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Doctor 2021 - رَوح - medicine - MU

pharmacology sheet

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Definition and Divisions

- **PHARMACOLOGY :** It is the science that deals with interaction of
  - drugs with living systems.
  - These inter interaction can lead to the benefical effect or defective effect

Drugs : These are chemical substances that shows biological activity (treatment or sometimes diagnosis).

The drug has mechanisms of action

- The first thing is to treat some diseases and relieve pain
- The second thing is used in diagnosis, for example, the use of radioactive iodine to diagnose thyroid diseases or the contrast media of CT scan

- **Divisions of Pharmacology:**

1. Pharmacodynamics :

(What the drug does to the body)

- This deals with the action of drugs on living tissues , namely the type or quality of action, its quantitative aspect , as well as the mechanism of action .
- Adverse effects and safety of drugs on body tissues or systems are also included
- The main organ or tissue on which the drug acts , and for which it is used therapeutically, is called the target organ or tissue of drug action

2. Pharmacokinetics :

(What the body does to drug)

- This includes administration and absorption of drugs, their distribution inside body, and their elimination by metabolism or excretion

Other topics linked with pharmacology (jargons)

1. Pharmacotherapeutics: It is concerned with the proper use of drugs in treatment of disease in man

Appropriate use for the treatment of diseases

2. Clinical Pharmacology: This includes :-

A. Drug pharmacology

B. Clinical evaluation of drugs in treating disease in man.

This is done by :

a. Clinical trials b. Surveillance studies

clinical trials can be either in vivo or in vitro

3.Chemotherapy : It is used to imply the use of drugs to inhibit growth or kill either :

a. Microbes (i.e. anti-microbial agents) even antibiotics are chemotherapy drugs

b. Cancer cells (Cyto-toxic anti-cancer drugs)

cytotoxic drugs can't distinguish between normal and cancerous cells, so they are harmful. However, other drugs called "targeting agents" attack the molecular basis of cancerous cells, therefore they have less side-effects.

4. Pharmacy : It is the science and profession that is

concerned with the preparation, storage, dispensing (way of administration of drugs), and proper utilization of drug products

5. Toxicology : It is the science that deals with the harmful effects of chemicals (including drugs) .

DRUG SOURCES

These may be either :-

I. Synthetic sources : common at present

- these drugs are prepared by the labs or factories of the pharmaceutical industry. Nowadays, computers greatly assist in discovery of new drugs

II. Semi-synthetic drugs :

- these are obtained from natural sources, but are modified by pharmaceutical industry in order to improve their physical or chemical properties or pharmacological activity.

The medicine extracted from nature may have a 3-hour effect or a bad taste, so it is chemically modified and its physical properties improved to be a modified medicine suitable for use.

III. Natural sources : These are less used now . They may be either :

1. Organic :

A. Plants : Any part of the plant (stem, leaves, flowers, seeds, roots) may be used to extract active ingredients for drugs; same plant may contain more than one active principle. All of this is dealt with in PHARMACOGNOSY

Pharmacognosy is the science that deals with drugs obtained from natural sources.

Examples of drugs from plants are : alkaloids, steroids, some vitamins, tannins, volatile oils, gums

Note :

Alkaloids are small organic molecules containing nitrogen . e.g. atropine, morphine, caffeine, theophylline, quinine

B. Animals : these may include either proteins , oils, enzymes from exocrine glands, hormones, vaccines and anti-sera, and some vitamins

C. Microbes : like fungi, and sometimes bacteria which are sources of antibiotics

2. Non-Organic sources :

- **metals : Platinum (build-up of anticancer drugs), Zinc (in anti-septics)**
- **non-metals : Sodium chloride (normal saline) , magnesium sulfate (antacid)**

Rational drug design:

- **This implies the ability to predict the chemical structure of drug molecule on basis of 3-dimensional structure of its receptor, employing at present suitable computer programs. Only few drugs in clinical use at present were developed in this rational way.**

The computer program 3D helps to design a medicine that looks close to the shape of the receptor it will be working on

