As Per New Syllabus ER 20

Diploma in Pharmacy 1st Year

Pharmaceutical Chemistry Notes

All Chapter in One PDF

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Chapter 1

Introduction to pharmaceutical chemistry

Topics
Pharmaceutical chemistry Objective Scope
Source and Types of Errors Accuracy Precision Significants
Impurities in pharmaceuticals
Limit Tests for Chlorides, Sulphates, Iron, Heavy Metals, and Arsenic.

INTRODUCTION TO PHARMACEUTICAL CHEMISTRY

Pharmaceutical chemistry

- The chemistry which studies about the drug design and synthesis of biologically active molecules is known as pharmaceutical chemistry
- Pharmaceutical Chemistry involves development and the study of drugs , Drug discovery, Metabolism, absorption, delivery etc. are included in this

Careers

- Pharmacetical companies
- Biotechnology companies
- Drug development & research facilities etc.

Objective

Its main aim is to ensure the fitness for the purpose of medicinal products by analsing and evaluating them as per the quality control standards

Following are some objectives of pharmaceutical chemistry

- To enhance the knowledge base required for synthesis, Isolation, Purification
- To enhance Skill for effective handling of chemicals, glasswear etc.
- To provide proper qualities and skills to the students required to fulfill their job responsibilities as chemist
- To train the students about effect of chemicals

Scope

Skills required in pharmaceutical chemistry

- Good writing and verbal communication skills
- Synthetic organic chemistry skills
- Ability to purify drugs and intermediates
- Spectoscopic techniques
- Understanding of biological roles drugs
- Team work and interpersonal skills
- Good communication skills etc.

ERRORS

→ Error is a mistake but rather a difference between a computed / estimated measured value and the accepted true / specified / theoretically correct value

Classification of error

- ❖ Systematic / Determinate / Non random errors
- ❖ Non systematic / Indeterminate / Random / Accidental errors
- ❖ Gross error

1) Systemic error :- The error is constant or changes slightly bu consistent fault during the analysis.
Eg : - error in titration

- **Instrumental error :-** Error occurs due to faulty instrument or reagent containing impurities
- **Operational / Personal :-** When error occur during operation or carryout the experiment is calles as operational error
- **Methological error :-** These error are most serious errorr of analysis most of above error can be minimized or corrected but errors that are not changeable unless the condition of the determinations are alterted.
  Eg : Errors occer due to co-precipitation of impurities

2) Non-systematic error :- The error unpredictable and difficult to identify

Source

- Presence of bubbles in burette
- Sample handling improperly

3) Gross error :- These error are a combination of both systematic and non-systematic error
They are the result of big mistake made during analysis and can be identified easily
Gross error is also known as Avoidable mistake

Source

- Calculation error
- Wrong sample sizes
- Mix up of samole / reagent
- Transcription error

Accuracy and Precision

Accuracy :- It can be said that the difference between calculated value and accepted real value is known as accuracy

Precision :- Reproducibility or Repeatability can be defined as the precision of measurement system in which the degree of repeated measurement is considered under the static condition given the same result

Repeatability :- It is the variation which arise in spite of all the efforts made to keep the condition constant wheather relased to instrument and repeating in short term span

Reproducibility :- It is the variation which arise by applying the same process for the measurement by using different instrument and operators over a longer time span

Significant figure

The significant figure of any number are the digits that add up to the precision

Rule

- Non – zero digits are significant
  Eg : 89, 56,78,etc
- Zero between teo non – zero digits are significant
  Eg : 108, 805 etc
- Leading zero are consider insignificant
  Eg : 0.00098, 0.000643 etc
- Trailing zeros after a decimal point are significant
  Eg : 12.7900, 6.900 etc

Impurities in pharmaceuticals

→ An impurities is generally considered as an there various organic material except the other drug substance that arises during the manufacturing process.

Raw material employed in manufacture :- Impurities resulting from raw material many affect the process of manufacture and contaminate the resultant product **Eg:** Calcium sulphate & magnesium chloride present rocksalt some amount of calcium & magnesium will present in sodium chloride

Reagents used in the manufacturing process :- The impurities from the reagents may contaminate the final product if they are not washed away properly.

Eg : Mixing mercuric chloride solution with dilute ammonia solution result in ammoniated

$$HgCl_2 + 2NH_4OH \longrightarrow NH_2Hgcl + NH_4cl + 2H_2O$$

Ammonium hydroxide present in the final product

Process used in manufacture :- Different manufacturing process are used for producing many drugs and chemicals during there process of manufacturing, some impurities get an access into the materials

- Formulation related impurities
- Synthesis intermedicates & byproduct
- Residual solvent
- Method related impurities
- Chemicals process used in manufacture

Environment related impurities :- Atmosphere in industial areas is adulterated with gases like Hydrogen, sulphide, smoke,etc

- Exposure to adverse temperature
- Uv ligits
- Humidity

Effects of impurities in pharmacopoeial substance

A little amount of impurities always remain in a material

- After a certain period , even a minute quantity of impurite cause toxic effect
- Impurities also bring about technical difficulties in the formulation
- Impurities also reduce the self-life of a substance
- Some impurities result in incompatility with other substance
- Impurities also effect in physical and chemical properties of substance

Limit tests

Quantitive tests intended for identifying and controlling small quanties of impurities which may occer in a substance are termed as limit test

Limit test used for :-

1. Finding out the quantity of harmful impurities
2. Finding out the quantity of avoidable impurities

Arsenic

This test is carried out for controlling the arsenic impurities on inorganic substance

Principal :- The limit test for arsenic is based on the reaction in which arsenic is converted in arsine (AsH_3) by undergoing reduction with zinc and hydrochloric acid. The use of Stannated hydrochloric acis is prescribed in the I.P

$$H_3Aso_4 \longrightarrow H_3Aso_3$$

Arsenic Acid — Arseneous Acid

$$H_2Aso_3 + 6H_2 \longrightarrow AsH_3 \uparrow + 3H_2o$$

Arsine

When arsine comes in contact with dry paper daturated with mercuric chloride | bomide it produce a yellow or brown stain

$$2AsH_3 + Hgcl_2 \longrightarrow Hg \rightarrow AgH_2 + 2Hcl$$
$$\searrow AgH_2$$

The intensity of the colour produce is proportional to the amount of arenic present, if the diameter of the paper exposed to arsine os constant

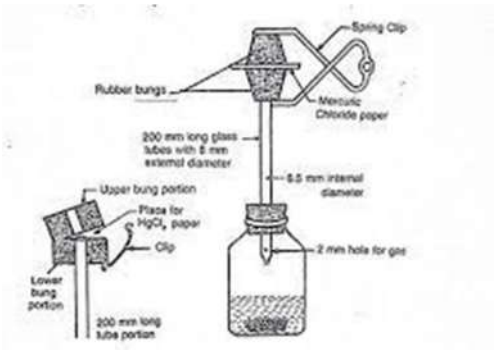
The test solution of the sample is compared with the standard solution with known amount of arsenic
The strain are the compared in natural light

Apparatus : Rubbercork,springclip,mercuric chloride,paper,200mm long glass tube with 8mm external diameter 200mm, etc

Procedure :

Test solution : The test solution is prepared as directed in the monograph and placed in the generator bottle 5 ml of 1m potassium iodide, 5ml of stannous chloride acid solution and 10gm of zinc AsT are added to the test solution

A test paper of mercuric chloride is placed in the rubber slit and the bottle is immediately stopped . The reaction is allowed to continus for 40 min at above 40°c.



. Apparatus used for arsenic limit test; on the left is an alternative device for securing mercuric chloride paper.

Standard solution : 0.33 gm of arsenic triocide is dissolved in 5 ml of 2m NaOH solution and volume is made up to 250 ml with water 1ml of this solotion is further diluted with distilled water up to 100 ml

The stain produced by the test sample passes the test if the stain produced by it is less intense than that of the standard solution

Chloride

Limit test of chloride

This test is carried out for identifying the chloride ions present in a standard solution

Principal

- The limit test for chloride is based on a reaction that occurs between silver nitrate and soluble chloride which is insoluable in dilute nitric acid.
- The test solution appears turbid due to the formation of silver chloride in the presence of dilute nitric acid . Amount of chloride present in the test samples influences the degree of turbidity.
- Test solution is compared with the standard solution.
- By viewing transversly through both the solution against a black background in nessler's cylinder is compared the samples passes the limit test if the test solution is less turbid than the standard solution and fails in vice versa condition.

Procedure

In this limit test a standard solution and test solution is prepared and then the appearance of there two solution is compared

Test solution :- 1.0 gm of sample is accurately weighted and transferred to nessler cylinder dislove in 10 ml distill water . 1 ml of nitric acid is added to this sol and volume up to 50 ml with distill water . 1 ml of silver nitrate be added to the solution stirring for 5 min after which turbidity develop

Specified substance (1gm) + 10 ml of water + 1 ml of nitric acid + water up to 50 ml + 1 ml silver nitrate turbidity

Standard solution :- 1 ml of 0.01 m Hcl is mixed with 1 ml of nitric acid in nessler cylinder B and volume up to 50 ml with distill water . 1 ml of silver nitrate solution which produce turbidity after 5 min

The sample passes the limit test if it is less turbid than the standard solution

Sulphate

Limit test for sulphate

This test is carried out for controlling the sulphate impurity in inorganic substance

Principle

In the limit test for sulphate, barium chloride reacts with soluable sulphate in the presence of dilute Hcl solution . The resulting turbid solution is compared with the standard solution of acceptable limit.

The barium sulphate reagent contain barium chloride , sulphate free alcohol, and potassium sulphate

Procedure

Test solution :- 1 gm of sulphate is weighted and 2 ml of Hcl is added to 45ml of solution. 5 ml of $BaSo_4$ reagent is added to prepare the solution

Standard Solution : 1 ml of 0.1089 % w/v solution of K_2So_4 is weighted and treated with 2ml of Hcl . This solution is diluated up to 45 ml .At the last the standard solution is prepared by adding 5 ml of $BaSo_4$ reagent

The limit test of sulphate is passes if it is less turbid than the standard solution

Iron

Limit test of Iron

This test is carried out for controlling the iron impurities in inorganic sunstance

Principle:- The limit test for iron relies on the reaction in which iron reacts with thioglycollic acid in a solution. With ammonium citrate buffer

It results in the formation of a purple colour solution due to the formation of mercaptoacetate

This purple colour is compared with the standard colour containing a known amount of iron

Procedure

Test solution :- 40 ml of water is added to the sampleand treated with 2 ml of 20% w/v citric acid .Then 2 drop of thioglucollic acid is added the solution is mixed made alkaline with ammonia , and

volume made up to 50 ml . Then the solution is allowed to stand for 5 min so that a colour develop which is viewed vertically & compared with the standard solution

Standard solution :- 40 ml of water is added to 2 ml of standard solution of iron .Then 2 ml of 20 % w/v citric acid and 2 drop of thioglycollic acid is added to the solution the solution is made alkaline with ammonium and volume is made up to 50 ml .The solution is allowed to stand for 5 min so that a colour develop which is viwed vertically and compared with the test solution

When the colour of both the solution is compared the intensity of the colour of the test solution should be less than that of standard solution

Heavy Metals

Limit test for Heavy metals

This limit test is carried out for determining the content of metallic impurities coloured by sulphide ion , under specific condition

Principle:-

Limit test for heavy metals are based on the reaction between a solution of a heavy metals and a saturated solution of H_2S in an acidic medium

A reddish / black colour resulted is compared with the standard solution of lead nitrate solution

Procedure:-

Test solution :- 25 ml of test solution is prepared in a 50 ml of nessler cylinder and ph is adjusted between 3-4 using dilute acetic acid or dilute ammonia solution , After PH adjustment the solution is diluted up to 35 ml with water

Standars solution :- 2 ml of standard lead solution is prepared out in a 50 ml nessler cylinder and diluted up to 25 ml with water. The pH is adjusted between 3-4 using dilute acetic acid pr dilute ammonia solution After pH adjustment the solution is diluted u to 35 ml with water

After that

10 ml of freshly prepared hydrogen sulphide solution is added into both the cylinder containing standard solution and test solution and diluted up to 50 ml with Water .After dilution the solution is krpt aside over a white surface for 5 min and viewed down wards the test solution colour is lighter than the standars solution colour

Chapter 2

Volumetric and Gravimetric Analysis

Topics
Volumetric and Gravimetric Analysis
Acid Base Titration
Non – Aqueous titration
Precipitation titration
Complexometric titration
Redox Titration

Volumetric and Gravimetric Analysis

→ The quantitative analytical method is widely used is volumetric analysis
→ It is defined as the method involved in measurment of the volume of a solution whose concentration is known
→ This method is also applied to determine the concentration of analyte
→ Volumetric analysis or titration is defined as the measurment of volume of second substance which combines with the first known concentration

Fundamentals of volumetric analysis

- Titration measures the volume which completes the reaction between the solution and reagent
- The amount of reagent and solution is determined by the volume and concentration of reagent which are used in the titration
- Mole fraction of the equation determines the amount of unknown chemicals in the specific volume of the solution

Procedure for volumetric analysis

- The solution that needs to be analysed should have a specific weight in the sample of +/- 0.0001g of the material
- It is important to choose right kind of material which is to be analysed to obtain accurate results
- Preference should be given to a substance that reacts rapidly and completely to produce a complete solution
- The titration should be continued untill the reaction is completed and the amount of rreactant added should be exactly the amount required to complete the reaction
- A weighted amount of reagent should be taken and dissolve into a solution if the reagent or reactant is to be made into a standard solution so that it is in a definitive volume within a volumetric flask

Acid Base Titration

- In chemistry, acid – base titration is used for analysis the unknown organic compound concentration of an acid and base
- The principle of acid-base titration is based on the neutralisation reaction occurring between acid & base
- Phenolphthalein is the most commonly used indicator for acid-base titration
- Acid-Base reaction involve transfer of proton,

  Example :- Base accept proton from Acid

  $H^+ + OH^- \rightarrow H_2O$
- It is most common Neutralisation reaction
- At bequivalent point, moles of H+ are equal to the moles of OH-
- During titration one rectant (mostly an acid) is added from the burette to the known volume of the other reactant (mostly base) in a conical flask to make the equivation point (end point) of the titration and indicator is used

Theories

There are 3 theories , explaining the comcept of acids and bases

- ➲ Arrhenius theory
- ➲ Bronsted Lowry theory
- ➲ Lewis theory

Theory	Acid	Base
Arrhenius	H+ Producer	OH- Producer
Bronsted lowry	H+ donar	H+ acceptor
Lewis	Electron pair acceptor	Electron pair donar

Arrhenius Theory

- The most commonly used concept of acids and bases was develop by Savante Arrhenius in 1884 termed as Arrhenius theory
- According to this theory an acid is a substance which dissociates in Aqu. Solution produce hydrogen ion on other hand a base is a substance which dissolve in aqueous solution to produce hydroxyl ion (OH-)

  For example
  - HCl is an Arrhenius acid HCL H+ + Cl-
  - NaOH is an Arrhenius base NaOH OH- + Na+
- Arrhenius theory was the first scientific theory that had given defination for acid and base as well as classified them It is the simplest theory and is useful in case of aqueous solution

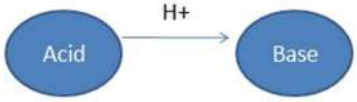
Limitations

- ❖ Acid and base have been defined only in terms of solution and not as a solid substance
- ❖ This theory also failed to explain the neutralistation of acid & base in the absence of solvent
- ❖ There are many basic substance (few organic substance) which do not have oh ions but are basie in nature this fact could not be explained by Arrhenius theory
- ❖ Acidic properties of many salts could not be explained by this theory

Bronsted Lowry theory

→ In 1923 J.N Bronsted and J.M Lowry was introduced a new concept of acid and base

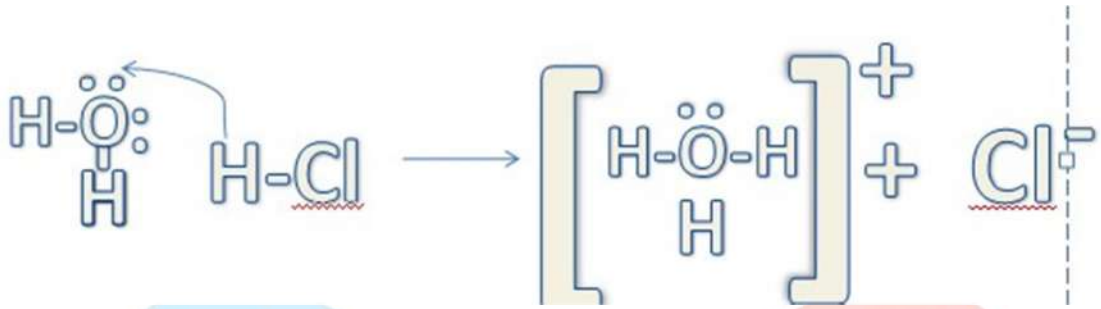
→ According to the theory an acid is any mol or ion that can donate a proton (h+) and base is any mol or ion that can accept a proton H+



An acid is a proton donor While base is a proton acceptor

- ➢ A base qualifying Bronsted lowry concept is termed as Bronsted lowry base or Bronsted base
- ➢ Where an acid qualifying Bronsted lowry concept is termed as Bronsted lowry acid or Bronsted acid

- **For example :-** On dissolving dry HCl gas in water , each molecule of HCl produces hydronium ion (H_3O^+)by donating a proton to a water molecule



There fore it can be concluded that water which accept a proton is a bronsted base where HCl gas which donate a proton is a Bronsted.

