Introduction

Pharmacology

- **Definition:**

  is the science which deals with drugs

- **Drugs:**

  Are chemical substances which increase or decrease the functional activity of a cell, but do not create a new function

- **Sources of Drugs:**

  1- Inorganic: → • **Iron**

  2- Organic: (A) Animal origin → • **Insulin** • **Heparin**

  (B) Plant origin → • **Atropine** • **Morphine**

  3 Synthetic: → • **Sulphonamides** • **Antibiotics**

  4 Microorganisms: → • **Penicillin** • **Streptomycin**

Branches of Pharmacology

1. Pharmacodynamics
2. Pharmacokinetics
3. Pharmacotherapeutic
4. Pharmacognosy
5. Clinical Pharmacology
6. Immunopharmacology
7. Pharmacogenomics
8. Drug toxicity

Types of Drug Action

Before it enters circulation	**1- Local action**
After it enters circulation	**2- Systemic action**
On **remote** site of action as **Camphor** (S/C)	**3- Reflex (Remote)**
On **specific** site of action as **Digoxin** on heart	**4- Specific action**

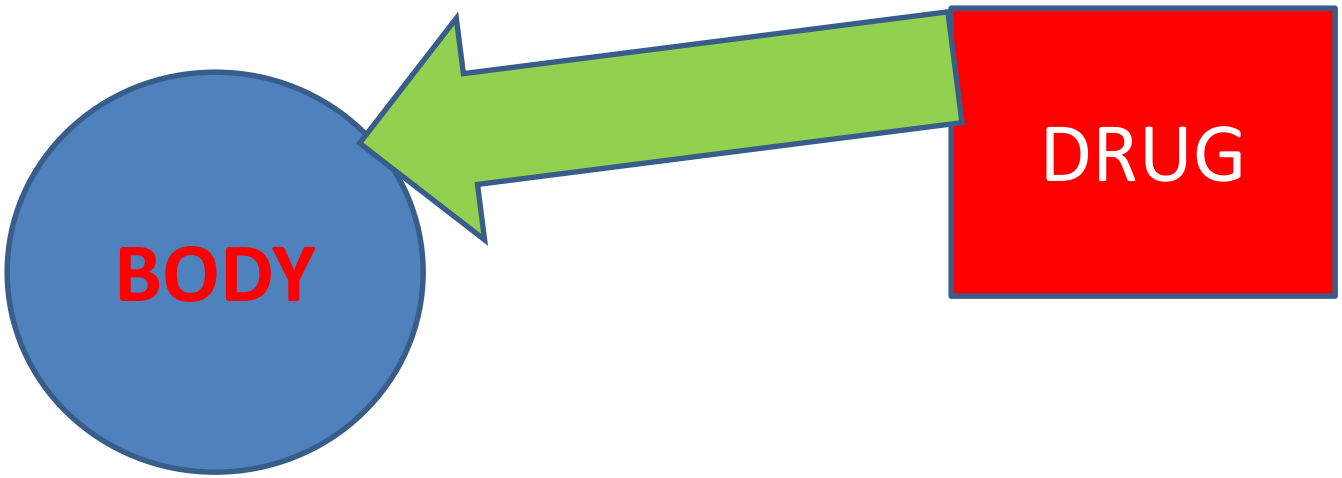
General MOA of drugs

1. **Mechanical:** e.g. Liquid paraffin (constipation)
2. **Physical:** e.g. Kaolin (diarrhea)
3. **Chemical:** e.g. Sodium bicarbonate (hyperacidity)
4. **By osmosis:** e.g. Magnesium sulfate (constipation)
5. **By replacement:** e.g. Vitamins and hormones
6. **By chelation:** e.g. BAL for mercury poisoning
7. **By binding to the cell receptors:**
   (Cell Receptor Theory)

Part I: Pharmacodynamics (PD)

- **Definition:**

  Study of drug action and mechanism of action on the cell function(Effect of the drug on the body



- **Cell receptors:** Chemically reactive macro-proteins found on cell membrane or in cytoplasm or nucleus. The drug can bind to its receptors and so initiate an effect (response)

Ka = Association constant Kd = Dissociation con.

