College of Pharmacy

Department of Pharmacology

جامعة الملك سعود
King Saud University
1957

CNS Depressants

Objectives

- Describe the general signs of CNS depression.
- Discuss the definition of sedative, hypnotic, tranquilizer and anesthetic.
- Elucidate sedative – hypnotic classification.
- Understand the mechanism of barbiturate and benzodiazepine. and illustrate some examples of each drug class.

Classification of CNS depressants according to their actions:

1- Sedative – hypnotics .

2- Tranquillizers .

3- Anesthetics .

General signs for CNS depressants

1- ↓ vitality .

2- ↓ excitability.

3- ↓ HR & RR .

I. Sedative – hypnotics

Sedatives:
Drugs which decrease the activity, calm the recipient, cause sedation and in large dose they induce sleep.

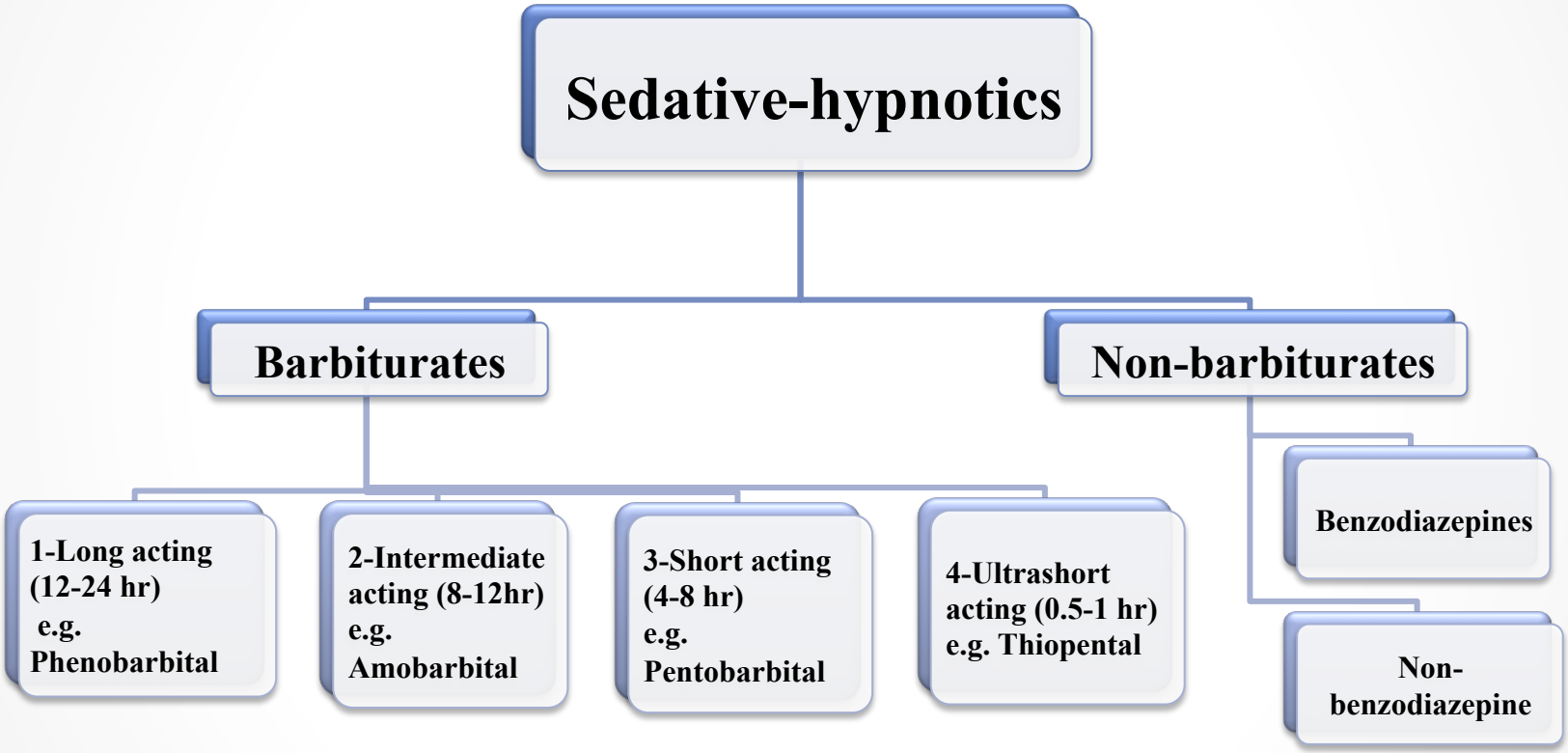
Hypnotics:
Drugs which induce sleep that resembles the natural sleep.