Advantages

- Much wider scope Bronsted lowry concept of acid and base cover wider range of molecules and ions accepting proton (base) or donating proton (acid)
- Where arrhenius concept of acid & base involve only those substance which release H+ or OH- ions in aqueous solution
- Not limited to aqueous solution Arrhenius concept is limited only to aqueous solution Bronsted lowry theory not only covers aqueous sol but also gas phases
- Release of OH- not necessary to qualify as a base Bronsted base is a substance which accept a proton, where Arrhenius base is a substance which release OH- ions in aqueous solution

Limitations

- Bronsted lowry theory of acid & base is based on transfer on proton commonly most of the acids as protonic in nature but some are not
- There are many acid base chemical reaction in which proton transfer not occurs

Lewis Theory of Acids & Bases

- This method of Acid & Base was given by G.N Lewis in the early 1930
- He defined Acid is an electron pair acceptor
  - Base is an electron pair donar
- In this theory the Lewis acid & Lewis base share an electron pair given by base result in the formation of a covalent or coordinate bond between them
- This resultant compaired bounded with a covalent bond is known as a complex
  - A + B = A-B
  - LA LB Complex

According to this concept

- Lewis base are anion or molecule having a long pair of electron
- Lewis Acid are cation or molecule lacking of electron pair

Advantages

- ★ It included the defination given by both Arrhenius and Bronsted Lowry.
- ★ The lewis concept explain the acidic & basic nature on the basis of transfer or gain of electron accompanied by loss/donation of electron pair.

Limitations

- ❖ Lewis acid and base can not arranged in their order of strength as their strength depend on the reaction type
- ❖ Lewis acid and base reaction are explained are excepted to be very fast but to the involvement of electron but some of there reaction slow

Neutralisation Curves

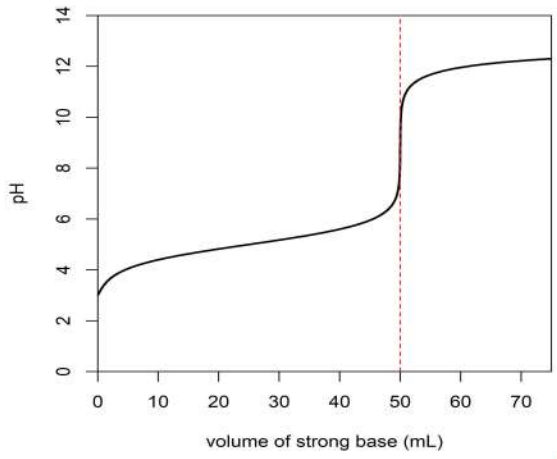
- ➢ A reaction in which an acid reacts with a base to produce a salt and a neutralised base is known as neutralisation reaction.
- ➢ **Example**

  Hydrochloric acid reacts with sodium hydroxide to formsodium chloride & water

  $HCl + NaOH \quad H_2O + NaCl$
- ➢ Neutralisation Curve is obtained when ph is plotted against the percentage of acid neutralisation or the no of millilitres of alkali added
- ➢ Neutralisation curve can be plootted between the following variabled
  - Weak acid & Strong base
  - Strong acid & Strong base
  - Strong acid &Weak base
  - Weak acid & Weak base

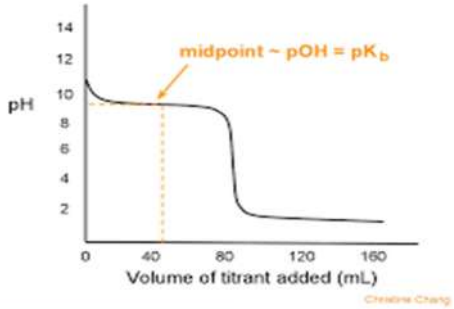
Strong acid & strong base

- ♦ In this titration Strong acid & Strong base are reacted with each other by using a suitable indicator
- ♦ Acid & Base compounds are rapidly break down in its ions (Cation & Anion) and react with each other and form the salt & Water
- ♦ Initially slow rise in PH
- ♦ Sharp rise in PH due to present of excess alkali
- ♦ Attain the neutral point PH=7



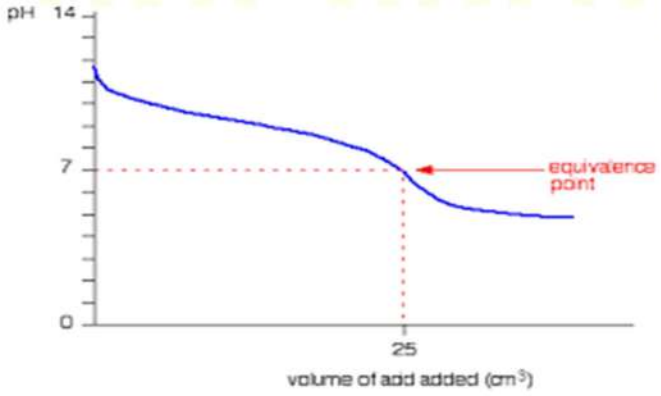
Weak Acid & Strong Base

- ★ In this Titration Method weak acid is treated with the strong base by using the suitable indicator to detech the end point
- ★ Doring the procedure weak acid are dissociated slowly in its compounts & strong base are dissociates rapidly in its componets
- ★ Initially the PH normally & where reaction processes the curve will not raise much This point is said to be half neutralisation point
- ★ Sharp rise in PH due to present of excess strong alkali



Weak Acid & Weak base

- In this titration method weak acid * weak base treated with each othe by using the suitable indicator
- The chief feature of the curve is that change of PH near equation point and during whole neutralisation is very gradual
- Hence the end point cannot be detected by ordinary indicator
- For detection of this titration mixed indicator are used .



Strong acid and Weak base

- In this Titration Method weak base is treated with the strong acid by using the suitable indicator to detech the end point
- During the procedure weak base are dissociated slowly in its compounts & strong acid are dissociates rapidly in its componets
- Initially the PH normally & where reaction processes the curve will not raise much This point is said to be half neutralisation point
- Sharp rise in PH due to present of excess strong alkali

Acid Base Indicators

- Acid Base indicator (weak organic acid or base) having different colours depending up on the concentration of H+ ions in the solution are available
- These indicator exhibit a colour change from an acidic colour to an alkaline colour although this colour change does not occurs suddenly or rapidly but take place with in a small PH range usually 2 PH unit which is indicator range
- The position of the colour change on the PH scale is different for different indicators
- The acid base indicators are also known as visual indicator
- Example p-nitrophenol is a weak acid that undergoes dissociation
- Phenolphthaline :- (most popular indicator) is a colourless & diprotic acid when it loses the first proton it gives a colourless solution but when loses another proton it produces a red colour by foeming an anion with the conjugated system

Application

- **Determination of Aspirin :-** Sample is dissolved in ethanol acid 2-3 drops of phenolphthalein is added as an indicator
- The resulting solution is treated with standard NaOH solution until pink colour is obtained
- Determination of Amino Acids :- Sample is added into 25ml of distilled water & small amount of HCl are added to maintain the PH up to 1.5
- The solution is titrated with standard NaOH solution using phenolphthalein as an indicator
- The procedure is continued until the PH reaches to 12

Non – Aqueous titration

→ Titration involving very weak acid or base with the help of non-aqueous solvents to obtain sharp end point are non-aqueous titration.

Principle

★ Organic acids & bases are water insoluable very weak & cannot be analysed via conventional titration method thus non-aqueous titration is used which relies on the principle that non-aqueous solvents are used to dissolve the sample.

Non-Aqueous Solvents

- The nature of solvent is a deciding factor for the behaviour of acid & base. Any solute when dissolved in any given solvent with exhibit acidic or alkaline behaviour
- The Non-aqueous solvents have a characteristic role in non-aqueous titration
    1. The solvent should be non-toxic for its wide use in analysis
    2. It should is liquid at he time of analysis
- These organic solvent are used but it is mainly depents on their properties such as capability of self dissociation dielectric constant & acid base character of solvent

The non-aqueous solvents are classified into

- **Aprotic solvent :**
    - These solvents are considered chemical neutral or inert under specific condition
    - Eg toluene & carbon tetrachloride

- These solvents have low dielectric constant which restrict the inosiation of solute and there is no reaction between there solvent & acid s and bases
- The Aprotic solvents are widely used as diluting agent for the reaction mixture

Protophilic solvents :- Solvents which have greater tendency to accept proton
Eg : Water, Alcohol

Protogenic solvents :- These solvents posses acidic character & have high affinity for donating protons
Eg : Alcohol , Organic acid

Amphiprotic solvents :- In this solvents have the ability to donate as well as accept proton because they caotain both protegenic & protophilic properties.
Eg : Water , Alcohol , & Organic acid (weak)

Frequently used non-aqueous solvents

- ★ For the determination of non-aqueous titration there are several solvents available (either organic or inorganic) but only few of them are employed for the purpose
- ★ The solvent used must be pure,Dry,& best analytical qualities to ensure precise and sharp end point
- ★ Alcolols : The organic salts of fatty acid can be determined with the help of glycol & alcohol mixture or glycol & hydrocarbon mixture
- ★ Dimethylformamide : DMF is an excellemt example of protophilic solvent 7 is used for the titration of benzonic acid 7 amide
- ★ Glacial Acetic Acid : Acetonitrile , Rioxane etc

Advantages of non-aqueous solvents

- ✓ The acids & bases of organic origin are easily soluable in non-aqueous solvent
- ✓ Non-aqueous solvent can dissolve two or more acids present in a mixture
- ✓ With the help of a suitable solvent or indicator the selective titrtion of biological ingredients present in a substance can be done whether it is acidic or basic
- ✓ Titration involving non-aqueous are comparatively simple & more accurate than aqueous titration

Indicators in Non-Aqueous Solvents

- A very narrow range of indicator are present which employed in non-aqueous titration
- Methyl Red : A 0.2 % W/V solution of Methyl Red is prepared using dioxane The end point is marked by a change in colour from yellow to red
- Naphthol Benzene :- Nephthol Benzene is used as a solution of 0.2 % W/V in acetic acid. It gives a sharp end point by changing its colour from yellow to green
- Thymol Blue : It is a widely used indicator especially for the substance behaves as acids in solution of DMF
- 0.2 % W/V solution is prepared using methyl alcohol & the end point detected by change in colour from yellow to blue

Application

The application of Non-Aqueous titration are

- Percentage of purity is determined by the assays
- Determination of Hydrophobic compounds
- Determination of the steroids
- Determination of Anti Tubercular drugs
- Determination of phenoburbitone

Precipitation titration

→ Precipitation titration is a type of titration which involves the formation of precipitate during the titration techniques

→ In precipitation titration the titrant reacts with analytic and forms an insoluble substance called precipitate

→ For example $AgNO_3$ is used as a precipitating agent for the determination of cl-

Principle

- Formation of an insoluble product by the combination of two ionic species is known as precipitation.
- Precipitation reaction are not frequently used in titration because of the precipitation reaction do not comply with desired specification.

Indicators used in precipitation

- The end point in precipitation titration can be marked using a regent known as indicator
- **Adsorption indicators**
- Adsorption indicators are substance that indicates an excess of a reactant in argentometric titration
    - Precipitation becomes coloured when adsorption indicators is adsorbed
    - Eg sodium salt of fluorescein
    - Sodium fluor can be used as an indicator in the titration of chloride with $AgNO_3$ solution in a neutral or slightly basic medium

Precipitation titration method

- The precipitation titration silver nitrate with chloride, bromide, iodide, and thiocyanade are most widely used
- These precipitation titration are also known as Argentometric titration
- Since silver is always involved during the reaction there fore concluding that there titration have limited use

There procedure are follow in precipitation titration

I. Mohr s method
II. Volhard s method
III. Modified volhard s method
IV. Farjan s method

Mohr' s method

- This method is named after Karl friedrich Mohr.
- In this method potassium chromate is used as an indicator which produces Red coloured silver chromate at the end point when all the chloride ions have reached.
- In mohrs method the end point is detected when a coloured precipitate of chloride or bromide is formed.
- A neutral sol of chloride ions is titrated with silver nitrate solution using a small quantity of potassium chromate solution as an indicator.
- The chromate ions combine with silver ions at the end point, forming a red coloured and sparingly soluble silver chromate.

Volhard s method

- This method is named after Jacob Volhard
- In this method a soluble coloured compound forms at the end point
- Thiocyanate is used to titrate silver ions in an acidic solution using ferric ions as an indicator
- In which an excess of a standard solution of silver nitrate is added to a chloride containing sample solution. The excess silver is then back titrated using a standardized Sol of potato or ammonium thiocyanate with ferric ions as an indicator

Modified volhard s method I.P 1985

- The principle of assay by volhard s method is based on indirect volumetric precipitation titration
- In this method nitric acid solution is used to acidify NaCl solution and then in the presence of nitrobenzene, this solution is treated with measured excess amount of standard solution of silver nitrate
- Some moles of silver nitrate are consumed in the reaction with NaCl and the remaining unreacted silver nitrate is determined by titration with a standard solution of ammonium thiocyanate. In this titration solution of ferric ammonium sulphate ferric alum is used as an indicator

Farjan s method

- This method named after kazimierz fajan
- Dichlorofluorescein uses as an indicator and the end point is observed when the green colour suspension turns pink
- Fajan s method involves the titration of chloride ions with silver ions using adsorption indicators
- These indicator are basically dyes that adsorb or desorb on the surface of the precipitate at the equivalence point and produces the colour change
- The indicator are acid dyes, fluorescein, etc
- Basic dyes rhodamine service

Application of precipitation titration

- Precipitation reaction are applicable in removal of salts from water during water treatment in qualitative inorganic analysis and also in manufacturing of pigments
- Products of any reaction can also be isolated during work up by the precipitation reaction
- Precipitation reaction are also used in metallurgy

Complexometric titration

→ Complexometric titration chelatometry is a form of volumetric analysis in which the formation of a coloured complex is used to indicate the end point of a titration

→ Cl- are particularly useful for the determination of a mixture of different metal ions in solution

Principle

- In complexometric titration the metal ions are titrated with a complexing or a chelating agent
- This method is an analytical application of a complexation reaction
- This method involves transforming simple ion into a complex ions and determing the equivalence point using metal indicatoror electrometrically
- This method is also termed as chilometric titration, chilometry titration, chilometric titration and EDTA titration Ethylene Diamine Titra Acetic Acid

Theory

- Complexometric titration involves the disappearance of the free metal ions as they are changed into complexia
- In any complexation reaction can be used as a volumetric techniques provided
- The reaction reaches equilibrium rapidly after each portion of titrant is added
- A complete titration indicator capable of locating equivalence point with fair accuracy is available

Classification

Complexometric titration following the four types

- **Direct titration :** This method is similar to acid base titration and involve adding the standard solution and chelon solution to the metal ion solution till the end point is attrived
- **Back titration :** In this method excess of standard EDTA solution is added to the metal solution and the excess is back titration with a standard solution of a second metal ion
- **Replacement titration :** In this method the metal to be analysed quantitatively displaces the metal from the Complex.
- **Indirect titration :** This is also known as alkalimetric titration. It is used for determination of anion which do not react with EDTA chelate protons from disodium EDTA are displaced by a heavy metal and titrated with sodium alkali

Application of complexometric titration

- Determination of permanent and temporary hardness of water separately
- Determination of total hardness of water
- Determination of magnesium and silicon dioxide in magnesium trisilicate
- Determination of calcium and lead in a mixture
- Determination of chromium 111 and Iron 111 in mixture kinetic masking
- Determination of manganese in the presence of Ironferromanganese
- Determination of lead and tin in a mixture
- Determination of phosphates

Redox Titration

→ In titration the redox/ oxidation- reduction reaction are more extensively used for analysis as compared to the precipitation reaction and acid base reaction

→ Reduction is defined as the gain of one or more electron by atomic species or molecules

→ Oxidation is loss of one or more electron by the atomic species or molecules oxidation is also known as de electronation

→ A titration which deals with a reaction involving oxidation and reduction of certain chemicals species are known as redox Titration

Agents

★ **Reducing agent :** Sodium thiosulphate, ferrous sulphate, titanous sulphate, oxalic acid are some of the reducing agents.