- **Agonist:** The drug which have affinity, Efficacy and rapid dissociation constant (Kd) & produce an effect

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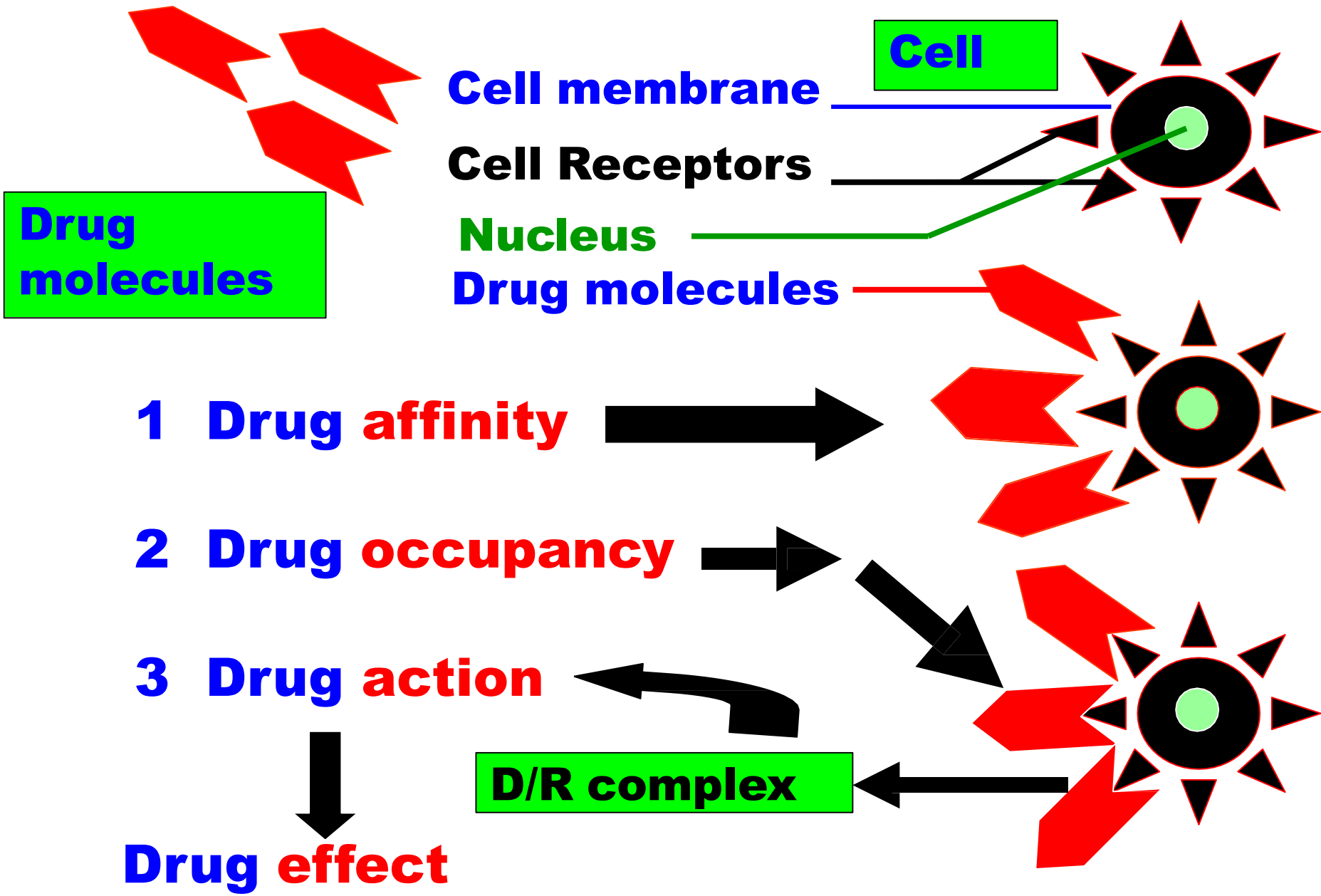
- Affinity = Tendency of drug to bind with its receptors
- Efficiency = Ability of drug to produce an effect
- Efficacy = Ability of drug to elicit its maximal effect

- **Antagonist:** The drug which block cell receptors and prevent action of the agonist.
  It has affinity, NO efficacy and slow Kd

Cell Receptor Theory of Clark& Gaddum



What happen when 2 drugs are given together ?

