

# Pharmacology of Antiseizure Drugs

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# Introduction

- Antiseizure drugs (ASDs) are used to prevent seizures, while hypnotics are used to induce sleep.
- Understanding their mechanisms, clinical applications, and side effects is crucial for safe and effective treatment.

Seizures are sudden, uncontrolled electrical disturbances in the brain. They cause changes in behavior, movements



As we know, the communication between neurons is done through the action potential which is considered an electrolytes movement through the synapse, so the brain send an output signals to the whole body by Action potential, however when we loss the control on those electrical signals and electrolytes (too much excitation with too little inhibition), the seizure will occur.

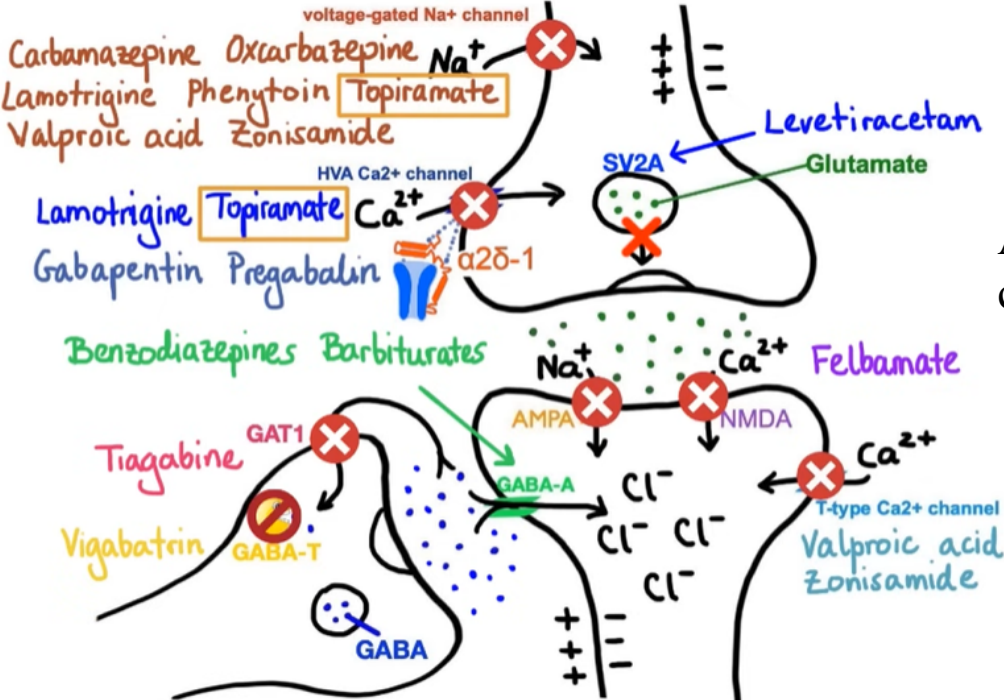
Negative ions >> Cl<sup>-</sup> (inhibition) >> GABA

positive ions >> Na<sup>+</sup> and Ca<sup>++</sup> >> excitation >> glutamate

So epilepsy will occur in one of both cases >> 1) too much Na<sup>+</sup> (glutamate) 2)too little Cl<sup>-</sup> (GABA)

-you should know your family history, because epilepsy maybe genetic.

Someone who addicted to CNS drugs shouldn't stop them suddenly, because it may result in epilepsy, as well as trauma and brain injury may cause it, also high body temperature (fever) considered a risk factor (fever result in infertility in boys).



Also we have specific Ca++ channels called alpha 2 delta 1

As we said above about the pathophysiology of the disease, now we going to think how to stop the causes by Na+ and Ca++ channels blockage (NMDA and AMPA as you can see in the pic above).

In normal situations, there is no continuous excitation, the Cl- will inhibit the signals (when the GABA enter through its channel, it would increase the influx of Cl-), in the epileptic patient who suffers from too little inhibition, I would preserve GABA by prevent its reuptake, or by inhibit GABA amino transferase (which degrades GABA).

We have a protein (SV2A) which found in the walls after the vesicles that store glutamate, so the anti SV2A drugs prevent the degradation of vesicles to prevent glutamate secretion. Remember the glutamate would activate the NMDA receptors.

# Classification of Antiseizure Drugs

- **Sodium Channel Blockers:** Phenytoin, Carbamazepine, Lamotrigine, Lacosamide
- **Calcium Channel Blockers:** Ethosuximide, Gabapentin, Pregabalin
- **GABAergic Enhancers:** Benzodiazepines (Diazepam, Lorazepam), Barbiturates (Phenobarbital), Vigabatrin
- **Mixed-Mechanism Drugs:** Valproate, Levetiracetam, Topiramate, Zonisamide
- **SV2A Modulators:** Levetiracetam, Brivaracetam
- **AMPA Receptor Inhibitors:** Perampanel




## Mechanism of Action - Antiseizure Drugs

- **Sodium Channel Blockers:** Reduce repetitive neuronal firing, stabilizing hyperexcitable neurons
- **Calcium Channel Blockers:** Inhibit T-type calcium currents (important in absence seizures)
- **GABAergic Enhancers:** Increase GABA activity, enhancing neuronal inhibition
- **SV2A Modulators:** Modulate synaptic vesicle protein 2A, reducing neurotransmitter release
- **AMPA Receptor Inhibitors:** Reduce excitatory glutamate neurotransmission

Brain is divided into 2 hemispheres, and we have 2 types of seizures : the focal one affect one hemisphere without loss of consciousness, and the generalized one involves both hemispheres with loss of consciousness

## Clinical Uses of Antiseizure Drugs

- **Focal Seizures:** Carbamazepine, Lamotrigine, Levetiracetam
- **Generalized Tonic-Clonic Seizures:** Valproate, Phenytoin, Levetiracetam
- **Absence Seizures:** Ethosuximide, Valproate *Usually occur in children*
- **Status Epilepticus:** Benzodiazepines (Lorazepam, Diazepam)
- **Neuropathic Pain:** Gabapentin, Pregabalin 
- **Migraine Prophylaxis:** Valproate, Topiramate

Benzodiazepines and barbiturates increase the Cl<sup>-</sup> influx

# Adverse Effects of Antiseizure

## Drugs

- Phenytoin: Gingival hyperplasia, ataxia, teratogenic effects
- Carbamazepine: Hyponatremia, agranulocytosis
- Valproate: Hepatotoxicity, teratogenicity (neural tube defects)
- Topiramate: Cognitive impairment, kidney stones
- Levetiracetam: Mood disturbances, aggression
- Ethosuximide: GI upset, fatigue

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# Adverse Effects & Drug Interactions

- Antiseizure Drugs: Sedation, hepatotoxicity, teratogenicity (Valproate, Phenytoin)
- Drug Interactions: CYP450 inducers (Carbamazepine, Phenytoin), increased sedation with alcohol

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# Latest Research and Future Directions

- Novel antiseizure drugs targeting specific ion channels
- Gene therapy for epilepsy



دعواتكم لنا، وبالتوفيق لكم.

**THANK YOU**

