3rd lec: pharmacodynamics II NO Date

- Relation () drug dose + clinical response exhibited as:

Ⓐ Graded dose_response relationships (individual)

Ⓑ Quantal dose_response relationships (population) = all or no response

- In this lec we will discuss Ⓐ:

The magnitude of drug effect depends on [Drug] in receptor site

graded dose_response curve is rectangular hyperbola

by this curve we can determine → potency
→ efficacy
of drug

- potency measure of the amount of drug neccessary to produce an effect of a given magnitude

EC50 is used to determine potency

amount of drug that is needed $\propto \frac{1}{\text{potency}}$

potency is affected by

[Receptor] | efficiency of S_R mechanism | Affinity

affinity ∝ potency

Efficacy

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Causes of variation in pharmacological responsiveness.

1_ varity in [drug] that reaches receptor

2_ Abnormality in num of receptor or function

3_ post receptor defect inside cells

4_ [endogenous receptor ligands]

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Receptor Regulation

Receptor up regulation: ↑num of receptors /↑affinity of specific receptors **(receptors supersensitivity)** occurs by:

① prolonged use of receptor antagonist

② Disease : e.g **hyperthyrodism**

Receptor down regulation (Receptor tolerance): ↓num of receptors/↓affinity of specific receptors ; **prolonged occupation by agonist.**

the dose of agonist must be increased to restore the intinsity of response

* **Tachyphylaxis** : rapidly developing receptor **tolerance** ; repeted use of large doses of direct receptor agonist at short intervals / Intra_venous injection of agonist

causes:

① Desensitization of receptors

② Depletion of intra_cellular stores of transmitter

to restore response stop agonist drugs for short time

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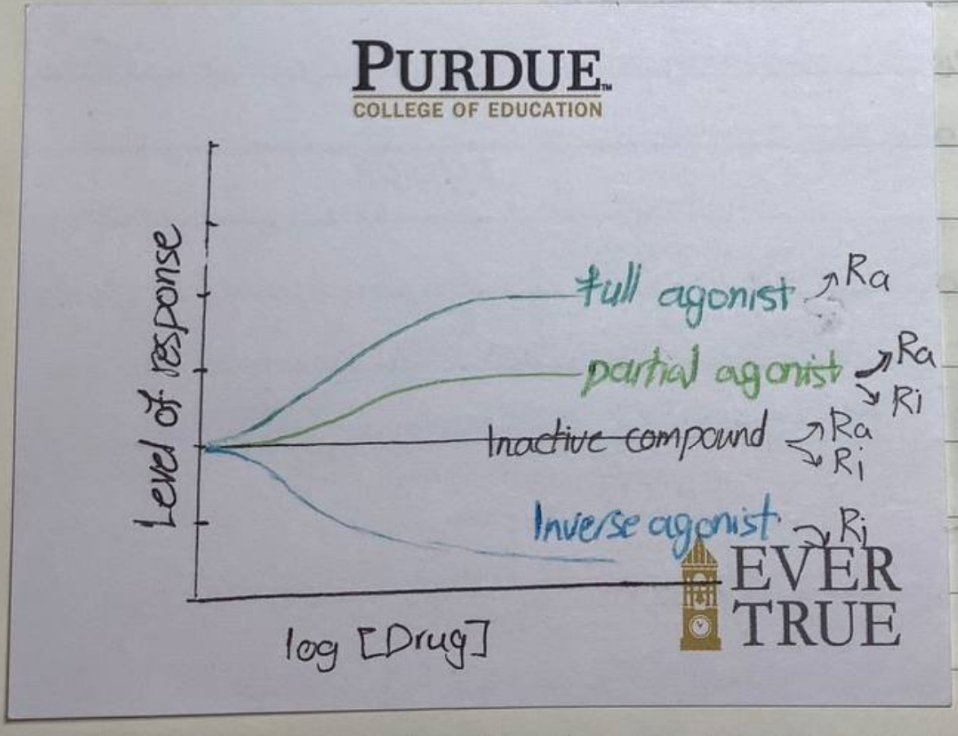
- Efficacy the ability of drug to elicit a response when its intract with receptor

Efficacy depend on → num of drug-receptor complexes form
→ cellular responses of receptor activation

* Drug + Receptor ⟷ Drug receptor complex → Biologic effict

* [drug] ∝ [bound receptors] / [Total receptors]



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Antagonist block the receptor

chemical
- alkaline antacids
- protamine
- chelating agents

physiological
different receptor
- agonist: histamine
- physiologic antagonist: Adrenaline
- condition: anaphylactic shock

pharmacological
- competitive reversible ✱
  - Drug Response curve to Rt
- Non competitive
  - irreversible DRC to Rt ~~↓~~
  - Allosteric antagonism ~~↓~~
  - dont confuse with enhancement
- Uncompetitive ~~↓~~
  - antagonist bind to different receptor so the effect of agonist blocked. ~~specificity~~

chemical: comines with agonist + inactivate it away from r

physiological: agonist in same tissue produce opposite effect...

pharmacological: have affinity for the receptor but have no intrinsic activity or efficacy

✱ compitive antagonists examples:

1_ Agonist: Ach / Antagonist: atropine at muscarinic receptors

2_ Agonist: Adrenaline / Antagonist: Beta blockers at adrenergic receptors