e.g. Barbiturates

Natural Sleep

NREM	REM
▪ Non rapid eye movement. ▪ Consists of 4 stages. ▪ Lasts for 90 min. ▪ Associates with thinking.	▪ Rapid eye movement. ▪ Consists of one stage (dreaming stage). ▪ Lasts for 20 min. ▪ Associates with dreaming.

Sedative – hypnotics: Classification



II- Tranquillizers

Definition:

Tranquillizers are drugs which relief mental anxiety and stress without affecting the consciousness.

e.g. Chlorpromazine (CPZ)

III- Anesthetics

Definition:

Drugs which cause unconsciousness and generalized loss of pain sensation to permit the performance of surgery.
e.g. thiopental (IV), halothane (inhalation).

MOA:

Decrease with propagation of nerve impulses by interfering with electrolytes conductance through the cell membrane.

1- Barbiturates

MOA:

They have GABA like action → ↑ opening time of chloride channels → ↑conductance of chloride ions → hyperpolarization.

Classification according to their duration of action:

1-Long-acting.
2-Intermediate-acting.
3-Short acting.
4-Ultrashort acting.

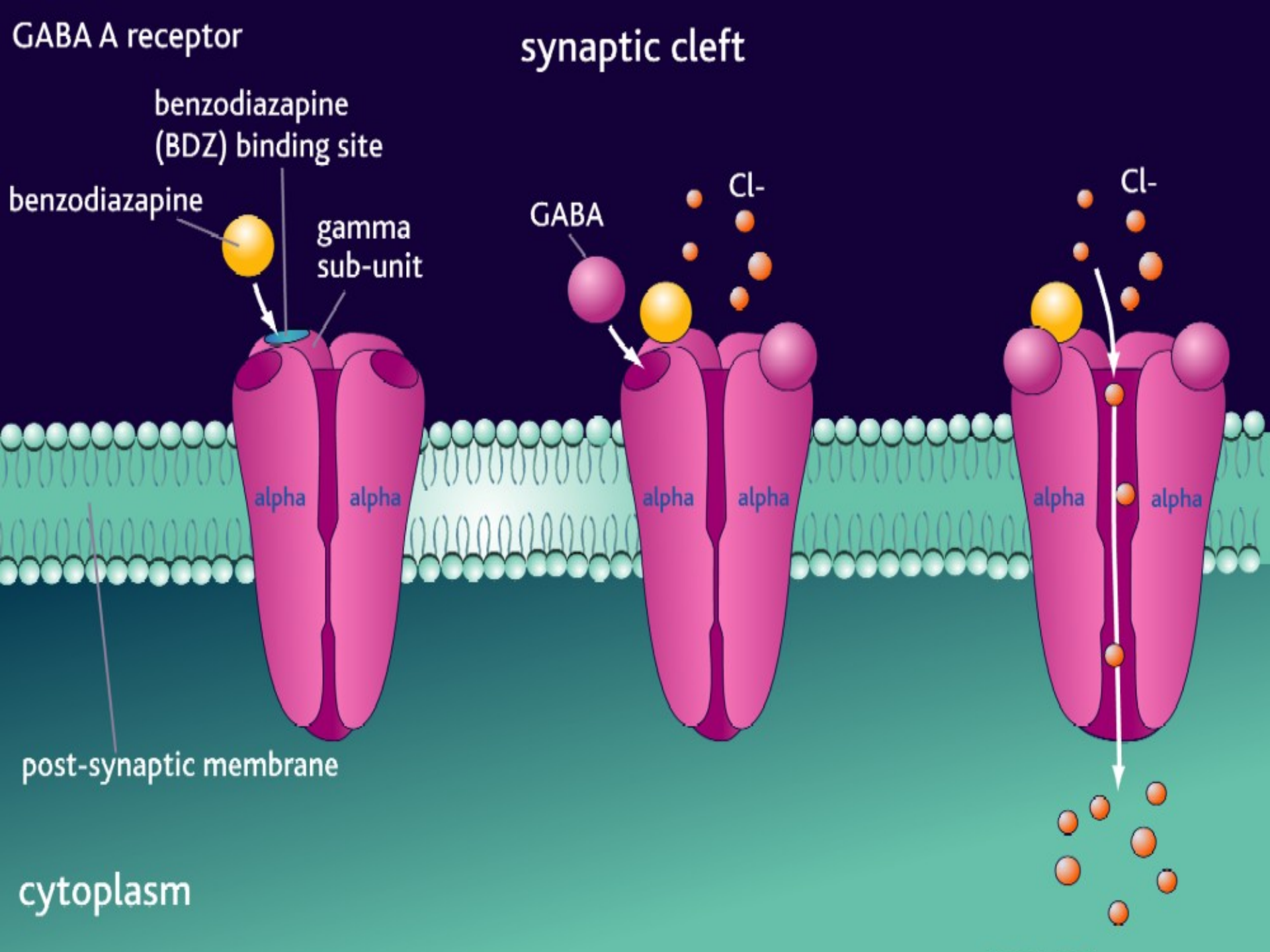
2- Benzodiazepines

MOA:

- Bind non-selectively to benzodiazepine receptors (GABA$_A$-dependent).
  - GABA$_A$ receptors → increase Cl influx → hyperpolarization
  - GABA$_B$ receptors → Gi protein → ↓cAMP → relaxation

