

UNIT – 4

Drugs Acting on the Central Nervous System: Sedatives and Hypnotics

A. Benzodiazepines:

Structure-Activity Relationship (SAR) of Benzodiazepines:

1. Chlordiazepoxide:

- Used for anxiety and alcohol withdrawal.
- Metabolized to active metabolites.

2. Diazepam:

- Used for anxiety, muscle spasms, and seizures.
- Metabolized to active metabolites.
- Long half-life.

3. Oxazepam:

- Used for anxiety.
- Does not form active metabolites.
- Shorter duration of action.

4. Chlorazepate:

- Used for anxiety.
- Prodrug converted to active metabolite desmethyldiazepam.

5. Lorazepam:

- Used for anxiety and seizures.
- Rapid onset of action.
- No active metabolites.

6. Alprazolam:

- Used for anxiety and panic disorder.
- Rapid onset of action.
- Short half-life.

7. Zolpidem:

- Used for insomnia.
- Binds selectively to the alpha-1 subunit of the GABA-A receptor.

B. Barbiturates:

Structure-Activity Relationship (SAR) of Barbiturates:

1. **Barbital:**

- Used as a hypnotic.
- Long-acting.

2. **Phenobarbital:**

- Used as an antiepileptic.
- Long-acting.

3. **Mephobarbital:**

- Used as a hypnotic.
- Intermediate duration of action.

4. **Amobarbital:**

- Used as a hypnotic.
- Short-acting.

5. **Butabarbital:**

- Used as a hypnotic.
- Intermediate duration of action.

6. **Pentobarbital:**

- Used as a sedative and for anesthesia.
- Short-acting.

7. **Secobarbital:**

- Used as a hypnotic.
- Short-acting.

Miscellaneous:

1. **Amides & Imides:**

• **Glutethimide:**

- Used as a sedative and hypnotic.
- Withdrawn due to abuse potential.

2. **Alcohol & Their Carbamate Derivatives:**

• **Meprobamate:**

- Used for anxiety.

- Carbamate derivative.
- **Ethchlorvynol:**
 - Used as a sedative and hypnotic.

3. Aldehydes & Their Derivatives:

- **Triclofos Sodium:**
 - Used as a sedative for pediatric patients.
 - Prodrug converted to trichloroethanol in the body.
- **Paraldehyde:**
 - Used as a sedative and anticonvulsant.

These drugs act on the central nervous system to produce sedative and hypnotic effects by enhancing the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) at GABA-A receptors. Understanding their structure-activity relationships is crucial for optimizing therapeutic effects while minimizing adverse effects and the risk of dependence.

Antipsychotics:

Antipsychotics, also known as neuroleptics, are a class of drugs used to manage symptoms of psychosis, including hallucinations, delusions, and disorganized thinking. They can be categorized into different classes based on their chemical structures and mechanisms of action.

B. Antipsychotics:

Phenothiazines:

Structure-Activity Relationship (SAR) of Phenothiazines:

1. **Promazine Hydrochloride:**
 - Used as an antipsychotic.
 - Low potency.
2. **Chlorpromazine Hydrochloride:**
 - First-generation antipsychotic.
 - Used for schizophrenia and other psychotic disorders.
 - Low to moderate potency.
3. **Triflupromazine:**
 - Used as an antipsychotic.
 - Moderate potency.

4. **Thioridazine Hydrochloride:**

- First-generation antipsychotic.
- Used for schizophrenia and other psychotic disorders.
- Moderate potency.

5. **Piperacetazine Hydrochloride:**

- Used as an antipsychotic.
- Moderate potency.

6. **Prochlorperazine Maleate:**

- Used for nausea, vomiting, and psychosis.
- Moderate potency.

7. **Trifluoperazine Hydrochloride:**

- First-generation antipsychotic.
- Used for schizophrenia and other psychotic disorders.
- High potency.

Ring Analogues of Phenthiazines:

1. **Chlorprothixene:**

- Used as an antipsychotic.
- High potency.

2. **Thiothixene:**

- Second-generation antipsychotic.
- High potency.

3. **Loxapine Succinate:**

- Second-generation antipsychotic.
- Also has antidepressant properties.

4. **Clozapine:**

- Second-generation antipsychotic.
- Used for treatment-resistant schizophrenia.
- Has a unique profile with reduced risk of extrapyramidal symptoms (EPS).
- Can cause agranulocytosis, requiring regular monitoring.

Fluorobutyrophenones:

1. **Haloperidol:**

- First-generation antipsychotic.
- High potency.
- Used for schizophrenia and acute psychotic episodes.
- Associated with a higher risk of EPS.

2. **Droperidol:**

- Used for sedation and the management of acute agitation.

3. **Risperidone:**

- Second-generation antipsychotic.
- Used for schizophrenia and bipolar disorder.
- Moderate to high potency.
- Can cause EPS.

Beta-Amino Ketones:

- **Molindone Hydrochloride:**

- Second-generation antipsychotic.
- Moderate potency.
- Used for schizophrenia.

Benzamides:

- **Sulpiride:**

- Second-generation antipsychotic.
- Used for schizophrenia.
- Also used for mood disorders and dysthymia.

Understanding the SAR of antipsychotics is essential for selecting appropriate agents based on their efficacy and side effect profiles. The development of second-generation antipsychotics aimed to reduce the risk of extrapyramidal symptoms associated with first-generation agents, offering a broader range of treatment options for psychiatric disorders.

Anticonvulsants:

Anticonvulsants are a class of medications used to treat seizures and prevent the recurrence of epileptic episodes. They act by stabilizing neural membranes, modulating neurotransmitter release, or altering ion channel function. The selection of an anticonvulsant depends on the type of seizure and individual patient characteristics.

Structure-Activity Relationship (SAR) of Anticonvulsants:

1. Barbiturates:

- **Phenobarbitone:**

- Enhances the inhibitory effect of GABA.
- Used for generalized tonic-clonic and partial seizures.

- **Metharbital:**

- Similar to phenobarbitone.
- Used for generalized tonic-clonic seizures.

2. Hydantoins:

- **Phenytoin:**

- Blocks voltage-gated sodium channels.
- Used for various types of seizures.
- Associated with gingival hyperplasia and hirsutism.

- **Mephenytoin:**

- Similar to phenytoin.
- Used for focal seizures.

- **Ethotoin:**

- Similar to phenytoin.
- Used for focal seizures.

3. Oxazolidine Diones:

- **Trimethadione:**

- Mechanism not fully understood.
- Used for absence seizures.

- **Paramethadione:**

- Mechanism not fully understood.
- Used for absence seizures.

4. Succinimides:

- **Phensuximide:**

- Mechanism not fully understood.
- Used for absence seizures.

- **Methsuximide:**

- Mechanism not fully understood.
 - Used for absence seizures.
 - **Ethosuximide:**
 - Blocks T-type calcium channels.
 - Used for absence seizures.
5. **Urea and Monoacylureas:**
- **Phenacemide:**
 - Mechanism not fully understood.
 - Used for various seizures.
 - **Carbamazepine:**
 - Blocks voltage-gated sodium channels.
 - Used for generalized tonic-clonic, focal, and trigeminal neuralgia.
6. **Benzodiazepines:**
- **Clonazepam:**
 - Enhances the effect of GABA.
 - Used for various seizure types, including absence seizures.
7. **Miscellaneous:**
- **Primidone:**
 - Converted to phenobarbitone and phenylethylmalonamide.
 - Used for generalized tonic-clonic and partial seizures.
 - **Valproic Acid:**
 - Enhances the effect of GABA, blocks sodium channels.
 - Used for generalized tonic-clonic, absence, and myoclonic seizures.
 - **Gabapentin:**
 - Mechanism not fully understood.
 - Used for partial seizures and neuropathic pain.
 - **Felbamate:**
 - NMDA receptor antagonist, enhances GABAergic activity.
 - Used for refractory partial seizures.

Understanding the SAR of anticonvulsants is crucial for optimizing therapeutic efficacy while minimizing side effects. The mechanisms of action vary, reflecting the diversity of epilepsy types and the need for different pharmacological approaches.

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