★ **Oxidising agents:** Potassium dichromate, potassium bromate etc are some of the oxidising agents.

Types of Redox Titration

Based on the method

- **Direct titration :** In this method initially coloured substance are used Thus end point detection does not require an indicator
- **Back titration :** In this method the sample solution is titrated with excess volume of titrant solution

Redox indicator

→ Compounds used in the redox titration and having different colours in the reduced and oxidised conditions are called redox indicator.

Types

Based on the Addition of the indicator

- **Self indicator :** These indicator are the titrant itself which develops an intense colour on reaching the end Point.
- **Internal indicator :** These indicator are incorporated into the reaction mixture during the titration.
- **External indicator :** These indicator are introduced externally through a groved title and mixed with the solution of the indicator.

Selection of indicator

- In an ideal indicator the colour change is observed near or at the equivalence point.
- For reversible and fast colour change the oxidation- reduction equilibrium for an indicator redox system needs to be established very fast.
- If the titration is feasible These could be a large change in potential at the end point that should be sufficient to bring above a change in colour of the indicator.
- Example Diphenylamine , ferroin etc

Application of Redox Titration

- Determination of phenol
- Determination of the presence of Iron in limonite
- Determination of calcium in lime stone
- Analysis of Isoniazid
- Analysis of tocophenol

Gravimetric Analysis

→ A quantitative analysis involving weight is known as gravimetric Analysis
→ In which the substance to be analysed is covered into an insoluble precipitate
→ This precipitate is collected, weighted using suitable method
→ Precipitation is the most suitable technique which employs formulation of a precipitate not soluble in the solution

Examples

Analyte	Precipitant
Piperazine adopted tablets BP	picric acid
Piperazine phosphate BP	picric acid

Principle

- Law of mass action and reversible reaction
- Principle of solubility product
- Common ion effect

Law of mass action and reversible reaction

- According to the law of mass action the rate of reaction is directly proportional to the product molecular concentration of the reacting substance

Principle of solubility product

- The solubility product expression for a compound is the product of the concentration of its constituent ions each raised to the power that corresponds to the number of ions in one formula unit of the compound
- The quantity is constant at constant temperature for a saturated solution of the compound
- The statement is the solubility product principle
- A slightly soluble Salt is decreased if excess of either of its ions are added

Common ion effect

→ The electron to the decrease in solubility of an ionic precipitation by the addition to the solution of a soluble compound with an ion in common with the precipitate

Types of Gravimetric Analysis

Physical Gravimetric : It is the commonest of all the types and is used in environment engineering. Environmental sample carry matter that is physically seperated and categoriesed on the basis of volatility and particle size.

Thermogravimetric : In this technique a substance is kept at a controlled temperature system and its mass is measured with respect to temperature This Techniques is used extensively in many discipline like pharmacy, food, polymer science, glasses, volatile solids.

Electro deposition : In this technique the electrochemical reduction and simultaneous deposition of metal ions occur at cathod before starting the electrolysis and after the process ends the cathod is weighted

Difference in the weight corresponds to the mass of analyte that was initially present in the sample This technique is applicable to environmental engineering analysis

Precipitative Gravimetry : This Techniques causes chemical precipitation of an analyte Precipitation method attract the concern of analyst working with gravimetric Analysis . In a gravimetric method precipitative is the major chemical reaction as it could be a highly selective means for separating the desired component from the metrix

Application

- Analysis of standard This is required during testing or instrument calibra ion.
- Analysis Requiring Accuracy This analysis can be conduct using gravimetry Which being time consuming allows only a few determination Pharmacopoeial analysis.
- Lead as chromate This method has less application due to insolubility of chromates.
- However This method helps in gaining experience in gravimetric Analysis.
- The best result are obtained by precipitating from homogeneous solution using the homogeneous generation of chromate ions produced by slow oxidation of chromium 111 by bromate at 90- 950 in the presence of an ethanoate buffer.

Chapter 3

Inorganic Pharmaceuticals

Topics

Haematinics :

1. Ferrous sulphate,
2. Ferrous fumarate,
3. Ferric ammonium citrate,
4. Ferrous ascorbate,
5. Carbonyl ion,

Antacids :

- Aluminium hydroxide gel,
- Magnesium hydroxide mixture,
- Magaldrate,
- Sodium bicarbonate,
- Calcium carbonate

Anti-Microbial Agents :

- ❖ Silver nitrate,
- ❖ Ionic silver,
- ❖ Chlorhexidine gluconate,
- ❖ Hydrogen peroxide,
- ❖ Boric acid,
- ❖ Bleaching powder,
- ❖ Potassium permanganate,

Dental Products :

- Cleaning agents,
- Dentifrices,
- Anticaries agents/fluorides,
- Desensitising agent,
- Cements and fillers,
- Oral antiseptics and astringents,
- Polishing/abrasive agents

MEDICINAL GASES

- → Oxygen
- → Carbon Dioxide
- → Nitrous Oxide

Inorganic Pharmaceuticals

Haematinics

→ Haematinics are the drugs used to increase the the Concentration of haemoglobin (iron) in blood or used to cure anaemia mainly due to iron deficiency.

Examples

→ These agents are required for the formation of blood.

→ Some common examples of haematinics used in treatment of iron-deficiency anaemia are

1. Ferrous sulphate,
2. Ferrous fumarate,
3. Ferric ammonium citrate,
4. Ferrous ascorbate,
5. Carbonyl ion, etc.

1.Ferrous Sulphate (FeSO4.7H20)

→ Ferrous sulphate, also known as green vitriol, contains not less than 98% of ferrous ion (Fe^{2+}) and not more than 103.3% of $FeSO_4.7H_2O$.

Preparation

- It can be prepared by when iron pyrites are exposed to air and moisture

$$2FeS+7O2 + 2H20\ 2 \longrightarrow Fe\ SOg+2H2SO4$$

Physical properties

- **Appearance :** Pale, bluish green crystals or granules.
- **Odour :** Odourless.
- **Taste :** Saline and styptic (astringent or bitter).
- **Solubility :** Soluble in water (43.5gm in 100gm of water at 150°C).
- **Acidic Nature :** Its solution is acidic to litmus paper at pH about 3.7.
- **Crystal Properties :** Crystals undergo oxidation when comes in contact with air, forming brown patches of sulphate due to efflorescent nature.

Chemical Properties

- It undergoes complete dehydration when heated at 300°C and in the absence of air it shows white colour. On further heating, the anhydrous solid produces sulphur dioxide, sulphur trioxide, and ferric oxide salts by undergoing decomposition.
- It undergoes rapid oxidation and forms ferrie sulphate, thus, it is an effective reducing agent. It also reduces potassium permanganate, potassium dichromate, etc.
- Being a reducing agent, it decolourises potassium permanganate and converts potassium dichromate into green.

Pharmaceutical Formulations

- Ferrous Sulphate Oral Solution,
- Ferrous Sulphate Tablets

Market Preparations

- Fer-In-Sol ,
- FerrouSul ,
- FeroSul ,
- Iron Supplement,
- Slow Fe, etc.

Storage Conditions

- It should be store out of the children's reach and in child-resistant containers.

Uses

- It is a haematinic preparation most widely used for treating iron-deficiency anaemia.
- Ferrous sulphate coated with brownish yellow basic ferric sulpnae should not be used.
- It is also used in agriculture as an insecticide

2.Ferrous Fumarate

→ Ferrous fumarate is the fumarate salt form of the minera iron

Preparation

- Anhydrous ferrous fumarate should be prepared by mixing a water-soluble ferrous salt and a water soluble salt of fumaric acid in aqueous medium at a temperature over about 70°C.

Physical Properties

- **Appearance** : Reddish-brown powder.
- **Odour** : Odorless powder.
- **Solubility** : Hardly soluble in water and very slightly soluble in alcohol.
- **Nature** : Basic in nature.

Chemical Properties

- ferrous fumarate is quite stable to oxidation and hydration.
- This salt remains stable in even hot, humid atmosphere in comparison to ferrous sulphate and ferrous gluconate.

Pharmaceutical Formulations

- Ferrous Fumarate and Folic Acid (Combination) Tablets,
- Ferrous Fumarate Syrup

Market preparations

- Feosol,
- Ferra-TD,
- Fer-in-Sol,

Storage Conditions

- It should be stored in clean, dry warehouse in the original unopened containers.
- It should be kept in cool condition.

Uses

- It is used to treat pernicious anaemia.
- It is used to treat iron deficiency anaemia.

3.Ferric Ammonium Citrate

→ It is a complex salt which contain 20.5 – 22.5 % of iron . It is the Scale Preparations of iron

Preparation

→ Ferric ammonium citrate (iron (III) ammonium citrate) is prepared by the **reaction of ferric hydroxide with citric acid, followed by treatment with ammonium hydroxide, evaporating, and drying**. The resulting product occurs in two forms depending on the stoichiometry of the initial reactants.

Physical Properties

- **Appearance** : Bright and brownish-red scales
- **Solubility** : Highly soluble in water, but insoluble in alcohol
- **Taste** : Slightly astringent in taste

Chemical properties

- Due to presence of different complexes ferric ammonium citrate is present in the form of bright scales which are brownish-red in colour.

Pharmaceutical Formulations

- Ferric Ammonium Citrate Tablets ,
- Ferric ammonium citrate solution

Market Preparations

- Deriton ,
- Geritol Liquid ,
- Iron, Vitamin and Min Supplement

Storage Conditions

- It should be stored in original package to protect it from light.
- It should not be stored above 30 °C.

Uses

- It acts as a haematinic agent.
- It is used as a source of iron for treating iron-deficiency anaemia.

4.Ferrous ascorbate

→ Ferrous ascorbate is an iron supplement which is used in the treatment of low iron levels in the blood. Ascorbic acid increases the absorption of iron from the stomach.

Preparation

- The present invention provides an improved and industrially feasible earth metal salts or its hydroxides are reacted with ferrous sulfate to get corresponding ferrous salts, which are reacted with ascorbic acid in an aqueous medium at slightly acidic or neutral condition followed by filtration to get ferrous ascorbate

Pharmaceutical Formulations

- Ferrous Ascorbate Capsules
- Ferrous Ascorbate Syrups

Market Preparation

- Ascofer Cap 275mg
- Solufer syrup 150ml
- Iron Ascorbate Caps

Storage Conditions

- It should be kept away from direct contact with heat, air and light because it may damage the medicines.
- The medicine must be kept in a safe place and out of children's reach.
- The drug should be kept at room temperature between 68°F and 77°F (20°C and 25°C).

Uses

- Iron deficiency aneamia.
- Anemia due to chronic kidney disease.

5.Carbonyl Iron

→ Carbonyl iron is an iron replacement product. Iron is obtained from the foods we eat. Red blood cells are produced with the help of iron that carries oxygen via the blood to tissues and then to organs.

Pharmaceutical Formulations

- Tablet
- Oral Suspension

Market Preparations

- Feosol (Carbonyl Fe)
- Icar Pediatric
- Icar C
- Irco

Storage Condition

- It should be stored in an airtight container at room temperature. Keep away from children

Uses

- As a dietary iron supplement.
- To treat iron deficiency anaemia.

ANTACIDS

- Antacids are such substances which are used to neutralise the excess amount of acid in our stomach.
- It may cause many severe problems like pain, ulceration, and also inactivate the pepsin (proteolytic enzyme).
- The stomach pH can range from pH 1, when empty to pH 7, when food is present.
- The low pH is due to the presence of endogenous hydrochloric acid, which is always present under physiological conditions.
- When hyperacidity develops, the results can range from gastritis (a general inflammation of the gastric mucosa) to peptic ulcer (specific circumscribed erosion)
- Patients with this condition will frequently suffer from "heartburn", which occurs due to the gastric acid entering the Oesophagus either during a belch or upon lying in bed.

Ideal Properties

- It should be non-absorbable
- It should not cause constipation.
- It should act rapidly for a prolonged time period.
- Its pH should lie within the range of 4-6.
- It should not evolve a large amount of gas on reacting with gastric hydrochloric acid.
- It should inhibit pepsin.
- It should not interfere with food absorption.

Classification

1) Systemic antacids (absorbable) : e-g., sodium bicarbonate which is soluble, readily absorbable and capable of producing systemic electrolytic alterations and alkalosis.

2)Non-systemic antacids (non-absorbable): Aluminium salts, magnesium salts, calcium carbonate, and sodium carboxyethylcellulose, which are not absorbed to a significant extent and thus do not exert a systemic effect.

some common examples of antacids:

1. Aluminium hydroxide gel,
2. Magnesium hydroxide mixture,
3. Magaldrate,
4. Sodium bicarbonate,
5. Calcium carbonate, etc.

1. Aluminium Hydroxide Gel

→ Preparations of aluminium hydroxide gel should not have less than 3.5% and not more than 4.4% w/w of aluminium oxide (Al_2O_3).

Preparation

- It can be formed by treating an aluminium salt (e.g, aluminium chloride or sulphate) with ammonium hydroxide.
- $AICl_3 + 3NH_4OH \longrightarrow Al(OH)_3 + 3NH_4CI$

Physical Properties

- **Appearance** : white amorphouse solid
- **Odour** : Odourless.
- **Solubility** : It is insoluble in water and ethanol, but soluble in acids and alkalis solutions.

Chemical Properties

- It gets converted to aluminium oxide on heating.
  $2AI(OH)_3 \longrightarrow Al_2O_3 + 3H_2O$
- It acts as an acid in the presence of an alkali.
  $Al(OH)_3 \longrightarrow 3H^+ + AlO_3^{3-}$

Pharmaceutical Formulation

- Oral Suspension

Market Preparations

- AlternaGEL
- Nephrox
- Amphojel

Storage Conditions

- It should be stored in well-closed containers and freezing should be avoided. It can be dispensed in blue or amber coloured bottles.

Uses

- To treat peptic ulcer, gastritis, peptic oesophagitis, gastric hyperactivity, and hiatal hernia,
- To protect the skin

2. Magnesium Hydroxide

→ Magnesium hydroxide (molecular weight 58.3197) or milk of magnesia contains not less than 95% and not more than 100.5% of $Mg(OH)_2$.

Preparation

- Treating the solution of different soluble magnesium salts with alkaline water induces the precipitation of the solid hydroxide $Mg(OH)_2$: $Mg_{2+} + 2OH- \rightarrow Mg(OH)$

Physical Properties

- **Appearance :** White powder
- **Solubility :** Soluable in water

Chemical properties

- At pH 10, magnesium hydroxide is alkaline to litmus solution and absorbs carbon dioxide from air.

Pharmaceutical Formulations

- Chewable Tablet
- Suspension

Market Preparations

- Milk of Magnesia

Storage Conditions

- It should be kept in original containers. Humidity
- It should be avoided in indoor storage areas and at least one metre away from heating devices.

Uses

- Magnesium hydroxide is a non-systemic gastric antacid and mild cathartic. But on continuous or prolonged use, kidney stones may develop.

3. Magaldrate

→ Magaldrate acts as an antacid which is used in the treatment of various conditions in GI tract, such as esophagitis, duodenal and gastric ulcers, and gastroesophageal reflux.

Properties

- It is white or almost white crystalline powder.
- It is practically insoluble in water and ethanol (96 per cent). It is soluble in dilute mineral acids.

Pharmaceutical Formulation

- Oral Suspension
- Market Preparation
- Riopan

Storage Condition

- The tablets and capsules should be stored at room Temperature
- Refrigerator is used to store the liquid form of this medication to improve taste.

Uses

- It is used to treat gastric and duodenal ulcer, GERD.
- It neutralies gastric acid and increases gastric pH.

4. Sodium Bicarbonate

→ Sodium Bicarbonate is not having less than 99% and not more than 101% of $NaHCO_3$.

Preparation

→ A similar method is used for the production of sodium bicarbonate on commercial scale. The soda ash (mined in the form of ore trona) is dissolved in water and treated with carbon dioxide. From this method, sodium bicarbonate is obtained as a solid precipitate.

$$Na_2CO_3 + CO_2 + H_2O \longrightarrow 2NaHCO_3$$

Physical Properties

- **Appperance** : white crystalline powder
- **Odour** : odourless
- **Stability** : It is stable only in dry air.
- **Solubility** : soluble in water and insoluble in other solvent like alcohol.

Chemical Properties

- It can be used as a wash for removing any acidic impurities from a crude liquid and resulting to a pure sample.
- It reacts with acetic acid (CH_3COOH) to give sodium acetate.

