Introduction to Pharmacodynamics

University of Hawai‘i Hilo Pre-Nursing Program
NURS 203 – General Pharmacology
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Learning objectives

- Understand the characteristics of the dose-response curves
- Understand the characteristics of the concentration over time curves
- Understand the terms efficacy, potency, affinity and spare receptors
- Know what agonists are and their different types
- Know what antagonists and their different types
- Know the importance of therapeutic window and the characteristics of a narrow and wide index
What is pharmacodynamics?

- Pharmacodynamics: The effects of the drugs on the body
- We are going to be focusing on the following:
  - Receptors and receptor sites
  - Dose-response curves
  - Concentration over time curves
  - Efficacy, potency, and spare receptors
  - Agonists and different types of agonists
  - Antagonists and different types of antagonists
  - Therapeutic window
  - Cell signaling and receptor regulation
Receptors

- Receptor: A molecule to which a drug binds to bring about a change in function of the biological system

- Receptors are:
  - Selective

- Receptors must:
  - Conformational change
Starting the process – after the drug binds receptor

Drug binds

Conformational change

Effector: A molecule that translates the drug-receptor interaction into a change in cellular activity.

- Not always just an on/off switch
- Effectors can play a role
  - Enzymes
    - Adenylyl cyclase
    - Tyrosine kinase
  - Ion channels
Drug dose and binding – Graded Dose response curve

- Percentage of receptors bound
  - Affinity
    - $K_d$
  - $B_{MAX}$
    - Maximum receptors bound
- Drug dose
- Potency & efficacy parameters
  - $ED_{50}$ (or $EC_{50}$)
    - Effective dose/effective concentration
  - $E_{MAX}$
    - Maximum efficacy

Drug dose increases as you go to the right
Which drug has a higher affinity? Which drug has a higher Kd?
Which drug is more potent?
1. At even low doses, some patients respond

2. Here is the dose where 50 percent of patients respond

3. Eventually most will respond

4. Toxic effects increase

5. Patients begin to die

6. Eventually most will die
Spare receptors

- Spare receptors exist when $E_{\text{MAX}}$ is achieved before $B_{\text{MAX}}$
  - May be due to
    - The effect of the drug is longer than the period of time the drug and receptor are bound
    - There are more receptors than effector molecules

- Spare receptors keep us safe from grizzly bears.
Agonists and Antagonists

- Introduction: Receptors at rest
  - Inactive
  - Active
  - Equilibrium
Agonists

- Constitutive activity
  - Effects when no substance present
- Full agonist
  - Exerts full receptor effects
  - Active state
- Partial agonist
  - Exerts less than full receptor effects
  - Active state > Inactive state
- Inverse agonist
  - Less activity than when receptor not being acted on by substance (constitutive activity)
  - Inactive state > active state
Antagonists

- Competitive
  - Reduced agonist effect but can be overcome by agonist dose
- Irreversible
  - Completely blocks receptor site
- Physiological
  - Antagonism through a different receptor
- Chemical
  - Intercept an antagonist
  - No receptor used
Antagonists

- Allosteric
  - Non-competitive
  - Could also be an agonist
Summary – Agonists and Antagonists
Therapeutic Index/Window

- Therapeutic window
  - Dose range between which a drug becomes effective and is not yet too toxic
  - Narrow or wide

Therapeutic window

- Peak of effect
- Side-effect
- Adverse response
- Therapeutic window
- Desired response
- Duration of action
- Sub-therapeutic
Therapeutic Window - Wide

- Relatively Wide
Therapeutic Window - Narrow
Cell signaling – The Effector

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Receptor Regulation

- Tachyphylaxis: Decrease in receptor response
  - Internal change to the receptor
  - Internalization of the agonist bound receptor
  - Depletion of downstream substances needed for activity
- Up-regulation: Increase in receptor number
- Down-regulation: Decrease in receptor number
Up/Down - regulation
Drug Nomenclature

- Chemical names
  - Atomic or molecular structure

- Brand names
  - Also known as the trade name
  - Copyright ®
  - Given by the company selling the drug product
  - One drug can have multiple trade names

- Generic names
  - Nonproprietary
  - Abbreviation of chemical name
Questions