

# **SEDATIVES AND HYPNOTICS**

## Introduction

**Sedative:** A sedative drug decreases activity, moderate excitement and calms the patient .

**Hypnotic drug:** A hypnotic drug produces drowsiness and facilitates the onset and maintenance of a state of sleep that resembles natural sleep .

Barbiturates & Benzodiazepines are widely used as sedative & hypnotic

**Barbiturates** are an old class of drugs used to relax the body and help people sleep.

**Benzodiazepines** are useful for treating insomnia and anxiety. They are the class of medications that work in the central nervous system and are used for a variety of medical conditions.

## Difference Between Sedative and Hypnotic

Sedatives are drugs that decrease activity and have a calming, relaxing effect. People use these drugs mainly to reduce anxiety. At higher doses, sedatives usually cause sleep. Drugs used mainly to cause sleep are called hypnotics.

The difference between sedatives and hypnotics, then, is usually the amount of the dose—lower doses have a calming effect and higher doses cause sleep.

## Classification of Barbiturates and Benzodiazepines

### Classification of Barbiturates:

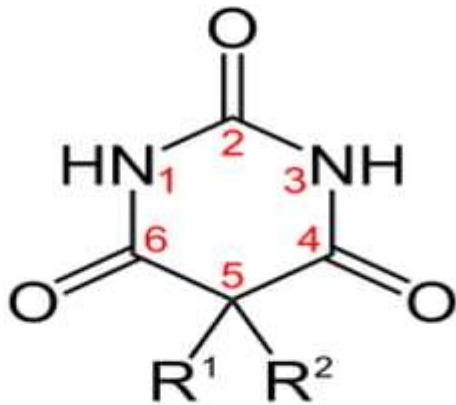
Based on duration of action:

- A long duration of action: (6 hours or more) e.g: Barbital, Phenobarbital.
- An intermediate duration of action: (3 to 6 hours ) e.g: Amobarbital, Talbutal.
- A short duration of action: (less than 3 hours) e.g: Pentobarbital, Secobarbital.

## **Classification of Benzodiazepines:**

- A long duration of action: (1-3 days) e.g: Diazepam, Nitrazepam
- An intermediate of action: ( 10-20 hours) e.g: Alprazolam, Lorazepam.
- A short duration of action: ( 3-8 hours) e.g: Oxazepam, Triazolam.

# Barbiturates



## Structure Activity Relationship (SAR) of Barbiturates

- 1) Both hydrogen atoms in position 5 of barbituric acid must be replaced for maximal activity.
- 2) Increasing the length of an alkyl chain in the 5 position enhances potency up to 5 or 6 carbon atoms.
- 3) Branched, cyclic or unsaturated in the 5 position generally produce a briefer duration of action than do normal saturated chains containing the same number of carbon atoms.

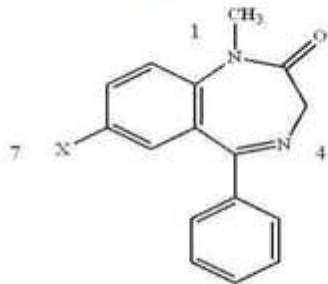


4) Compounds with alkyl groups in the 1 or 3 position may have a shorter onset & duration of action.

5) Replacement of oxygen by sulfur on the 2 carbon shortens onset & duration of action.

These are the Structure-Activity-Relationship of barbiturates.

# Benzodiazepines SAR



- 1,4 benzodiazepine
- Electron withdrawing group (EWG) → 7 position,
  - X= Cl < Br < F < CN < CF<sub>3</sub> < NO<sub>2</sub>
  - Stronger EWG give more potent compounds

## SAR of benzodiazepines

1. The presence of an electron attracting substituent at position 7 is required for activity
2. Position 6,8 and 9 should not be substituted .
3. A phenyl group at the 5 position promotes activity if this group is ortho or di ortho substituted with electron attracting groups , activity is increased.  
  
On the other hand ,para substitution decreases activity greatly.
- 5.The 2 carbonyl function is optimal for activity as in the nitrogen atom at 1 position .
- 6.The N-substituent should be small .

## Adverse effects of barbiturate

1. CNS: Barbiturates cause drowsiness, impaired concentration.
2. Drug hangover: Hypnotic doses of barbiturates produce a feeling of tiredness well after the patient wakes.
3. Barbiturates induce the P450 system.
4. By inducing aminolevulinic acid (ALA) synthetase, barbiturates increase porphyrin synthesis, and are contraindicated in patients with acute intermittent porphyria.

## Adverse effects of benzodiazepines

1. Light-headedness
2. Fatigue
3. Increased reaction time
4. Motor incoordination
5. Impairment of mental and motor functions
6. Confusion
7. Antero-grade amnesia
8. Cognition appears to be affected less than motor performance.
9. All of these effects can greatly impair driving and other psychomotor skills, especially if combined with ethanol.

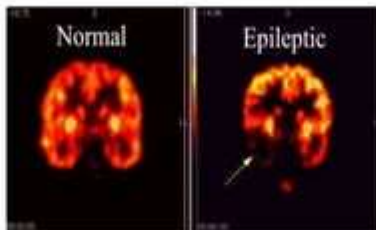
## Clinical use of Barbiturates



- Treatment of INSOMNIA



- Thiopentane for ANAESTHESIA



## Clinical use of Barbiturates



Treatment of seizure disorder



- Adjuvants in psychosomatic disorders

### **Dosages:**

- Average doses are between 50 to 100 milligrams.
- Barbiturates are available in pill, liquid, rectal, and injectable forms. Their effects last between 4 and 16 hours

## Clinical use of Benzodiazepine

- Sedative-Hypnotics
- Seizure control, anxiety
- Alcohol withdrawal
- Insomnia
- Control of drug-associated agitation, as muscle relaxants, and as pre-anesthetic agents; combined frequently with other medications for procedural sedation.