Pharmaceutical Formulations

- Injectable Solution
- Tablet

Market Preparations

- Sellymin
- Brioschi
- Sodium Bicarbonate
- Neut

Storage Condition

- It should be stored in well-closed containers.

Uses

- Aqueous solution of sodium bicarbonate is used as an antacid which is given orally to treat acid indigestion and heartburn.
- It is used in urinary alkalinisation for treating uric acid renal stones.

5. Calcium Carbonate

→ Calcium carbonate is a chemical compound with chemical formula the $CaCO_3$.

→ It is having not less than 98.0% and not more than 100.5% of $CaCO_3$ which is calculated with reference to the sample dried at 105°C.

Preparation

$CaCO_3$ is obtained by using carbon dioxide and slaked lime as raw materials. When carbon dioxide is passed through slaked lime, calcite is obtained. Another method to obtain calcite is by adding sodium carbonate to calcium chloride.

Physical Properties

- Apperance : White Powder
- Solubility : Soluble in dilute acids

Chemical Properties

- Action of Heat: When heated, calcium carbonate gives a reversible reaction.
- $CaCO_3 \longrightarrow Cao + CO_2 \uparrow$

Pharmaceutical Formulations

- Tablet
- Chewables

Market Preparations

- Tums
- Tums Chewy Delights
- Tums Extra, Tums Freshers , Tums Kids, Tums Regular
- Tums Ultra
- Tums Smoothies
- Children's Pepto

Storage Conditions

- Should be stored in well closed container.

Uses

- It is a rapidly acting non – systemic antacid .

Anti-Microbial Agents

- Chemicals or agents that are used to kill or to inhibit the growth of microorganism (bacteria, fungi, or protozoans) are known as antimicrobial.
- They are either Microbicidal (kill microbes) or microbiostatic (prevent the growth of microbes) in nature.
- Antimicrobial substance like disinfectants are generally used to clean non – living objects

Classification

- **Antiseptics :** These substance are used to inhibit the microbial growth and are specifically applied to living tissue. Antiseptic agents are used for treating sepsis, putrefaction,etc
- **Disinfectants :** These substance kill the pathogenic microorganisms to prevent infection. Disinfectants are usually applied to non-living objects.
- **Germicides :** These are used to kill microorganisms. More precise terms like bactericide (against bacteria), fungicide (against fungi), virucide (against virus), etc
- **Bacteriostatic Agents:** These are used to inhibit bacterial growth. They do not kill but hamper bacterial growth.
- **Sanitizers:** These are used to maintain general public health standards and to clean or wash away the organic matter (e.g., saliva, mucous, etc.).

Example

- Silver nitrate,
- Ionic silver,
- Chlorhexidine gluconate,
- Hydrogen peroxide,
- Boric acid,
- Bleaching powder,
- Potassium permanganate, etc

1. Silver Nitrate

→ Silver nitrate (or lunar caustic) is a soluble chemical compounds, having not less than 99.5 % and not more than the equivalent of 100.5% of AgNo3

Preparation

- It is prepared bu dissolving metallic silver in cold and dilute nitric acid
- $Ag + 2HNO_3 \longrightarrow AgNO_3 + NO_2 + H_2O$

Physical Properties

- **Apperance** : Colourless or White crystals.
- **Odour** : Odoueless
- **Taste** : Bitter in taste
- **Solubility** : Solubile in boiling alcohol, Water , Slightly soluble in alcohol

Chemical properties

➲ Raction with Potassium Chromate: It reacts with potassium chromate to give a reddish brown colour.

$2AgNO_3$ + K_2CrO_4 ⟶ Ag_2CrO_4 + $2KNO$

(Silver nitrate) (Potassium Chromate) (Reddish brown) (Potassium nitrate)

Pharmaceutical Formulations

- Topical Solution
- Applicator Sticks

Market Preparations

- Avoca Flexible Caustic Applicator
- Silver Nitrate

Storage Conditions

- It should be stored in amber coloured bottles in a cool and dark place.

Uses

- It is used as a disinfectant, astringent, and an irritant.
- In cosmetics, it is used to dye eyebrows, eye lashes, and hair.

2. Ionic Silver

- A Silver ion is an atom of silver that has one missing electron.
- Silver ion is obtained by removing one electron from a silver atom.

Pharmaceutical Formulations

- Solution ,
- Powder ,
- Gel

Market Preparations

- Antibacterial Hand Wash
- Ave Silvergen
- Argentyn 23 Professional Silver First Aid Gel

Storage Condition

- Many advertised products as ionic silver are actually ionic silver solutions that should be stored in glass.

Uses

♠ Ionic silver has been used for numerous years as "ultimate" antibiotic, antifungal and antiviral altermative.

3. Chlorhexidine Gluconate

→ Since 1950, Chlorhexidine gluconate is known to be broad spectrum antiseptic. It is first generation antiplaque, anti-gingivitis agent and chemical plaque control agent.

Preparation

➢ It can be prepared from 1,6 hexamethylenebis(dicyandiamide) and 4-chloroaniline hydrochloride.

Properties

➢ It is solid or crystal from methanol.
➢ It is soluble in water at 20 °C.
➢ It is stable under ambient warehouse conditions to moisture and simulated sunlight.

Pharmaceutical Formulations

♦ Mucous inserts
♦ Mucous membrane liquid

Market Preparations

▪ Paroex
▪ PerioChip
▪ Peridex
▪ Periogard

Storage Conditions

♦ It should be stored at 66°F- 90°F (19°C- 32°C).

Uses

- It is used in dairy cattle, the operation of dairy facilities or production of dairy products.
- By these different types of pesticide which are used to destroy or inhibit the growth of disease-causing mechanisms can be impregnated into clothing.,

4. Hydrogen Peroxide

Preparation

→ A thick paste of barium peroxide is added to ice-cold water. This mixture is added to a calculated volume of Ice-cold dilute sulphuric acid. The solution is filtered and the insoluble sulphate is separated.

$BaO_2 + H_2SO_4 \longrightarrow BaSO_4 \downarrow + H_2O_2$

Physical Properties

- Apperance : Colourless
- Odour : Odourless
- Solubility : It is soluble in ether and insoluble in water.

Chemical Properties

- As an Oxidising Agent: It oxidises ferrous to ferric in the presence of dilute sulphuric acid; and the solution turns yellow from green.

Pharmaceutical Formulation

- Solution

Market Preparations

- Eskata
- Orajel Antiseptic Mouth Sore Rinse
- Proxacol
- Peroxyl

Storage Conditions

- It should be stored in light-resistant containers.
- It is kept in a dark and cool place.

Uses

- It is used as a disinfectant, anti-infective, and deodorant.
- It is used to clean septic sockets and root canals in dentistry.
- It is available as ear drops used for removing wax.
- It is also used as a bleaching and oxidising agent.

5. Boric Acid

Preparation

→ By Decomposition of Borax: Hot aqueous solution of borax is mixed with a mixture of concentrated sulphuric acid, followed by addition of water. The hot solution is fltered and cooled resulting in the crystallisation of boric acid which is separated by filtration.

$$Na_2B_4O_7 + H_2SO_4 + 5H_2O \longrightarrow Na_2SO_4 + 4H_3BO_3$$

Physical Properties

- It is a colourless and odourless powder.
- It is stable in air.
- It is soluble in water and alcohol; and freely soluble in glycerine, boiling water, and boiling alcohol.

Chemical Properties

- It is a weak acid which turns litmus paper slightly red.
- On treating with boric acid, colour of turmeric paper changes to brown which when dipped in sodiumn hydroxide solution turns blackish.

Pharmaceutical Formulations

- Boric acid ophthalmic
- Boric acid otic
- Boric acid topical

Market Preparations

- Borofax
- Dri-Ear
- Hylafem
- Collyrium Fresh

Storage Conditions

➲ It is stored in tightly closed containers.

Uses

- It is used in eyewash and mouthwash in the form of solutions at a concentration of 2.5-4.5%.
- It is also used as a dusting powder.
- It is used as a buffer and as an antimicrobial in eye drops.

6. Bleaching Powder or Chlorinated Lime [CaOCl (Cl) H2O]

→ Chlorinated lime is also known as calcium hypochlorite and bleaching powder. It should not have less than 30.0% w/w of available chlorine

Preparation

★ Bleaching powder is prepared by **passing dry chlorine gas over dry slaked lime**. The reaction being essentially:

$2Ca(OH)2+2Cl2 \rightarrow Ca(OCl)2+CaCl2+2H2O$.

Properties

- It is a dull white powder with a characteristic odour.
- After being exposed to air it absorbs moisture and decomposes slowly.

Pharmaceutical Formulations

♦ Powder
♦ Liquid

Market Preparations

- Haktiman
- Vikram
- Lion

Storage Conditions

➲ It should be stored in a well-closed containers and kept in a cool place away from moisture and heat.

Uses

- It is used as a bleaching agent.
- It is used as an antiseptic.
- It is used as a cleaning solution for patients.

7. Potassium Permanganate

→ Potassium permanganate, formerly known as permanganate of potash or Condy's crystals is the inorganic, water-soluble chemical compound which consists equal moles of potassium (K^+) and permanganate (MnO_4^-) officially called manganate (VII) ions.

Preparation

- Industrial Preparation (Large Scale Preparation): It is prepared by mixing KOH solution, powdered manganese oxide, and potassium chlorate. The resultant mixture is boiled and evaporated. The residue obtained is heated in iron pans till it forms a paste of desired consistency.

$$KOH + 3MnO_2 + KClO_3 \longrightarrow K_2MnO_4 + KCl + 3H_2O$$

Physical Properties

- It is found in the form of dark purple coloured monoclinic prism.
- It is odourless
- It is soluble in water and boiling water

Chemical Properties

➲ On heating at 240°C, it disintegrates and deteriorates.

$$2KMnO_4 \longrightarrow K_2MnO_4 + Mno_2 + o_2 \uparrow$$

Pharmaceutical Formulations

- Oral Tablet
- Topical Solution

Market Preparations

- Permasol
- Kalii permanganas RFF
- Koi Med Tricho-Ex

Storage Conditions

- It should be stored in closed containers.
- It must be handled carefully.

Uses

- It is used as an antiseptic in mouthwashes.
- It is used in the treatment of urethritis.
- Its solution destroys the effect of a poison and prevents its absorption.

DENTAL PRODUCTS

- At the present time dental products of different category are available which are used to maintain dental health and hygiene.
- Dental decay and other dental problems mainly caused by poor oral hygiene.
- Inorganic compounds which are used as dental products or in dentistry can be categorised under the following heads
    - Cleaning agents,
    - Dentifrices,
    - Anticaries agents/fluorides,
    - Desensitising agent,
    - Cements and fillers,
    - Oral antiseptics and astringents, and
    - Polishing/abrasive agents.

1. Cleaning Agents

- An efficient cleaning agent must comprise of fine particles having suitable abrasive property. It must provide suitable abrasiveness in order to remove stains from teeth.
- The phosphates are generally used as anticaries and cleaning agents.

Dentifrices

- A dentifrice is a substance used for cleaning the reachable surfaces of the teeth with a toothbrush.
- The main objective of a dentifrice is to help the toothbrush clean the teeth.
- A dentifrice is used to maintain good oral hygiene.
- Toothpaste is the most common dentifrice that dentists recommend to use with a toothbrush for removing dental plaque and food debris.

Types

Dentifrices are of three types depending on whether they are solid, semi-solid or liquid:

I. **Toothpaste:** It is used with a toothbrush for maintaining oral hygiene. Toothpaste is mainly used for removing debris and plaque. It also has some additional functions, like whitening teeth and freshening breath.

II. **Tooth powder:** It is a substitute of toothpaste and is available in both fluoride and non-fluoride forms.

III. **Mouthwash:** It is available in a variety of compositions, claiming to kill bacteria forming plaque or bad breath, and freshen up breath on regular use

Examples

- Calcium carbonate,

Calcium Carbonate

→ Calcium carbonate is a chemical compound with the chemical formula $CaCO_3$.

Preparation

- $CaCO_3$ is obtained by using carbon dioxide and slaked lime as raw materials.

Properties

- It is a fine white powder, and is soluable in dilute acids .

Pharmaceutical Formulation

- Tablet
- Chewables

Market preparations

- Tums,
- Tums freshers,
- Tums kids, etc

Storage condition

- It stored in well closed containers.

2. Denture Cleaners

→ A dentures cleaner 9 also termed denture cleanser) is used to clean dentures when they are out of the mouth.

Properties

- Non-toxic
- Easy to remove
- Harmless to patient if accidentally spilled/splashed
- Harmless to denture base materials, denture teeth and soft liners
- Long shelf life and cheap

Pharmaceutical Formulations

- Liquid Solutions
- Powders
- Pastes
- Tablets

Market Preparations

- Polient ,
- Corega,
- Secure

Storage Conditions

- It should be stored in hygienic place

Uses

- They help the denture to intact in place.
- They fight bad breath with its antibacterial ingredients.
- The adhesive locks out any food particles from getting between the gum and the denture.

3. Mouth Washes

→ Mouthwashes are concentrated, clear aqueous solution having a pleasant taste that is used to clean and deodorise the mouth or buckle cavity.

Preparation

➢ Dissolve the benzoic acid in the chloroform, add the glycerin and mix. Dissolve the cinnamon, peppermint and phenol in alcohol and mix two solutions together.Mix for two hours, chill and filter.

Properties

- It should be quick in action and potent enough to show its intended action at specific dilution.
- Flavour must be strong enough to mask foul smell of mouth.
- It should have an acceptable taste, in most cases, sweet taste is considered.
- Low cost of production.
- No irritation should be caused to oral cavity or mucous membrane.
- It must be non-toxic.

Pharmaceutical Formulations

- Oral solution

Market Preparations

- Colgate
- Listerine
- Closeup
- Freshclor

Storage Condition

➲ Mouthwashes should be supplied in a well closed air tight plastic container having screw cap

Uses

- It is used as an antiseptic/antibacterial.
- It is used as cooling and refreshing action.

MEDICINAL GASES

- Gases like oxyger and water and food are therapeutically significant and essential for the maintenance of living organisms.
- Among oxygen, food and water (the three basic needs of life), oxygen deficiency leads to death most rapidly.
- In case of many diseases and intoxication, intereferin with normal oxygenation of blood or tissues, oxygen therapy is required.

Oxygen (O2)

- Mol. wt-32.0
- Oxygen is a living gas, constituting one-fifth by weight of air in its free form. It contains not less than 99.0% of v/v of O_2

Preparation

→ Laboratory Method: Electrolysis of aqueous solutions of alkalis or acids liberates oxygen. Here, H^+ drifts to the cathode, accepts an electron and converts into a neutral atom forming hydrogen molecules whereas, OH^- discharges at anode forming water and oxygen.

Physical Properties

- It is a colourless, odourless, and tasteless gas which supports combustion.

Chemical Properties

- Many non-metals, when heated with oxygen, burns rapidly, producing a non-metal oxide, e.g., CO_2, P_2O_5, and SO_2.

$$C + O_2 \longrightarrow CO_2$$
$$S + O_2 \longrightarrow SO_2$$
$$P_4 + 5O_2 \longrightarrow P_4O_{10}$$

Pharmaceutical Formulation

- Medical gas

Market Preparation

- EZ-Ox

Storage Conditions

- It is stored and supplied in metallic cylinders under pressure with a pressure gauge.

Uses

- It is used for treating hypoxia.
- It is used in anaesthesia.
- It is used for treating carbon monoxide poisoning.

Carbon Dioxide

→ Carbon dioxide with not less than 99.0% W/w of CO_2 is stored and compressed in metal cylinders.

Preparation

➢ It is obtained when carbon containing compounds likecoal, coke, oil, etc., are burned with an excess of oxygen.

$C + O_2 \longrightarrow CO_2$

Physical Properties

♦ It is a heavy, colourless, odourless gas with a faintly acidic taste. It can be liquefied under water, is soluble in water.

Chemical Properties

➢ Carbon dioxide forms carbonic acid when passed in water. This carbonic acid produces sodium bicarbonate when added to sodium hydroxide.

Pharmaceutical Formulation

- Medical gas

Market Preparation

♦ Carbon dioxide

Storage Conditions

➲ It is stored and supplied in metal cylinders in compressed form.

Uses

➢ It is inhaled to be used as a respiratory stimulant which stimulates the respiratory and cardio accelerator centres.

➢ Mixture of carbon dioxide and oxygen are used for treating carbon monoxide poisoning.

Nitrous Oxide

→ Nitrous oxide contains not less than 99.0% v/v of N_2O. It is also known as laughing gas because if inhaled an exhilarating/ exciting effect is produced.

