
النادي الطبي
Pharmacology
Subject : -
Lec no : 9
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للوصول الى guidance الفارما و تفاريغ المادة كاملة :

كل اعمال الفريق العلمي تنشر على قناة التيليغرام

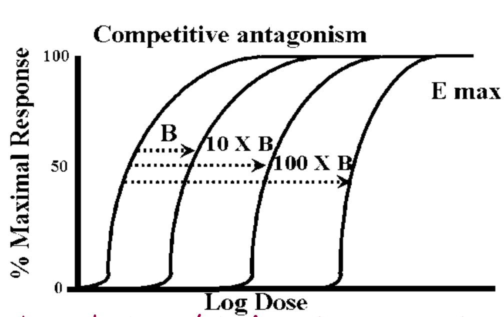
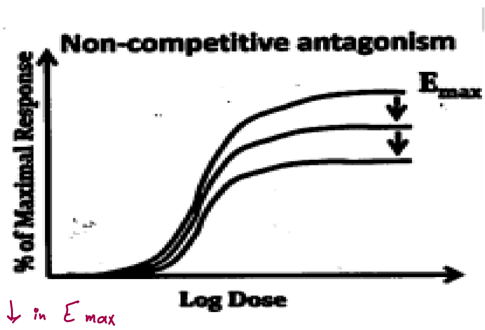
تجدون في guidance مادة الفارما على موقع النادي :

→ This drug doesn't have any effects on the cell it only blocks the agonest

→ blocks the agonest by taking its place on the receptor

2. Antagonist effect:

- Antagonist has: **1. Affinity** **2. No Efficacy** **3. Slow Rate** of ass. & diss.
  - Types of **receptor (pharmacological) antagonists:**

1- Competitive Antagonist	2- Noncompetitive Antagonist
• Antagonist ***competes with the agonist*** for the ***same recognition site*** of the receptor.	• Antagonist ***binds irreversibly with recognition site*** of the receptor ***or to an allosteric site*** (a site away from recognition site) to prevent binding of agonist with receptor or prevent activation of receptor by agonist
• ***Duration*** of antagonism depends on the relative ***plasma concentrations of agonist and antagonist.*** • Antagonist can be ***Displaced*** by excess agonist ***(surmountable)*** (Displacable)	• ***Duration*** of antagonism depends on ***synthesis of new receptors*** • Antagonist can ***Not*** be Displaced by agonist ***(non-surmountable)*** (غير قابل للإزاحة)
• Causes ***parallel shift to the right*** in the log dose-response curve i.e. ***No change in E_{max} but ↓↓ in potency (↑↑ in ED_{50})***	• Causes ***downward shift*** in the log dose-response curve with ***↓↓ in E_{max}***, ***but No change in potency (ED_{50})***
 → higher dose is needed of the drug as competitive antagonist ↓ potency	 ↓ in E max
• Examples: **Atropine** (muscarinic blocker) → Antagonist for Ach	• Example: **Phenoxybenzamine** (α – blocker)

→ Receptors become "non-functional"

→ Allosteric site: a site that is close to recognition site but they're not the same one

→ As the number of functional receptors decrease maximum response also decreases

→ potency remains the same

← بشكل عام ال Antagonist وظيفته انه يصعب حياة ال Agonist لكن الاسلوب الذي يتخذه ال Antagonist في تصعيب حياة ال Agonist هو الذي يختلف .

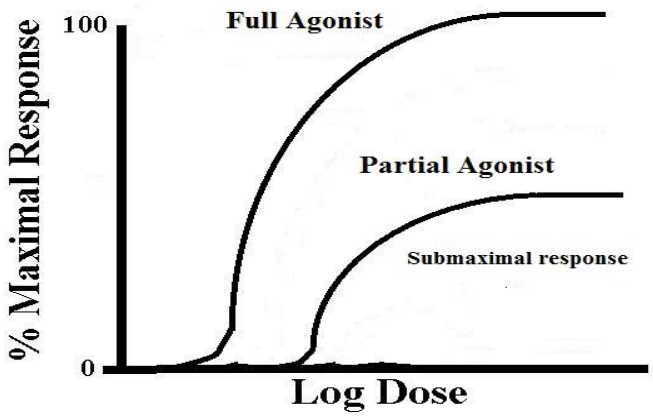
← عندك اسلوبين (1) Competitive Antagonist منافسة بين الاثنين على المستقبلات لهون مدة الاعاقة تعتمد على التراكيز كل ما كان تركيز ال Antagonist أعلى الإعاقة زادت؛ لكن الحل يكون في زيادة تراكيز ال Agonist حتى يجبر عندي displacment of antagonist

(2) Non competitive Antagonism هون ما عندي منافسة إلي بجبر إنه ال Antagonist يخرب المستقبلات ويخلي ال Agonist منها تماما و هون زيادة التراكيز ما إلها أي تأثير وحكي هذا الموضوع بحتاج انتاج مستقبلات جديدة لأنه الأصلية تم اتلافها .

3. Partial Agonist (Agonist-Antagonist)

- In absence of the agonist: it has:
  1. **Affinity**
  2. **Moderate efficacy (submaximal effect)** whatever its concentration.
  3. **Moderate or slow rate** of association & dissociation.

