University of Basrah\College of Nursing
Branch of Basic Sciences
Pharmacology for Nurses1 (1st course)
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# Basic concepts and processes in Pharmacology

## Pharmacodynamics

**Objectives:** Upon completion of this lecture, student will be able to answer the following questions:

1. Define the pharmacodynamics and discuss the mechanism of drug action.
2. What are factors that determine how an individual will respond to a specific drug and dosage.
3. Define the types of adverse effects of drugs and describe the adverse effects of drugs in general.
4. Describe various drug interactions: Drug-drug interactions and Drug-food interactions.

**Pharmacodynamics:** The study of the biochemical and physiologic effects of drugs and the molecular mechanisms by which those effects are produced (mode of action of drugs). There are varied and complex physiological systems that control bodily functions (homeostasis). Drugs exert their effect by acting on those physiological systems

**Pharmacodynamics:** derived from two Greek words: **Pharmakon** = "Drug" **dynamics** = "change" (drug action)

In short, pharmacodynamics is the study of what drugs do to the body and how they do it.

***Drug action*** is the mechanism by which drug exerts its effects.

***Drug effect*** is the biochemical or physiological changes result from drug action – drug responses or effects observed when the drug is administered.

E.g., drug act on vascular smooth muscle and cause relaxation (drug action) → cause vasodilation and hypotension (drug effects).

## Mechanism of drug action:

1) **Receptor:** Most of the drugs act by interacting with receptor → **Receptor drug interactions**. These drugs act on the body by **altering cellular function**. A drug can modify cell function or rate of function, but it cannot impart a new function to a cell or to a target "drugs can only alter the rate of pre-existing processes".

Receptors are any functional macromolecules in a cell to which a drug binds to produce its effects. Receptors may be found on membrane, within membrane, on

inner surface of membrane or within a cell on which natural hormones and neurotransmitters can bind to and cause a specific effect.

In order for a drug to act at a specific receptor site, it must have a complementary structure to the receptor – sometimes referred to as a 'lock and key' action. When drugs bind to receptors they can do one of two things: they can either mimic the action of endogenous regulatory molecules – cause an effect called agonists or they can block the action of endogenous regulatory molecules called antagonists.

Drug (Ligand) + Receptor ↔ Drug–receptor complex →Biologic effect → **Response**

2) Some drugs **act through simple physical or chemical reactions** – Non receptor – drug interactions:

These drugs produce their therapeutic effects on the body by **changing the cellular environment** through nonspecific chemical or physical interactions without receptor interactions include changes in osmotic pressures, lubrication or PH. Common examples include antacids. Antacids neutralize gastric acidity by direct chemical interaction with stomach acid.

3) **Interference with ion channels** – some drug act directly on ion channels and alters their function. E.g., local anesthesia act by block $Na^+$ channels
4) **Alteration of the enzymes activity**. An enzyme is a protein which acts as a catalyst that also controls many body activities. The action of a drug depends upon the role of the enzyme it affects - which can promote or accelerate biochemical reactions. e.g., inhibition of angiotensin converting enzyme by Captopril drug.
5) **Carrier or transport mechanisms**: drugs act by interfering with passage of molecules across the cell membrane - acting as carrier inhibitors.
   e.g., digoxin, which blocks the sodium pump in the heart, and omeprazole, which blocks the potassium pump in the gastric mucosa.
6) Interfering with cell growth and division e.g., Cancer drugs
7) Interfering with the cell processes of invading microorganisms e.g., Antibiotics

## Affinity and Intrinsic activity of the drugs:

### Affinity:

### Intrinsic activity

Drugs with high intrinsic activity have high maximal efficacy. That is, by causing intense receptor activation, they are able to cause intense responses. Conversely, if intrinsic activity is low, maximal efficacy will be low as well.

**Agonists:**

Agonists have two main properties:

1) **Affinity:** the ability of the agonist to "bind to" the receptor
2) **High intrinsic activity** or Efficacy: the ability to cause a response via the receptor interaction

**Full agonist:** can elicit a maximal effect at a receptor.

**Partial agonists** also mimic the actions of endogenous regulatory molecules, but they produce responses of intermediate intensity – have only moderate intrinsic activity and reduced efficacy as compared with full agonist.

**Antagonists:** Antagonists have:

1) **Affinity** for a receptor (can bind with receptors) but
2) **Little or no intrinsic activity**, (no efficacy).

## Receptors and selectivity of drug action

1. **Selective drug**
2. **Nonselective drug**

**Receptor Regulation**: Receptors are dynamic cellular components that can be synthesized by body cells. In response to continuous activation or continuous inhibition, the number of receptors on the cell surface can change.