- **Most drugs were in the past developed through random testing of chemicals , or modified molecules of known drugs that are known to have some pharmacological effect.**

However, as more becomes known about detailed structure of receptors, rational drug design with the aid of computers would become more feasible

DRUG CLASSIFICATION

There is no fixed rule; classification is usually done according to their :

1. Therapeutic use : e.g. anti-hypertensive drugs ; anti-microbial drugs ; anaesthetics; hypoglycemic drugs; anticoagulants;

2. Type of pharmacological action :

This should be precise. e.g. local or general anaesthetics; vasodilators; anticoagulants OR according to molecular or cellular site of action in target cells e.g. enzyme inhibitors, receptor blockers , ion channel blockers, inhibitors of transporters, antimicobials acting on l wall, DNA, or ribosomes

3. Physiological systems on which they act : Drugs acting on cardio-vascular system; drugs acting on GIT or CNS or respiratory system

4. Chemical nature or Source :

Common chemical groups or structures can be used to classify drugs that have similarity in their pharmacological profile e.g. benzodiazepines (anti-depressents), steroids.

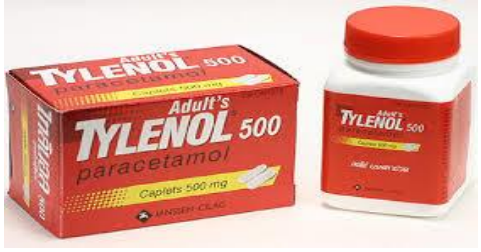
For drugs derived from nature, both the plant species or genus and drug chemistry are included e.g. belladona alkaloids from *atropa belladona* , digitalis glycosides (for heart muscle) from *Digitalis* leaves .

A special case when the medicine is extracted from nature, it is named by plant name + drug chemistry

DRUG NAMES

1. Chemical name :

- **Because of its complexity , the chemical structure is not usually used to name drugs.**
- **However, sometimes a shorthand name based on a simple chemical structure is employed e.g. acetylsalisylic acid (aspirin) , acetaminophen (parectamol)**



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2. Generic (non-proprietory) name :

- **This is a unique name that is given by official pharmaceutical bodies;**
- **It is present in pharmacopeas (BP or USP) (files of all medicines).**
- **It is the approved scientific name, and must be used in scientific publications as well as in prescriptions esp. in hospitals .**
- **Its use makes it easier for pharmacist to choose from many available brands of same drug.**
- **Only few drugs show more than one generic name :**

Noradrenaline & adrenaline in UK but are named Nor-epinephrine and epinephrine, respectively, in USA & WHO; salbutamol in UK while albuterol in USA

- **Generic names of drugs in a classified group may have common endings e.g. – olol for beta-adrenoceptor blockers; -caine for local anaesthetic drugs. These endings may give a hint about the drug pharmacotherapeutic action**

3. Commercial or trade or brand or proprietory name:

- **This name is given by the specific pharmaceutical company synthesizing and marketing the drug.**
- **Examples: Diclofenac Na (Voltaren, Inflaban, Diclogesic)**
- **A single drug can have many brand names (this may be confusing) due to its manufacture and marketing by many pharmaceutical companies.**

DOSE FORMS OF DRUGS

- **It is the physical form of drug product that is suitable for administration to man. It contains specified dose or amount of drug in a specified quantity or unit of the formulation.**
- **Types of drug dose forms:**

1. **Oral**
2. **Inhalational**
3. **Parenteral**
4. **Topical**
5. **Suppository**

1. Oral dose forms: It includes the following

A. Pill: Tablets and capsules

B. Liquid: Syrup or suspension

C. Powder

D. Herbal plants: seeds, leaves etc..

E. Pastes

2. Inhalational:

A. Aerosol (without specified dose)

B. Inhaler (with specified dose)

C. Vaporizer (Solutions)

3. Parenteral:

A. Intradermal (ID) B. Intramuscular (IM)

C. Intraperitoneal (IP) D. Intravenous (IV)

E. Subcutanous (SC) F. Intrathecal (IT) (in vertebral column)

4. Topical:

A. Cream, gel, ointment, lotion

B. Eye drops (ophthalmic)

C. Ear drops (otic)

D. Skin patch (transdermal)

5. Suppository:

A. Vaginal . B. Rectal

PRINCIPLES OF PHARMACODYNAMICS

MECHANISMS OF DRUG ACTION

Drugs can act through:

1. Physical action:

Drug can produce a therapeutic response because of it's physical properties. e.g: Mannitol as diuretic because it increase osmalerity, Radio-isotopes : emit ionizing radialarge

Mannitol Diuretic: It is a sugar whose chemical structure is very large and complex

And because it is large in size, the body tries to expel it outside the body, and it becomes eliminated outside the body through the kidneys, but it needs large amounts of water inside the body to help remove sugar.

Radio Isotops: Because of its radioactive properties, it is used in treatment

Whether nuclear medicine or imaging diagnostics

2. Simple chemical reaction:

Drug may act through a chemical reaction. e.g: Gastric antacids work by neutralizing the stomach acidity with a base, Chelating agents that bind heavy metals in body and inactivate their toxic effect.

The drug works and produces effects through a chemical reaction

For example: a person who suffers from acidity in the stomach as a result of that takes magnesium sulfate

(Antacid)

So it will produce

Magnesium Sulfate + HCL=neutralizing effect

3. Receptors:

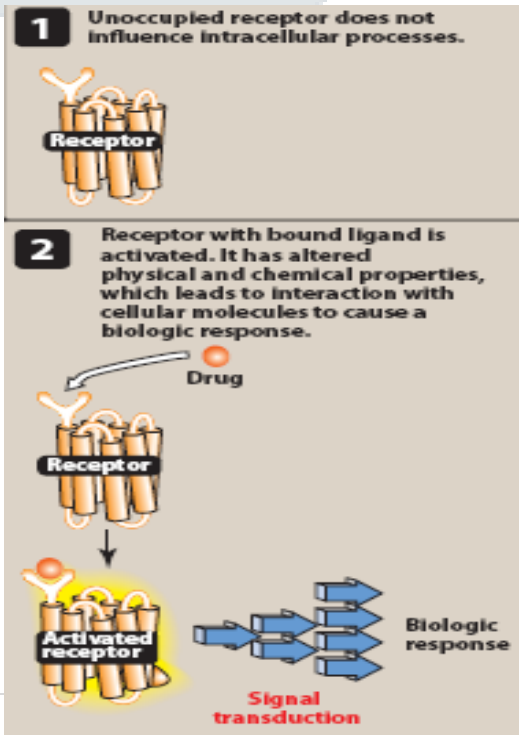
Receptor: a molecule found on or within the cell membrane

There is also an activation binding site on the receptor that binds to the ligand

A receptor is a specialized target macromolecule mostly protein, present on the cell surface or intracellular, that binds a drug and mediates it's pharmacological actions.

- Receptors can either be enzymes, nucleic acids or structural proteins to which drugs may interact.
- A molecule that binds to a receptor is called a ligand, and can be a peptide or another small molecule like a neurotransmitter, hormone, or drug.

- Ligand binding changes the conformation (three-dimensional shape) of



the receptor molecule. This alters the shape at a different part of the protein, changing the interaction of the receptor molecule with associated biochemicals, leading in turn to a cellular response mediated by the associated biochemical pathway.

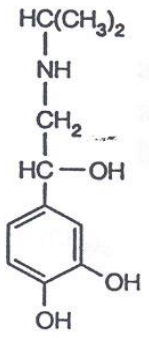
TYPES OF LIGAND-RECEPTOR INTERACTIONS

- **Not every ligand that binds to a receptor also activates the receptor. The following classes of ligands exist:**
- **1. (Full) agonists are able to activate the receptor and result in a maximal biological response. The natural endogenous ligand with greatest efficacy for a given receptor is by definition a full agonist (100% efficacy).**
- • This ligand binds to and stimulates the receptor, resulting in a maximal response such as epinephrine and acetylcholine
- **2. Partial agonists do not activate receptors thoroughly, causing responses which are partial compared to those of full agonists (efficacy between 0 and 100%).**
- The receptor is activated, but it does not reach the maximum level
- **3. Antagonists bind to receptors but do not activate them. This results in receptor blockage, inhibiting the binding of agonists and inverse agonists.**
- It is associated to the receptor and it works as a block, so there is no activation