Preparation

★ When sulfamic acid is heated with 73% nitric acid solution, pure nitrous oxide is liberated.

Physical Properties

- It is a colourless, non-flammable gas, with a pleasant and slightly sweet odour and taste.

Chemical Properties

♦ At low temperature (about 600°C), it dissociates into nitrogen and oxygen.

♦ Sulphur and phosphorus burn in its atmosphere.

♦ It reduces to nitrogen when passed over red hot copper.

Pharmaceutical Formulation

- Medical gas

Market Preparation

- Nitrous Oxide

Storage condition

- It is stored and supplied in metal cylinders.

Uses

- It is used as an anaesthetic.
- Mixture of oxygen and nitrous oxide in 65:35 ratio is used in myocardial infarction.
- It is used as a good analgesic. In low concentration, it reduces the sensitivity of pain.
- In high concentration, it has a stimulating effect on the nervous system as it is a laughing gas.

Chapter 4

Organic Chemistry

Topics

Organic Chemistry
Nomenclature of organic chemical System

Organic Chemistry

- Organic chemistry deals with the study of chemistry of carbon compounds.
- The term organic was used for branch of chemistry because at a time when most of the compounds studied in this branch of chemistry were obtained from living sources (plants or animals).
- However at the present time, organic chemistry studies the chemistry of carbon compounds irrespective of their Source. Carbon can combine with each other to form long chains and different sized rings. This process is known as catenation.
- The other few elements (apart from carbon) present in organic compounds are hydrogen, halogens, oxygen, sulphur, nitrogen, phosphorus, etc.
- Thus, organic molecules can be very large and complicated.
- The concepts of structure, homology isomerism, and functional groups are to be studied in organic chemistry.

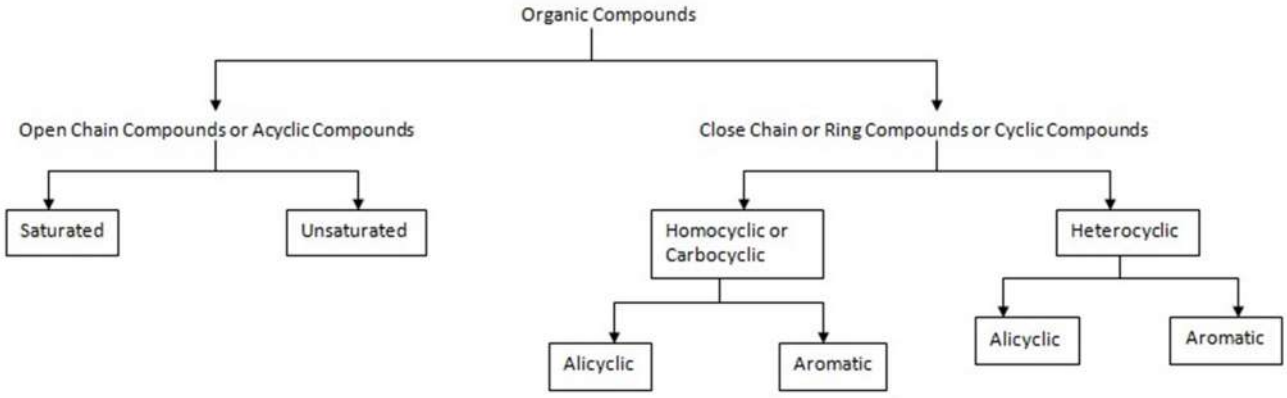
Classification of Organic Compounds

Organic compounds can be classified on the basis of following two ways:

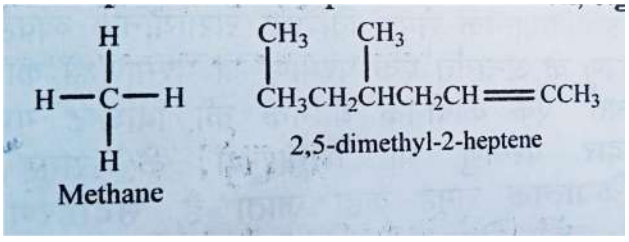
- On the basis of structure, and
- On the basis of functional group.

On the Basis of Structure

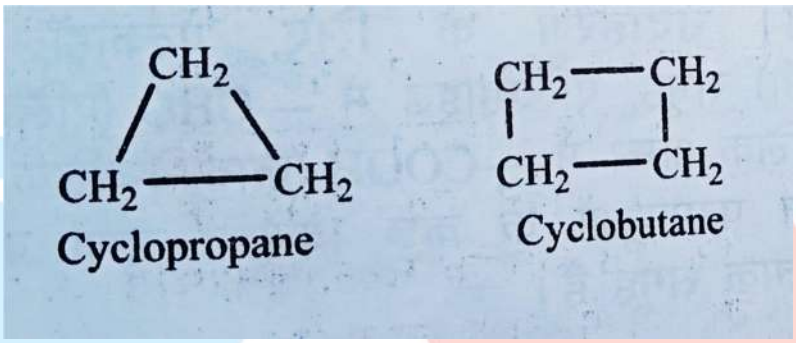
Based on structure, organic compounds are classified as shown below:



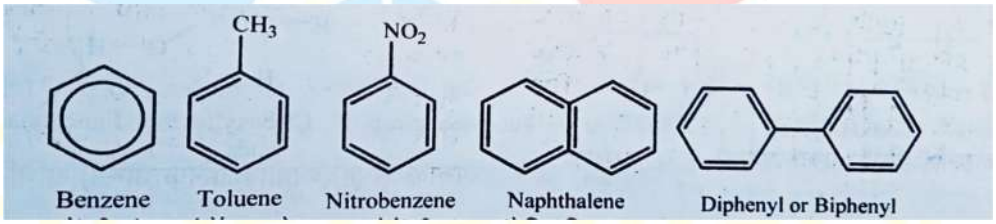
- **Acyclic or Open Chain Compounds :** These organic compound have open chain skeleton, e.g,



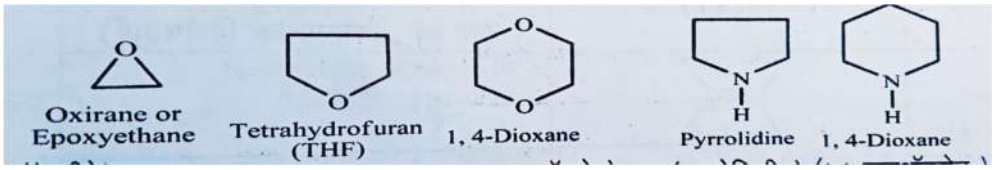
- **Cyclic or Closed Chain Compounds:** These organic compounds have closed rings and are further divided into:
  i. **Homocyclic or Carbocyclic Compounds:** In these organic compounds, the ring of compound has carbon atoms only. These compounds are further classified into:
    a) **Alicyclic Compounds:** These homocyclic compounds are similar to acyclic compounds and do not have a benzene ring, e.g.,



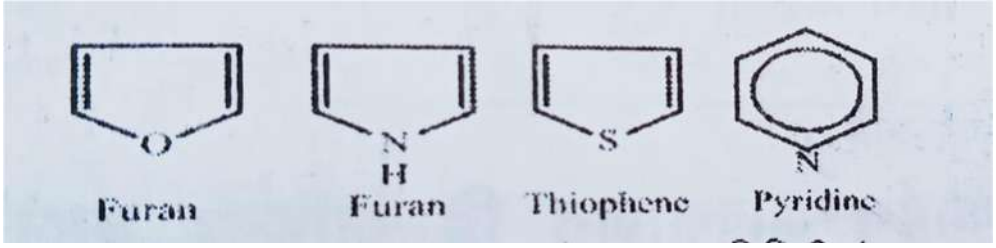
    b) **Aromatic Compounds :** These Homocylic compounds have a benzene ring eg.



  ii. **Heterocyclic Compounds:** These organic compounds have one or more heteroatoms (e.g., o, N, S, etc.) in the ring. These compounds are further classified into:
    a. **Alicycic Compounds:** These heterocyclic compounds are compounds are similar to alphatic compounds in properties, eg



    b. **Aromatic Compounts :** These heterocylic compoundsare similar to benzene and other aromatic compounds in properties eg



On the Basis of Functional Group

→ A functional group is an atom or group of atoms within a specific chemical behaviour. Thus, an atom or group of atoms responsible for the characteristic features of an organic compound is termed as a functional group eg : Carbon-carbon double bond (one of the simplest functional groups forming alkenes).

Nomenclature of organic chemical System

The two nomenclature system which are in use for naming organic compounds are :

1. Trivial or common system and
2. IUPAC System

Trivial or Common System

→ The trivial or common system of nomenclature of the organic compounds is based on various factors like the source, name of discoverer, structure etc:

- **On the basis of property :** some example of organic compounds which were named on the basis of their properties are:
  - i) Glucose (sweet in test),
  - ii) Glycol (sweet poisonous),
  - iii) Glycerol (sweet)
- **On the Basis of Discovery:** Some examples of organic compounds which were named on the basis of their discoverer are:
  - RMgx (Grignard reagent),
  - RZn (Frankland reagent).

Some of the drawbacks associated with trivial system of nomenclature are:

- ➲ This method of naming compounds was not systematic, thus naming large number of compounds was not possible.
- ➲ The naming of various organic compounds was not scientific.
- ➲ Often a compound isolated from different sources or by different discoverers or at different places was named in a different way. For example,
  - The name acetic acid originated from the Latin word acetum meaning vinegar.
  - The name methyl alcohol name originated from wood spirit (the compound was first isolated by destructive distillation of wood).
- ➲ This system of nomenclature thus caused confusion while naming compounds.

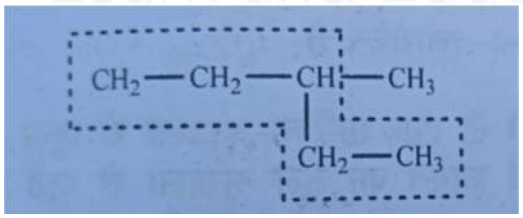
IUPAC System of Nomenclature

→ The International Union of Pure and Applied Chemistry (IUPAC) put forward a systematic method of naming organic compounds; this method is termed IUPAC nomenclature. This method eases the identification of different compounds. Each and every organic compound should be named so that their structural formula can be drawn.

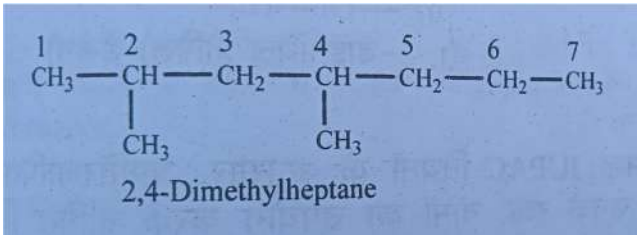
Rules Governing IUPAC Nomenclature of Branched Chain Alkanes.

Branched chain alkanes can be named by the given rules of IUPAC nomenclature system:

1. The longest continous chain of carbon atoms is identified as the parent chain and the compounds is considered its derivative.

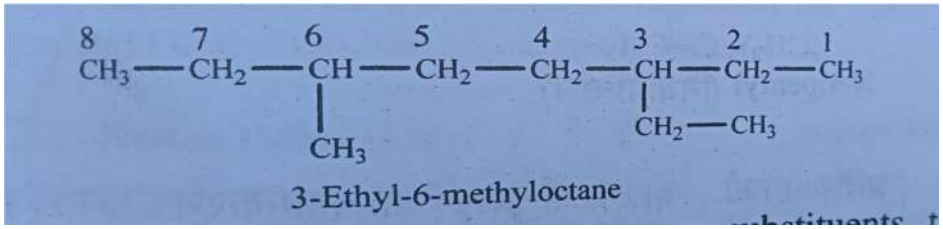


2. The carbon atom in the parent chain are numbered from one end so that the substituent carrying carbon atoms receive the lowest numbers.
3. For naming the organic compounds the position of each substituent and its name of parent alkane.

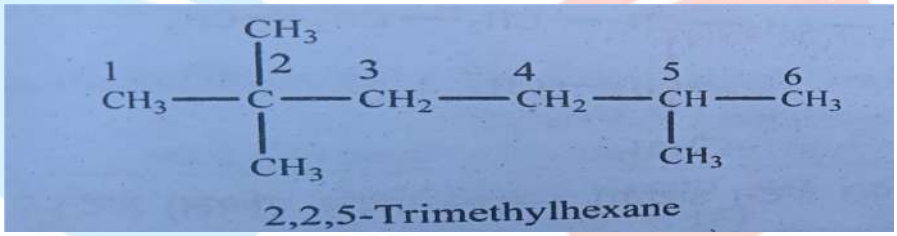


4. The names of different alkyl substituents present in the parent chain are written alphabetically

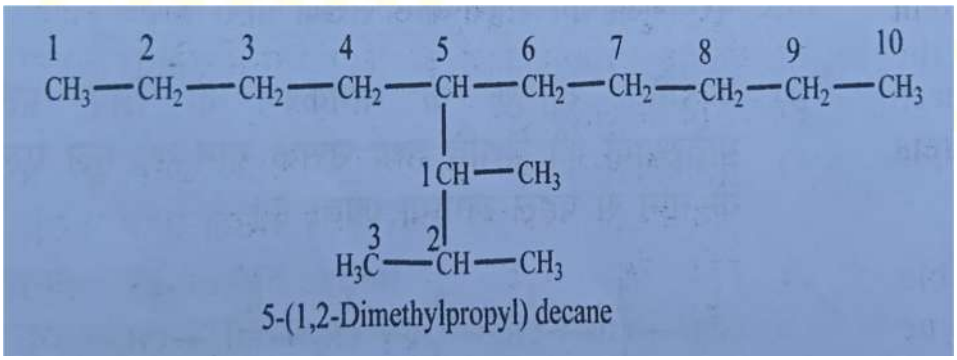
5. If the parent chain has two or more substituents at equivalent position the first substituent in the alphabetical order is given the lowest number.



6. In the presence of two or more same substituent their number position is sepersted by commas and the appropriate predix-di, tri, tetra, etc., are added to the name of each.

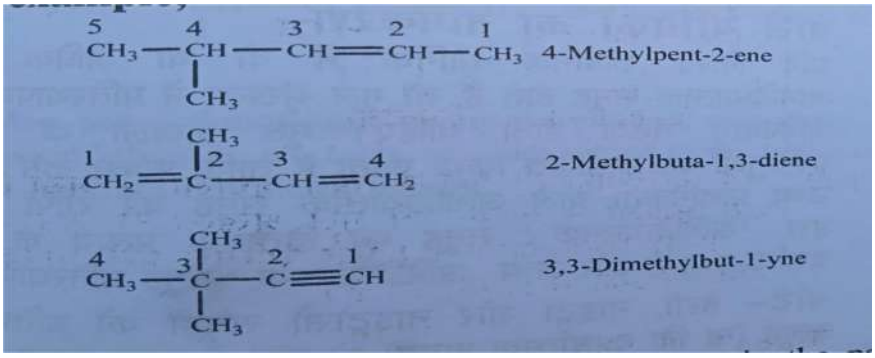


7. If the substiturnt also carries a branched chain the carbon in the chain are numbered separately beginning from the carbon attached to the parent chain. The names of such complex substituents are written within brackets.



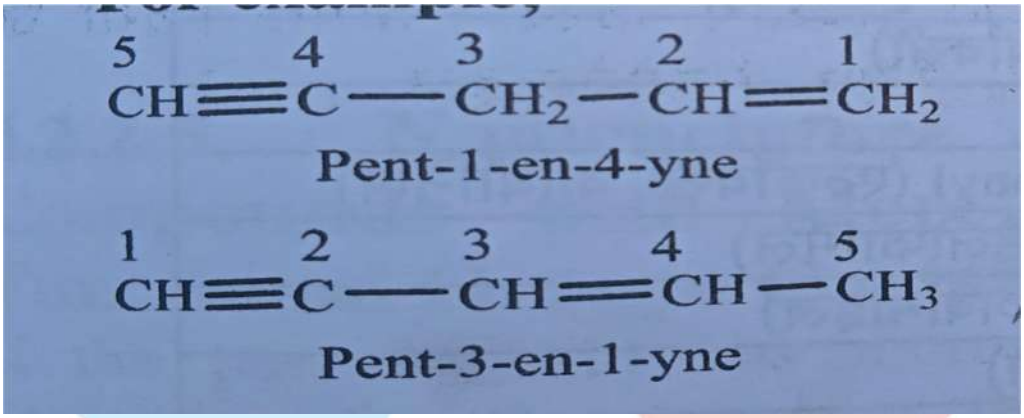
Nomenclature of Alkenes and Alkynes

Alkene and alkyne are assigned IUPAC names derived from the corresponding alkane. In the IUPAC name of alkene, the suffix -ane is replaced with ene; while in alkyne, ane is replaced with -yne.



