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Chapter one

Introduction and Definitions

Pharmaceutical chemistry:

Intersection of chemistry and pharmacology, involved with designing, synthesizing and developing pharmaceutical drugs. It involves the identification(assay), synthesis and development of new chemicals suitable for therapeutic use. It also includes the study of existing drugs, their biological properties, metabolism, distribution and their structure-activity relationships (SAR).

Important definitions:

Chemical names:

Is a well-known name, used generally for chemicals and drugs.

e.g. acetylsalicylic acid for aspirin and acetaminophen for paracetamol.

IUPAC Name:

The IUPAC nomenclature of organic chemistry, is a systematic method of naming organic chemical compounds as recommended by the **International Union of Pure and Applied Chemistry (IUPAC)**. e.g. aspirin is 2-acetoxy benzoic acid and paracetamol is N-(4-hydroxyphenyl) ethanamide.

Trade name (Brand Name):

A trade name is a proprietary name, that is applied to a product by a company for the purposes of marketing and sales. It generally doesn't convey much chemical information. A trademark is a legal concept, not a scientific concept. e.g. for aspirin: Aspro (Roche); aspirin (Bayer); Aspin(samara), and for paracetamol: Panadol, Paralen, Phenaphen and Tylenol.

Generic Name:

is a name describes the form that the drug is present in final production e.g. aspirin tablets.

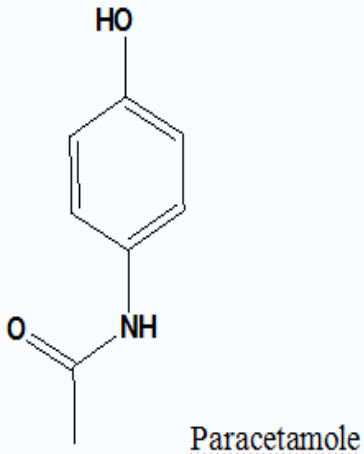
Molecular formula:

Expressing the information about the atoms that constitute a particular chemical compound, For example Methane, a simple molecule consisting of one carbon atom bonded to four hydrogen atoms has the chemical formula (CH4) and Glucose with six carbon atoms, twelve hydrogen atoms and six oxygen atoms has the chemical formula (C6H12O6). While Aspirin is (C9H8O4) and Paracetamol is (C8H9NO2).

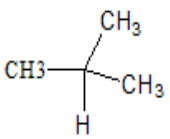
Chemical structure:

supplies information about the types and spatial arrangement of bonds in the chemicals, for example:

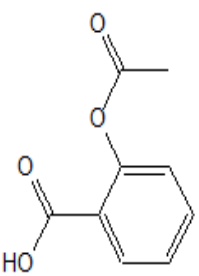
2-methylpropane as (CH3)3CH implies a chain of three carbon atoms, with the middle carbon atom bonded to another carbon as in (a).



Paracetamole



(a)2-methylpropane



(b)acetylsalicylic acid

Preparation equations (Manufacture):

Equations described the reactions to prepare a well-known compound.

For e.g.:

1- preparation equation of Aspirin:

The synthesis of Aspirin is classified as an esterification reaction, where the alcohol group from the salicylic acid reacts with an acid (acetyl anhydride) to form an ester.

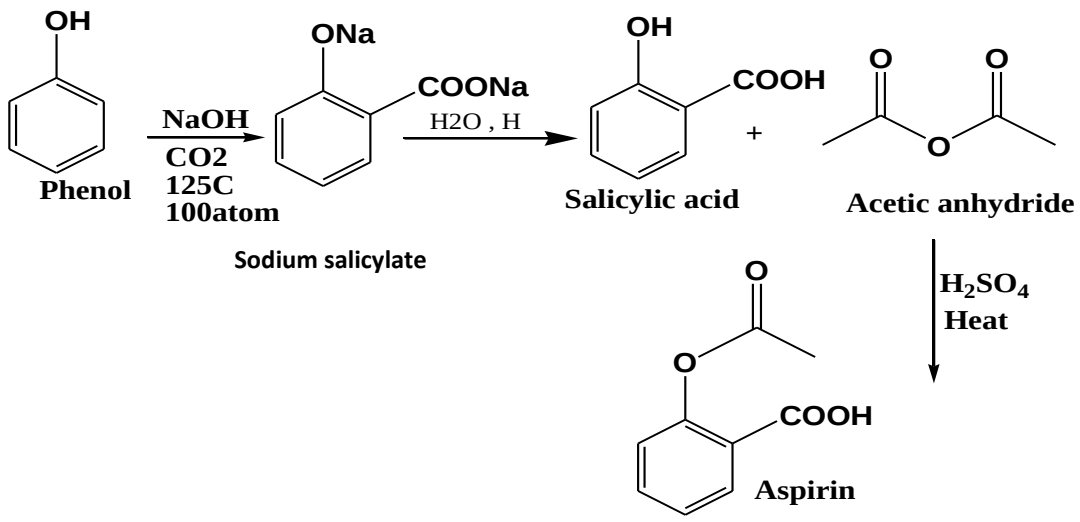
Aspirin is commercially synthesized using a two-step process:

First, (the Kolbe-Schmitt reaction):

phenol (generally extracted from coal tar) is treated with a sodium base which generates sodium phenoxide, which is then reacted with carbon dioxide under high temperature and pressure to yield salicylate, which is acidified, yielding salicylic acid.

Second, (acetylation):

Salicylic acid is then acetylated using acetic anhydride, yielding aspirin and acetic acid as a byproduct.



2- preparation equation of paracetamol:

paracetamol can be made in the following manner:

a-Phenol is nitrated using sulfuric acid and sodium nitrate .

b-The para isomer is separated from the ortho isomer by fractional distillation.

c-The p-nitrophenol is reduced to p-aminophenol using a reducing agent such as sodium borohydride in basic medium.

d- p-aminophenol is reacted with ethanoic anhydride (acetic anhydride) to give paracetamol .

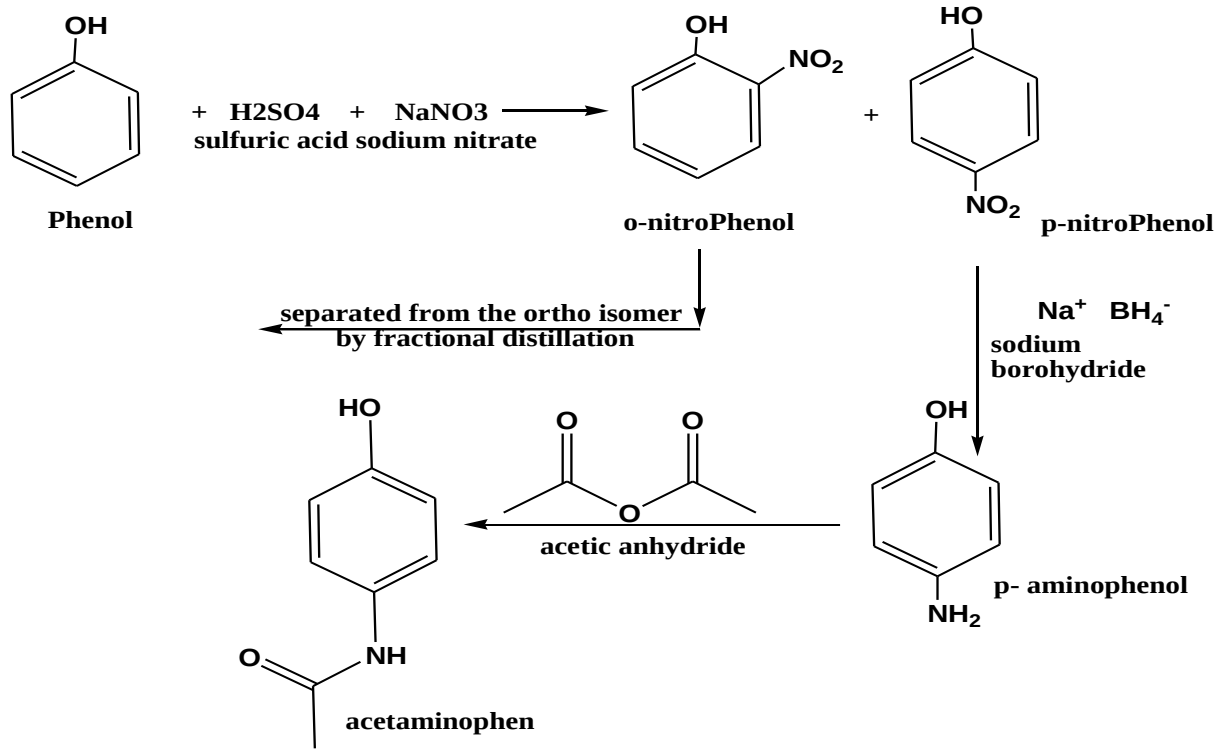


Fig (5)
Preparation of paracetamol

Synthesis equations:

Equations describes the reactions to prepared anticipated compounds (new compounds).

Properties:

The complete descriptions of the drug (odor, solubility, affecting by heat, LD50, MP, etc.)

LD50: a test in which the dose kills 50% of a group of test animals is calculated

e.g. as for Aspirin

a- Is odorless, but in moist air it is gradually hydrolyzed into salicylic and acetic acids and acquires the odor of acetic acid. Stable in dry air.

b- One-gram dissolves in 300 ml water at 25degrees, in 100 ml water at 37degrees, in 5 ml alcohol, 17 ml chloroform, 10-15 ml ether. Less soluble in anhydrous ether.

c- Decomposed by boiling water or when dissolved in solutions of alkali hydroxides and carbonates.

d- LD 50 orally in mice, rats: 1.1, 1.5 g/kg (Hart).

Pharmacology:

The study of desirable effects, therapeutic or beneficial responses of drugs, especially the ways in which they react biologically at receptor sites in the body and affect the body in more than one way.

e.g. pharmacology of aspirin

1-Antithrombotic [Anticoagulant] (Cardioprotective). **2-**Antirheumatic, strong analgesic, antipyretic and anti-inflammatory properties. **3-**Anticancer.

e.g. pharmacology of Paracetamol

Paracetamol has analgesic and antipyretic properties comparable to those of Aspirin, it fails to exert significant anti-inflammatory action due to

paracetamol's susceptibility to the high level of peroxides present in inflammatory lesions.

Side effects:

Undesirable or harmful effects are called adverse reactions. Some adverse reactions, or side effects, can be predicted.

e.g. side effects of aspirin

1-Ingestion of large amounts can cause vomiting, abdominal pain, increased respiration, acidosis, mental disturbances. May cause skin rashes in sensitive individuals.

2-GIT Irritations, allergic reactions, asthma, urticaria.

Dosage Forms:

The forms that the drug is present in final production e.g. aspirin dosage forms are;

Powder, capsule, suppository, tablet, ointment.

Excretion:

Is the discharged of waste matter (as urine or sweat but especially feces) from the body.

e.g. aspirin 52-75 % excreted in the urine.

Doses:

Prescribes the amount of medication or a measured quantity of medication administered once or at specific intervals to obtain the pharmacological effects .

e.g.: 81 mg of aspirin daily decreases the cardiovascular risk and thrombotic strokes.

300-900 mg of aspirin for every 4-6 hrs. are used for the other therapeutic uses. (analgesic, antipyretic and anti-inflammatory, ect.)

Max dose per day 4 gm

Contraindications:

Inadvisable taking particular medication because of a likely adverse reaction.

