

Sedative – Hypnotic Drugs

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Sedative : a drug that reduces anxiety & exerts calming effects.

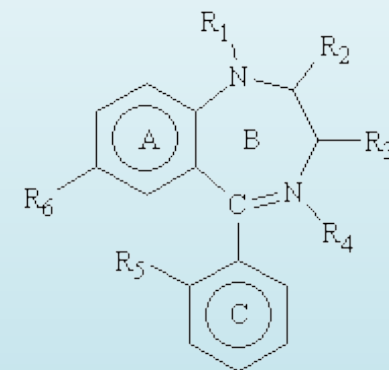


Hypnotic : a drug that produces drowsiness & encourages onset of sleep.



Sedative - Hypnotics

1. Benzodiazepines (BDZ):-

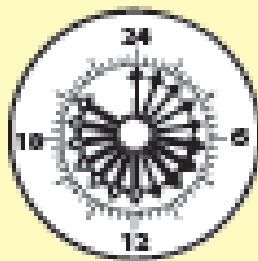


Long-acting



*Clonazepam
Chlordiazepoxide
Diazepam
Flurazepam
Quazepam*

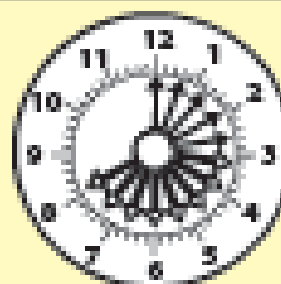
Intermediate-acting



10-20 Hours

*Alprazolam
Estazolam
Lorazepam
Temazepam*

Short-acting



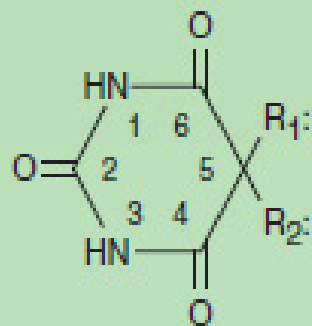
3-8 Hours

*Oxazepam
Triazolam*

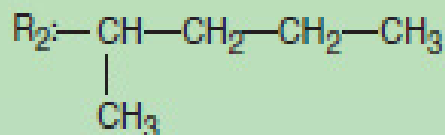
Other BDZ :

Nitrazepam, Clonazepam and Midazolam.

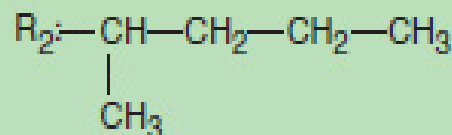
2. Barbiturates (barb.) :-



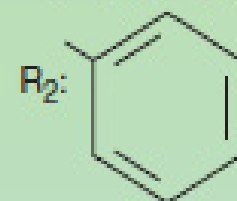
Barbiturate nucleus



Pentobarbital



Secobarbital



Phenobarbital

Long-acting	Short-acting	Ultra-short-acting
<i>Phenobarbital</i>	<i>Pentobarbital</i> <i>Secobarbital</i> <i>Amobarbital</i>	<i>Thiopental</i>

Other barb. : Thiamylal and Methohexital .

