

تفريغ فارما ١

اسم الموضوع: *Lec 5*

إعداد الصيدلاني / *Farah Aljundi*



4. Intracellular receptors

- The ligand must diffuse into the cell to interact with the receptor
- Drug factors are crucial
- Upon binding its target, the drug-receptor complex stimulate a transcriptional factor to induce certain genes.
- Response occurs in hours to days
- Example : Steroids

thyroid hormone.



e.g. : Salbutamol (ventoline)
 - beta₂ agonist → bronchodilation / with side effect (rise in heart rate)
 adrenergic
 - beta blockers → bronchoconstriction.

Signal transduction

➤ Signal amplification :

- More than one G-protein may be activated
- Secondary messenger activation lasts for long time

The end result is an amplified response

➤ Desensitization and down-regulation of receptors

- Chronic exposure of the ligand to the receptor leads to its downregulation (as a protective mechanism).
- Receptor expression may be reduced or it may be engulfed by endocytosis.

تضخيم

الاستجابة المتضخمة

عدم الاستجابة

لأن التعرض المستمر للليجند للجسم عن طريق الاتصال
للـ toxic

* antidote

Receptor desensitization

- Also termed as down regulation
- Prolonged exposure of receptors to agonists
- Common consequence in clinical practice
- May occur only for a particular agonist (homologous desensitization) or
- To more than one agonist (Heterogenous Desensitization)
- Associated with tolerance to drugs : as in BDZ and morphine
Benzodiazepine

Agonist/ Antagonist

- “Drugs that bind to physiological receptors and mimic the regulatory effects of the endogenous signaling compounds are termed ***agonists***”
- “Drugs bind to receptors without regulatory effect, but their binding blocks the binding of the endogenous agonist are termed ***antagonists***”

Partial Agonist/Inverse Agonist

- Agents that are **only partly as effective as agonists** no matter the amount employed are termed **partial agonists**

بعض ما يزيد أو لا Dose مع تغير التأثير
بعض effect به ما يصل 100%

- and those which **stabilize the receptor in its inactive conformation** are termed **inverse agonists**