- Why is it related to the receptor?
- In order to prevent some substances from binding to the receptor
- **4. Inverse agonists: is a drug that binds to the same receptor as an agonist (negative efficacy).**
- **Nearly all antihistamines acting at H1 receptors and H2 receptors have been shown to be inverse agonists**

For example, I have a receptor that attaches to adrenaline and produces effects (this is called an agonist).
But after a while the inverse agonists work and give a signaling cascad that differs from an agonist and reverses its effect

TYPES OF LIGAND-RECEPTOR INTERACTIONS



Isoproterenol

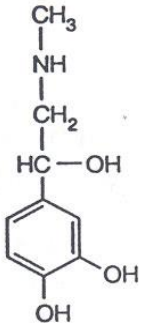
Agonist

e.g. important therapy

in asthma

binds β_2 receptor in heart muscle →

increased heart rate

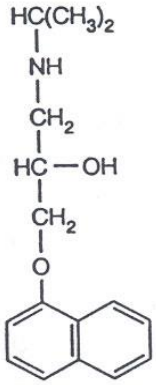


Epinephrine

Hormone

binds β_2 receptor in lung →

bronchial relaxation



Propranolol

Antagonist

control heart beat

TYPES OF DRUG-RECEPTOR BONDING

Drugs interact with receptors by means of chemical forces or bonds. These are of three major types:

1. **Covalent:** It is very strong and in many cases not reversible under biologic conditions. Thus, the duration of drug action is frequently, but not necessarily, prolonged (irreversible)

   Its connection is strong and cannot be untied (uncommon bond)

2. **Electrostatic:** is much more common than covalent bonding in drug-receptor interactions. These vary from relatively strong linkages between permanently charged ionic molecules to weaker hydrogen bonds and very weak induced dipole interactions such as van der Waals forces. Electrostatic bonds are weaker than covalent bonds. (reversible)

3. **Hydrophobic:** are usually quite weak and are probably important in the interactions of highly lipid-soluble drugs with the lipids of cell membranes and perhaps in the interaction of drugs with the internal walls of receptor "pockets."

   - Drugs which bind through weak bonds to their receptors are generally more selective than drugs which bind through very strong bonds.
   - Drugs that bind to the receptor through a weak limit such as van der Waals are selective
   - High selective drugs give 1) good therapeutic effect
     2) minimum adverse effects

- This is because weak bonds require a very precise fit of the drug to its receptor if an interaction is to occur

DURATION OF DRUG ACTION مهم جداااا

Termination of drug action at the receptor level results from one of several processes:

1. The effect lasts only as long as the drug occupies the receptor, so that dissociation of drug from the receptor automatically terminates the effect.

   When the drug is attached to the recptor directly it gives an effect

   And if you remove the drug directly the effect ends

2. The action may persist after the drug has dissociated, because, for example, some coupling molecule is still present in activated form.

3. Drugs that bind covalently to the receptor, the effect may persist until the drug-receptor complex is destroyed and new receptors are synthesized.

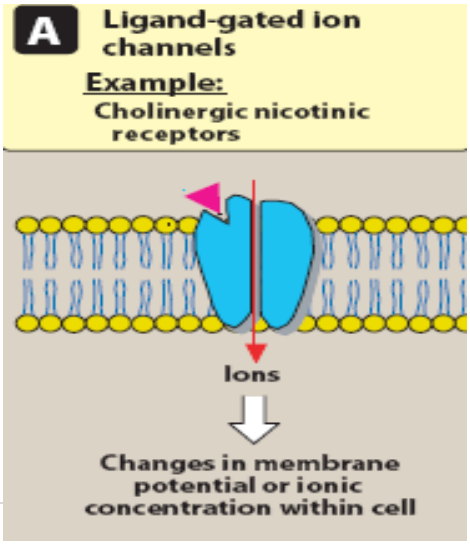
4. Many receptor-effector systems incorporate desensitization mechanisms for preventing excessive activation when agonist molecules continue to be present for long periods

CLASSIFCATION OF RECEPTORS

This is based on the type of the transduction mechanism that these receptors activate when stimulated by their agonists:

1. Transmembrane ligand-gated ion channels: These receptors are present in the walls of ion channels in cell membranes. When activated by their specific agonist, they open these ion channels & lead to movement of ions across cell membrane.