Won't reach the same E_{max} as a Normal Agonist



- In the presence of the agonist, it acts as an antagonist i.e blocks effect of agonist.
- e.g. **Buprenorphine:** In the absence of a pure agonist e.g. morphine, it exhibits analgesic effects. In the presence of morphine it acts as an antagonist reducing its analgesic effect.

→ Bupernorphine works as Analgesic in case there aren't another one Agonist but in case there are another agonist e.g Morphine. it will work as Antagonist

← يعني بشكل عام تأثيره لـ مسكن متوسط حالن اعطي لوحده وفي حال اعطي مع مسكن آخر يجعل تأثيره متوسط ايضا (حيث يصبح الـ Antagonist للمسكن الآخر)

Receptor Cycling or Turnover

- The number of receptors is not constant but the receptors are cycling (old receptors are internalized inside the cell and the new ones are externalized to the outside) and their number is continuously changing depending on the rate of recycling
- Binding of the **agonist** → ↓ number of receptors **[down regulation]** Decreasing the number of receptors
- Binding of the **antagonist** → ↑ the number of receptors **[up regulation]** Increasing the number of receptors

→ Agonist binding to Receptor Activating it (stimulating it) ↑ cellular Response After a while the cell starts to ↓ numbers of Reseptors in order to ↓ cellular response

→ Antagonist binds to a Receptor blocking it thus cellular response ↓ so the cell ↑ Receptors to ↑ cellular Response

2) Drugs acting on ion channels: drugs can modulate ion channels through:

Drug act directly on the ion channel:

- Voltage-gated ion channels: **Local anesthetics** (Na^+ channels). → Cells won't be able to generate AP
  → Those are ion channels that requires ATP to function
- ATPase-sensitive ion channels: **Oral hypoglycemics** (ATPase-sensitive K^+ channels in pancreatic β cells) — Low glucose drug that lowers glucose levels in the blood → used to treat Diabetes

Not directly:

- Ion channels modulated by G protein-linked receptors (2^{ry} messenger) — Drug → G protein ↓ 2nd messenger ↓ Cellular response (ion channels opening)
- Ligand-gated ion channels (ion channel-linked receptors) — Drug → Receptor

3) Drugs Acting on Enzymes: drugs can modulate enzyme through:

في الـbiotransformation أخذنا عن بعض الأدوية التي تأثر على الـ HME حيث تعمل induction أو inhibition لكن هنا كان كتأثير جانبي لذلك
← يعني المقصود بالإنزيمات هنا الانزيمات التي لها وظائف بالجسم غير التي تهضم الأدوية

→ Most drugs work by inhibition

- Activation of enzyme systems.
- Inhibition of enzyme:
  - Neostigmine inhibit cholinesterase enzyme → increase Ach. (The enzyme which breaks Ach)
  - Aspirin inhibits cyclooxygenase enzyme → decreases PGs synthesis

→ The are two types of enzyme inhibition:
1) Reversible — Neostigmine → Cholinesterase
2) Irreversible — OPC → Cholinesterase "Organophosphorus compounds"

4) Drugs Acting on carrier systems

- Drugs may affect carrier systems or transport processes in the plasmatic membrane. Examples:
  - **Digitalis** (e.g. digoxin) inhibit Na^+/K^+ ATPase pump in cardiac cell.
  - **Diuretics** (مدرات للبول) affect ions transporters in renal tubules

5) Drugs Acting on Subcellular Structures

(Organnels within the cell)

Microtubules (→ Components of the cell cytoskeleton): **Colchicine** disrupts microtubules inhibiting mitosis. (→ used to treat gout as it prevents mitoses of inflammatory cells)

6) Drugs Acting on the Genetic Apparatus

→ Works on nucleic acid

- **Aminoglycosides** inhibit **bacterial protein** synthesis.
- **Anticancer** drugs affect **DNA** synthesis or function.

→ Mechanism in which drug act doesn't require cellular response

7) Drugs Acting Physically:

- **Demulcents** (soothing): **bismuth salts** coat intestinal mucosa.
- **Lubricants**: **liquid paraffin** is used in constipation.
- **Adsorbent**: **Kaolin** in treatment of diarrhea

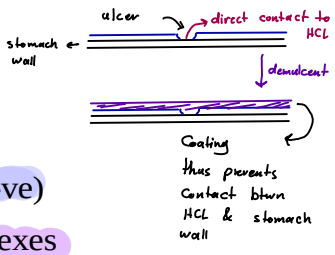
  Activated charcoal in treatment of drug toxicity

→ Used to relieve ulcer

↓

hole in the mucus membrane of the stomach

What demulcent dose is to coat this hole & thus prevents (HCL) from reaching under the mucus membrane (preventing pain)



8) Drugs Acting Chemically:

We basicly are making salts as when nutralizing an acid we give base those two compine & nutralize each other & the resault is salt

Acid + Base

a. Neutralization: - **Antacids** neutralize HCL in peptic ulcer.

- Protamin sulfate (basic, +ve) for toxcicty of heparin (acidic, -ve)

b. Chelation; is the capacity of organic compounds to form complexes with metals (chelates). The chelate may become more water-soluble and easily excreted. It is useful in treatment of heavy metal poisoning e.g. **EDTA** for lead & calcium) - **Deferrioxamine** for iron

→ Chelation Organic compound that works by making complexes with metals