1. **Desensitization or receptor down-regulation:**

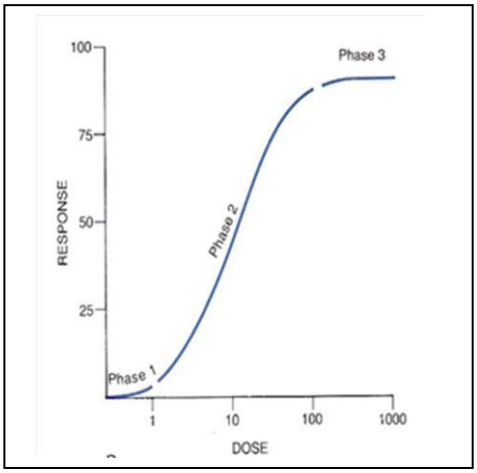
**Tachyphylaxis**

**Tolerance**.

2. **Receptor up-regulation:**

## Dose–Response curve

Dose-response curve represent relationships between the size of an administered dose and the intensity of the response produced. The dose-response relationship is a fundamental concern in therapeutics.




The most obvious and important characteristic revealed by these curves is that the dose-response relationship is graded.

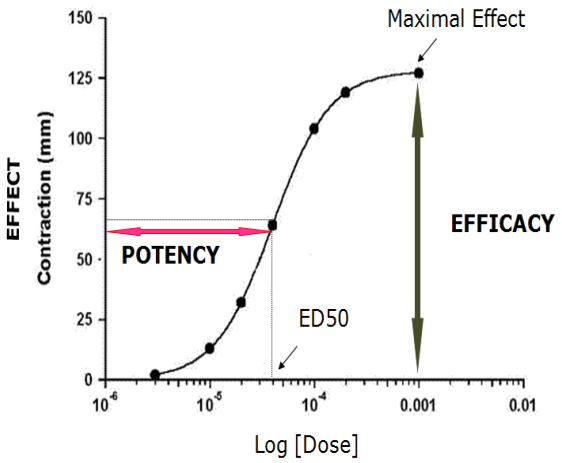
The graded nature of the dose-response relationship is essential for successful drug therapy. That is, as the dosage increases, the response becomes progressively larger. Because drug responses are graded, therapeutic effects can be adjusted to fit the needs of each patient. ⇒ all we need to do is raise or lower the dosage until a response of the desired intensity is achieved.

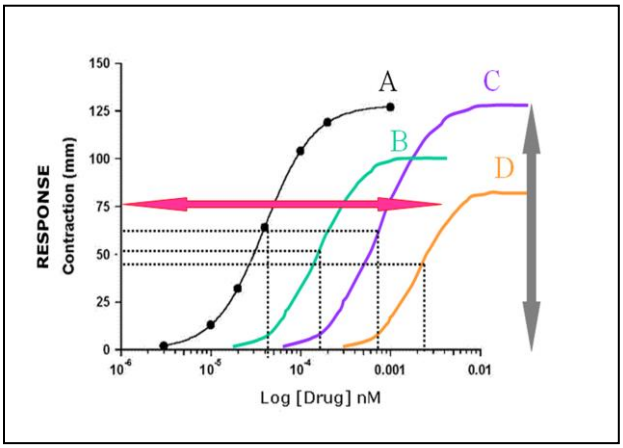
**Dose-response curves reveal two characteristic properties of drugs:**

**Maximal Efficacy** is defined as the largest effect that a drug can produce. Maximal efficacy is indicated by the height of the dose-response curve.

**Relative Potency** refer to the amount of drug we must give to elicit an effect. Potency is indicated by (dosage).

E.g. if Drug A causes a greater maximum intensity of response than Drug B (regardless of dose), ➔➔ Drug A is more efficacious than Drug B.




