جامعة ساوة الاهلية
كلية التقنيات الصحية والطبية
قسم التخدير - اللجنة العلمية

SAWA UNIVERSITY

PHARMACODYNAMIC

جامعة ساوة

كلية التقنيات الصحية والطبية

قسم تقنيات التخدير

المرحلة الثانية

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رقم المحاضرة :3

1. Hydrophobic drug	2. Hydrophilic drug
Uniform distribution of electrons.	Non-uniform distribution of electrons.
No charge.	Positive/negative charge.
Readily penetrate most biological membranes.	Don't readily penetrate biological membranes, must go through the slit junctions
Can dissolve in the lipid membranes.	-

Drug metabolism:

Drugs are eliminated by:

1. Biotransformation.
2. Excretion into the urine/bile.

Liver ⟶ major site of drug metabolism.

Specific drugs may undergo ⟶ biotransformation in other tissues

Kidney ⟶ cannot eliminate lipophilic drugs, that readily cross cell membranes and are reabsorbed in the distal tubules.

*Lipid-soluble agents: must be first metabolized in the liver, using two phases:

Phase I:

This involves microsomal oxidation , non microsomal

oxidation , reduction and hydrolysis . Phase I reaction convert

lipophilic molecules into more polar molecules by introducing or unmasking a polar function group

Phase I metabolism may increase , decrease or uncharged the pharmacologic activity of the drug

Cytochrome P-450: iso-enzymes located in ⟶ cells of liver and intestinal tract.

Phase II: 2.

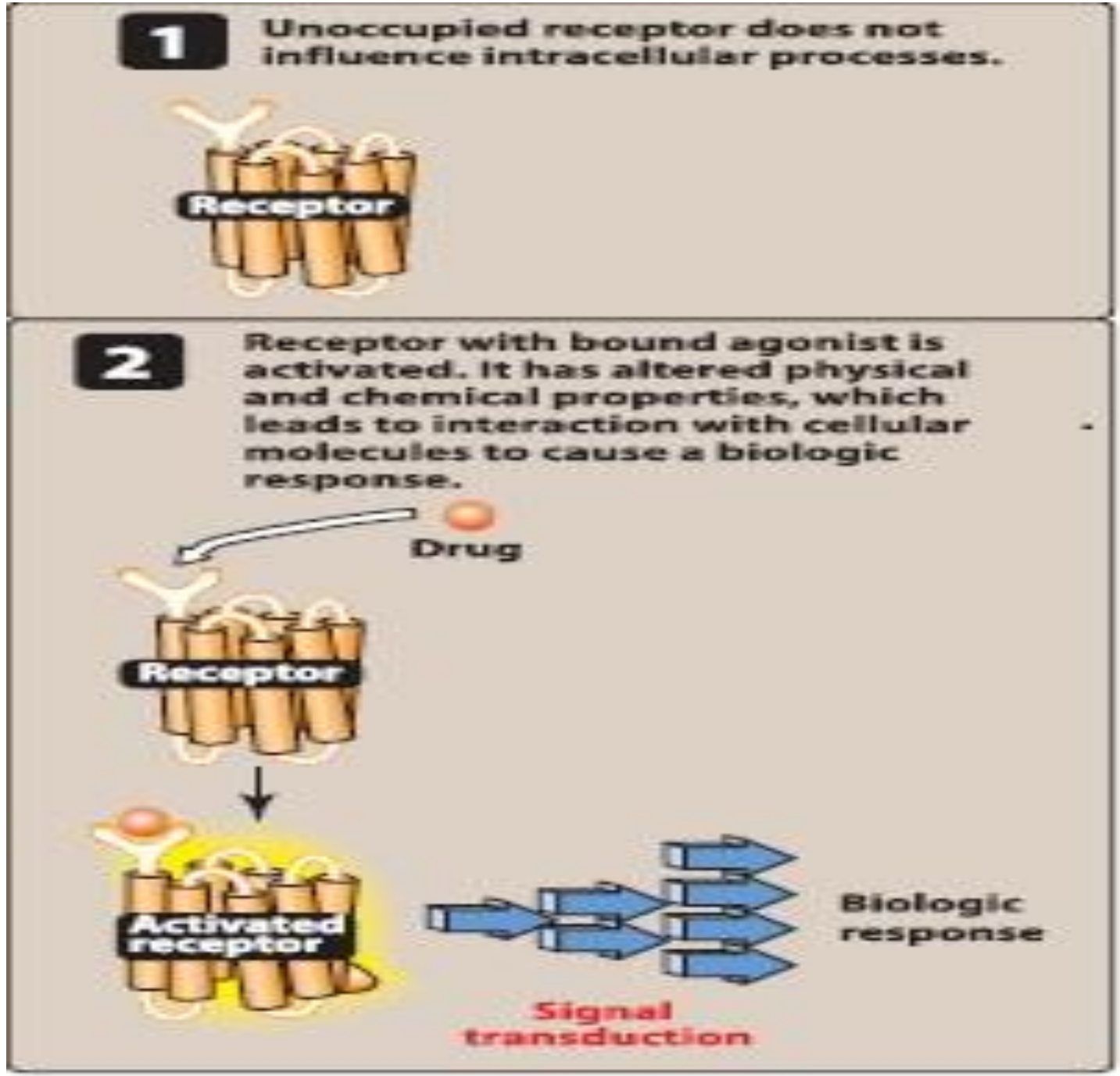
This phase consists of conjugation reactions. If the metabolite from Phase I metabolism sufficiently polar, it can be excreted by the kidneys. However, many Phase I metabolites are too lipophilic, so they are retained in the kidney tubules.

