	Poor to moderate	Moderate to good	Good to excellent
Use in elderly	Limited	Improved	Preferred
Current clinical role	Effective but limited by toxicity	Widely used first-line options	Preferred for refractory epilepsy and special populations

better biocompatibility and low systemic peripheral exposure and side effects (Zhang *et al*., 2024).

CHALLENGES AND LIMITATIONS

There are still some translational issues as immunogenicity, safety issues, limited human use evidence, synthesis scalability, firm robust regulatory obstacles. Mucociliary clearance and small nasal dose quantities, requiring high solubility and or loading efficiency are additional formulation difficulties (Musumeci *et al*., 2019).

FUTURE DIRECTIONS

Translational Steps and Clinical Integration

Epilepsy personalized nanomedicine, multi-disciplinary collaboration, and firm rigorous preclinical-to-clinical translation are recommended (Prentice and Rizwan, 2023).

CONCLUSION

Drug delivery system has been a serious problem in the treatment of epilepsy. Nanotechnology based drug delivery system addressed the limitations associated with conventional antiepileptic drugs therapy by enhancing drug stability, better penetration through blood brain barrier, targeting the brain delivery, reducing the peripheral drug concentrations leading to better therapeutic response and reducing the adverse effects of these AEDs. Various nanocarriers, including liposomes, polymeric nanoparticles, solid lipid nanoparticles, nanoemulsions, and magnetic nanoparticles, have demonstrated encouraging preclinical outcomes in enhancing the therapeutic efficacy of antiepileptic drugs which are based on preclinical trials. However, large scale formulation batch preparation, safety in long term use, regulatory approval remains to be folded. Future research should emphasize on epilepsy personalized nanomedicine, multi-disciplinary collaboration, and firm rigorous preclinical to clinical translation are recommended.

ABBREVIATIONS

AEDs: Antiepileptic Drugs; **BBB:** Blood-Brain Barrier; **BSA:** Bovine Serum Albumin; **BSA-LDHs:** Bovine Serum Albumin-Coated Layered Double Hydroxides; **CNS:** Central Nervous System; **EEG:** Electroencephalogram; **FDA:** Food and Drug Administration; **fMRI:** Functional Magnetic Resonance Imaging; **GABA:** Gamma-Aminobutyric Acid; **IEDs:** Interictal Epileptiform Discharges; **LDHs:** Layered Double Hydroxides; **MMSE:** Mini-Mental State Examination; **MNP:** Magnetic Nanoparticle; **MoCA:** Montreal Cognitive Assessment; **NMDA:** N-Methyl-D-aspartate; **PBSEs:** Psychiatric and Behavioural Side Effects; **PEG:** Polyethylene Glycol; **PLGA:** Poly(Lactic-Co-Glycolic Acid); **SLNs:** Solid Lipid Nanoparticles.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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