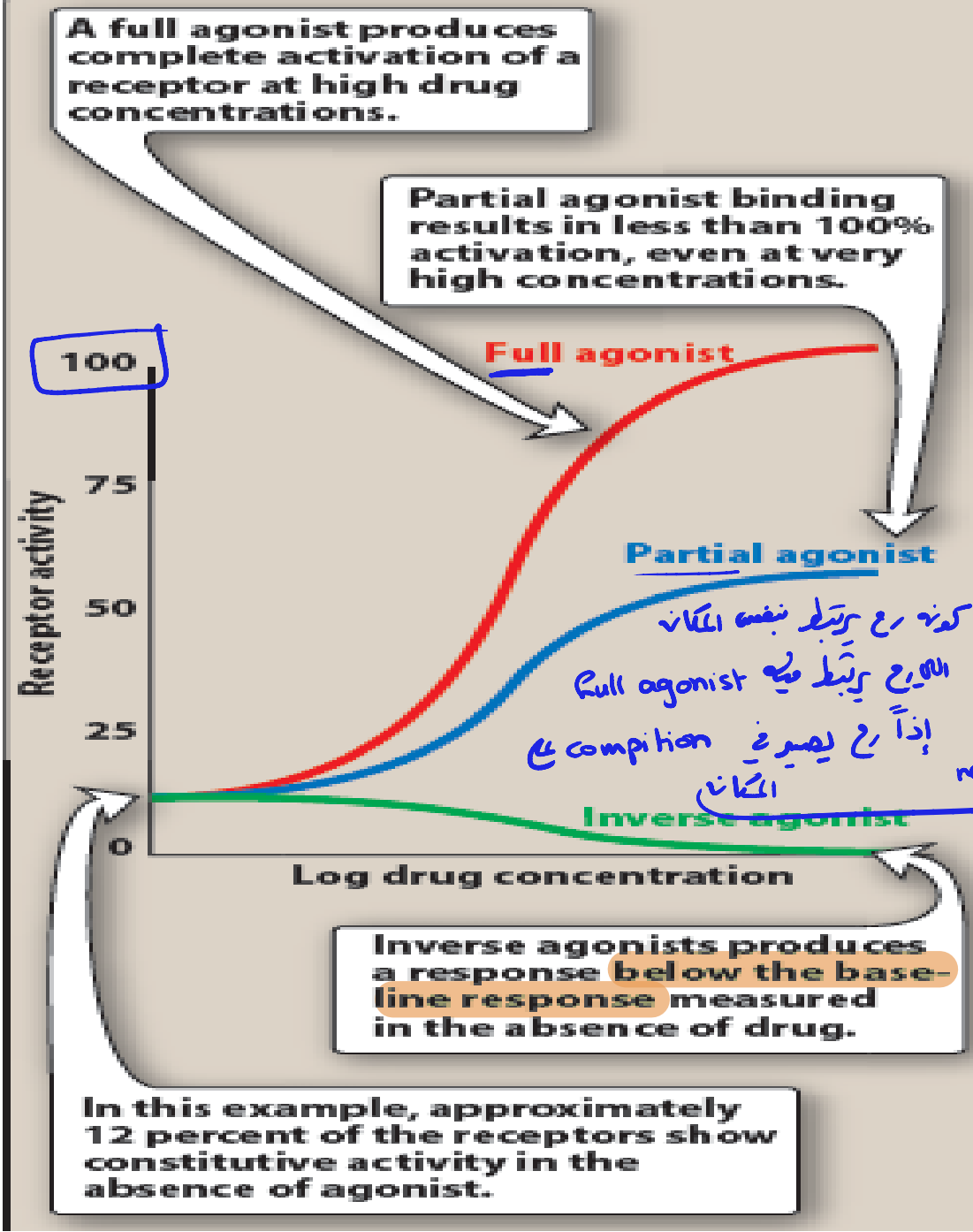
بكون نزلت ال consistence activity
له بعض تأثير أقل من التأثير العادي (الطبيعي)
ليس مسبقا كونه صفر وتفسير
بار minus !

🤔 شوية منع



Partial Agonist

- ❑ combine with receptors and activate them, but are incapable of eliciting a maximal response, no matter how high their concentration may be.(low efficacy)
- ❑ Ex: **buprenorphine** (a **partial agonist** at morphine mu-receptors)
- ❑ partial agonists antagonize the effect of a full agonist sine they both compete for the same receptor



كثرة ربح يرتبط بنفس المكان
الربح يرتبط فيه Full agonist
إذا ربح يصير في competition مع المكان

∴ بالتالي ربح يقل التأثير لدرجة صفر
عند Full agonist
أكثر ارتباط receptor

Antagonism

بعضلة أو بالكملة

Competitive Antagonist

- Compete with Agonist on the same receptor (reversible)