Aspirin Contraindications:

1- Less than 12 years
2- Breast - feeding
3- GIT (ulceration)
4- Hemophilia
5- Asthma

Mode of Actions or (mechanism of action):

The specific biochemical interaction through which a drug substance produces its pharmacological effect on the body (on the enzymes or receptors).

e.g. mod of action of aspirin (Antithrombotic action):

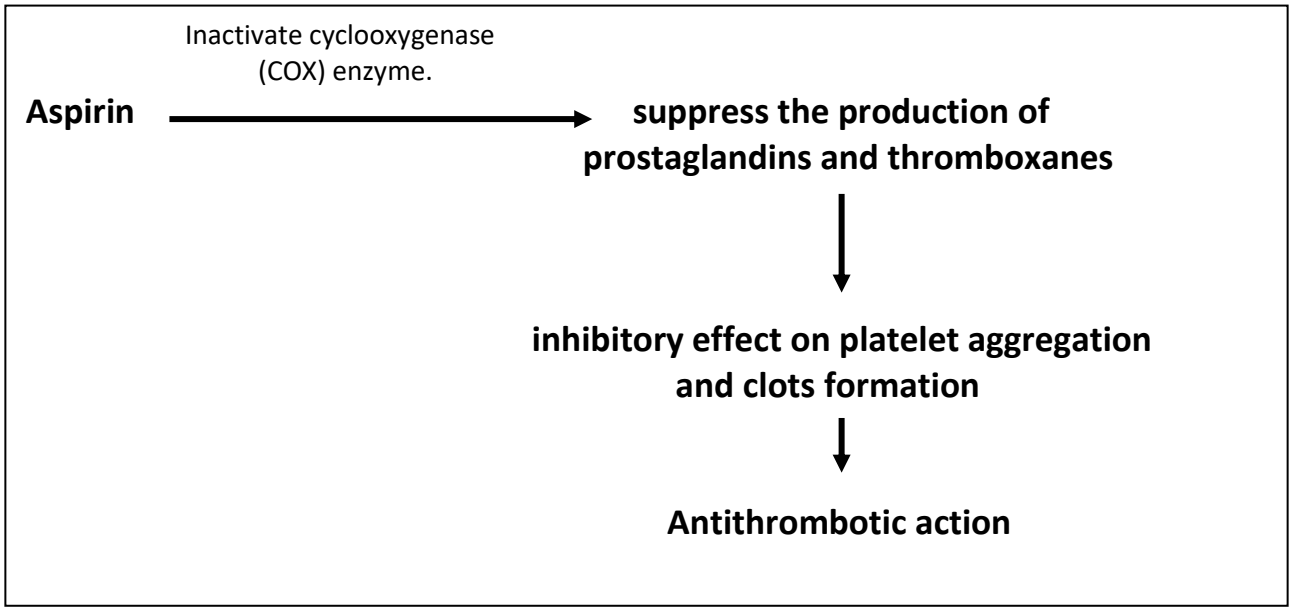
Aspirin's ability to suppress the production of prostaglandins and thromboxane is due to its competitive and irreversible inactivation of the cyclooxygenase (COX) enzyme.

Cyclooxygenase is required for prostaglandin and thromboxane synthesis.

Aspirin acts as an acetylating agent where an acetyl group is covalently attached to a serine residue in the active site of the COX enzyme producing an inhibitory effect on platelet aggregation.

Thromboxane are responsible for the aggregation of platelets that form blood clots.

Heart attacks are primarily caused by blood clots, and their reduction with the introduction of small amounts of aspirin has been seen to be an effective medical intervention.



Metabolism:

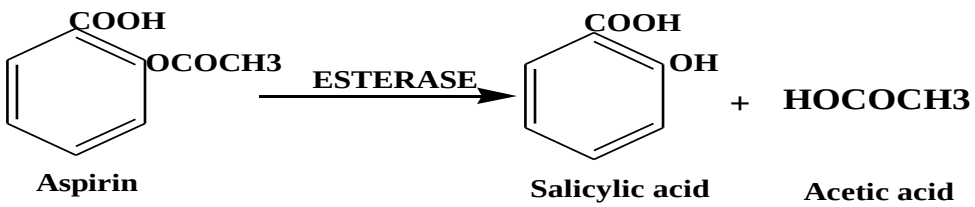
The whole range of biochemical processes that occur within any living organism.

Metabolism consists both of anabolism and catabolism (the buildup and breakdown of substances).

The term is commonly used to refer specifically to the breakdown of food and its transformation into energy, or drug and transformation into another form of compound.

e.g. Metabolism of aspirin

The enzyme esterase in liver, kidney, intestine and plasma. carrying out ester hydrolysis of Aspirin into the salicylic acid and acetic acid.



chapter two 2

Physico-chemical Properties in Relation to Pharmaceutical Activities

A drug is a chemical molecule.

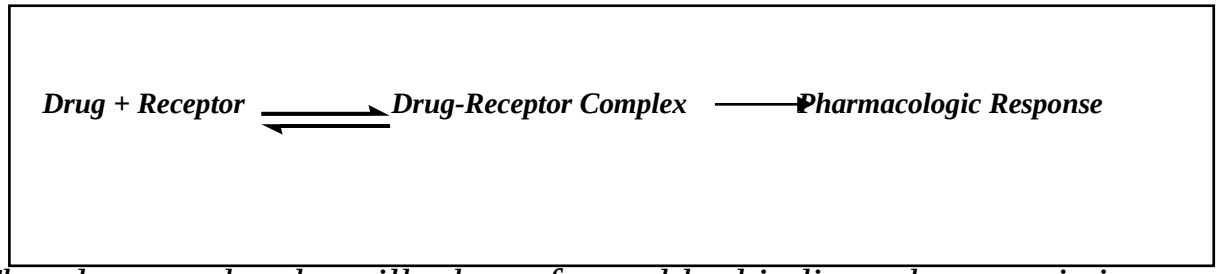
Following introduction into the body, and before it reaches the site of action, a drug must pass through:

1. many barriersحواجز ,
2. survive alternate sites of attachment مواقع اتصالات بديلة
3. storage sites,مواقع تخزين
4. avoid significant metabolic destruction تجنب التحلل الايضي

The receptor

A (cell or group of cells) surface that receives stimuli by their chemical group or molecules (as a protein), that has an affinity for a specific chemical group, molecules or virus that the most drugs are produce their effects by interacting with, or binds to modify biological function.

At the receptor, the following equilibrium usually holds:

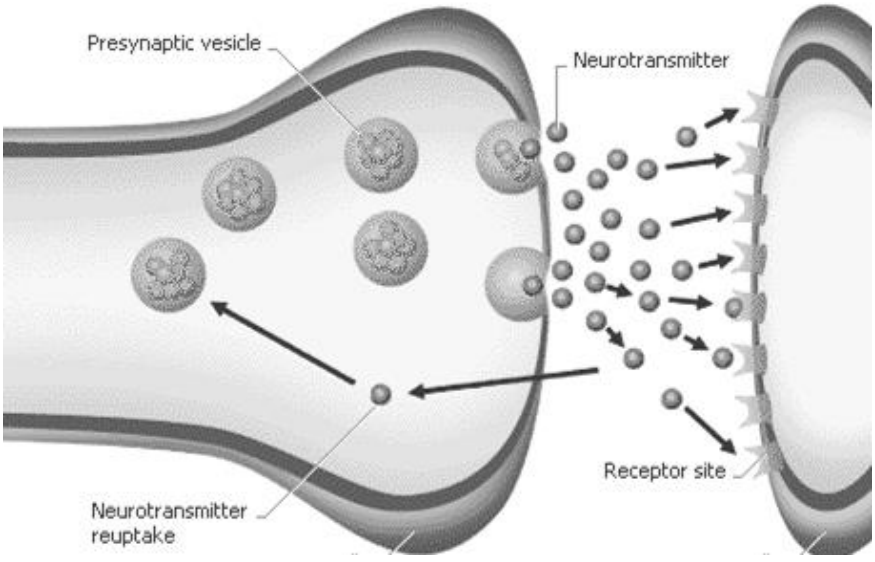


The drug molecule will show favorable binding characteristics to the receptor, and the equilibrium will lie to the right. At the same time, the drug will be expected to dissociate from the receptor and re-enter the systemic circulation to be excreted.

In other words, the usual use of drugs in medical treatment calls for the drug's effect to last for a finite period of time. Then, if it is to be repeated, the drug will be administered again. If the patient does not tolerate the drug well, it is even more important that the agent dissociate from the receptor and be excreted from the body.

***Example**:*

The neurotransmitter receptor in the membrane of nerve cell relating to the parasympathetic nervous system in which acetylcholine (ACh) sending electrical impulses across synapses between nerve cells causing the muscle cells to contract. The effect of acetylcholine can be neutralized by an enzyme, such as acetyl cholinesterase, which decomposes acetylcholine through the process of hydrolysis. When acetylcholine is decomposed, the muscle relaxes.



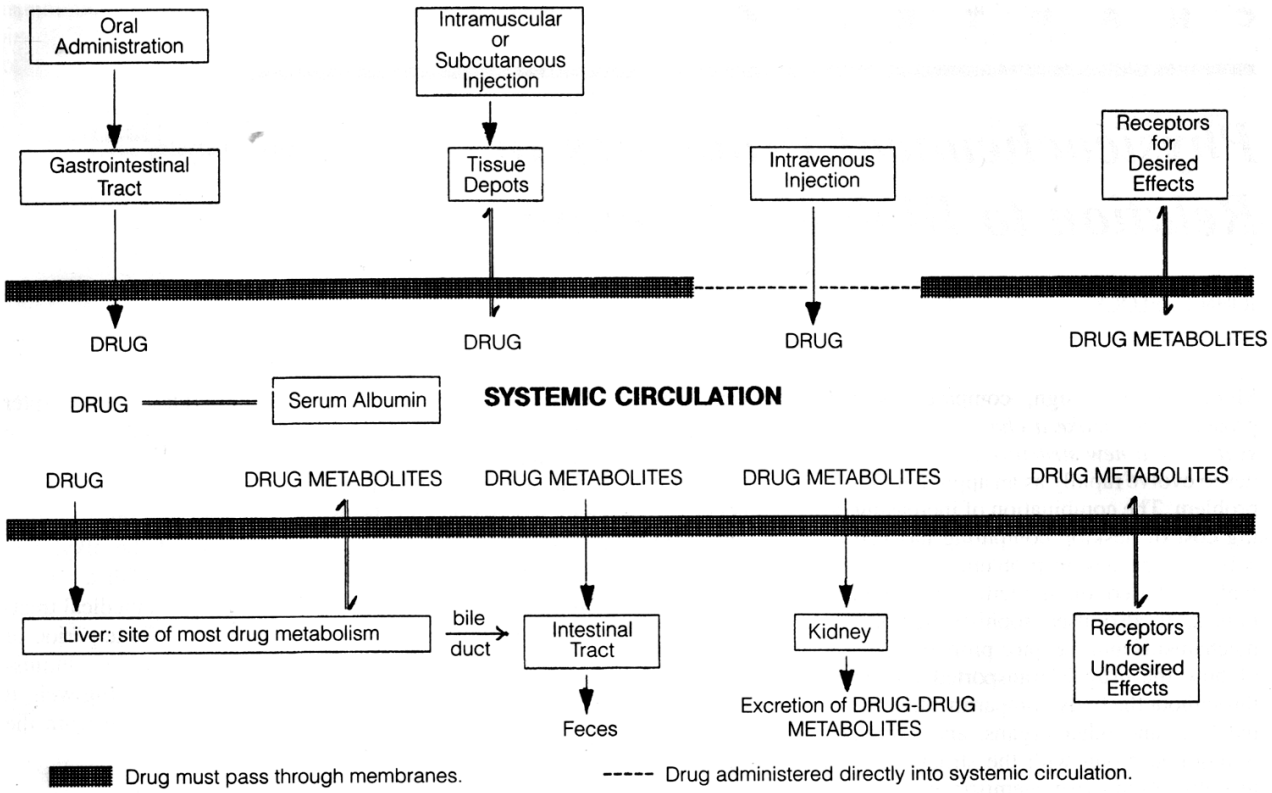
Rout of administration

Oral Administration:

Assume that the drug is administered orally. The drug must dissolve into a solution to pass through the gastrointestinal mucosa. Even drugs administered as true solutions may not remain in solution as they enter the acidic stomach and then pass into the alkaline intestinal tract. before reaching the colon.

The ability of the drug to dissolve is governed by several factors including:

1. Its chemical structure.
2. Variation in particle size.
3. Particle surface area.
4. Nature of the crystal form.
5. Type of tablet coating.
6. Type of tablet matrix قالب.



The therapeutic advantages are to bypassing the intestinal barrier and hepatic circulation by using parenteral (injectable) dosage forms.

This is common in:

1. Patients who, because of illness, cannot tolerate or are incapable of accepting drugs orally.
2. Some drugs are so rapidly and completely metabolized to inactive products in the liver (first-pass effect) that oral administration is precluded تستبعد.