1-Drug Antagonism

decrease or disappearance of effect of one of the 2 drugs when given together

2-Enhancement of drug effect

A- Addition

B- Potentiation

C- Synergism

Drug Antagonism

Is a condition which occurs when 2 drugs are given together and result in a decrease or disappearance of effect of one of them.

opposite actions of two drugs on the same physiological system

- **Significance:** 1- To treat of drug toxicity
  2- To overcome side effects of drugs

Antagonism between drugs

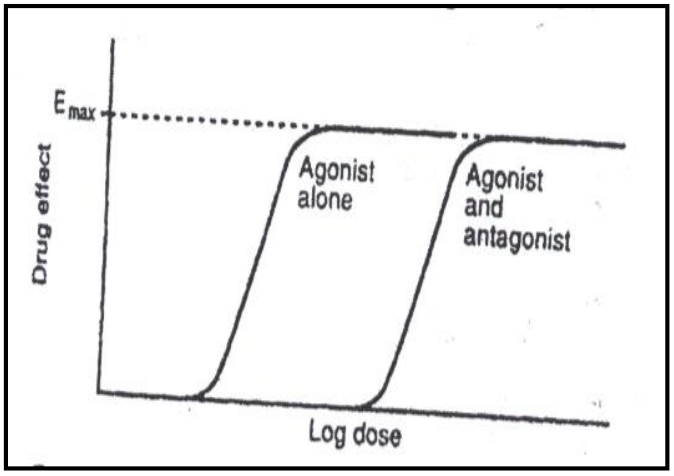
A. Pharmacological antagonism: Occurs when an antagonist prevents an agonist from interacting with its receptors to produce an effect. This type of antagonism can be either competitive or noncompetitive.

Competitive antagonism

(a) Competitive antagonists compete with agonists in a reversible fashion for the same receptor site.

(b) When the antagonist is present, the log dose-response curve is shifted to the right, indicating that a higher concentration of agonist is necessary to achieve the same response as when the antagonist is absent.

(c) In the presence of the antagonist, if enough agonist is given, the E_{max} can be achieved, indicating that the action of the antagonist has been overcome. This results in a parallel shift of the dose-response curve, as shown.



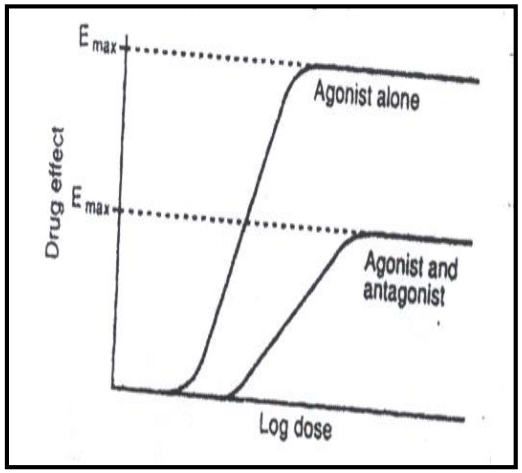
Shift in the log dose-response curve that occurs when an agonist is administered in the presence of a competitive antagonist.

Non Competitive antagonism

a) The non competitive antagonist binds irreversibly to the receptor site or to another site that inhibits the response to the agonist.

(b) **No matter how much agonist is given, the action of the antagonist cannot be overcome**.

(c) **This results in a nonparallel shift of the log dose-response curve with a lower E_{max}**



Shift in the log dose-response curve and lowering of the maximum effect (E_{max}) that occurs when an agonist is given in the presence of a noncompetitive antagonist

■ Types of Agonists:

Total (complete) Agonist	Partial Agonist
Stimulate receptors and produce maximal effect (Emax) i.e. have a high efficacy	Stimulate & block Rescep. and produce submaximal effect i.e. have a moderate efficacy
e.g. Ach on M. receptors Adrenaline on Ad. Recp.	Oxyprenolol on β receptors L.D.of Nicotine on N. Recp.

■ Types of Antagonists:

Competitive	Non competitive
Compete with the agonist for the same receptor site in a reversible manner e.g. Atropine and ACh	Compete with the agonist for different receptor sites e.g. Papaverine on muscle and Ach on nerve

B.Physiologic antagonism:

the drugs act independently on two different receptors.