Examples : Famotidine Vs histamine on H₂ receptors

- Increasing Comp. Agonist dose decreases Antagonist effect

إبطال مفعول

Non competitive Antagonist

- Does not compete with Agonist
- Bind irreversibly, to receptor

Example :
phenoxylbenzamine on adrenaline receptors

تزيد جرعة واحد منهم
بغالب عائلتي

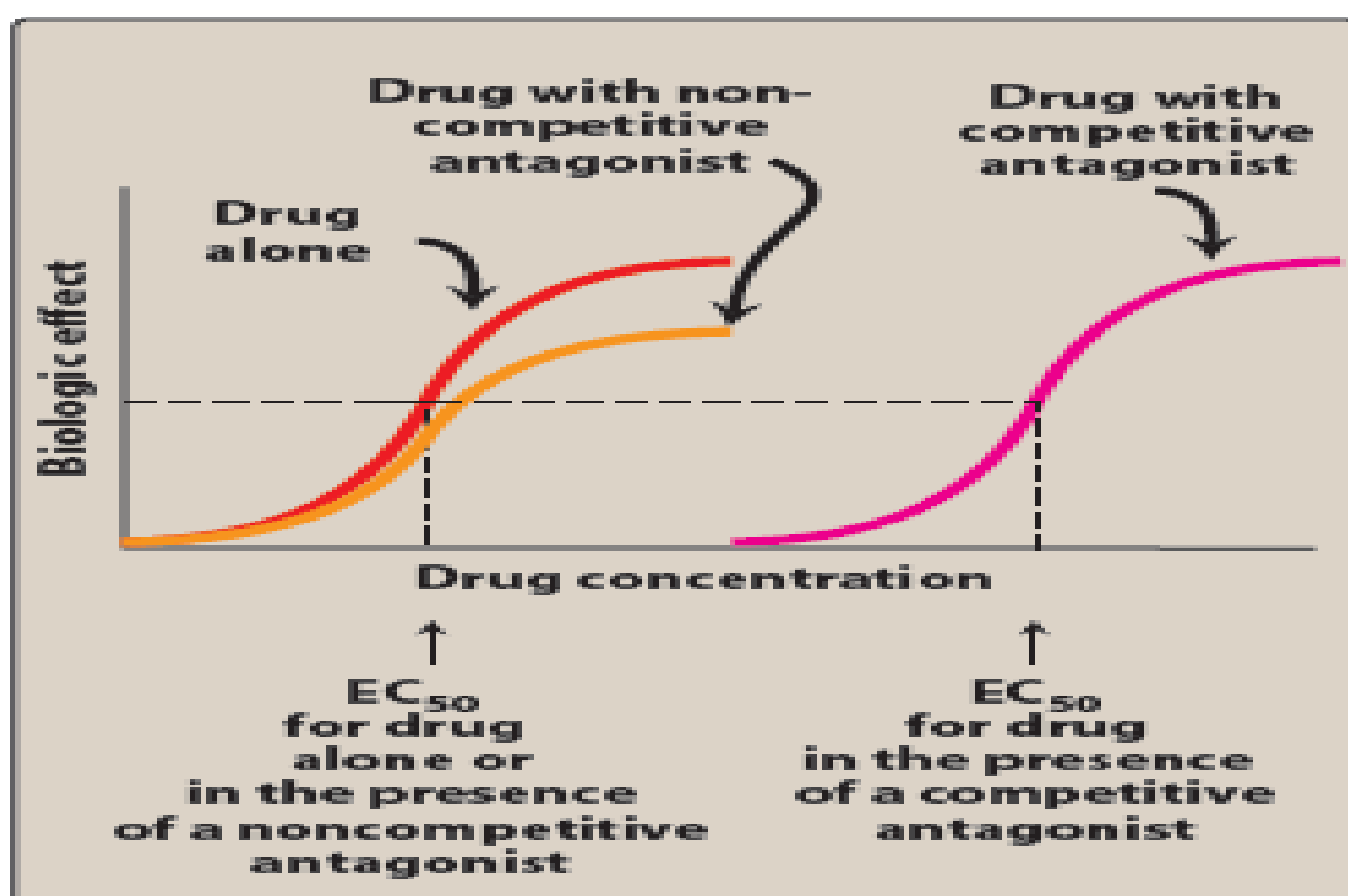


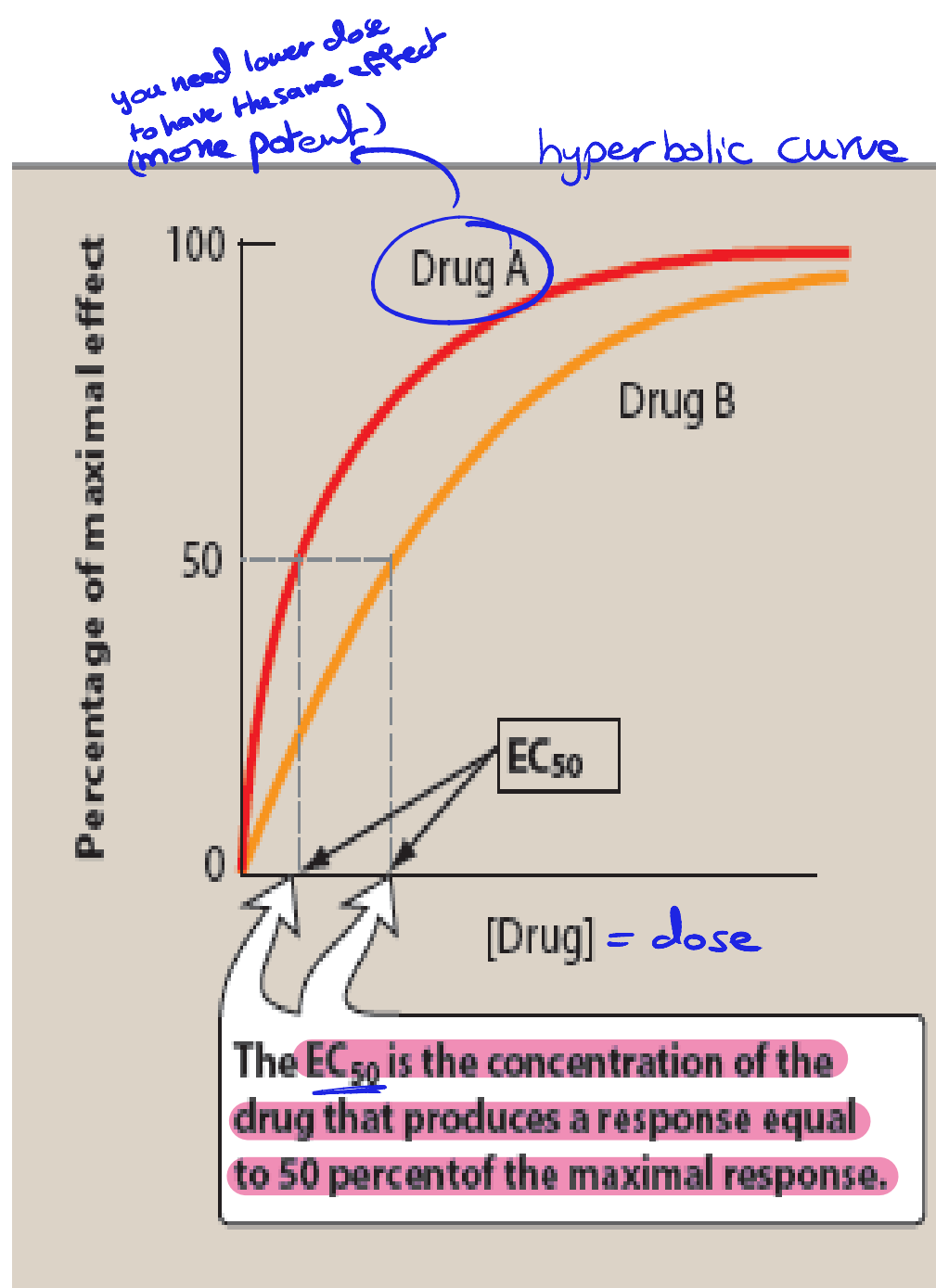
Figure 2.12

Effects of drug antagonists. EC₅₀ = drug dose that shows 50 percent of maximal response.

DOSE–RESPONSE RELATIONSHIPS

1. Graded dose–response relations

- As the concentration of a drug increases, the magnitude of its pharmacologic effect also increases
- The response is continuous and gradual بمعدل تدريجي
- A graded dose–response curves can be used to determine :
 - Drug Potency → dose مقدار الدواء
 - Drug Efficacy → response الاستجابة