Intravenous administration *places the drug directly into the circulatory system, where it will be rapidly distributed throughout the body.*

Subcutaneous and intramuscular injections *slow distribution of the drug because it must diffuse from the site of injection into systemic circulation.*

Examples of Administration of a drug directly into the its site of action

Local anesthetics are examples of administration of a drug directly into the desired nerve. A spinal block is a form of anesthesia performed by injecting a local anesthetic directly into the spinal cord at a specific location to block

Drug Distribution

The transport of drug from the blood stream to tissue sites where it will be effective, as well as to sites where the drug may be stored, metabolized, or eliminated from the body.

Many drugs need to pass through several barriers to reach their site of action.

These barriers include the walls of blood vessels, the walls of the intestines, the walls of the kidneys, etc.

All these walls consist of several types of cells and each cell has its cell membrane.

A common feature of all cell membranes is a phospholipid bilayer, about 10 nm thick, each layer arranged with the hydrophilic heads on the outside and the lipophilic chains facing inwards.

This gives a sandwich effect, with two hydrophilic layers surrounding the central hydrophobic one.

Glycoproteins Spanning(يمتد) this bilayer or attached to the outer or inner leaflets of the cell membrane, which may act as ion channels, receptors, intermediate messengers (G-proteins) or enzymes.

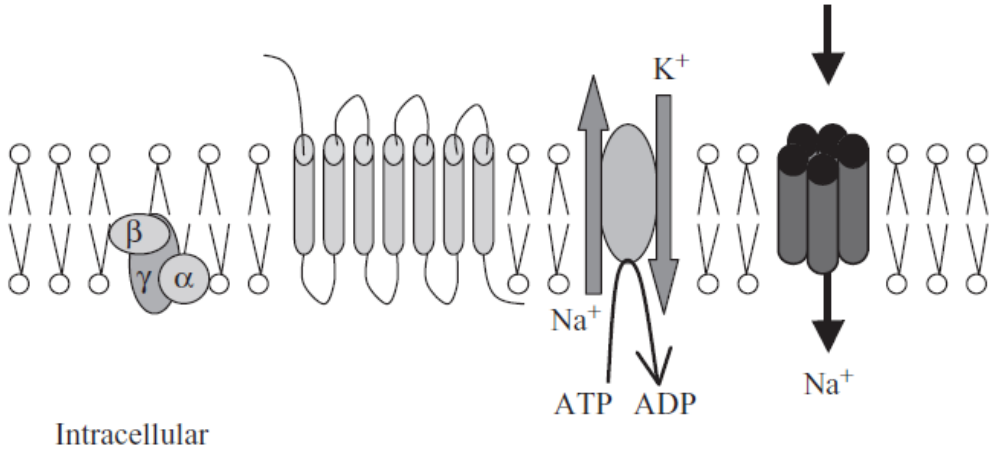


Figure 1.1. Representation of the cell membrane structure. The integral proteins embedded in this phospholipid bilayer are G-protein, G-protein-coupled receptors, transport proteins and ligand-gated ion channels. Additionally, enzymes or voltage-gated ion channels may also be present.

Drugs Diffusions

Passive diffusion:

This is the commonest method for crossing the cell membrane.

Drug molecules move down a concentration gradient, from an area of high concentration to one of low concentration, and the process requires no energy to proceed.

Many drugs are weak acids or weak bases and can exist in either the unionized or ionized form, depending on the pH.

The unionized form of a drug is lipid-soluble and diffuses easily by dissolution in the lipid bilayer.

Thus, the rate at which transfer occurs depends on the pKa of the drug in question.

Active transport:

Active transport is an energy-requiring process.

The molecule is transported against its concentration gradient by a molecular pump, which requires energy to function.

Energy can be supplied either directly to the ion pump, or indirectly by coupling pump-action to an ionic gradient that is actively maintained.

Active transport is encountered يصادف commonly in gut القناة الهضمية mucosa, the liver, renal tubules and the blood-brain barrier (BBB) [is a separation of circulating blood and cerebrospinal fluid (CSF)]

Pinocytosis:

The lipid membranes are very complex with a highly ordered structure.

Part of this membrane is a series of channels or tunnels that form, disappear, and reform.

There are receptors that move compounds into the cell by a process called pino-cytosis.

Pinocytosis is the process by which an area of the cell membrane invaginates التفاف around the (usually large) target molecule and moves it into the cell.

The molecule may then be released into the cell or may remain in the vacuole حويصلة so created, until the reverse process occurs on the opposite side of the cell.

The process is usually used for molecules that are too large to traverse the membrane easily via another mechanism.

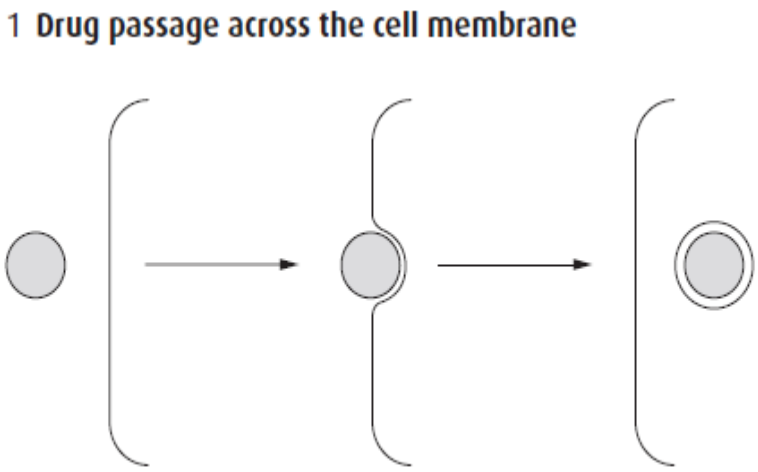


Figure 1.5. Pinocytosis.

Protein Binding

Only the unbound fraction of drug in plasma is free to cross the cell membrane; drugs vary greatly in the degree of plasma protein binding.

In practice, the extent of this binding is of importance only if the drug is highly protein-bound (more than 90%).

In these cases, small changes in the bound fraction produce large changes in the amount of unbound drug.

Drug + Albumin = Drug-Albumin Complex

Both albumin and globulins bind drugs, each has many binding sites, the number and characteristics of which are determined by the pH of plasma. In general, albumin binds neutral or acidic drugs (e.g. barbiturates), and globulins bind basic drugs (e.g. morphine).

Protein binding can have a profound عميق effect on the drug

1. effective solubility
2. bio-distribution
3. half-life in the body

4. and interaction with other drugs.

While this process may increase the amount of time the drug is active in the body, it may decrease the amount of the drug available to the tissues.

Drug-drug interactions

A drug interaction is a situation in which a first drug affects the activity of a second drug, by increased or decreased, or they produce a new effect that neither produces on its own. It may also exist between drugs & foods (drug-food interactions), as well as drugs & herbs (drug-herb interactions).

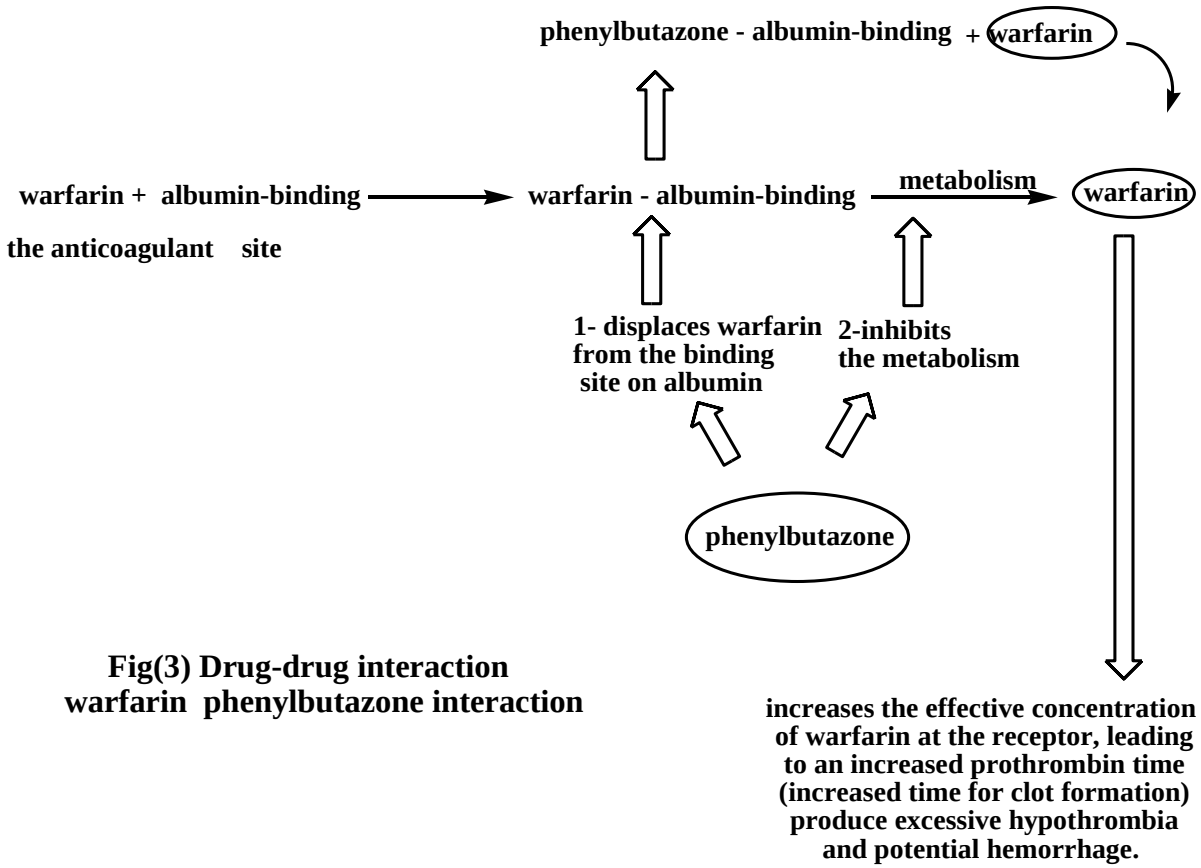
The drug-protein binding phenomenon can lead to some clinically significant drug-drug interactions resulting when one drug displaces another from the binding site on albumin.

Example.: A large number of drugs can displace the anticoagulant warfarin from its albumin-binding sites. This increases the effective concentration of warfarin at the receptor, leading to an increased prothrombin time (increased time for clot formation) and potential hemorrhage

Example:

drug –drug interaction between Phenylbutazone and warfarin

Phenylbutazone is a nonsteroidal anti-inflammatory drug (NSAID) effective in treating fever, pain, and inflammation in the body. Phenylbutazone is generally used with caution in patients taking blood thinning medications (anticoagulants), such as warfarin (Coumadin), because of an increased risk of bleeding.



Fig(3) Drug-drug interaction
warfarin phenylbutazone interaction

Tissue Depots ***مستودعات الانسجة***

The drug can also be stored in tissue depots. neutral fat constitutes some 20 to 50% of body weight and constitutes a depot of considerable importance. The more lipophilic the drug, the more likely it will concentrate in these pharmacologically inert depots.

The ultra-short-acting, lipophilic barbiturate thiopental's concentration rapidly decreases below its effective concentration following administration.

It "disappears" into tissue protein, redistributes into body fat, and then slowly diffuses back out of the tissue depots but in concentrations too low for a pharmacological response.

Thus, only the initially administered thiopental is present in high enough concentrations to combine with its receptors.

The remaining thiopental diffuses out of the tissue depots into systemic circulation in concentrations too small to be effective, is metabolized in the liver, and is excreted.

Excretion

The main route of excretion of a drug and its metabolites is through the kidney and liver.

Either the drug or drug metabolite can reenter systemic circulation by passing once again through the intestinal mucosa.

Nursing mothers must be concerned because drugs and their metabolites can be excreted in human milk and be ingested by the nursing infant.

ACID-BASE PROPERTIES

Most drugs used today can be classified as acids or bases.

As is noted shortly, a large number of drugs can behave as either acids or bases as they begin their journey in the body in different dosage forms and end up in systemic circulation.