Adrenaline acting on the sympathetic nervous system causing vasoconstriction to Blood vessels,

Histamine acting on H receptor decreases the causes vasodilatation to Blood vessels

C- Chemical antagonism

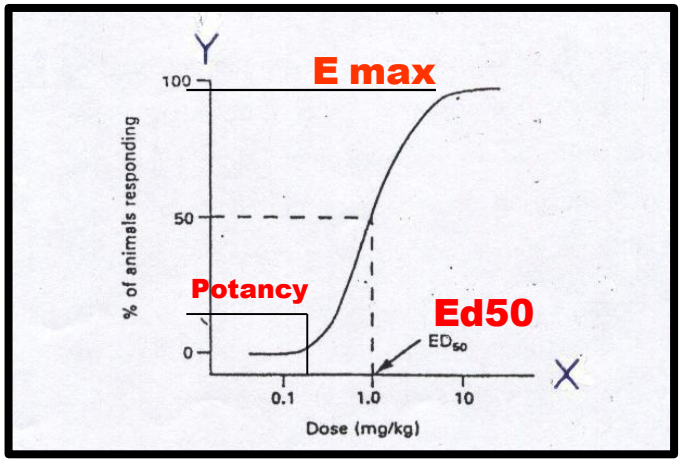
Antagonism by neutralization: occurs when two drugs combine with one another to form an inactive compound. For example,

in the neutralization of gastric hyperacidity by (Antacids) the alkaline salts of sodium and potassium such as acetates, citrates and bicarbonates.

Body Response According to given Dose

I- Graded response:

- The response is **increased** by **increasing the dose** till reach the maximal effect at which **most of receptors** are occupied.



Potency is how much drug is required to start its effect

- **Importance:**
  For determination of **ED50, E max and Potency**

II- Quantal response:

- The response start to appear only when the dose reach to certain limit or quantity
- **Importance**: For determination of **LD50**

Therapeutic index (TI) = LD50 / ED50

2- Enhancement of Drug Effect

Additive effect (Addition or summation):

Occur when 2 drugs have the same effect are given together and the resultant effect equal the sum of both effects when 2 drugs are given individually i.e.

$$E_{AB} = E_A + E_B \quad \text{i.e.} \quad 1 + 1 = 2$$

Synergism:

Occur when 2 drugs have the same effect are given together and the resultant effect is greater than the sum of both effects when drugs are given individually

$$E_{AB} > E_A + E_B \quad \text{i.e.} \quad 1 + 1 > 2$$

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Potentiation:

Occur when one drug has no effect but it increases the effect of a second active drug i.e.

$$E_{AB} > E_A + E_B \quad \text{i.e.} \quad 0 + 1 > 1$$

3-Species Variations in Drug Response

- **Causes:** Anatomical & physiological differences between different species of animals.
- **Examples:**

1- Cats are sensitive to phenol derivatives

2- Dogs and cats are sensitive to strychnine

3Cats are exited by CNS depressant morphine

4Ruminants can tolerate large amounts of Digoxin

5- Rabbits can tolerate large amounts of atropine

6- Poultry can tolerate large amounts of organic mercurial compounds

Cumulative Effect of Drugs

- **Definition:**

  It occurs when a drug is **rapidly absorbed** and **slowly excreted** and is given **repeatedly** it may accumulate to a **toxic** level or cause **death.**

- **Examples of cumulative drugs:**

  1-Digoxin 2-Strychnine 3-Long acting sulpha drugs

- **To avoid cumulative effect of drugs:**

  1Start therapy with **initial therapeutic** dose followed by **small maintenance** dose

  2Give a **period of rest** during course of therapy

  3- Give a **diuretic** to help excretion of the drug

  4- **Stop** administration of the cumulative drug once toxic symptoms appear

Drug Tolerance

It is the unusual resistance of the body to the ordinary dose of a drug, or

when a large dose of a drug is required to produce an effect produced by normal therapeutic dose of the drug.

Types of drug tolerance

Species (natural, congenital tolerance): Certain animal species can tolerate certain drugs than other species. Rabbits can tolerate large quantity of Atropa belladonna due to the presence of atropinase enzyme in liver and plasma of rabbits which rapidly detoxifies atropine.

Acquired tolerance: develops only due to repeated administration of certain drugs as morphine, barbiturates, caffeine, nitrites…etc. After a period of administration, the therapeutic dose of the drug becomes ineffective.