**Rank order of efficacy: A = C > B > D**

**Rank order of potency: A > C > B > D**

**A potent drug is one that produces its effects at low doses**

## Factors that determine the intensity of drug responses

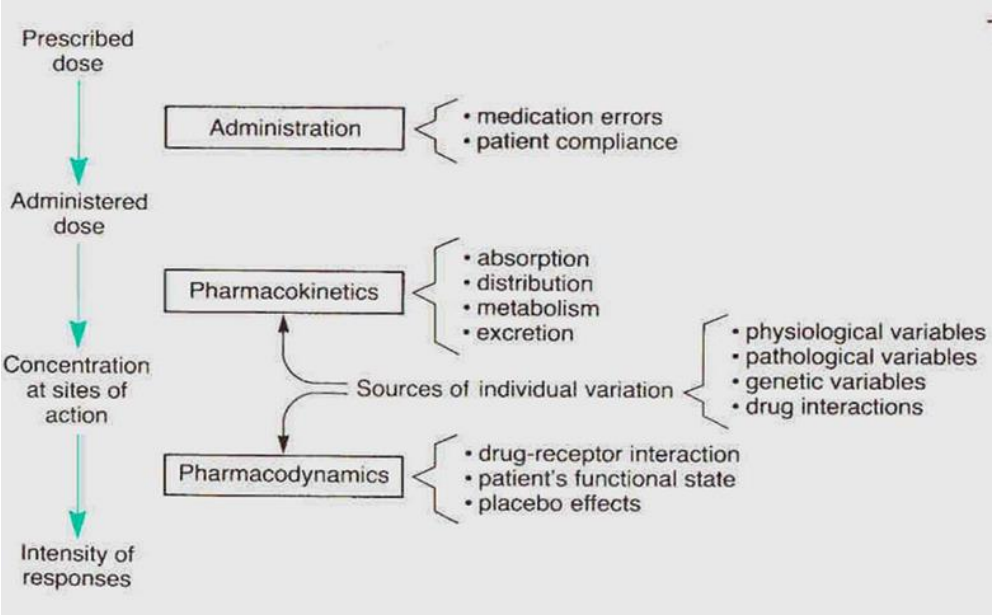
Multiple factors determine how an individual will respond to a prescribed dose of a particular drug

### 1. Administration

Dosage size, the route and the timing of administration are important determinants of drug responses. Accordingly, the prescribing clinician will consider these variables with care.

Unfortunately, drugs are not always administered as prescribed: **poor patient compliance and medication errors** by health care providers can result in major discrepancies between the dose that is prescribed and the dose that is actually administered. Such discrepancies can significantly alter the outcome of treatment. To help to minimize errors caused by poor patient compliance, you should give patients complete instruction about their medication and how to take it.

Medication errors made by health care providers may result in a drug being administered by the wrong route, in the wrong dose, or at the wrong time; the patient may even be given the wrong drug. Any of these errors will detract from achieving the therapeutic objective.




2. **Pharmacokinetics**: 1) drug absorption 2) drug distribution 3) drug metabolism 4) drug excretion

3. **Pharmacodynamics**

Once a drug has reached its sites of action, pharmacodynamic processes determine the nature and intensity of the response.

- **Drug – receptor interaction**:
- **Patient's functional state** can influence pharmacodynamic processes. e.g., a patient who has developed tolerance to morphine will respond less to a particular dose than will a patient that lacks tolerance.
- **Placebo (psychological) effects** also help to determine the responses that a drug elicits.

**"Placebo"** is a drug dosage form, such as a tablet or capsule, that has no pharmacologic activity because it contains no active ingredients. When taken, the patient may report a therapeutic response. This response can be beneficial in patient's being treated for illnesses such as anxiety, because the patient tends to take fewer potentially habit-forming drugs

4. **Individual Variations in Drug Responses**: Variables that affect drug action. Many factors that can cause one patient respond to drugs differently than another. When you know these factors, you well be better prepared to reduce individual variation in drug responses, thereby maximizing the benefits of treatment and reducing potential for harm.

   1) **Physiological variables**
      **Body weight and composition:** Dosages must be adapted to size. The "body surface area" calculation is better than body weight because it takes into account weight as well as percentage of body fat.
      **Age:** Infants very sensitive to drugs: due to organ immaturity and/or receptor numbers on cells – Elderly very sensitive to drugs-due to organ system degeneration (decreased metabolic inactivation and receptor number)
      **Gender**: Response is different to same drug and dosage between men and women – due to hormonal differences, Some drug more effective in men, other more effective in women – Until recently, all drug research done in males
   2) **Pathological variables** (especially diminished function of the kidneys and liver, the major organs of drug elimination)
   3) **Genetic variables:** Genetic factors can alter the metabolism of drugs and can predispose the patient to unique drug reaction. Genetic variations can result in ↑or↓ metabolism of certain drugs.
   4) **Drug Interactions**

## Self-assessment

- What are mechanisms of drug action?
- What are Affinity and Intrinsic activity of the drugs?
- What are Agonists and Antagonists drugs?
- What is Receptor Regulation?
- What is up regulation and down regulation of receptors?
- What is the Dose–Response curve ?
- What are factors that determine the intensity of drug responses?