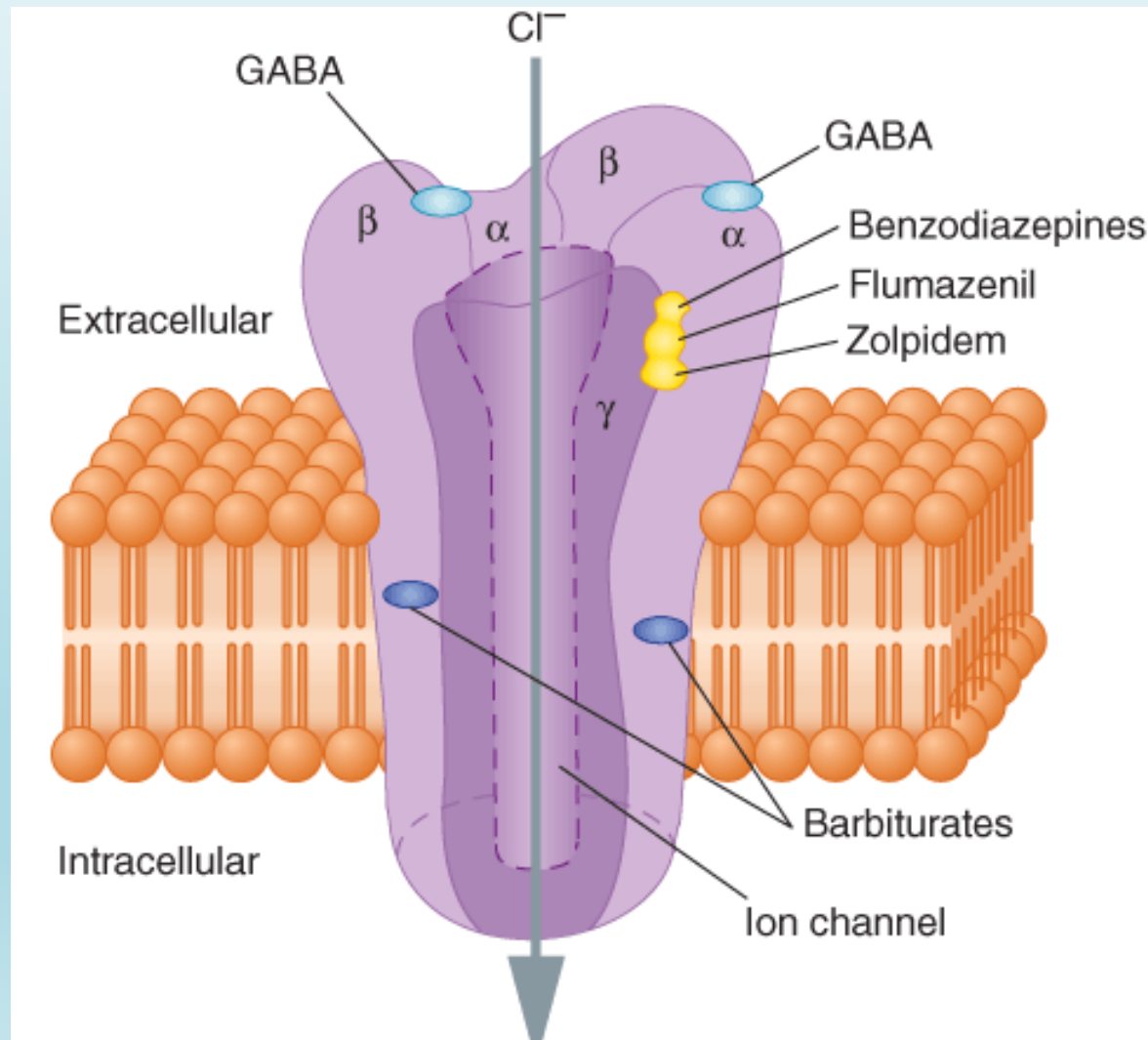
3. Non-BDZ that have similar mechanism of action to BDZ :-

e.g. **Zolpidem, Zaleplon and Eszopiclone.**

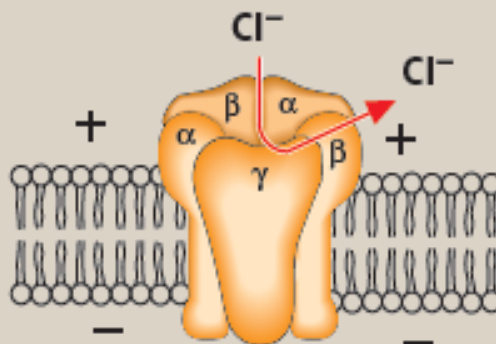
4. Non-barb. that have similar mechanism of action to barb. :-

e.g. **Meprobamate, Chloralhydrate and Glutethimide.**

Pharmacodynamics

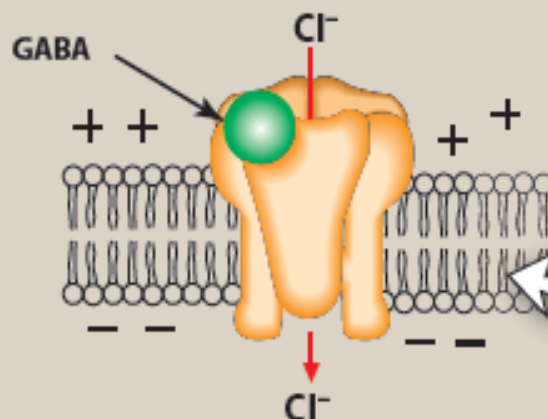


A Receptor empty
(no agonists)