If double as well as triple bonds are present in the parent chain, following rules are considered for naming the compound.

1) Parent chain is numbered so, that the double and triple bonds receive the lowest numbers.
2) If possible lowest number is assigned to the double bond, such a hydrocarbon is considered an alkyne derivative.



Nomenclature of compound Containing Functional Groups

→ The functional group (apart from C=C and C=C) present in a molecule is written by adding secondary suffix after the primary suffix. The 'e' terminal of the primary suffix is removed before the secondary suffix is added if its name begins with a, i, o, u, or y.

Nomenclature of Compounds with More than One Functional Group

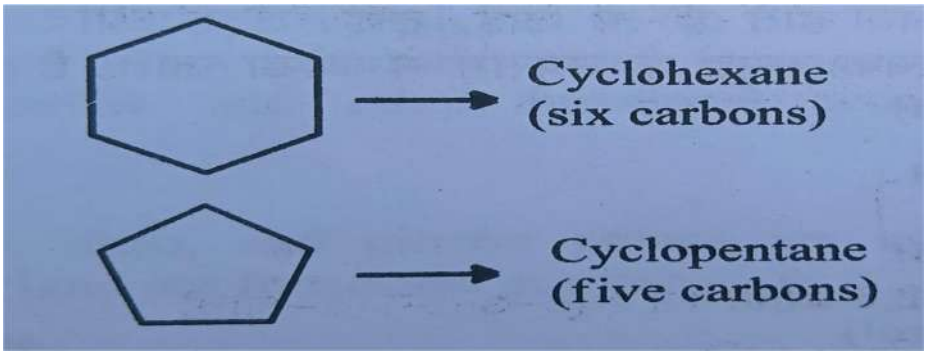
→ If an organic compound has two or more different functional groups, then the parent chain must have maximum number of Substituents. The carbon atoms of parent chain are numbered so that lowest number is assigned to the functional group of higher priority. This functional group is represented with a secondary suffix and other functional groups are the substituents.

Nomenclature of Alicyclic Compounds

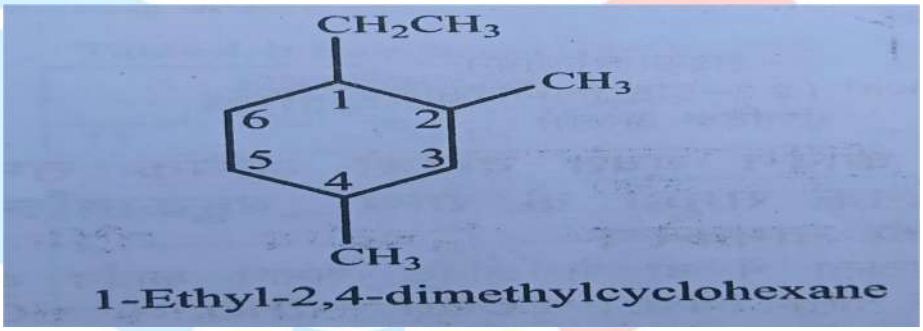
Organic Compounds having closed chain compounds and resembling with aliphatic compounds in their properties are referred as alicylic compounds Cycloalkanes , Cycloalkenes and non aromatic carbocyclic compounds are classified as alicyclic compounds

Alicylic compounds can be named based on the following rules :

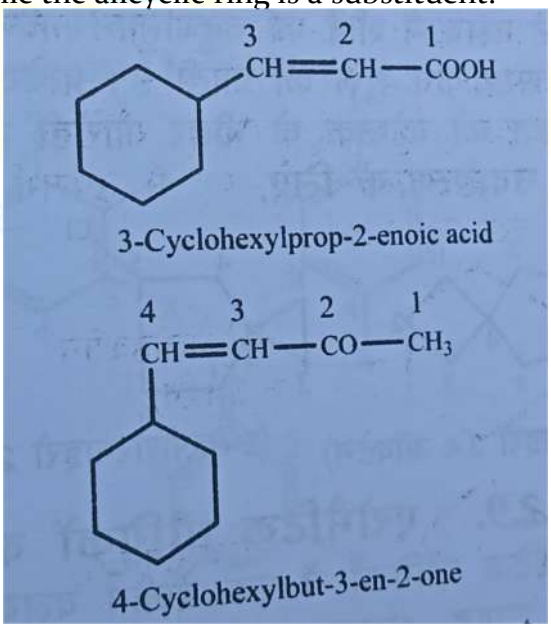
1) A saturated monocyclic compound is named prefix cyclo- to the name of the corresponding cycloalkane.



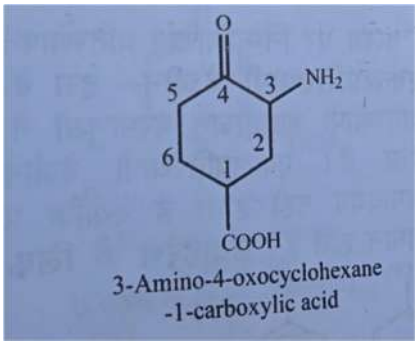
2) In the presence of two or more substituents, beginning from the one coming first in alphabetical order numbering is continued up to the last substituent so that it receives the lowest number.



3) In case, a functional group is attached to the side chain, the compound is considered as acyclic (irrespective of the ring size); while the alicyclic ring is a substituent.

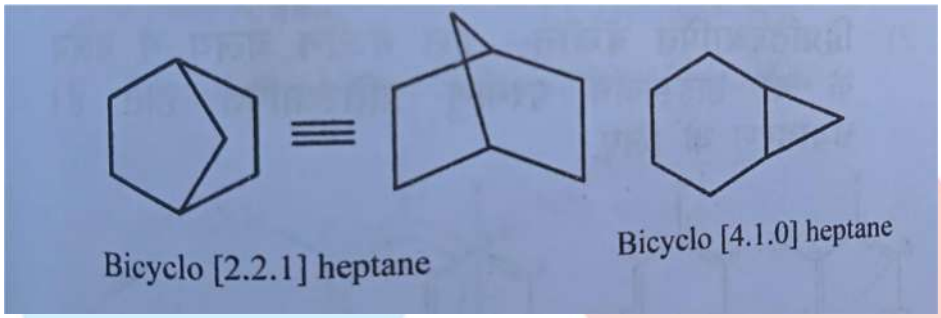


4) In case, the functional groups form a part of the ring system, the functional groups of highest priority are assigned with lowest number.



Nomenclature of Bicyclic Compounds

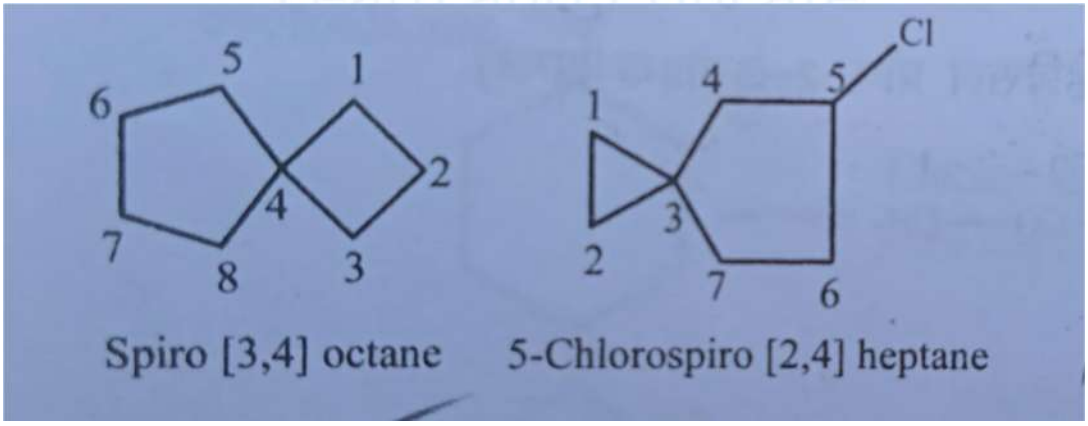
→ Bicyclic compounds have two fused rings joined by two tertiary carbon atoms. While naming these compounds, the alkane name (containing the same number of carbon as the bicyclic compound) is added after the prefix bicyclo- .The number of carbons in each of the three bridges is given within the brackets in descending order. For example,



Nomenclature of Spiro Compounds

→ Spiro compounds have two rings joined by a common quatermary carbon at the apex. While naming these compounds the name of the alkane (containin same number of carbons as part of the ring term system (s) is added: after the prefix spiro-.

→ Numbering is started from the carbon next to the quaternary carbon at the apex in the smaller ring Number of carbons in each bridge is written with in the brackets in ascending order for Example

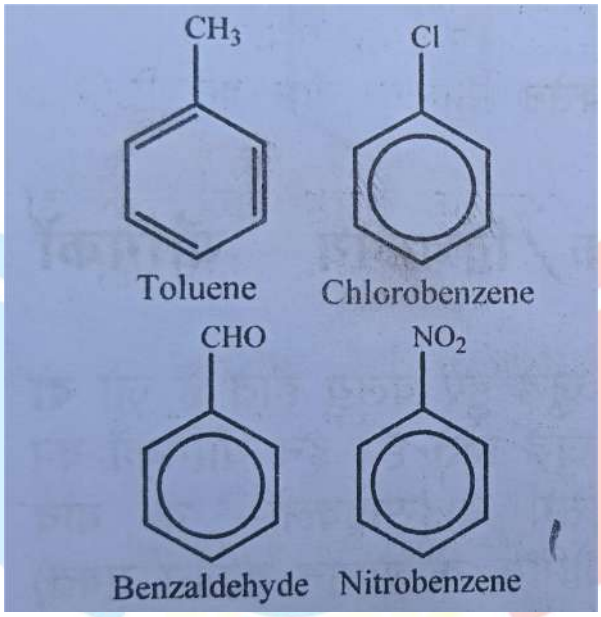


Nomenclature of Aromatic Compounds

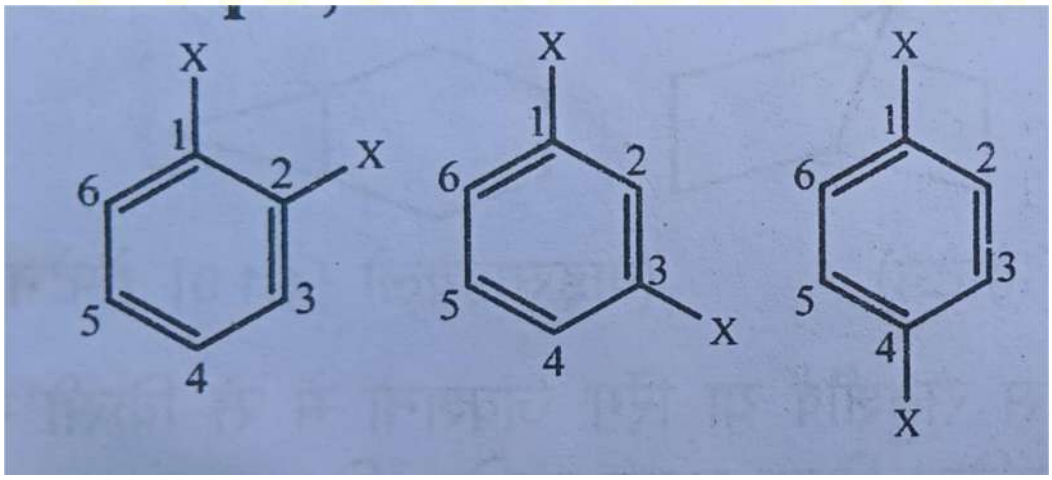
Aromatic compounds have a benzene ring and a Side chain or substituent (the group attached to benzene ring).

Follwing substitutions are possible on benzene ring

- **Monosubstituted Benzene:** In this benzene ring, a substituent replaces one of the hydrogen atoms. Monosubstituted benzene ring has no isomer as the nuclear carbons are all similar. For example.



- **Disubstituted Benzene:** In this benzene ring, two hydrogen atoms of the ring are substituted. For example,



Chapter 5

Drugs Acting on Central Nervous System

Topics

Anaesthetics

- Thiopental sodium *
- Ketamine hydrochloride *
- Propofol

Sedative-hypnotic

- Diazepam, *
- Nitrazepam,
- Phenobarbital, *
- Alprazolam, *

ANTIPSYCHOTICS

- Chlorprozamine hydrochloride *
- Risperidone *
- Olanzapine
- Lurasidone
- Haloperidol *
- Sulpiride *
- Quetiapine

ANTICONVULSANTS

- Phenytoin *
- Carbamazepine *
- Clonazepam
- Valproic acid *
- Gabapentin *
- Topiramate
- Vigabatrin
- Lamotrigine

ANTIDEPRESSANTS

- Amitriptyline Hydrochloride *
- Fluoxetine *
- Duloxetine
- Citalopram
- Escitalopram
- Imipramine Hydrochloride *
- Venlafaxine
- Sertraline
- Fluvoxamine
- Paroxetine

Anaesthetics

→ General anaesthetics are CNS depressants which include non-awareness of all sensations and loss of pain. The term anaesthetic is of Greek origin and means without perception or insensibility. They cause non-selective and reversible CNS depression.

Classification General anaesthetics are classified as follows:

- ★ **Inhalational Anaesthetics:** These substances are either volatile liquids or gases and are usually delivered using an anaesthetic machine, e.g.. Enflurane (liquid), Desflurane, Halothane, and Ether.
- ★ **Intravenous Anaesthetics:** These substances produce anaesthetic effect when injected into the bloodstream via venepuncture, e.g. Thiopentone sodium, Etomidate Ketamine, Fentanyl, and Diazepam.
- ★ **Gaseous Anaesthetics:** Nitrous oxide.

Examples

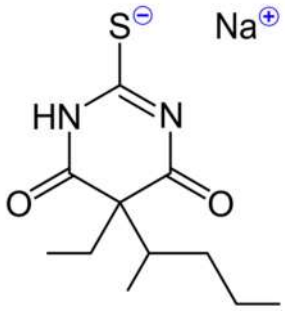
1. Thiopental sodium *
2. Ketamine hydrochloride *
3. Propofol

Thiopental sodium *

→ Thiopental Sodium sodium is administered intravenously for inducing general anaesthesia aesthesia or for producing complete anaesthesia of short duration.

Chemical Name and Structure

Sodium 5-ethyl-5-(1-methylbutyl)-2-thiobarbiturate



Mechanism of Action

- ★ Thiopental binds at a distinct binding site associated with a Cl^- ionopore at the $GABA_A$ receptor, increasing the duration of time for which the Cl^- ionopore is open. The post-synaptic inhibitory effect of GABA in the thalamus is, therefore, prolonged.

Uses

- ❖ It is used as a sole anaesthetic agent for short procedures 15 min

Stability and Storage Conditions

- ★ It should be stored at 22°C. Thiopental remains stable and sterile for 6 days and well beyond 7 days at 3°C.

Types of Formulations

- ➢ Injection,
- ➢ Powder,
- ➢ Solution,

Popular Brand Names

- Pentothal,
- Anesthal,
- Thiosol,
- Thiojex,
- Pentone

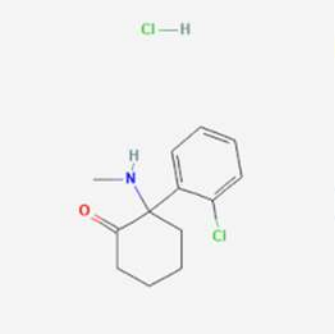
Ketamine Hydrochloride *

→ Ketamine is an NMDA receptor antagonist having a potent anaesthetic effect.

→ It was developed as a replacement for phencyclidine by Calvin stevens at Parke Davis Laboratories in 1963.

Chemical Name and Structure

2-(2-chlorophenyl)-2-(methylamino)cyclohexan-1-one



Mechanism of Action

- ★ Unlike other general anaesthetic agents, ketamine does not interact with GABA receptors; but it interacts with NMDA receptors, opioid receptors, monoaminergic receptors, muscarinic receptors, and voltage sensitive Ca ion channels.

Uses

- ♠ It is used as an anaesthetic agent in various diagnostic and surgical procedures. It is combined with a muscle relaxant if skeletal muscle relaxation is needed.
- ♠ It should be combined with a visceral pain desensitising agent if the surgical procedure involves visceral pain.
- ♠ It can also be used for inducing anaesthesia before using other general anaesthetics and as a complement for low potency agents.

Storage and Stability Condition

- ➢ It should be kept in tightly closed container and in dry and well ventilated place.