A subsequent conjugation reaction with an endogenous substrate, such as glucuronic acid, sulfuric acid, acetic acid, or an amino acid results in polar, usually more water-soluble compounds that are most often therapeutically inactive. These conjugated drugs are highly polar and may be excreted by the kidney or in bile

Pharmacodynamics

- **Pharmacodynamics** describes the actions of a drug on the body. Most drugs exert effects, both beneficial and harmful, by interacting with specialized target macromolecules called receptors, which are present on or in the cell.
- The drug-receptor complex initiates alterations in biochemical and/or molecular activity of a cell by a process called signal transduction

- the cellular response is proportional to the number of drug-receptor complexes
- Drug + receptor  drug- receptor complex  biological effect
- it is important to know that **not** all drugs exert effects by interacting with a receptor. Antacids, for instance, chemically neutralize excess gastric acid, thereby reducing stomach upset.


1
Unoccupied receptor does not influence intracellular processes.
Receptor
2
Receptor with bound agonist is activated. It has altered physical and chemical properties, which leads to interaction with cellular molecules to cause a biologic response.
Drug
Receptor
Activated receptor
Signal transduction
Biologic response

 Occurs when medication reaches the → target cell, tissue, organ and a therapeutic effect occurs.

Mechanism of drug action:

1. **Physical action:** alter the environment of the cell through physical action (Kaolin adsorbs toxins in → diarrhea).
2. **Chemical action:** alter the environment of the cell through chemical action (NaHCO3 in → hyperacidity).
3. **Cytotoxic action:** stop cell division (anti-cancer drugs)
4. **Interfere with selective passage of ions** (Ca+2 and Na+ entry → local anesthetics drugs)
5. **Interference with normal metabolic pathway** (Sulphon-amides competes with PABA → essential for bacterial growth).

6- Action on enzyme stimulation/inhibition:

enzyme inhibition could be:

- **Reversible:** short-term (Neostigmine → Cholin-esterase inhibitor).
- **Irreversible:** long-term for new enzyme synthesis (irreversible Anti-cholin-esterase).

7-Action on specific receptors (drug receptor interaction):

- Receptors: are macromolecular protein structures, present on → cell membrane / within the cell.

Graded dose-response relationship

- 1. **Potency**: is a measure of the amount of drug necessary to produce an effect. The concentration of drug producing 50% of the maximum effect (EC50).
- 2. **Efficacy**: is the magnitude of response a drug causes when it interacts with a receptor. Efficacy is dependent on the number of drug-receptor complexes formed and the intrinsic activity of the drug (its ability to activate the receptor and cause a cellular response)
- **Maximal efficacy of a drug (Emax)** assumes that the drug occupies all receptors, and no increase in response is observed in response to higher concentrations of drug .

Type of receptors according to efficacy

1. **Full agonists** If a drug binds to a receptor and produces a maximal biologic response that mimics the response to the endogenous ligand.
2. **Partial agonists** have intrinsic activities greater than zero but less than one ,Even when all the receptors are occupied, partial agonists cannot produce the same Emax as a full agonist

Antagonists

- **Antagonists** bind to a receptor with high affinity but possess zero intrinsic activity. An antagonist has no effect on biological function in the absence of an agonist, but can decrease the effect of an agonist when present.
- Antagonism may occur either by blocking the drug's ability to bind to the receptor or by blocking its ability to activate the receptor

Type of antagonist recptors

1. **Competitive antagonists**: If the antagonist binds to the same site on the receptor as the agonist in a reversible manner, example, the antihypertensive drug terazosin competes with the endogenous ligand norepinephrine at a1-adrenoceptors, thus decreasing vascular smooth muscle tone and reducing blood pressure.

- increasing the concentration of agonist relative to antagonist can overcome this inhibition

2. Irreversible antagonists bind covalently

to the active site of the receptor, thereby permanently reducing the number of receptors available to the agonist.