A drug's acid-base properties can greatly influence its biodistribution and partitioning characteristics.

Over the years, at least four major definitions of acids and bases have been developed. The model commonly used in pharmacy and biochemistry was developed independently by Lowry and Bronsted. In their definition, an acid

is defined as a proton donor and a base is defined as a proton acceptor. Notice that for a base, there is no mention of the hydroxide ion.

Ionization

The lipophilic nature of the cell membrane only permits the passage of the uncharged fraction of any drug.

The degree to which a drug is ionized in a solution depends on:

1. the molecular structure of the drug and
2. the pH of the solution in which it is dissolved.

***The pKa** is the pH at which 50% of the drug molecules are ionized – thus the concentrations of ionized and unionized portions are equal.*

The value for pKa depends on the molecular structure of the drug and is independent of whether it is acidic or basic.

1. At a Ph below their pKa weak acids will be more unionized;
2. At a pH above their pKa they will be more ionized.

The reverse is true for weak bases, which are:

3- More ionized at a pH below their pKa and
4- More unionized at a pH above their pKa.

Chapter 3

ANALGESICS

An analgesic (painkiller) is any drug used to relieve pain .

The name derived from Greek (an-), "without", and (-algia), "pain".

Analgesic drugs act in various ways on the peripheral and central nervous system.

Classification according to mode of actions and chemical structures:

A. Morphine and related compounds.

B. Non-Steroidal Anti-inflammatory drugs (NSAID).

C. Aniline and p-Aminophenol derivatives.

D. Pyrazolone and pyrazolidine derivatives.

A. Morphine and related compounds:

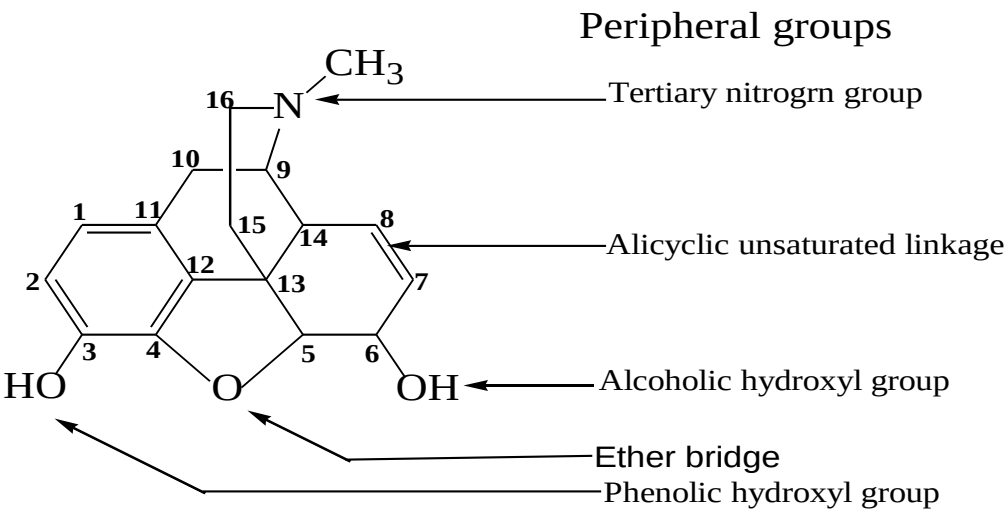
a) Opium:(morphine)

Narcotic drug produced from the drying resin of unripe capsules of the opium poppy.

Opium is grown mainly in Burma and Afghanistan.

Morphine is isolated from opium.

Chemical structure:



Morpholine and its Peripheral groups

b) Heroin

The diacetyl derivatives of morphine.

Heroin is more addictive than morphine but causes less nausea.

It is one of the most abused drugs in the United States; heroin addicts in the United States number close to 2 million people.

Because of its powerful habit-forming qualities, its manufacture and import are forbidden in the United States, even for medical use.

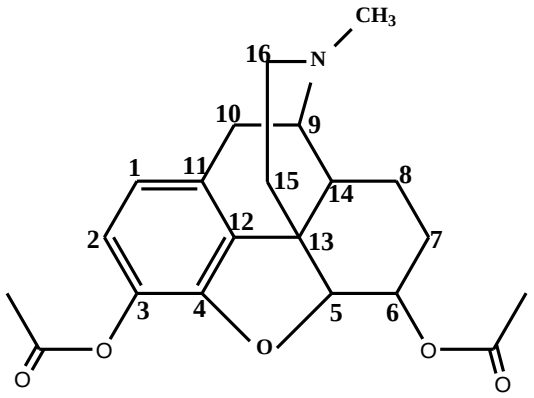
Heroin is a semi-synthetic opioid synthesized from morphine, a derivative of the opium poppy. It is the 3, 6-diacetyl ester of morphine (hence diacetylmorphine) and is processed by acetylation, making it a prodrug for the systemic delivery of morphine.

The white crystalline form is commonly the hydrochloride salt diacetylmorphine hydrochloride.

Upon crossing the blood-brain barrier, which occurs soon after introduction of the drug into the bloodstream, heroin is converted into morphine.

One of the most common methods of heroin use is via intravenous injection.

Chemical structure:



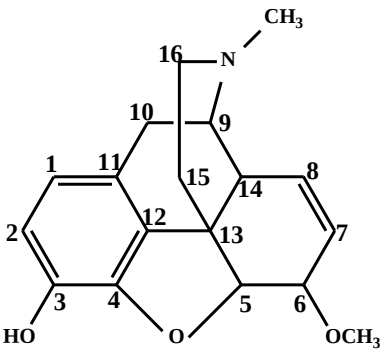
c) Codeine (methylmorphine):

The phenolic methyl ether of morphine, it has similar physiological effects but to a lesser degree, particularly because it is less habit-forming, it used for its analgesic, antitussive and antidiarrheal properties.

Codeine is an alkaloid found in opium in concentrations ranging from 0.3 to 3.0 percent.

While codeine can be extracted from opium, most codeine is synthesized from morphine through the process of O-methylation.

Chemical structure:



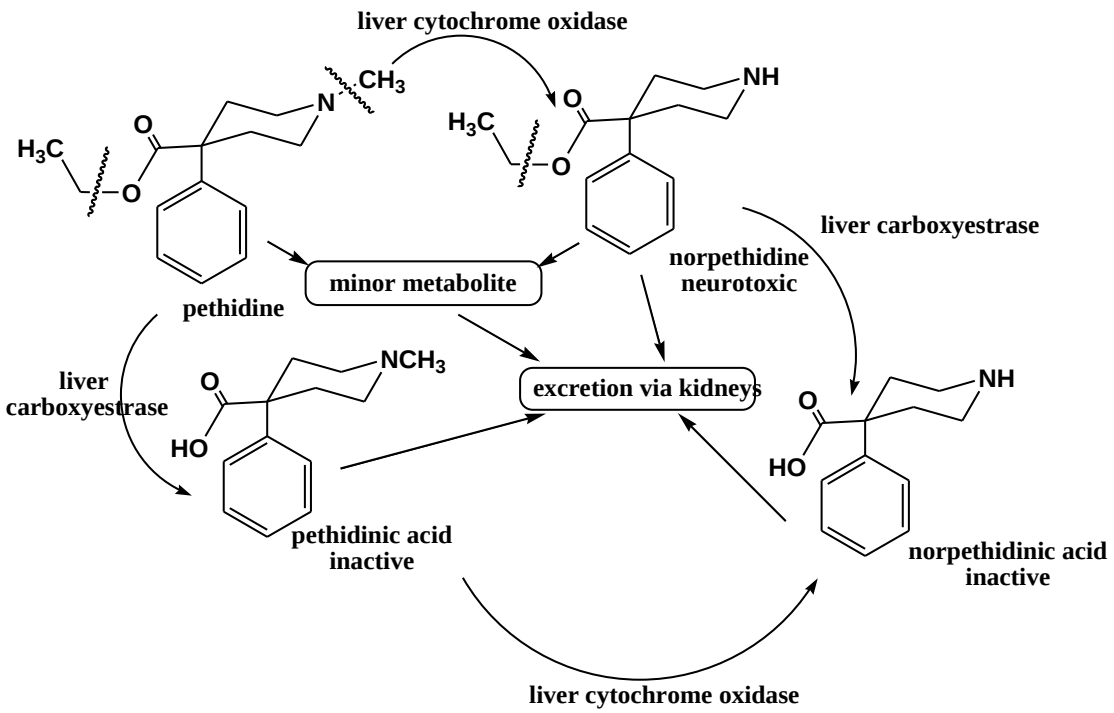
d) Meperidine (Pethidine)

Compared to morphine, pethidine was supposed to be safer and carry less risk of addiction, and to be superior in treating the pain associated with biliary spasm or renal colic due to its antispasmodic effects.

iupac name: Ethyl-1-methyl-4-phenylpiperidine-4-carboxylate

Metabolism:

1. Pethidine is quickly hydrolyzed to pethidinic acid by liver carboxyestrase enzyme.
2. Pethidine is also demethylated in the liver to norpethidine by liver cytochrome oxidase enzyme, which has half the analgesic activity of pethidine but a longer elimination half-life (8-12 hours); accumulating with regular administration, or in renal failure, norpethidine is toxic and has convulsant and hallucinogenic effects.
3. Norpethidine is converted to inactive norpethidinic acid by hydrolysis in the liver, by liver carboxyestrase enzyme.
4. pethidinic acid is converted to inactive norpethidinic acid by demethylation in the liver, by liver cytochrome oxidase enzyme.
5. norpethidinic acid excreted in the urine by the kidney.



Metabolism of Pethidine

B. Non-Steroid Anti-inflammatory drugs (NSAIDs):

a) 2-hydroxybenzoic acid derivatives (salicylic acid, aspirin)

1- salicylic acid:

This colorless crystalline organic acid is widely used in organic synthesis, It is probably best known as a compound that is chemically similar but not identical to the active component of aspirin (acetylsalicylic acid).

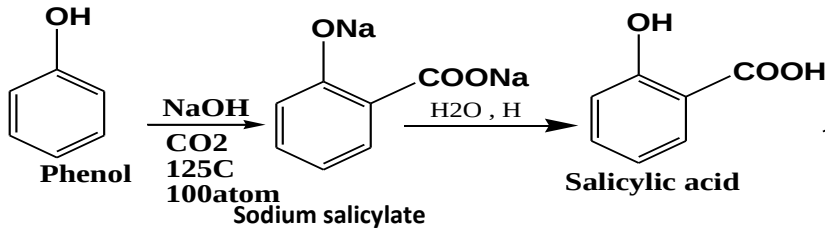
Uses:

1- salicylic acid is a key ingredient in many skin-care products for the treatment of acne, psoriasis, calluses, corns, keratosis pilaris, and warts.
2- Because of its effect on skin cells, salicylic acid is used in several shampoos used to treat dandruff.
3- The medicinal properties of salicylate, mainly for fever relief, have been known since ancient times, and was used as an inflammatory drug.

Chemistry and preparation:

(the Kolbe-Schmitt reaction)

phenol (generally extracted from coal tar) is treated with a sodium base which generates sodium phenoxide, which is then reacted with carbon dioxide under high temperature and pressure to yield salicylate, which is acidified, yielding salicylic acid



Important example: (combinations)

Whitfield Ointment:

contains 6% w/w benzoic acid and 3% w/w salicylic acid, it is highly effective in the treatment of tinea, of the chronic dry-scaling variety.

The ingredient Benzoic Acid has antibacterial and antifungal properties. It is applied topically for fungal skin infections such as ringworm and tinea. Salicylic Acid has keratolytic and fungicidal properties. It is applied topically in the treatment of fungal skin infections.

DOSAGE & ADMINISTRATION

Clean and dry the affected area, apply the ointment to affected area by gentle massage once or twice daily or as directed by the physician.

The Ointment should not be applied to broken or inflamed skin. Its use should be discontinued if excessive dryness or irritation of the skin occurs.