Type of Formulation

- ❖ Liquid solution

Popular Brand Names

- ❖ Ketalar,
- ❖ Anket,
- ❖ Ketmin,
- ❖ Verket,

Propofol

→ Propofol is a class of hypnotic alkylphenol derivatives. They are formulated for intravenous introduction of sedation and hypnosis during anaesthesia.

Mechanism of Action

➲ The action of propofol comprises of positive modulation of the inhibitory function of the neurotransmitter Gamma- Amino Butyric Acid (GABA) via GABA-A receptors.

Uses

- Propofol slows down the activity of brain and nervous system
- Propofol act as sedation and keeps asleep during general anaesthesia-for surgery or other medical procedures. It is used in adults as well as children 2 months and older.
- It is also used to sedate a patient who is in case of critical care and needs a mechanical ventilator (breathing machine).

Stability and Storage conditions

- It should be stored between the temperatures of 4°C to 22°C (40°F to 72°F). Refrigeration is not required.

Types for Formulations

- Emulsion,
- Suspension,
- Injectable

Popular Brand Names

- ➢ Diprivan,
- ➢ Propoven,

Sedative-hypnotic

→ Sedative-hypnotic drugs reduce tension and anxiety, and induce calmness (sedative effect) or sleep (hypnotic effect). Low doses of these drugs exert a calming effect and higher doses have a sleep-inducing effect. Sedative- hypnotic drugs depress the CNS.

→ Drugs like opiates can also produce these actions, thus sedative-hypnotics have a distinctive feature that they are capable of producing effects without altering the mood or reducing sensitivity to pain.

Classification

Urea Derivatives:

i) Diureides: Barbiturates.

- **Long Acting Barbiturates:** Phenobarbitone and Mephobarbitone.
- **Short Acting Barbiturates:** Butobarbitone, Secobarbitone,and Pentobarbitone.
- **Ultra Short Acting:** Thiopentone and Hexobarbitone.

ii) Related Ureides: Glutethimide.

Benzodiazepines: These are divided as follows as per their primary use

- **Hypnotics:** Flurazepam, and Nitrazepam.
- **Antianxiety:** Diazepam, Chlordiazepoxide, and Lorazepam.
- **Anticonvulsants:** Diazepam, Clonazepam, anda Oxazepam.

Newer Non-Benzodiazepines Hypnotics: Zopiclone and Zolpidem.

Miscellaneous: Chloral hydrates, Triclophos, and Paraldehyde.

Examples of sedatives and hypnotics are given below:

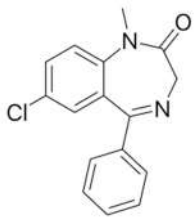
I. Diazepam, *
II. Nitrazepam,
III. Phenobarbital, *
IV. Alprazolam, *

Diazepam *

→ Diazepam is a benzodiazepine having anticonvulsant, anxiolytic, muscle relaxant, amnestic, and sedative properties. It has a long duration of action.

Chemical Name and Structure

7-chloro-1, 3-dihydro-1-methyl-5-phenyl-2H-1, 4-benzodiazepin 2-one



Mechanism of Action

➲ Diazepam is a benzodiazepine that exerts anxiolytic, sedative, muscle- relaxant, anticonvulsant and amnestic effects. Most of these effects are thought to result from **a facilitation of the action of gamma aminobutyric acid (GABA), an inhibitory neurotransmitter in the central nervous system**.

Uses

★ It is used for treating severe anxiety disorders, alcohol withdrawal syndrome, and for managing insomnia for a short-term. It is also used as a pre-medicant, anticonvulsant, and sedative.

Stability and Storage Conditions

- Diazepam injection is chemically stable as 5-mg doses in disposable glass syringes for 90 days when stored at 4°C om 30°C. It should be stored in refrigerator.

Types of Formulations

- Tablet,
- Oral solution,
- Rectal gel,
- Injectable solution

Popular Brand Names

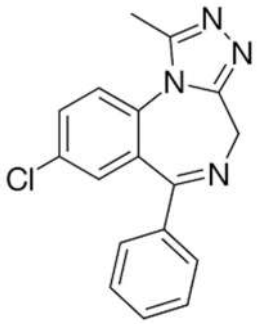
- Valium,
- Diastat,
- Diastat AcuDial

Alprazolam *

→ Alprazolam is a triazolobenzodiazepine compound having antianxiety and sedative-hypnotic properties. It is used effectively for treating panic disorders and generalised anxiety disorders.

Chemical Name and Structure

8-chloro-1-methyl-6-phenyl-4H-s-triazolo [4,3- α] [1,4] benzodiazepine.



Mechanism of Action

- **The exact mechanism of action of alprazolam is unknown**. Benzodiazepines bind to gamma aminobutyric acid (GABA) receptors in the brain and enhance GABA-mediated synaptic inhibition; such actions may be responsible for the efficacy of alprazolam in anxiety disorder and panic disorder.

Uses

- It is used for managing anxiety disorder, for short-term treatment of anxiety symptoms, and for treating panicdisorders with or without agoraphobia.

Stability and Storage Conditions

- It should be stored in a dry place at room temperature . Also, keep bottle out of direct sunlight and out of the reach of Children and pets. Make sure it stays in its original Container

Types of Formulation

- Tablet,
- Extended release

Popular Brand Names

- Xanax,
- Alprazolam
- Intensol,
- Xanax XR,
- Niravam

Nitrazepam

→ Nitrazepam is a DEA Schedule IV controlled substance. Substances in the DEA Schedule IV have a low potential for abuse as compared to substances in Schedule lIl. It act as a role in anticonvulsant, an antispasmodic drug, a GABA modulator, a sedative and a drug metabolitd.

→ It is a 14-benzodiazepinone and a C-nitro compound.

Mechanism of Action

- Nitrazepam is a benzodiazepine. Benzodiazepines presumably exert their effects by **binding at stereo specific receptors at several sites within the central nervous system**. All benzodiazepines cause a dose-related central nervous system depressant activity.

Uses

- Nitrazepam is a long-acting benzodiazepine with intermediate onset commonly used to treat:
    1. Panic disorders
    2. Insomnia
    3. Severe anxiety
    4. Seizures

Stability and Storage Condition

- It should be stored at room temperature and away from heat and light.

Type of Formulation

- Tablets

Popular Brand Names

- Mogadon,
- Nitrazadon,
- Nitrazepam,
- Hypnotex, Nitavan

Phenobarbital *

→ Phenobarbital is a barbituricacid derivative which acts as a non-selective depressant of CNS. It modulates chloride currents through receptor channels and promotes binding to inhibitory GABA sub-type receptors.

Chemical Name and Structure

5-ethyl-5-phenyı-2, 4, 6(ıH, 3H, 5H)-pyrimidinetrione.

Mechanism of Action

→ Phenobarbital **acts on GABAA receptors, increasing synaptic inhibition**. This has the effect of elevating seizure threshold and reducing the spread of seizure activity from a seizure focus. Phenobarbital may also inhibit calcium channels, resulting in a decrease in excitatory transmitter release.

Uses

- It is used as a hypnotic, sedative, and an antiepileptic drug. It is used in symptomatic therapy of epilepsy, and in nervous and tension related states.

Stability and Storage Conditions

➲ According to USP, it should be dispensed in well-closed containers at controlled room temperature.

Types of Formulations

- Oral elixir,
- Oral tablet

Popular Brand Names

- Luminal,
- Solfoton

ANTIPSYCHOTICS

→ Anti-psychotic drugs are mainly used for treating Schizophrenia; however they can also be used in mania, with much agitation.

→ Anti-psychotic agents are also called mood-altering gents.

Classification

Antipsychotics are classified as follows:

1) **Phenothiazines Derivatives:** Chlorpromazine and Trifluoperazine.
2) **Butyrophenones:** Haloperidol and Trifluperidol.
3) **Rauwolfia Alkaloids:** Reserpine.
4) **Diphenylbutyl Piperidines:** Pimozide and Penfluridol.
5) **Atypical Neuroleptics:** Clozapine, Olanzapine, and Risperidone.
6) **Indole Derivatives:** Malingole.
7) **Thioxanthine Derivatives:** Chlorprothixene and Flupenthixol.
8) **Substituted Benzamides:** Sulpirides.

Examples

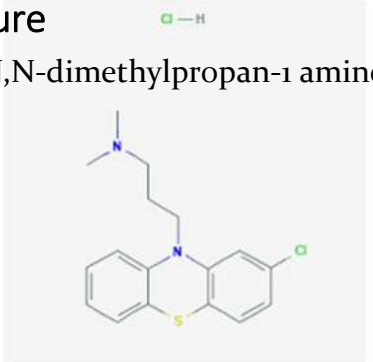
1. Chlorprozamine hydrochloride *
2. Risperidone *
3. Olanzapine
4. Lurasidone
5. Haloperidol *
6. Sulpiride *
7. Quetiapine

Chlorpromazine Hydrochloride *

→ Chlorpromazine is a psychotropic agent prescribed for treating schizophrenia. It also consists of sedative and antiemetic activity.

Chemical Name and Structure

3-(2-chlorophenothiazin-10-yl)-N,N-dimethylpropan-1 amine



Mechanism of Action

➢ Chlorpromazine is a member of the typical antipsychotic or neuroleptic drug class, also known as first-generation antipsychotics (FGAs). **It produces its antipsychotic effect by the post-synaptic blockade at the D2 receptors in the mesolimbic pathway**.

Uses

- It is used for treating schizophrenia, controlling nausea and vomiting, relieving pre-operative restlessness and apprehension, as an adjunct for treating tetanus, for acute intermittent porphyria, for controlling manifestations of the manic type of manic-depressive illness

Stability and Storage Conditions

- Chlorpromazine hydrochloride like oral solutions, tablets and injection should be stored at temperature less than 40 °C,

Types of Formulations

- Injectable solution,
- Oral tablet,

Popular Brand Names

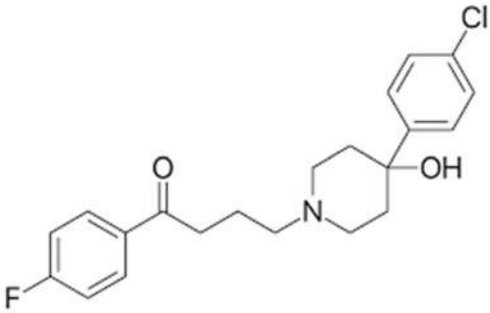
- Ormazine,
- Thorazine,
- Thorazine Spansule

Haloperidol *

- Haloperidol is a phenyl-piperidinyl-butyrophenone and a traditional antipsychotic drug used for treating schizophrenia and other psychoses.

Chemical Name and Structure

[4-(4-chlorophenyl)1-1[4-(4-fluorophenyl)-4-oxobutyl]piperdin-4-yl] decanoate



Mechanism of Action

- The accurate mechanism of haloperidol is not known but it seems to be depressing the CNS at the subcortical level of brain, midbrain, and brainstem reticular formation. It interrupts the impulse between diencephalon and cortex by inhibiting the ascending reticular system of the brain stem.

Uses

- It is used in acute psychosis, such as drug psychosis (LSD, psilocybin, amphetamines, ketamine, and phencyclidine), and psychosis associated with high fever or metabolic disease

Stability and Storage Conditions

- The haloperidol injection should be stored at a temperature of 20° to 25°C. It should be protected from light and should not be refrigerated.

Types of Formulations

- Tablets,
- Oral Concentration

Popular Brand Names

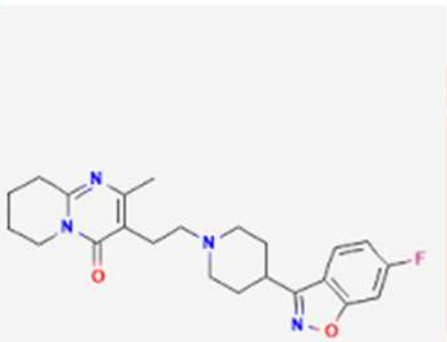
- ★ Haldol,
- ★ Haldol Decanoate,
- ★ Haloperidol LA, Peridol

Risperidone *

→ Risperidone is a second generation atypical antipsychotic drug

Chemical Name and Structure

3-{2-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1- yl]ethyl}-2-methyl-4H,6H,7H,8H,9H-pyrido[1,2-a]pyrimidin-4-one



Mechanism of Action

- ➢ The primary action of risperidone is to decrease dopaminergic and serotonergic pathway activity in the brain, therefore decreasing symptoms of schizophrenia and mood disorders. Risperidone has a high binding affinity for serotonergic 5-HT2A receptors when compared to dopaminergic D2 receptors in the brain.

Uses

- ♦ It is widely used for treating schizophrenia and mood disorders like bipolar disorder and depression with psychosis.

Stability and Storage Conditions

- It should be stored at room temperature and away from light and moisture. The liquid form of this medication should not be refrigerated and should be kept away from children

Types of Formulations

- ❖ Tablets,
- ❖ Oral Suspension

Popular Brand Names

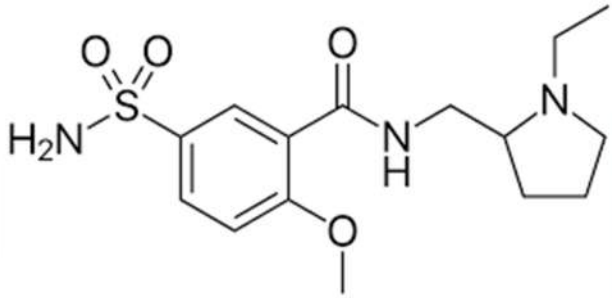
- ♣ Perseris,
- ♣ Risperdal

Sulpiride *

→ Sulpiride is a dopamine D_2-receptor antagonist which is therapeutically used as a digestive aid, antipsychotic, and an antidepressant,

Chemical Name and Structure

N-[(1-ethypyrrolidin-2-yl)methyl]-2-metgoxy-5-sulfamoylbenzamide



Mechanism of Action

➲ Sulpiride acts selectively as a dopamine receptor antagonist in the brain, its effects on other neuronal systems being extremely limited. Indeed, it may act even selectively within the dopamine systems in that it would appear it specifically interacts with one sub-population of cerebral dopamine receptors.

Uses

★ It is prescribed for treating schizophrenia.

Stability and Storage Conditions

♠ It should be stored in a cool and dry place. It should be kept away from direct heat and light.

Types of Formulations

- Tablets,
- Capsules,
- Solutions

Popular Brand Names

- Dogmatil,
- Espiride,
- Sulpor,
- Dolmatil,
- Eglonyl,
- Modal,
- Prometar

Olanzapine

→ Olanzapine is a class of thienobenzodiazepine classified as an atypical or second-generation antipsychotic agent. It is an antipsychotic drug which is used in the management of schizophrenia, bipolar 1 disorder, and agitation associated with these disorders.

Mechanism of Action

➲ Olanzapine is an atypical (second-generation) antipsychotic that **exerts its action primarily on dopamine and serotonin receptors**. It works on dopamine D2 receptors in the mesolimbic pathway as an antagonist, blocking dopamine from potential action at the post-synaptic receptor.

Uses

❖ It is an antipsychotic medication which is used in the and treatment of psychotic conditions such as schizophrenia bipolar disorder (manic depression) in adults and Children at least 13 years old.

Stability and Storage Conditions

- Olanzapine should be stored at room temperature. This drug should be kept away from light. This medication should not be stored in moist or damp areas, like bathrooms

Type of Formulation

- Tablets

Popular Brand Names

- ZyPREXA,
- ZyPREXA Zydis

Quetiapine

→ Quetiapine is a class of an antipsychotic medicine which is used in the treatment of schizophrenia in adults and children who are at least 13 years old. It is used in the treatment of bipolar disorder (manic depression) in adults and children who are at least 10 years old.

Mechanism of Action

➢ Quetiapine is a second-generation antipsychotic that has affinity for D2, 5-HT2A, H1, alpha 1 and 5-HT1A receptors. Its precise mechanism of action is unknown, but according to the dopamine theory of schizophrenia, antipsychotic effects might be related to the drug's ability to reduce dopaminergic neurotransmission in the mesolimbic pathway.

Uses

- It is used to treat schizophrenia.
- It is used to treat bipolar disorder.
- It is also used together with antidepressant medications to treat major depressive disorder.

Stability and Storage Conditions

- ♦ Quetiapine should be stored at room temperature. This drug should be kept away from light. This medication should not be stored in moist or damp areas.

Types of Formulations

- Tablets,
- Capsules

Popular Brand Names

- SEROquel,
- SEROquel XR

Lurasidone

→ Lurasidone is a class of atypical antipsychotic which is used in the treatment of schizophrenia and depressive episodes associated with bipolar I disorder.