   - These mediate diverse functions, including neurotransmission, cardiac conduction, and muscle contraction.



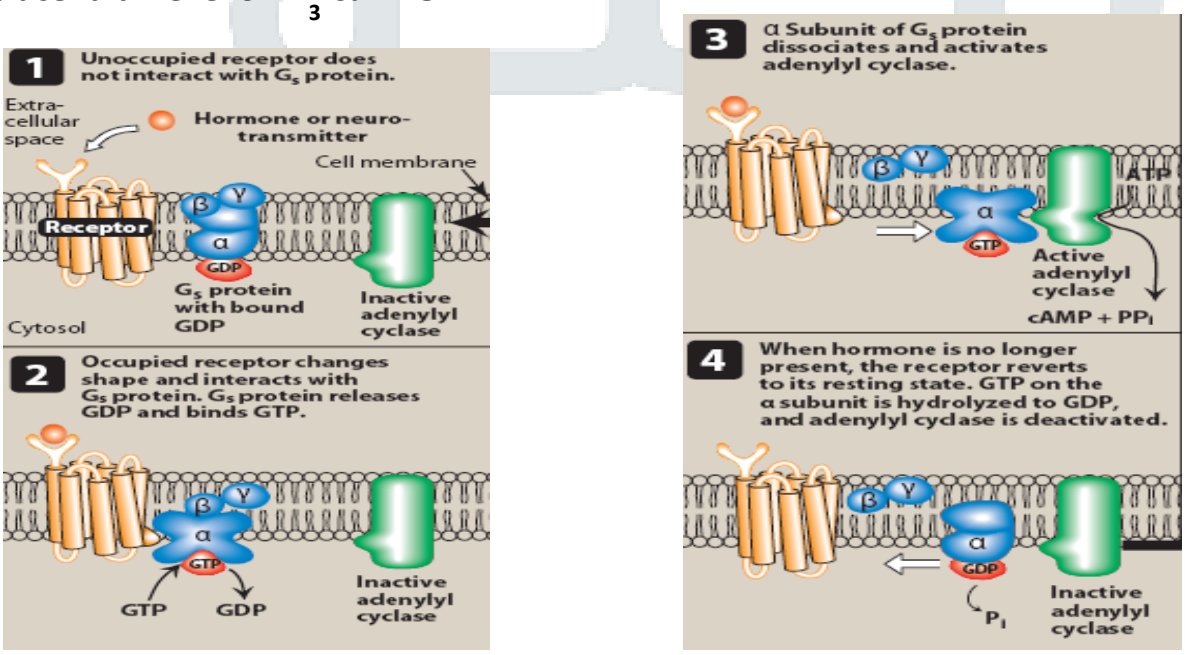
Examples :

- **1. Nicotinic receptors for acetylcholine (Ach.) : when stimulated, they open receptor-operated Na^+ channels, and thus increase influx of sodium ions across membranes of neurons or NMJ(neuromuscular junction) in skeletal muscle and therefore activation of contraction in muscle.**
- **2. γ-aminobutyric acid (GABA) receptors:**
- **Benzodiazepines enhance the stimulation of the GABA receptor by GABA, resulting in increased chloride influx and hyperpolarization of the respective cell.**

2. Transmembrane G protein–coupled receptors:

- **When these receptors are stimulated by their specific agonists, they will activate a regulatory G-protein in cell membrane which in turn change activity of membrane enzymes (either adenyl cyclase or phospholipase C) leading to a change in intracellular level of a second messenger like cAMP (cyclic adenosine monophosphate), or IP_3 (inositol triphosphate), respectively, and this would lead to cell response.**