2- aspirin: which is given previously

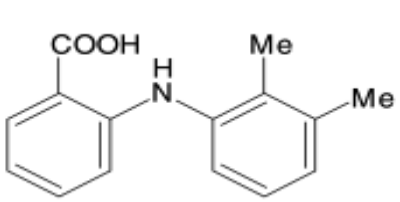
b) N-aryl-anthranilic acid derivatives

Mefenamic acid Ponstan®

is a non-steroidal anti-inflammatory drug used to treat pain, including menstrual pain. It is commercially available as Ponstel. It is also prescribed as an antipyretic drug. It is typically prescribed for oral administration.

Mefenamic acid is known to cause an upset stomach, therefore it is recommended to take prescribed doses together with food or milk.

Chemical structure:



(IUPAC) name : 2-(2,3-dimethylphenyl)aminobenzoic acid

c) aryl acetic acid derivatives

drugs with analgesic, antipyretic and anti-inflammatory effects, they reduce pain, fever and inflammation. The most prominent members of this group of drugs are aspirin and ibuprofen.

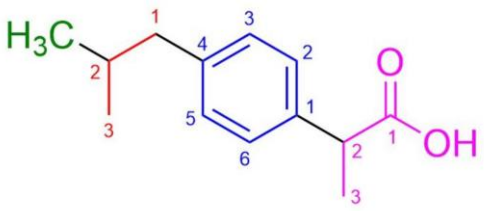
Ibuprofen:

Trade name: marketed as Nurofen and since under various trademarks including Brufen, Dorival, …etc.

It is used for relief of symptoms of arthritis, primary dysmenorrhea عسر الطمث , fever, and as an analgesic, especially where there is an inflammatory component.

Ibuprofen has no antiplatelet effect.

Chemical structure and (IUPAC) name :



2-(4-(2-methylpropyl)phenyl)propanoic acid

Mode of action:

is believed to work through inhibition of cyclooxygenase (COX), thus inhibiting prostaglandin synthesis.

Side effects include:

nausea, dyspepsia, gastrointestinal ulceration/bleeding, raised liver enzymes, diarrhea, headache, dizziness, unexplained rash, salt and fluid retention, and hypertension. along with several other NSAIDs, ibuprofen has been implicated in elevating the risk of myocardial infarction, particularly among those chronically using high doses.

ketoprofen :

non-steroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic effects.

Mod of action:

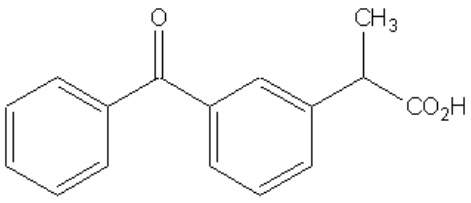
It acts by inhibiting the body's production of prostaglandin.

Dosage from:

available 12.5 mg coated tablets (25, 50, 75, 100, 150, and 200 mg) capsules.

Ketoprofen also comes in a 2,5% gel for topical application.

Chemical structure:



(IUPAC) name :

2-(3-benzoylphenyl) propanoic acid

C.Aniline and p-Aminophenol derivatives:

Aminophenol derv. (paracetamol)

Paracetamol is a common analgesic and antipyretic drug that is used for the relief of fever, headaches, and other minor aches and pains.

Paracetamol is also useful in managing more severe pain, It is a major ingredient in numerous cold and flu medications, as well as many prescription analgesics.

It is considered safe for human use in recommended doses, but because of its wide availability, deliberate or accidental overdoses are fairly common.

Paracetamol has similar analgesic and antipyretic effect as NSAIDs but unlike NSAIDs it has no antiplatelet effect as aspirin, and has little or no anti-inflammatory effect

Also, it has no GI side effects as NSAIDs.

Names:

1- Common brand names for the drug include Tylenol ,paracetol and Panadol.
2- acetaminophen and paracetamol (both come from the chemical names for the compound)
3- chemical names: N-acetyl-para-aminophenol and para-acetyl-amino-phenol. In some contexts, it is shortened to APAP, for N-acetyl-para-aminophenol.

4- Systematic(iupac)name: N-(4-Hydroxphyenyl) ethanamide

Preparation:

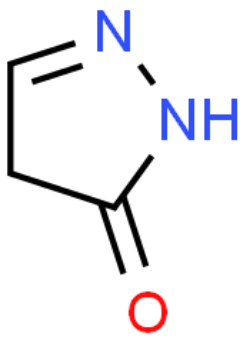
which is given previously in lec. 1

Mode of action:

The exact mechanism of action of paracetamol/acetaminophen is uncertain, but it appears to be acting centrally.

D.Pyrazolone and pyrazolidine derv:

Pyrazolone, a five-membered-ring lactam, is a derivative of pyrazole that has an additional keto (=O) group.



It has a molecular formula of C3H4N2O.

Ph. Yaarub Al Shakargy
2022-2023

Chapter 4
ANTI-INFECTIVE AGENTS & ANTIBACTERIAL ANTIBIOTICS

CLASSIFICATIONS:

i. **<u>ANTI-INFECTIVE AGENTS:</u>**

A. GENERAL COMPOUNDS:

1. ALCOHOLS AND RELATED COMPOUNDS

2. PHENOLS AND THEIR DEREVATIVES

3. OXIDIZING AGENTS

4. HALOGEN-CONTAINING COMPOUNDS

5. CATIONIC SURFACTANTS

6. DYS

7. MERCURY COMPOUNDS

8. PRESERVATIVES

B. ANTIFUNGAL AGENTS

C. SYNTHETICS ANTIBACTERIAL AGENTS

D. ANTIPROTOZOAL AGENTS

E. ANTHELMINTICS

F. ANTISCABIOUS AND ANTIPEDICULAR AGENTS

G. ANTIBACTERIAL SULFONAMIDES

H. DIHYDROFOLATE REDUCTASE INHIBITORS

I. SULFONES

ii. **<u>Antibacterial Antibiotics</u>**

a) ß Lactam: Penicillin's, cephalosporin's

b) Amino glycosides: Streptomycin, Neomycin

c) Tetracyclines

d) The macrolides: Erythromycin, Azithromycin

e) Lincomycin

f) Unclassified Antibiotics

i. <u>ANTI-INFECTIVE AGENTS:</u>

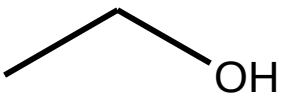
A. GENERAL COMPOUNDS:

This compd. is used locally and called germicides, which kill or prevent the growth of microorganisms when applied to living tissue.

1. Alcohols And Related Compounds:

Ethanol (Ethyl Alcohol)

CH3CH2OH.



Uses of ethanol:

1. Externally as antiseptic
2. Preservative
3. Solvent
4. In practice pharmacy for preparation of spirits, tinctures and fluid extracts

Preparation (Industry):

$$C_2H_4 + H_2O \rightarrow \mathbf{CH_3CH_2OH}$$

ايثانول ماء ايثلين

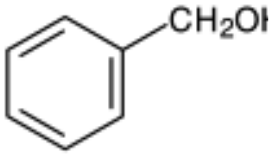
Side effects:

- Ethanol is a central nervous system depressant and has significant psychoactive effects in sublethal doses.
- Enzymes break down Ethanol into a byproduct (Acetaldehyde) causes nausea, vomiting and vasodilation (flashing).

Mode of action (as anti-infection):

The ability of alcohol's as polar solvents to penetrate of microorganism membranes and denature the important proteins & carbohydrates and kill or prevent their growth on the living tissue.

Benzyl Alcohol:



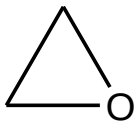
Uses:

1. Local anesthetic.
2. Disinfectant.
3. Preservative.

Ethylene Oxide:

C2H4O

A colorless flammable gas that liquefies at 12°C.



Ethylene oxide

Uses:

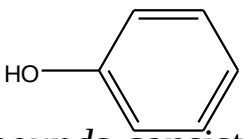
Ethylene oxide forms explosive mixtures in air at concentrations ranging from 3 to 80% by volume.

The explosion hazard is eliminated when the gas is mixed with sufficient concentrations of carbon dioxide.

Carboxide is a commercial sterilant containing 10% ethylene oxide and 90% carbon dioxide by volume that can be handled and released in air without danger of explosion.

2. PHENOLS AND THEIR DEREVATIVES:

Phenol:



Are a class of *chemical compounds* consisting of a *hydroxyl group* (*-OH*) attached to an *aromatic hydrocarbon* group.

The simplest of the class is *phenol* (C6H5OH).

Although similar to *alcohols*, phenols have unique properties and are not classified as alcohols

They have relatively higher *acidities* due to the aromatic ring tightly coupling with the oxygen and a relatively loose bond between the *oxygen* and *hydrogen*.

thus, making it very suitable as a cleaning and disinfectant agent.

Uses:

1. Disinfection
2. Aspirin preparation, and other drugs

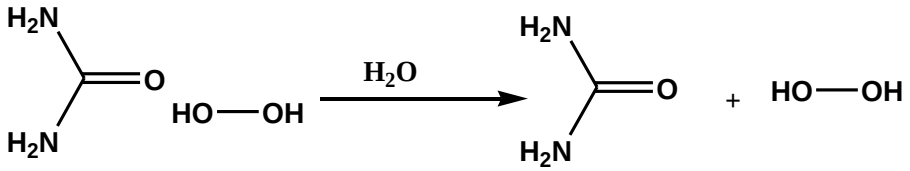
3. OXIDIZING AGENTS:

Substances such as hydrogen peroxide (H2O2) and potassium permanganate (KMnO4) are most commonly had tendency to liberate oxygen.

Mode of action:

By their ability to liberate oxygen in the tissues thus they modifying vital cell components, including DNA and proteins, thereby leading to cellular dysfunction, denature proteins in microorganisms through a direct oxidation reaction such as KMnO4, oxidizing agents are especially effective against anaerobic bacteria & can be used in cleansing contaminated wounds. The bubbles that form during the liberation of oxygen help to dislodgeازالة debrisبقايا الانسجة المتحطمة.

Carbamide peroxide:



Carbamide peroxide urea Hydrogenperoxide

also called urea peroxide, is an oxidizing agent, consisting of *hydrogen peroxide* compounded with *urea*.

The *molecular formula* is CH6N2O3, or CH4N2O.H2O2. It is white crystalline material that releases oxygen in contact with water.

Uses of Carbamide peroxide:

1. Antiseptics
2. Disinfectants

4. HALOGEN-CONTAINING COMPOUNDS:

Compd. Contains halogens (iodine, chlorine or bromine)

Iodophors:

Lugol's iodine(Lugol's solution), a solution of *iodine* (*French* physician *J.G.A. Lugol*.)

Uses:

- Lugol's iodine solution is often used as an germicides (*antiseptic* and *disinfectant*).
- As an indicator to test for the presence of *starches* in *organic compounds*.
- For emergency disinfection of drinking water.
- In the treatment of gout.
- A first line treatment for hypothyroidism in adults.

It consists of 10% *iodine* (I2) and 10% *potassium iodide* (KI) in 80% *distilled water* with a total iodine content of 130 mg/ml.

5-CATIONIC SURFACTANTS:

Benzalkonium chloride:

Benzalkonium chloride is an organic salt used in cleaning agents, classified as a quaternary ammonium cationic (positively charged ions) detergent.

- Used for the disinfecting of the intact skin.
- In the treatment of superficial injuries and infected wounds.
- It is also used to preserve the sterility of surgical instruments.

- Preserve the sterility of ophthalmic solutions.

Mode of action:

Dissolute in to the microbial cell membrane, destabilizing it, and interfere with enzymes

6-DYS:

Organic dyes use, as anti-infection agents against Gram-positive bacteria & many fungi but Gram-negative are generally resistant.

Gentian Violet:

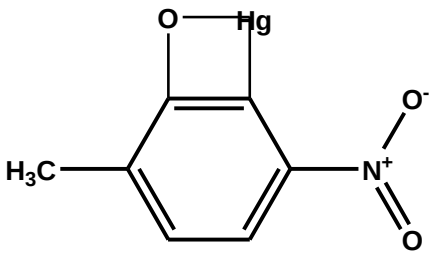
Uses

- Vaginal suppositories for treatment of yeast infections.
- Used for treatment of oral yeast and fungal infections.
- Orally as an anthelmintic to destroy parasitic worms (ringworm) in solution (1-3%).