Examples:

- Diazepam (sedative) .
- Triazolam (hypnotic) .


GABA A receptor
synaptic cleft
benzodiazapine
(BDZ) binding site
benzodiazapine
gamma
sub-unit
GABA
Cl-
Cl-
alpha
alpha
alpha
alpha
alpha
alpha
post-synaptic membrane
cytoplasm

3- Non-barbiturate Non-BZD

1. 5-HTA1 agonist e.g. buspirone.
2. Chloral hydrate (prodrug) converted to trichloroethanol.
3. Antihistamine e.g. diphenhydramine.
4. Paraldehyde.
5. Promethazine.

Specific signs of sedative-hypnotic

Drugs:

Thiopental, Phenobarbital and Chloral hydrate .

Signs:

1- Staggering gait .
2- Sleeping posture .
3- Loss of righting reflex (onset time) .
4- ↓ Touch & pain reflexes (**lost** with thiopental) .

Specific signs for CPZ

Signs:

1- No loss of righting reflex.
2- Creeping gait.
3- Abdomen touches the ground.
4- State of catalepsy (loss of muscles control) → onset time.
5- ↓ Touch & pain reflexes.

CPZ mechanism of action:

- It is D2 , 5 HT , H1 and alpha 1 antagonist .

Lab work

Drug	Conc.	Dose	Route
Thiopental	2.5 %	100 mg/kg	IP
Phenobarbital	2 %	200 mg/kg	
Chloralhydrate	3 %	300 mg/kg	
C.P.Z	0.1%	15 mg/kg	

References

- H.P. Rang, M.M. Dale, M.J Ritter, R.J. Flower (2007). Anxiolytic and hypnotic drugs. Rang and Dale's Pharmacology, 6th edition, Elsevier health sciences, London.