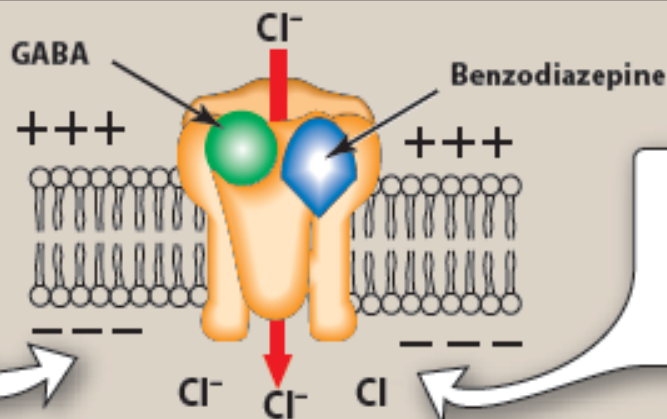
Empty receptor is inactive, and the coupled chloride channel is closed.

B Receptor binding GABA



Binding of GABA causes the chloride ion channel to open, leading to hyperpolarization of the cell.

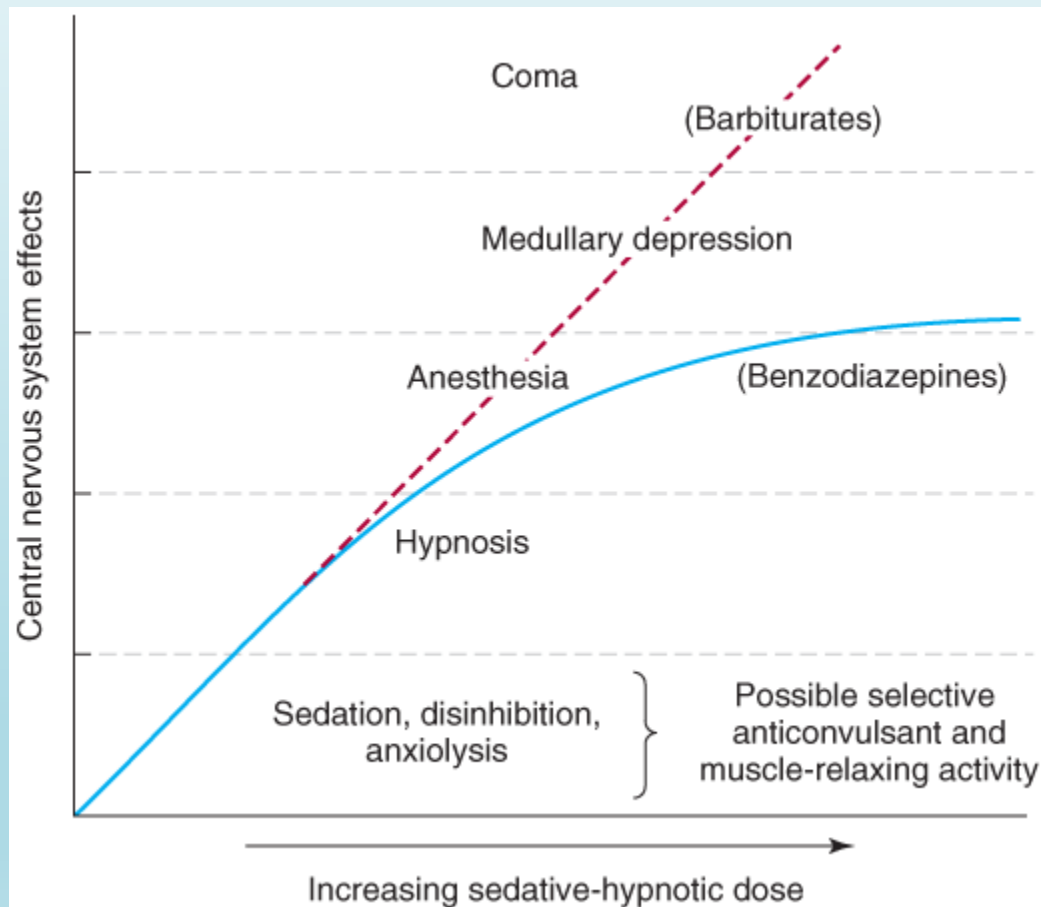
C Receptor binding GABA and benzodiazepine