7. MERCURY COMPOUNDS:

Synthetic *mercury*-containing organic compound

Nitromersol (Metaphor):



4-nitro-3-hydroxymercuriorthocresol

uses:

- As an *antiseptic* for the skin and mucous membranes.

- As a *disinfectant* for sterilizing surgical instruments.

8. PRESERVATIVES:

A preservative is a *chemical* that is added to products (foods, pharmaceuticals ... etc.) to prevent *spoilage*, whether from microbial growth or undesirable chemical changes.

What should be an ideal preservative:

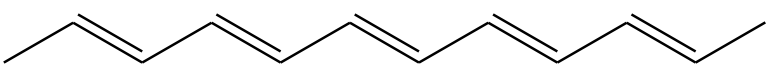
1-Effective at low conc. against all possible microorganisms.
2-Compatible with other constituents of the preparation.
3-Nontoxic.
4-Stable.

B. ANTIFUNGAL AGENTS:

1- Polyenes

Polyenes are poly-unsaturated organic compounds that contain one or more sequences of alternating double and single carbon-carbon bonds. These double carbon-carbon bonds interact in a process known as conjugation, which results in an overall lower energy state of the molecule.

Organic compounds with two carbon-carbon double bonds are dienes; those with three such double bonds are trienes; those with four are tetraenes, etc.

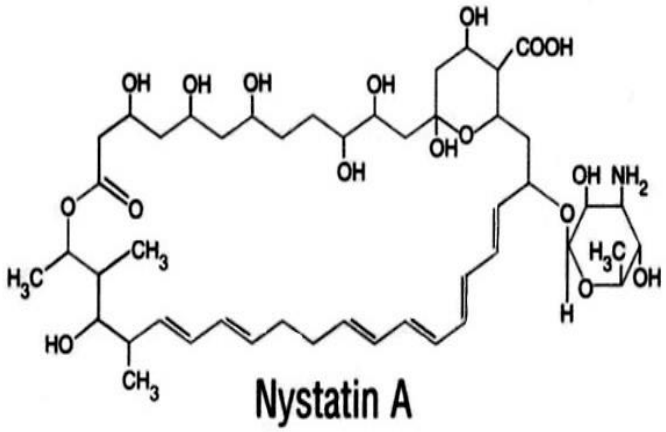


Structurally complex isolated from soil bacteria of genus streptomyces:

EXAMPLES:

Nystatin (Mycostatin):

Nystatin is the first polyene antifungal drug that could be used safely and effectively in humans to treat fungal infections. It is not absorbed across intact skin or mucous membranes. It's too toxic to be administered parentally. It's used as a topical agent as cream ointment and powder, It is considered a relatively safe drug for treating oral, gastrointestinal or Vaginal fungal infections.



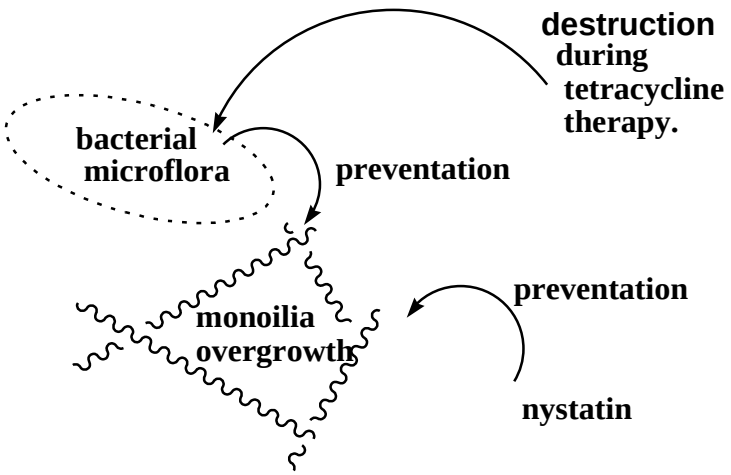
Nystatin A

Mode of action:

Nystatin binds to ergosterol, a major component of the fungal cell membrane. When present in sufficient concentrations, it forms pores in the membrane that lead to K+ leakage and death of the fungus.

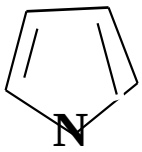
Combination of Nystatin with Tetracycline:

A combination of nystatin with tetracycline use to prevent monilia overgrowth caused by the destruction of bacterial microflora of the intestine during tetracycline therapy.



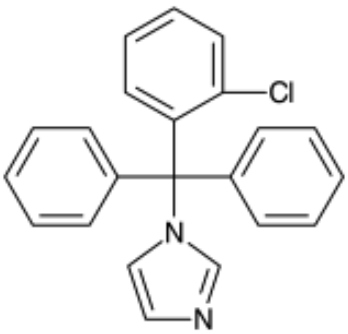
***2*- Azoles:**

Azoles: five members heterocyclic rings Compounds containing nitrogen atom.

Diazoles: when this ring  containing two nitrogen atoms.

Examples:

Clotrimazole:



1-[(2-chloroph]-1H-imidazole

Mode of action:

The drug works by damaging the cell walls of the invading fungus, thereby inhibiting its growth.

Uses:

broad spectrum anti-fungal drug that used for treat a variety of fungal infections, especially on the skin and in the mouth and vagina.

C. **Synthetic antibacterial drug**

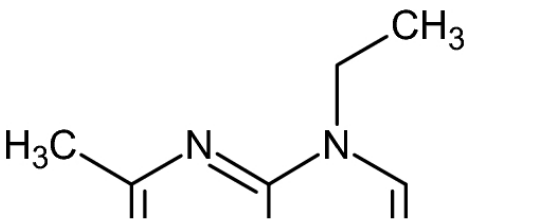
A family of broad-spectrum series of synthetic antibacterial antibiotic

1- **Quinolones:**

Examples:

nalidixic acid (NegGram)

The parent of the group of these drugs is nalidixic acid.

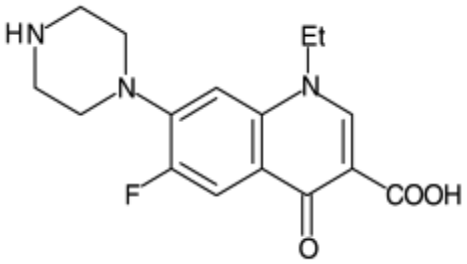


used in treatment of UTI (against common Gram-negative urinary pathogens).

Mode of action

Inhibition of DNA synthesis

Norfloxacin {Noroxin}: Also called fluoroquinolone

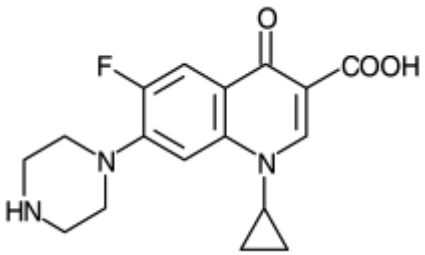


Is an oral broad-spectrum antibacterial agent used in the treatment of urinary tract infections.

Mode of action

Inhibition of DNA synthesis

Ciprofloxacin (ciprodar):



Uses:

Drug used to treat bacterial infections in the lower respiratory tract, urinary tract, bones, joints, and skin. It is also used to treat serious ear, and eye infections, cholera, tuberculosis, infectious diarrhea, and infections associated with acquired immunodeficiency syndrome (AIDS) and anthrax.

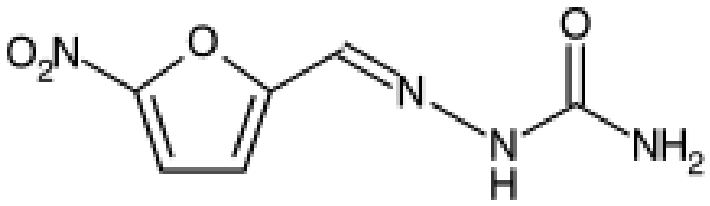
***2*- Nitrofurans:**

Mode of action:

they act by breaking down cell walls and interfering with the bacteria's metabolism.

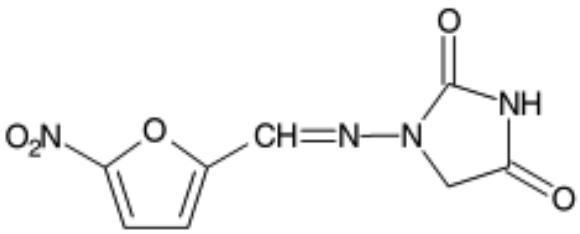
Examples:

Nitrofurazone



This bactericidal compound is used as an antibiotic most commonly in the form of ointments. Its use in medicine has become less frequent as safer and more effective products have become available.

Nitrofurantoin



Brand Names: Furadantin, Macrobid, Macrodantin

Uses:

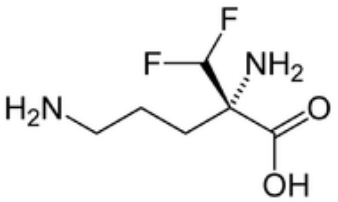
Antibiotic drug used to treat bacterial infections of the bladder and kidneys.

D. ANTIPROTOZOAL AGENTS

Is a class of pharmaceuticals used in treatment of protozoan infection (parasitic diseases).

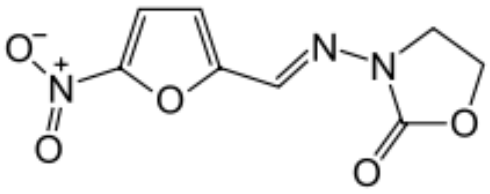
Examples:

Eflornithine (α-difluoromethylornithine or DFMO):



It was initially developed for cancer treatment, but while having little use in treating malignancies, it was found to be highly effective in African trypanosomiasis (sleeping sickness).

Furazolidone:



is an antibacterial drug used to treat diarrhea and enteritis caused by bacteria or protozoan infections. It has been used in aquaculture.تربية الاحياء المائية

E. ANTHELMINTICS

Anthelmintics or anti-helminthics:

Drugs that have the capability of ridding طرد the body parasitic worms (helminths) from the body, by either stunningتعطيل الفعاليات الحيوية or killing them. They may also be called vermifuges (stunning) or vermicides (killing).

Examples:

1- **Albendazole**: effective against threadworms, roundworms, whipworms, tapeworms, hookworms.

2- **Mebendazole:** effective against pinworms, roundworms and hookworms

3- **Niclosamide:** effective against tapeworms

4- **Ivermectin**: effective against most common intestinal worms (except tapeworms)

5- **Thiabendazole:** effective against roundworms, hookworms

F. ANTISCABIOUS AND ANTIPEDICULAR AGENTS

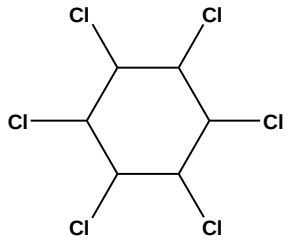
1- ANTISCABIOUS

Examples:

a) **Permethrin 5% Cream**

b) **Lindane 1% Lotion or cream:**

Lindane, also known as gamma-hexachlorocyclohexane (γ-HCH) and benzene hexachloride (BHC), is an organochlorine insecticide that has been used in agriculture الزراعة and as a treatment for headlice and scabies



1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE

It has an oral LD50 of 88 mg/kg in rats and a dermal LD50 of 1000 mg/kg. In humans, lindane primarily affects the nervous system, liver and kidneys, and may be a carcinogenic and/or endocrine disruptor معطل او مثبط.

c) **Benzyl benzoate 10% or 25% Lotion:**

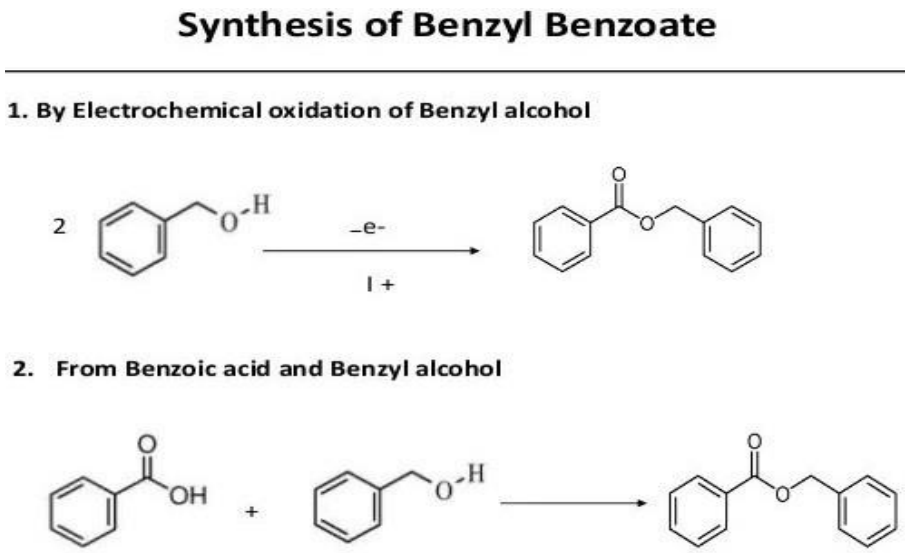
As an antiparasitic insecticide that kills lice and the mites العث responsible for skin scabies.