Examples : e.g. Receptors for transmitters : Stimulation of muscarinic receptors (M_1 and M_3) for Ach will activate G and leads to increase intracellular level of IP_3 & DAG

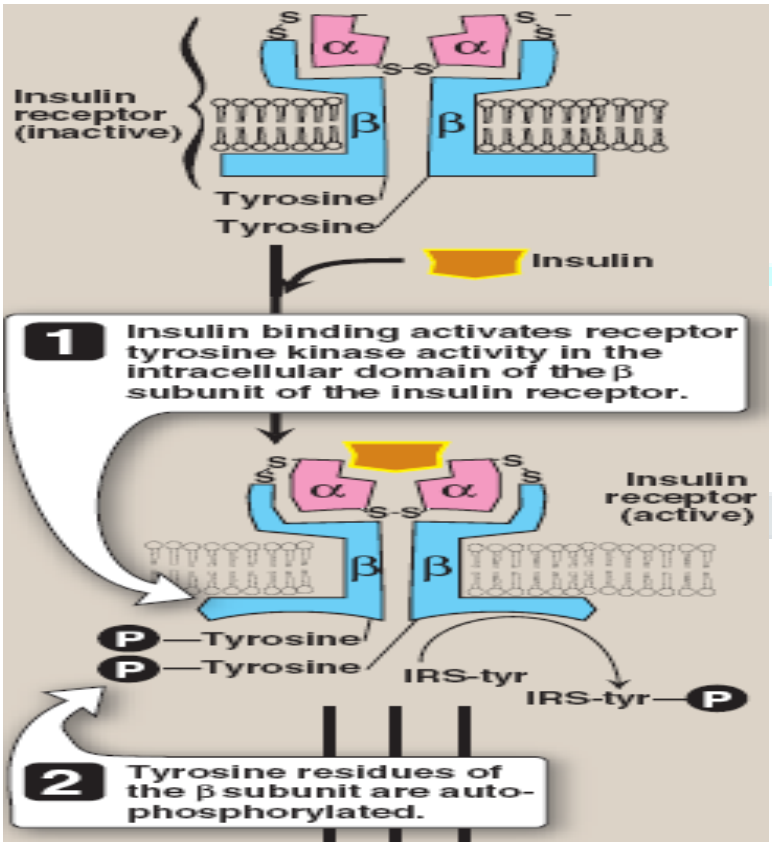


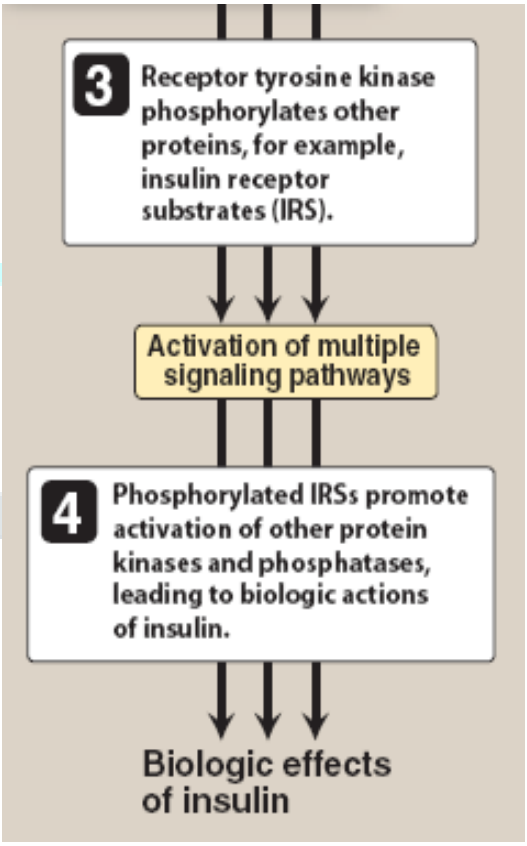
guanosine triphosphate (GTP), guanosine diphosphate (GDP)