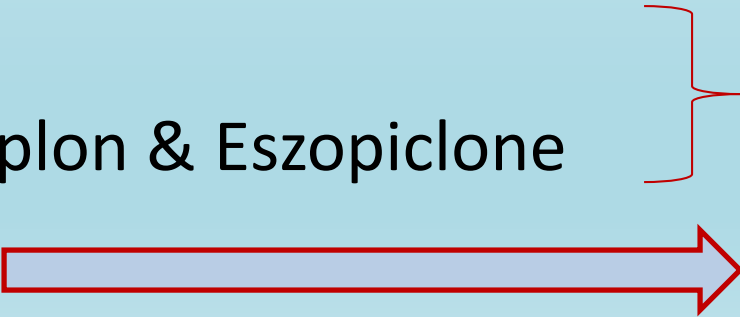
Entry of Cl^- hyperpolarizes the cell, making it more difficult to depolarize, and therefore reduces neural excitability.

Binding of GABA is enhanced by benzodiazepine, resulting in a greater entry of chloride ion.

Graded dose-dependent CNS depression



Respiratory depression induced by Sedative-Hypnotics

- Which carries a greater risk for induction of respiratory depression BDZ or barb.?
 - Is there a specific antidote for overdose of:
 - BDZ
 - Zolpidem, Zaleplon & Eszopiclone
 - Barbiturates.
- Flumazenil
- Sorry , No.
- 

Pharmacological actions

1. Sedation: Reduce anxiety and have calming effects, they may impair psychomotor & cognitive functions.

2. Anti-convulsant effects:

Clonazepam, Nitrazepam , Diazepam and Lorazepam and Phenobarbital.

➤ *Zolpidem, Zaleplon & Eszopiclone lack anticonvulsant effects.*



3. Hypnosis: ↓ latency of sleep onset
↑ duration of sleep



4. Anesthesia: thiopental, thiamylal and methohexital.

5. Muscle relaxation: BDZ and Meprobamate have muscle relaxing activity.

➤ *Zolpidem, Zaleplon & Eszopiclone lack muscle relaxing effects.*



Tolerance and Dependence



Tolerance and Dependence

- **Tolerance:** is decreased responsiveness to drug following repeated exposure.
- Then what ???
- Tolerance is very common with Sedative-Hypnotics use which occurs mostly in long treatment courses.
- Why does tolerance occur?
- Minimal tolerance has been observed with Zolpidem, Zaleplon & Eszopiclone.

- **Physiologic dependence:** is altered physiologic state that requires continuous drug administration to prevent withdrawal symptoms.
- What are withdrawal symptoms associated with discontinuation of Sedative-Hypnotics?
- When do withdrawal symptoms appear?

Buspirone: (5HT_{1A} partial agonist): an anxiolytic without causing marked sedation, hypnosis or euphoria.



Suvorexant: Orexin receptors antagonist.

Ramelteon: MT₁ and MT₂ (melatonin) receptor agonist.

AE: ↓ testosterone
↑ prolactin



Clinical uses of Sedative-Hypnotics

- Anxiety.
- Insomnia.
- Epilepsy.
- Anesthesia.
- Control of withdrawal symptoms during abuse of other drugs (e.g. ethanol , opioids).

Thank you

References

- Basic & Clinical Pharmacology , Bertram G. Katzung
12th edition .
- Lippincott's Illustrated Reviews: Pharmacology ,
5th edition .
- Goodman & Gilman's The Pharmacological Basis of
Therapeutics, 12th ed. .