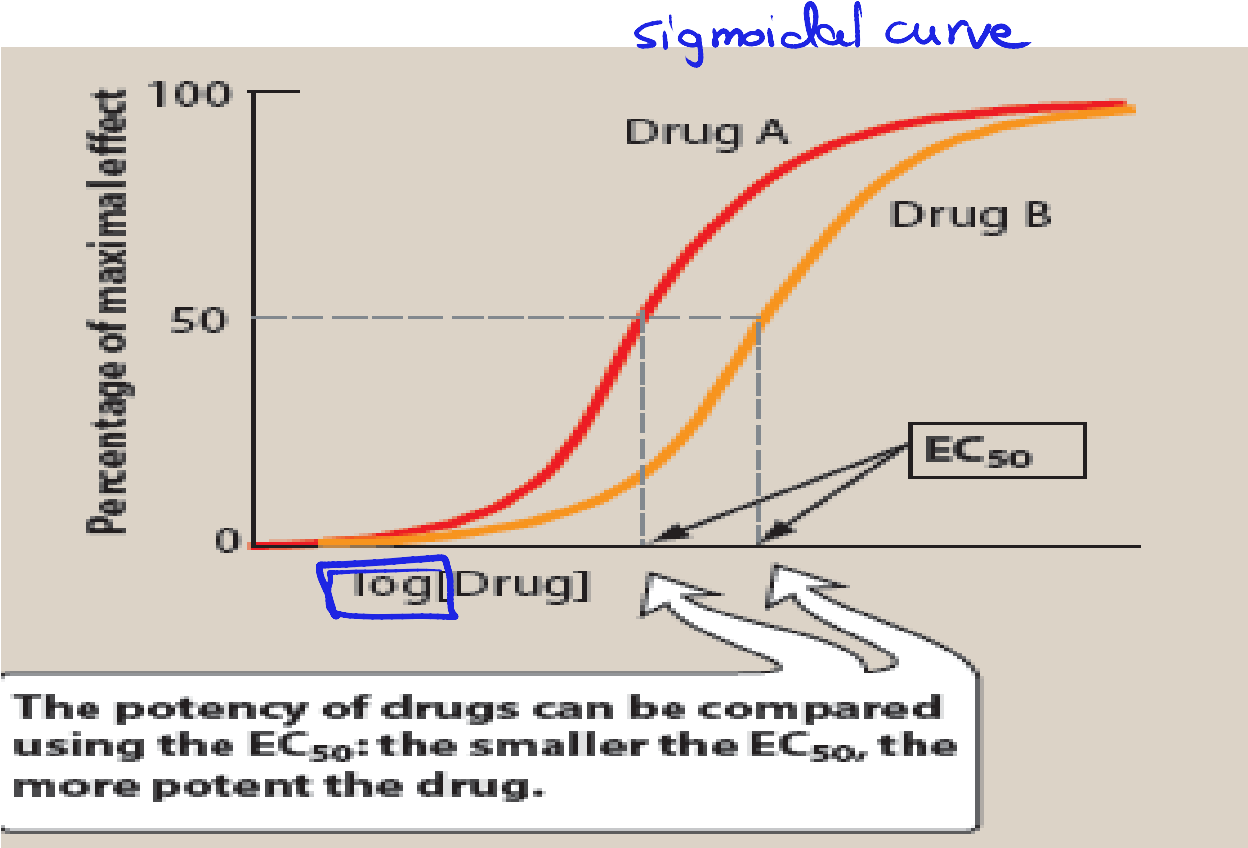
Graded dose-response curve:

- Shows gradual increase
- EC₅₀ can be determined (potency)
- Also Efficacy can be determined

پختہ

Potency

- “A measure of the **amount of drug** necessary to produce an effect of a given magnitude.”
- The concentration of drug producing an effect that is 50 percent of the maximum is used to determine potency and is commonly designated as the EC50