3. Allosteric antagonists: An allosteric antagonist binds to a site (allosteric site) other than the agonist-binding site and prevents receptor activation by the agonist.

4. Functional antagonism: An antagonist may act at a completely separate receptor, initiating effects that are functionally opposite those of the agonist.

A classic example is the functional antagonism by epinephrine to histamine-induced bronchoconstriction.

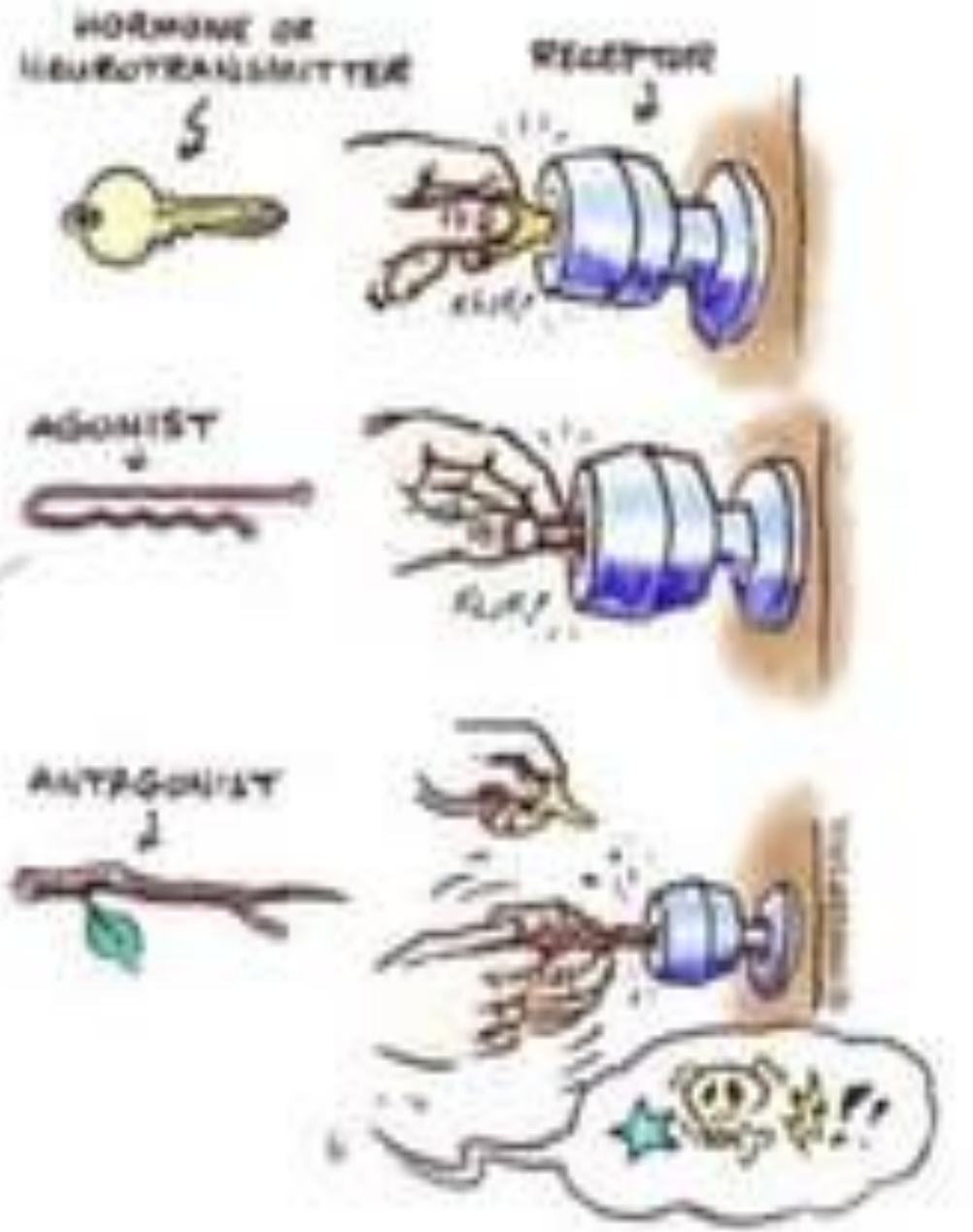
- Histamine binds to H1 histamine receptors on bronchial smooth muscle, causing bronchoconstriction of the bronchial tree. Epinephrine is an agonist at B2-adrenoceptors on bronchial smooth muscle, which causes the muscles to relax.
- This functional antagonism is also known as "physiologic antagonism."

Agonism and Antagonism

Agonists facilitate receptor response

Antagonists inhibit receptor response

(direct ant/agonists)



Thank you for listening

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