Types of drug tolerance

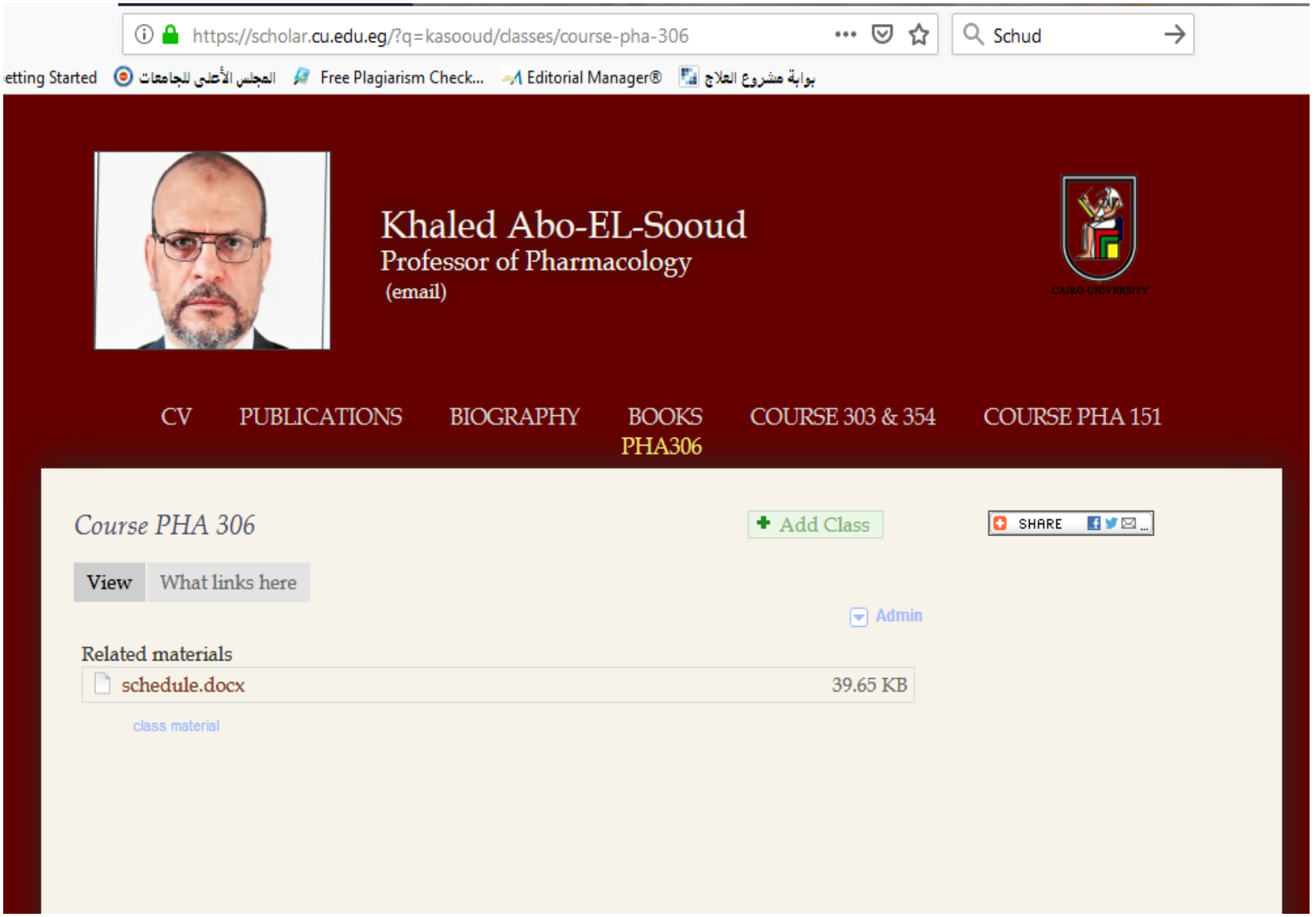
Cross tolerance: which develops to one drug by the administration of another one related, e.g.: tolerance between alcohol and volatile anaesthetics or antibiotics from the same group.

Apparent or Pseudotolerance: This is usually manifested by ingesting small doses of poisons orally, where animals become immune to oral poisons but poisoning could occur if any route was a chosen. This tolerance to oral administration of the poison is probably due to the immunity developed by the GI tract which prevents the poison from getting absorbed into the systemic circulation.

Adverse Effects of Drugs

Idiosyncrasy: Abnormal response to some drugs in certain individuals reactions due to genetic or enzymic defect as

- **Penicillin** injection into guinea pigs causes fatal respiratory anaphylaxes
- **Sulphonamide** administration produces skin rashes.
- Horses may suffer from fatal colitis after administration of some broad spectrum antibiotics as **oxytetracycline.**



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