Synthesis:

This colorless liquid is formed by

1- Electrochemical oxidation of benzyl alcohol

2- The condensation product of benzoic acid and benzyl alcohol



d) **Allethrin 0.6% Aerosol**

e) **Crotamiton 10% Cream**

f) **Precipitated sulfur 3–6% Lotion or 5%,10%, or 40% in petrolatum** applied for 24 hr. and then reapplied every 24 hr. for the next 2 days (with a bath taken between each application)

2- **Anti-pedicular agents:**

Are agents used to eliminate head, body and crab lice (pubic lice) by kill the adult lice (pediculicides) and destroy their eggs.

IVERMECTIN:

is a broad-spectrum anti-parasite medication, traditionally used against worms (except tapeworms), but more recently found to be effective against most mites and some lice too.

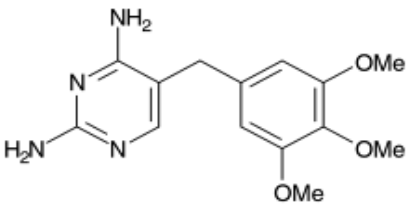
MODE OF ACTIONS:

Ivermectin kills by interfering with nervous system and muscle function, in a particular by enhancing the inhibitory neurotransmission.

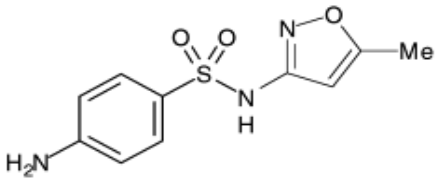
G. ANTIBACTERIAL SULFONAMIDES

Example:

Mixed Sulphonamides(Methaprime):



Trimethoprim



Sulfamethoxazole

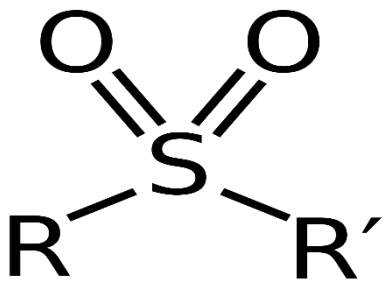
H. DIHYDROFOLATE REDUCTASE INHIBITORS:

Trimethoprim and sulfamethoxazole are also considered as examples of dihydrofolate reductase inhibitors.

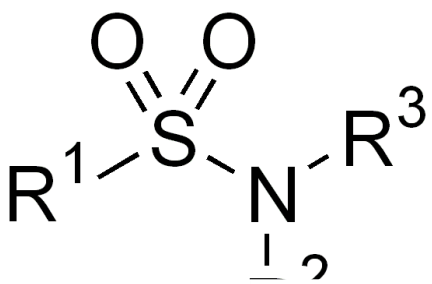
I. SULFONES:

Trimethoprim and sulfamethoxazole are also considered as examples of sulfones and sulfonamide.

Sulfones: -



Sulfonamides: -



Gram's method

(Hans Christian Joachim Gram)

Bacteria are first stained with gentian violet (dye) and then treated with Gram's solution, (consisting of 1 part iodine, 2 parts potassium iodides, and 300 parts water).

After being washed with ethyl alcohol, the bacteria will either retain the strong blue color of gentian violet or be completely decolorized.

Gram- variable bacteria:

Organisms that sometimes retain the blue color and sometimes do not are known as gram-variable; typical gram-variable bacteria are the bacilli that cause tuberculosis.

Gram- positive bacteria:

Bacteria that retain the blue stain are known as gram-positive; typical gram-positive bacteria are those staphylococci that produce boils.

Gram- negative bacteria:

Bacteria that do not retain the blue stain are known as gram-negative. Typical gram-negative bacteria are the bacilli that cause whooping cough.

Anti-bacterial drugs can be further subdivided into:

1. **The narrow-spectrum**

The antibacterial antibiotics that effective against gram-positive or gram-negative (penicillin acts against many gram-positive bacteria).

2. The broad -spectrum

The anti-bacteria antibiotics that effective against both gram-positive and gram-negative bacteria, (The tetracycline and chloramphenicol are both broad-spectrum drugs because they are effective against both gram-positive and gram-negative

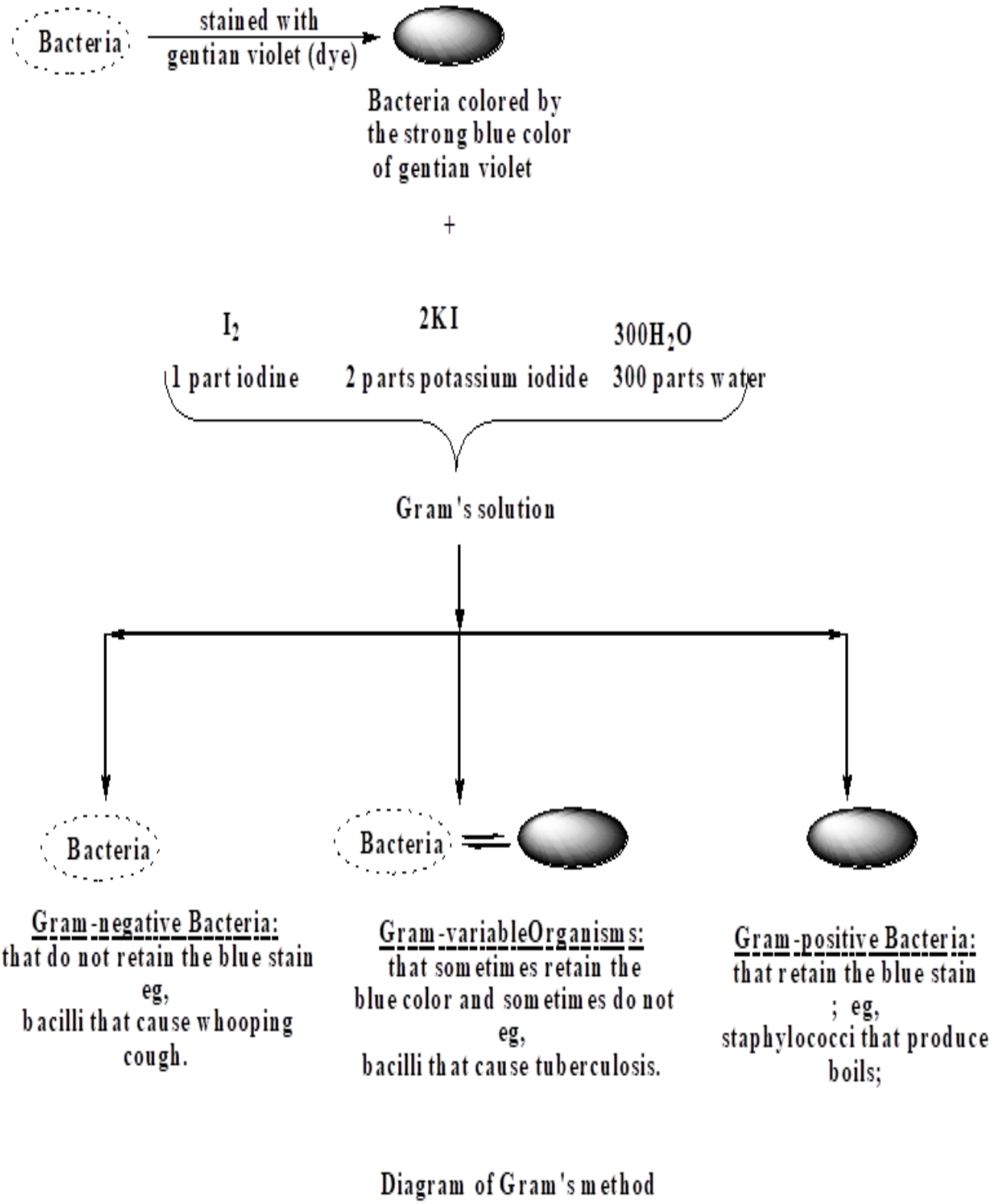


Diagram of Gram's method

II-Antibacterial Antibiotics

Classifications:

Antibiotics can be classified in several ways. The most common method classifies them according to:

1. their action against the infecting organism. Some antibiotics attack the cell wall. some disrupt the cell membrane; and the majority inhibit the synthesis of nucleic acids and proteins, the polymers that make up the bacterial cell.
2. Another method classifies antibiotics according to which bacterial strains they affect: staphylococcus, streptococcus, or Escherichia coli.
3. Antibiotics are also classified on the basis of chemical structure:
   a) ß Lactam as penicillin, cephalosporins.
   b) Aminoglycosides.
   c) Tetracyclines.
   d) Polypeptides. [macrolides]
   e) Lincomycin.
   f) Unclassified antibiotics.

a) ß Lactam

1. Penicillin's

Penicillin Discovered by Scottish bacteriologist Alexander Fleming discovers that Penicillium mold produces a substance that has an antibiotic effect. He recognizes the potential value of this substance, which comes to be called penicillin, but another decade passes before studying it by other scientists.

Penicillin, is a group of antibiotics derived from *Penicillium* fungi.

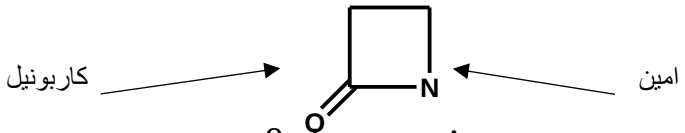
They are *Beta-lactam antibiotics* used in the treatment of *bacterial infections* caused by susceptible, usually *Gram-positive* organisms.

It was discovered accidentally in 1928 by Fleming, who showed its effectiveness in laboratory cultures against many disease-producing bacteria.

This discovery marked the beginning of the development of antibacterial compounds produced by living organisms.

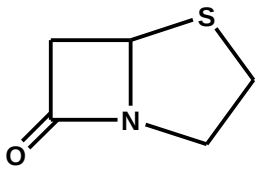
Structure:

Penicillin, is antibiotics contain a ß -lactam ring as a critical part of their chemical structure.



ß -lactam ring

[a four –membered cyclic amide]



general structure of Penicillin

[two fused heterocyclic rings. a ß -lactam and thiophen]

Mode of actions:

binding to the *enzyme* (*DD-transpeptidase*) that links the molecules in bacterial cell wall, and this weakens this wall ,causes *cytolysis* or *death*.

Penicillin acts both by killing bacteria and by inhibiting their growth. It does not kill organisms in the resting stage but only those growing and reproducing (bactericidal).

Penicillin is effective against a wide range of disease-bearing microorganisms, including pneumococci, streptococci, gonococci, meningococci, the clostridium that cause tetanus, and the syphilis spirochete. The drug has been successfully used to treat such deadly diseases as endocarditis, septicemia, gas gangrene, gonorrhea, and scarlet fever.

Adverse effects(allergy):

Common *adverse drug reactions* associated with use of the penicillin include diarrhea, hypersensitivity, nausea, rash, neurotoxicity *urticaria*الشرى, and/or superinfection (including *candidiasis*). Infrequent adverse effects include fever, vomiting, *erythema*, dermatitis, *angioedema*وذمة وعائية, seizures (especially in epileptics), and/or *pseudomembranous colitis* التهاب القولون الغشائي الكاذب.

Pain and inflammation at the injection site is also common for *parenterally* administered benzathine benzylpenicillin and, to a lesser extent, procaine benzylpenicillin.