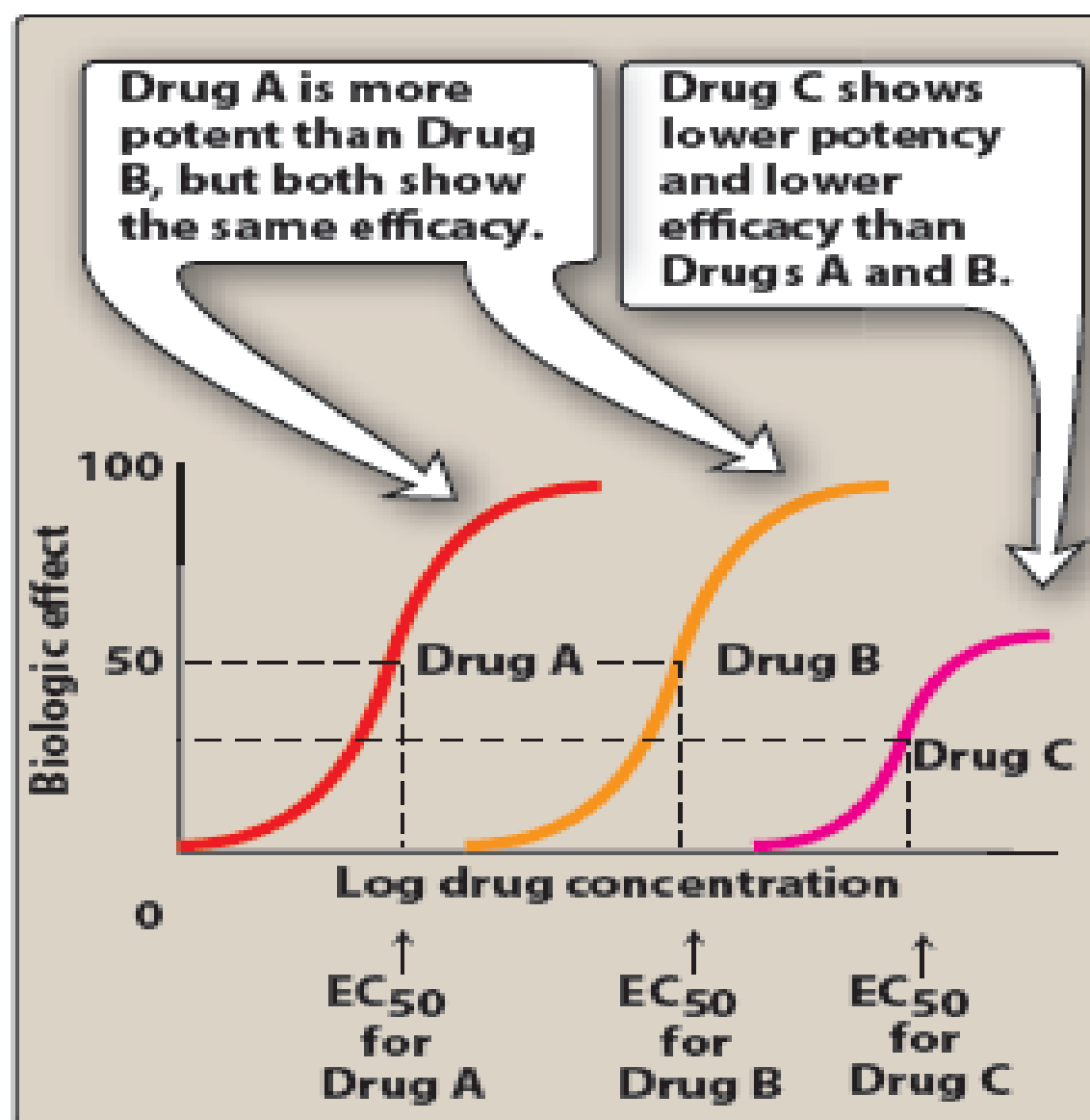
Efficacy

خوفاً و كذا

قد نسي ما دار الدواء بطلين تاشي
لا يرتبط بال receptor

- “The ability of a drug to elicit a **response** when it interacts with a receptor”
- Efficacy, is more important than drug potency. A drug with greater efficacy is more therapeutically beneficial than one that is more potent.
- Efficacy deals with drug ability to bind receptor and exert a clinical response

رنا لا ندر نفينا
ارتنا ندر ما نفينا
در dose



Efficacy(E_{max})

Non receptor mechanisms

- No specific biological receptor
- Based on properties of the drug(chemical)
- EX :antiacids, osmotic diuretics