3. Enzyme-linked receptors: (with enzymatic activity)

- These membrane receptors have an extra-cellular site that binds to specific agonists and an intra-cytoplasmic domain which contains tyrosine and other amino acids.
- Binding to specific agonist and activation of these receptors usually lead to phosphorylation of tyrosine in intra-cellular domain which then acquires kinase activity and leads to activation of intracellular substrates or enzymes that finally leads to cell response.
- Examples:

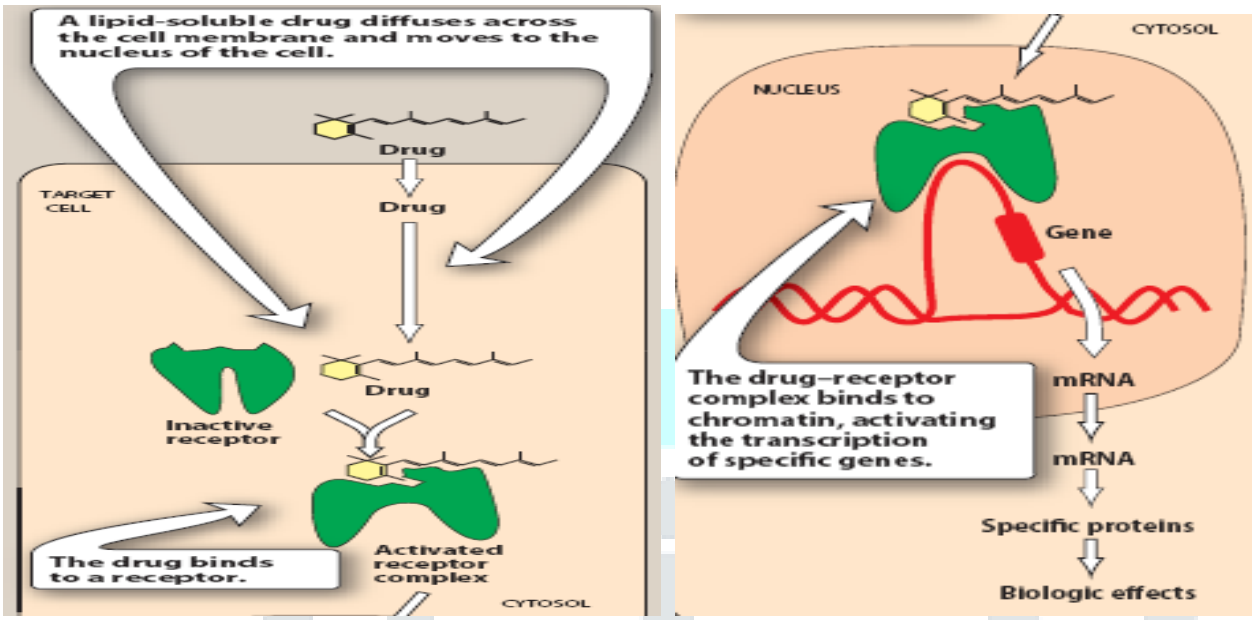
- Receptors for insulin,
- Receptors for growth factors like EGF or PDGF,
- Receptors for immune cytokines





4. Intracellular receptors:

- **These receptors are located in cytoplasm (e.g. steroid receptors) or nucleus (receptors for thyroid hormones or vitamin D_3) .**
- **The <u>specific agonist must cross cell membrane to inside of cell</u>, binds and activates these receptors, which will then bind to DNA gene response elements in nucleus and lead to change in gene transcription , and thus synthesis of new proteins**



للبدايات الجديدة دائما ألَق، خفقة في القلب، وغبطة بالنجاة من الوقت الصعب...
لم تكن قوتنا كافيةً قط، لكن الله مرَّر الوقت العصيب دون أن يمسَّ قلوبنا، وأوصلنا إلى هذه الليلة، هنا والآن، بأرواح معافاة وعيون ما زالت قادرة على النظر إلى السماء ومخزون هائل من القدرة على الضحك"
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