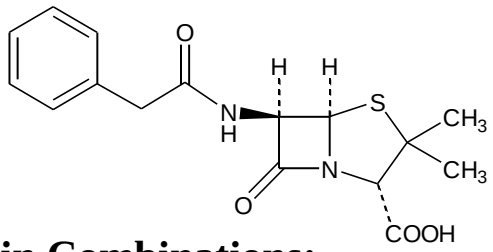
Resistant to Penicillin:

Infections caused by certain strains of staphylococci cannot be cured by this antibiotic because the organism produces an enzyme, penicillinase, capable of destroying the antibiotic.

In addition, enterococci and other bacteria known to cause respiratory and urinary tract infections were found resistant to the action of penicillin.

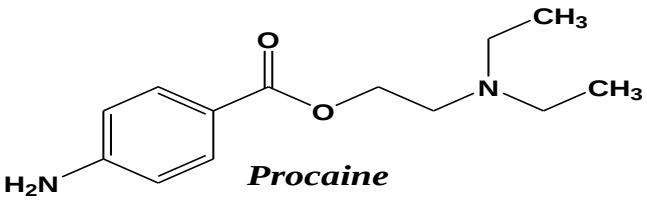
Benzyl penicillin; penicillanic acid; penicillin G

Chemical structure:



Procaine benzyl penicillin Combinations:

Procaine benzyl penicillin also known as procaine penicillin, is a combination of benzylpenicillin (penicillin G)with the *local anesthetic* agent *procaine*

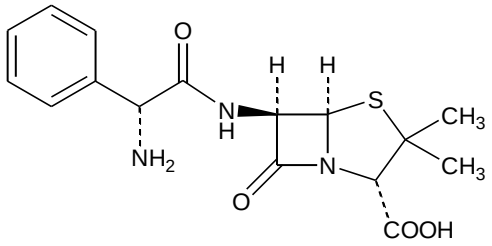


Procaine

(4-Aminobenzoic acid 2-(diethylamino)ethyl ester]).

This combination is aimed at reducing the pain and discomfort associated with a large *intramuscular* injection of penicillin.

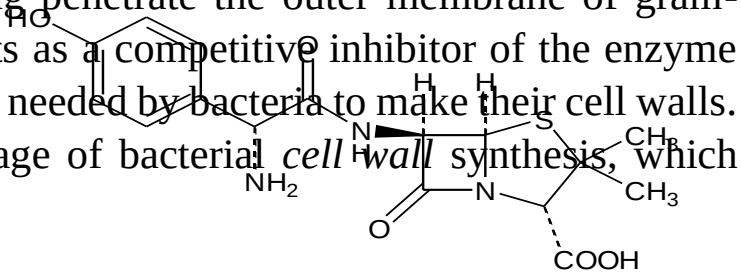
Ampicillin



It is active against all organisms normally killed by penicillin.

Mechanism of action:

Ampicillin is able to penetrate *Gram-positive* and some *Gram-negative* bacteria. It differs from penicillin only by the presence of an *amino* group. That amino group helps the drug penetrate the outer membrane of gram-negative bacteria. Ampicillin acts as a competitive inhibitor of the enzyme transpeptidase. Transpeptidase is needed by bacteria to make their cell walls. It inhibits the third and final stage of bacterial *cell wall* synthesis, which ultimately leads to cell *lysis*.



Amoxycillin (*INN*)

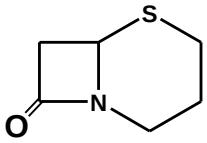
Mechanism of action:

Amoxicillin acts by inhibiting the synthesis of bacterial *cell wall*. It inhibits *cross-linkage* between the linear peptidoglycan polymer chains that make up a major component of the *cell wall* of *Gram-positive* bacteria.

It is one of the most common antibiotics prescribed for children, and the liquid forms are helpful where the patient might find it difficult to take tablets or capsules.

2. Cephalosporin's

Are a class of *β-lactam antibiotics* originally derived from *Acremonium,* which was previously known as "Cephalosporium".



general structure of Cephalosporin's
[two fused heterocyclic rings. a ß -lactam and thiopyran]

Cephalosporin's are more effective than penicillin against gram-negative bacilli and equally effective against gram-positive cocci.

Cephalosporin’s may be used to treat strains of meningitis التهاب السحايا and as a prophylactic for orthopedicالعظام, abdominal, and pelvic surgery.

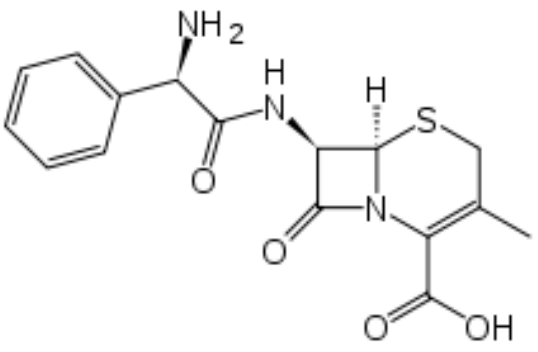
Mode of action:

Cephalosporins disrupt the synthesis of the *peptidoglycan* layer of bacterial *cell walls*. The peptidoglycan layer is important for cell wall structural integrity.

Hypersensitivity reactions:

Rare hypersensitive reactions from the cephalosporin’s include skin rash and, less frequently, anaphylactic shock.

Cephalexin [Keflex, Biocef]



The first-generation *cephalosporin antibiotic*. It is an orally administered agent with commonly marketed under the trade name Keflex

Uses:

Cephalexin, bacteria-fighting drug used to treat infections of the middle ear ; urinary tract ; reproductive system ; skin, and bones.

Availability:

This drug is available by prescription in tablet, capsule, and liquid form, all of which are taken orally. The typical adult dosage is 500 mg every 12 hours (sometimes prescribed as 250 mg every 6 hours). Children should take the liquid form of this drug, which is usually prescribed in two or four daily doses.

Important notes:

- The total daily dosage for children is determined by body weight and the type of infection being treated.
- Cephalexin works fastest when taken on an empty stomach, but it may be taken with food if it causes stomach upset.
- The drug is effective within three to five days, but to prevent a recurrence عودة of infection, the entire course كامل of medication should be taken.
- However, prolonged use is not recommended as it may lead to a secondary infection.
- Patients with diabetes should be aware that cephalexin may affect the accuracy of urine glucose monitoring tests.
- Patients with drug allergies, kidney disorders, colitis (inflamed colon) or other gastrointestinal problems should use this drug with caution.
- Its safety for use during pregnancy has not been determined. It is known to appear in breast milk.

Side effects:

Diarrhea is this drug's most common side effect. Less common side effects include indigestion سوء الهضم , abdominal pain, colitis, vomiting, dizziness دوخة, confusion تشوش , hallucinations, skin rash, joint pain, fluid retention, vaginitis, and yellowing of the eyes or skin.

A severe allergic reaction to cephalexin may occur in patients who are sensitive to both cephalosporin antibiotics and penicillin. This drug may interact adversely with diarrhea medications and oral contraceptives.

Cefotaxime (Claforan)

is a third-generation *cephalosporin antibiotic*, it has broad spectrum activity against *Gram positive* and *Gram negative bacteria*. In most cases, it is considered to be equivalent to *ceftriaxone* in terms of safety and efficacy.

Clinical use:

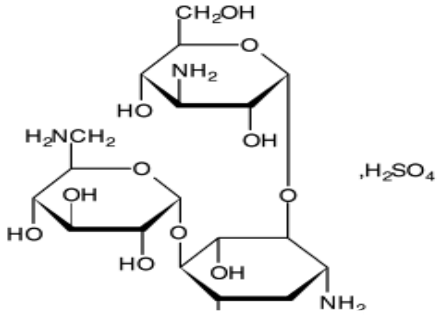
Cefotaxime is used for infections of the *respiratory tract*, *skin*, *bones*, *joints*, *urogenital system*, *meningitis*, and *septicemia*. It generally has good coverage against most *Gram-negative bacteria*, with the notable exception of *Pseudomonas*. It is also effective against most *Gram-positive cocci* except for *Enterococcus*. It is active against *penicillin*-resistant strains of *Streptococcus pneumoniae*. It has modest activity against the anaerobic *Bacteroides fragilis*.

b) **<u>Amino glycosides</u>**

Streptomycin

Effective against Microorganisms that cause many serious diseases, such as tuberculosis, leprosy جذام , and cholera**.**

structure of Streptomycin:



Spectrum Activity:

Broad spectrum vs. aerobic Gram-negative and Gram-positive, TB, Brucellosis and Tularemiaحُمَّى الأرانب infections.

Mechanism of actions:

Streptomycin stops bacterial growth by damaging cell membranes and inhibiting protein synthesis. Specifically, it binds to the rRNA of the bacterial ribosome. This prevents initiation of protein synthesis.

Humans have structurally different ribosomes from bacteria, thereby allowing the selectivity of this antibiotic for bacteria. Streptomycin cannot be given orally, but must be administered by regular *intramuscular injection*. An adverse effect of this medicine is *ototoxicity*. It can result in permanent hearing loss.

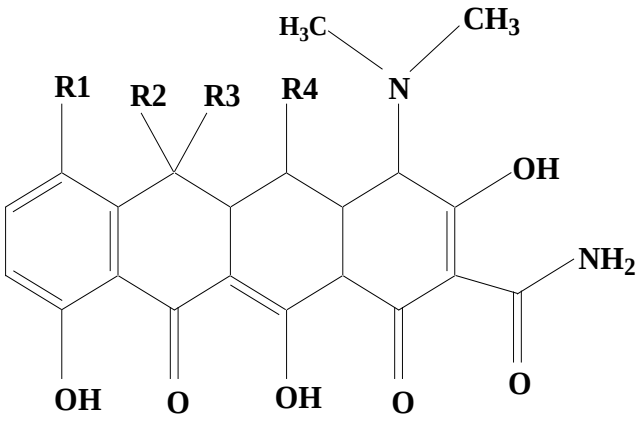
Neomycin

antibiotic drug most commonly used in combination-drug preparations to treat skin, eye, and ear infections.

c) **Tetracycline'**

drugs used to treat various bacterial infections.

Structures:



TETRACYCLINES

	R1	R2	R3	R4
TETRACYCLINE	H	CH3	OH	H
DOXYCYCLINE	H	H	CH3	OH
METHACYCLINE	H	C H3	--	OH

Mode Of Actions: it inhibits bacterial protein synthesis, bacteriostatic.

Tetracycline

Availability:

Tetracycline is available by prescription in capsule form, taken orally, and in a reconstituted powder solution, applied topically.

Cautions, contraindications of TETRACYCLINE

- Can stain developing *teeth* (even when taken by the mother during pregnancy).
- Inactivated by Ca+ *ion*, not advised to be taken with *milk* or *yogurt*.
- Inactivated by *aluminum*, *iron* and *zinc*, not to be taken at the same time with drugs contain these metals.
- Inactivated by common antacids and over the counter heart burn medicines.
- *Skin photo sensitivity*, not advised to be exposed to the *Sun* or intense *light*.
- Drug induced *lupus الذئبة*, and *hepatitis*

d) The macrolides

MODE OF ACTIONS:

The macrolides are bacteriostatic, binding with bacterial ribosomes to inhibit protein synthesis.

Erythromycin

is a *macrolide antibiotic* which has an antimicrobial spectrum similar to or slightly wider than that of *penicillin*, and is often used for people who have an *allergy* to penicillin's. For respiratory tract infections.

Erythromycin is easily inactivated by gastric acids, therefore all orally administered formulations are given as either enteric coated or as more stable salts or *esters.*

e) Lincomycin (Lincocin)

is an antibiotic with a completely new type of molecular structure. It is therefore unlikely to cause reactions in patients sensitive to other antibiotics. Bacterial resistance is also less likely. Although not a broad-spectrum antibiotic, Lincomycin is effective against the most important gram-positive organisms, including resistant staphylococcus. It is effective by mouth and by injection, which is essentially painless.

f) Unclassified antibiotics.

Chloramphenicol

bacteriostatic antimicrobial, it has very serious side effect *aplastic anemia*.

the main use of chloramphenicol is in *eye drops* or *ointment* for bacterial *conjunctivitis*.

Structures: