BARBITURATES
CHEMISTRY

Derivatives of Barbituric acid.
DISADVANTAGES

- Low Therapeutic Index
- Potent Enzyme Inducers: Drug Interactions
- Drug of Abuse
- Risk of Physical Dependence
- Svere withdrawal Syndrome
CLASSIFICATION OF BARBITURATES

According to duration of action

I. Long acting barbiturates (DOA: 8-12hrs)
   - Phenobarbitone
   - Barbitone
   - Methyl phenobarbitone

II. Intermediate acting (DOA: 4-8hrs)
   - Amylobarbitone
   - Butobarbitone
   - Cyclobarbitone
   - Pentobarbitone
III. Short-acting barbiturates (DOA: 2-4hrs)
   Quinal barbitone

IV. Ultrashort Acting (DOA: 15-30 min)
   Thiopentone Sodium
   Methohexital
   Thiamylal
PHARMACOKINETICS
MOA

Multiple MOA at multiple sites in brain:

1.(a) Acts on $\text{GABA}_A$ Receptor chloride channel.

Site of action: Different from BDZ & GABA.

- **GABA**ergic at low doses. Prolongation of Chloride channel openings.
- **GABA** mimetic at high doses. Activate the Chloride channel.
2. Depress voltage activated Ca\(^+\) currents in isolated Hippocampal neurons.

3. Depress Glutamate induced depolarizations.

4. Inhibition of Na\(^+\) channel.--- at high conc. (GA)

5. Inhibition of K\(^+\) channel.--- at still higher conc. (GA)
GROUP ACTIONS

- Sedation
- Hypnosis
- Antiepileptic
- Anticonvulsant
- Hyperalgesia
- Amnesia & Automatism
- Action on Respiratory System
- Action on Liver
- Action on GIT
- Action on CVS
- Action on Kidneys
- Action on ANS
- Dependence
THERAPEUTIC USES

- Hypnotic
- Sedatives
- GA
- Antiepileptic
- Anticonvulsant
- Potentiation of Anesthesia
- Neonatal jaundice & Kernicterus
- In narcoanalysis
ADVERSE EFFECTS

- Hangover
- Drug Automatism
- Skin rashes
- GIT disturbances
- Idiosyncracy---Excitation Restlessness
- Attacks of Ac. Porphyria,
- Enzyme Induction
- Megaloblastic anaemia
- Depression of fetal respiration
# DIFFERENCE BETWEEN BZP & BARBITURATES

<table>
<thead>
<tr>
<th>BENZODIAZEPINES</th>
<th>BARBITURATES</th>
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<tbody>
<tr>
<td><strong>GABA ergic</strong></td>
<td>GABA mimetic in large doses</td>
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<tr>
<td>Commonly used sedative hypnotic</td>
<td>Blockade of Ca, Na, K channels, Ih</td>
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<td>NMDA rec</td>
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<td>Safe in patients of porphyria</td>
<td>Causes hyperalgesia</td>
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<td></td>
<td>More resp depression may be fatal in toxic doses</td>
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<tr>
<td>No role in neonatal jaundice</td>
<td>CI in porphyria</td>
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<tr>
<td>More commonly used for premedication</td>
<td>Enzyme inducer, used in neonatal jaundice</td>
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<td>Midazolam for induction</td>
<td>Ultra-short acting as i/v GA, for induction</td>
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<tr>
<td>Floppy baby syndrome, if given prior to delivery</td>
<td>Pronounced resp depression</td>
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Acute Poisoning:

- Symptoms
- General Treatment
- Specific Treatment

Drug Dependance:
CONTRAINDICATIONS

- Hepatic failure
- Severe pulmonary insufficiency.
- Porphyria
Buspirone

- Newer selective anti-anxiety agent.
- Partial agonist at brain $5\text{HT}_{1A}$ Receptors.
- Agonist at brain Dopamine $D_2$ Receptors

CLINICAL USE

mainly used for GAD
Differences from BDZ:

- OOA more than a week. Unsuitable for acute anxiety states.
- No marked **Sedative, Euphoric & Hypnotic** effect
- Less **psychocntor impairment**
- No Rebound anxiety.
- No withdrawal signs on abrupt discontinue
- Minimal abuse liability.
- No potentiation of other CNS depressants.
- Elderly patients are not more sensitive to its effects.
Adverse Effects

- Tachycardia
- Palpitations
- Nervousness
- Gastrointestinal distress
- Paresthesias
- Elevated Blood Pressure
ZOLPIDEM

Imidazopyridine. St. related to BDZ zaleflon.

MOA:- BZ1 – Omega subtype and facilitates GABA mediated neuronal inhibition
- Sedative anxiolytic, Hypnotic.
- Minimal muscle relaxing and anticonvulsant effects.
- Larger doses produce amnesia.
- Minor effects on sleep pattern.
- Suppress REM sleep at higher doseses.
- Rebound insomnia may occur on abrupt discontinuance.
- Resp. depression with larger doses.
- Actions are antagonised by flemazenil
- Less risk of dependence and tolerance.
ZALEPLON

- Binds to BZ$_1$
- Facilitates inhibitory actions of GABA.

Effect on Sleep:
- Less risk of tolerance and withdrawal syndrome.
- Potentiate effects of Ethanol and other sedative Hypnotics.
PARALDEHYDE

- CYCLIC ETHER
- Colorless transparent
- Pungent smell
PHARMACOKINETICS

- Absorption
- Metabolism
- Excretion
CLINICAL USES

- Orally ___ hypnotic
- I/M _____

Mania
Alcohol withdrawal
Anticonvulsant
Status epilepticus
Tetanus
Eclampsia
TOXICITY

1. GIT upset on oral adm
2. I/M adm – abscess formation
3. Accidental I/V administration
   Violent coughing
   Pulmonary edema
   Coma & sudden death
4. Administration of expired drug
   (or drug exposed to sunlight)
   Acetic acid & Acetaldehyde is formed
   Hypotension
   Respiratory depression
   Coma

5. Tolerance & addiction

6. Over dosage toxicity
   1. Acidosis
   2. GIT Bleeding
   3. Toxic hepatitis
   4. Nephrosis
CONTRAINDICATION

- Hepatic & pulmonary impairment
- Never given to patients taking Disulfiram
  (Aldehyde dehydrogenase inhibitor)