Mechanism of Action

- ➢ It is a class of an atypical antipsychotic that is a D2 and 5- HT2A (mixed serotoninand dopamine activity)to improve cognition

Uses

- Schizophrenia in adults and adolescents
- Depressive episode associated with Bipolar I disorder

Stability and Storage Conditions

- ❖ It should be stored at room temperature and kept away from light and moisture.

Type of Formulation

- Tablets

Popular Brand Name

- ♦ Latuda 5

ANTICONVULSANTS

→ Anticonvulsants are also known as antiepileptic or anti-seizure drugs. They are used for adequately controlling and managing CNS disorders manifested by recurrent transient attacks of disturbed brain function, producing motor (convulsive), sensory (seizure), and psychic sequence of events.

→ Anticonvulsants suppress the rapid and excessive firing of neurons which starts a seizure.

→ If it fails then an efficient anticonvulsant will prevent the spreading of seizure within the brain and offer protection gainst possible excitotoxic effects which may result in brain damage.

Classification

Based on Mechanism of Action:

They are classified as follows:

1. **Enhancement of Na Channel Inactivation:** Phenytoin, Carbamazepine, Lamotrigine, and Valproate.
2. **Enhanced GABA Synaptic Transmission**
    a. Agents acting on the GABA/CI ionophore complex, e.g., Progabide.
    b. Agents that potentiate GABA:
        - GABA transaminase inhibitors, e.g., Vigabatrin, and
        - GABA reuptake inhibitors, e.g., Tiagabine.
    c. Agents binding to benzodiazepine receptors, e.g., Clobazam and Flumazenil.
    d. Agents binding to barbiturate receptors, e.g., Phenobarbital and Mephobarbital.
3. **Reduction of Current Through T-type Ca2+ Channels: e.g.,** Ethosuximide, Dimethadione, and Valproate.

Examples

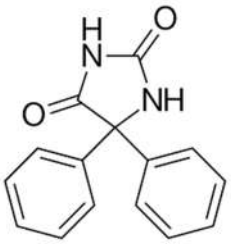
1. Phenytoin *
2. Carbamazepinev *
3. Clonazepam
4. Valproic acid *
5. Gabapentin *
6. Topiramate
7. Vigabatrin
8. Lamotrigine

Phenytoin *

→ Phenytoi is an antico convulsant used in various types of seizures.

Chemical Name and Structure

Sodium 5,5-diphenyl-2, 4-imidazolidinedione



Mechanism of Action

➢ Phenytoin is believed to protect against seizures by causing voltage-dependent block of voltage gated sodium channels. This blocks sustained high frequency repetitive firing of action potentials.

Uses

Phenytoin is widely used for controlling:

1) Status Epilepticus: Administered by slow intravenous injection.
2) Trigenminal Neuralgia: Second choice drug to carbamazepine.
3) Cardiac Arrhythmias: Especially digitalis induced.
4) Generalised tonic: clonic, simple and complex partial seizures.

Stability and Storage Conditions

♠ It s be stored in the tightly closed or sealed container or bottle

Types of Formulations

- Capsule,
- Oral suspension,
- Tablet,
- Injectable solution

Popular Brand Names

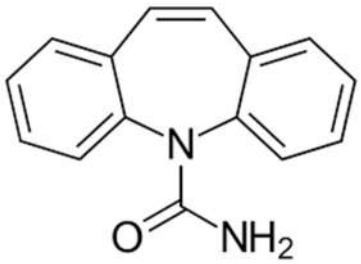
❖ Dilantin,
❖ Phenytoin Sodium,
❖ Prompt,
❖ Extended Release

Carbamazepine *

→ Carbamazepine (CBZ) is an anticonvulsant and mood stabilising drug which is mainly used for treating epilepsy, bipolar disorder, and trigeminal neuralgia.

Chemical Name and Structure

5H-dibenzo[b,f]azepine-5-carboxamide



Mechanism of Action

- Carbamazepine is a sodium channel blocker. It binds preferentially to voltage-gated sodium channels in their inactive conformation, which prevents repetitive and sustained firing of an action potential.

Uses

- It is used for treating epilepsy and pain related to true trigeminal neuralgia.

Stability and Storage Conditions

- It should be kept away from children and should be kept in a cool, dry place and stored at room temperature. Direct sunlight is prohibited.

Types of Formulation

- Tablet,
- Suspension,
- Capsule

Popular Brand Names

- Tegretol,
- Equetro,
- Tegretol XR,
- Carbamazepine CR,
- Epitol Carbamazepine Chewtabs,
- Teril, Carbatrol, Carnexiv

Clonazepam

→ Clonazepam is a benzodiazepine that is mainly used as an anticonvulsant for treating absence seizures, petit mal variant seizures (Lennox-Gastaut syndrome), myoclonic and akinetic seizures, and nocturnal myoclonus.

Mechanism of Action

- Clonazepam is highly potent and a long-acting benzodiazepine. It exerts pharmacological effects by **acting as a positive allosteric modulator on GABA-A receptors**. The GABA-A receptor is a ligand-gated chloride ion-selective channel which endogenous ligand is GABA (gamma-aminobutyric acid).

Uses

- It is used for treating various types of seizures such as myotonic or atonic seizures, photosensitive epilepsy, and absence seizures but it may develop tolerance. It is rarely effective in general tonic-chronic or partial seizures.

Stability and Storage Conditions

- It should be stored at 59°F and 86°F (15°C and 30°C).
- This medication should not be stored in moist or damp areas like bathrooms.

Types of Formulation

- Tablets,
- Solution,

Popular Brand Names

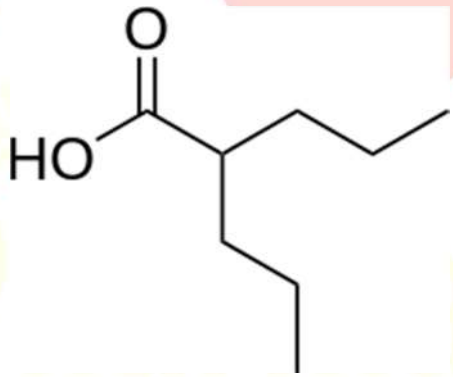
- Klonopin,
- Rivotril

Valproic Acid *

→ Valproic acid is a fatty acid having anticonvulsant properties and is used for treating epilepsy. It is supplied as its sodium salt valproate semisodium or divalproex sodium.

Chemical Name and Structure

2-propylpentanoic acid



Mechanism of Action

➲ Valproic acid exhibits its pharmacologic effects in a couple of ways, such as by acting on GABA (γ aminobutyric acid) levels in the CNS, blocking voltage-gated ion channels, and inhibiting histone deacetylase.

Uses

❖ It is used for managing and treating seizure disorders, mania, and prophylactic treatment of migraine headache.

❖ It is also used for controlling absence seizures, tonic-clonic seizures (grand mal), complex partial seizures. and seizures related to Lennox-Gastaut syndrome.

Stability and Storage Conditions

- It should be stored between 15 and 30 °C (59 and 86 °F) and in a tight container.
- It should be protected from freezing

Types of Formulation

- Capsule,
- Syrup,
- Injectable solution

Popular Brand Names

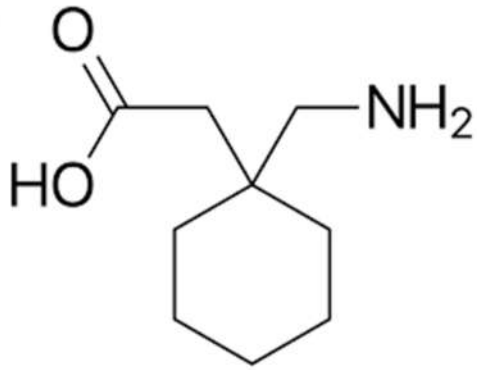
- Valproate Sodium,
- Depacon,
- Depakene, Stavzor

Gabapentin *

→ Gabapentin is a drug initially developed for treating epilepsy.

Chemical Name and Structure

1-(aminomethyl)cyclohexaneacetic acid



Mechanism of Action

➢ Gabapentin **crosses several lipid membrane barriers via system L amino acid transporters**. In vitro, gabapentin modulates the action of the GABA synthetic enzyme, glutamic acid decarboxylase (GAD) and the glutamate synthesizing enzyme, branched-chain amino acid transaminase.

Uses

➢ It is used for managing postherpetic neuralgia in adults and as an adjunctive therapy for treating partial seizures with and without secondary generalisation in epilepsy patients over 12 years of age.

Stability and Storage Conditions

- It should be stored between 15 and 30 °C (59 and 86 °F) and in a tight container.
- It should be protected from freezing

Types of Formulations

- Capsule,
- Tablet,
- Solution,
- Suspension

Popular Brand Names

- Neurontin,
- Gralise,
- Fanatrex,
- Gabaron

Topiramate

→ Topiramate is an anticonvulsant drug which is used in controlling epilepsy, prophylaxis and migraines treatment.

Mechanism of Action

➢ Topiramate has been observed to exert actions on voltage-dependent sodium channels, GABA receptors, and glutamate receptors. Topiramate **stimulates GABA-A receptor activity at brain non-benzodiazepine receptor sites and reduces glutamate activity at both AMPA and kainate receptors**.

Uses

- Treating certain types of seizures.
- Preventing migraine headaches.

Stability and Storage Conditions

- Tablets and extended-release capsules should be stored at room temperature and away from excess heat and moisture (not in the bathroom).

Types of Formulations

- Tablets,
- Capsules

Popular Brand Names

- Topamax,
- Topamax Sprinkle,
- Trokendi XR,
- Qudexy XR

Vigabatrin

→ VGB (4-amino-5-hexenoic acid or gamma-vinyl-GABA) is a structural analogue of GABA that contains a vinyl appendage.

Mechanism of Action

- The main mechanism of action of vigabatrin is thought to be **irreversible inhibition of GABA transaminase resulting in increased GABA levels**. Vigabatrin has been successfully tested

in animal models of epilepsy such as subcutaneous pentylenetetrazol-induced seizures and electrical kindling.

Uses

- As an adjunct therapy to treat refractory complex partial seizures.
- As monotherapy to treat infantile spasms in infants 1 month to 2 years.

Stability and Storage Conditions

- The oral syringes are provided separately by the pharmacy. It should be properly stored and handled. It should be stored at 20°C to 25°C.

Types of Formulations

- Tablets,
- Powders

Popular Brand Names

- Sabril,
- Vigadrone

Lamotrigine

→ Lamotrigine is a phenyltriazine antiepileptic used to treat some types of epilepsy and bipolar I disorder.

Mechanism of Action

➢ The mechanism of action for lamotrigine is not entirely understood. It is a triazine, and research has shown that lamotrigine selectively binds and inhibits voltage-gated sodium channels, stabilizing presynaptic neuronal membranes and inhibiting presynaptic glutamate and aspartate release.

Uses

- Alone or with other medications to treat epileptic seizures in adults and children.
- To delay mood episodes in adults with bipolar disorder.

Stability and Storage Conditions

★ It should be stored in tightly closed or sealed.

Type of Formulation

➲ Tablets

Popular Brand Name

→ Lamictal

ANTIDEPRESSANTS

→ A major class of psychoses comprised of affective disorders are different from schizophrenia and characterised by mood changing (depression or mania) instead of thought disturbances.

→ Two main types of depression are recognized:

1. Unipolar, and
2. Bipolar

→ In bipolar depression, mood and behaviour fluctuate between depression and mania.

→ Unipolar depression arises earlier in life and tends to be inherited.

→ It may have common features with schizophrenia.

→ Unipolar depression is more common than bipolar depression, and more frequently related to adverse circumstances.

Examples

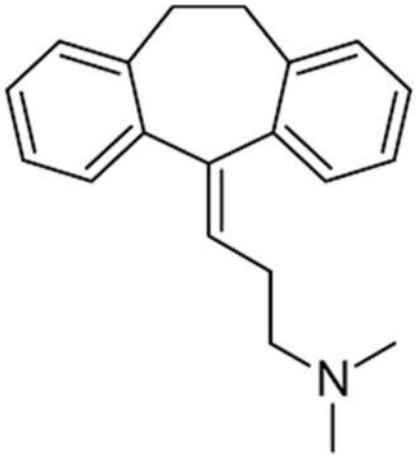
- Amitriptyline Hydrochloride *
- Fluoxetine *
- Duloxetine
- Citalopram
- Escitalopram
- Imipramine Hydrochloride *
- Venlafaxine
- Sertraline
- Fluvoxamine
- Paroxetine

Amitriptyline Hydrochloride *

→ Amitriptyline is a class of tricyclic antidepressants (TCA). It is the most extensively used TCA and is the most effective drug against depression.

Chemical Name and Structure

N,N-dimethyl-3-(2-tricyclo[9.4.0.03,8]pentadeca-1(15),3,5,7,11,13-hexaenylidene)propan-1-amine;hydrochloride



Mechanism of Action

- Amitriptyline increases noradrenergic or serotonergic neurotransmission by blocking the norepinephrine or serotonin transporter (NET or SERT) at presynaptic terminals.

Uses

- It is widely used in the cases like anxiety,which accompanies depression.
- At the side chain of nitrogen forming Nortriptyline, it is monodemethylated.

Stability and Storage Conditions

- It should be stored in a well-closed container at 20°-25°C (68°-77°F). Additionally, amitriptyline tablets must be protected from light therefore should be stored in a light resistant container.

Types of Formulations

- Tablets,
- Oral solutions

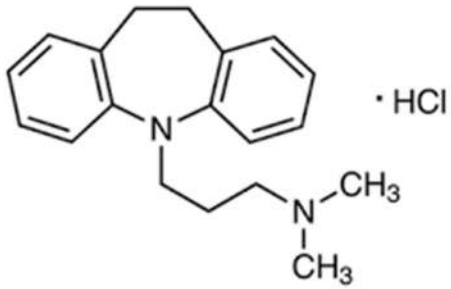
Popular Brand Names

- Elavil,
- Tryptizol,
- Laroxyl,
- Sarotex

Imipramine Hydrochloride *

Chemical Name and Structure

3-(10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)-N,Ndimethylpropan-1-amine



Mechanism of Action

- Imipramine is a tricyclic antidepressant that has been used since the 1950s. Its primary mechanism of action is to **inhibit the reuptake of serotonin and norepinephrine**, thus elevating the levels of these neurotransmitters in the brain.

Uses

- It is useful in the treatment of endogenous depression.
- It is formed after undergoing metabolic N demethylation, that appears to have a somewhat shorter onset of action than imipramine and less sedating.

Stability and Storage Conditions

- It should be stored in a tightly closed container and at well-ventilated place.

Types of Formulations

- Capsule,
- Tablet

Popular Brand Name

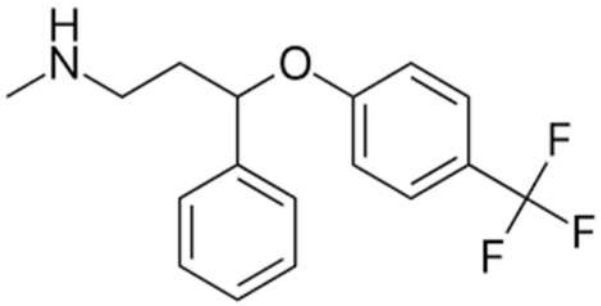
- Tofranil

Fluoxetine *

→ Fluoxetine is a class of Selective Serotonin Reuptake Inhibitors (SSRI) antidepressant. The chemicals in the brain get affected and become unbalanced, which may cause depression, panic, anxiety, or obsessive-compulsive symptoms.

Chemical Name and Structure

N-methyl-3-phenyl-3-[4-(trifluoromethyl)phenoxy]propan-1-amine



Mechanism of Action

- Presynaptic serotonin (5HT1A) receptors are in the dorsal raphe nucleus and project to the prefrontal cortex. Fluoxetine exerts its effects by **blocking the** reuptake of serotonin **into presynaptic serotonin neurons by blocking the reuptake transporter protein located in the presynaptic terminal**.

Uses

- It is used in the treatment of endogenous depression.
- It may be useful in the treatment of obsessive compulsive disorder, obesity and alcoholism

Stability and Storage Conditions

- It should be stored at room temperature between 59°F and 86°F (15°C to 30°C).
- It should be kept away from light. The bottle should be tightly closed. Keep all medicines out of the reach of children.

Types of Formulations

- Capsule,
- Tablet,
- Solution

Popular Brand Names

- Act Fluoxetine,
- Prozac,
- Sarafem,
- Symbyax

Venlafaxine

→ Venlafaxine is a class of selective serotonin and norepinephrine reuptake inhibitor(SNRI) which is used in the treatment of major depression.

Mechanism of Action

♦ Venlafaxine works by increasing serotonin levels, norepinephrine, and dopamine in the brain by blocking transport proteins and stopping their reuptake at the presynaptic terminal.

Uses

- The chemicals in the brain get affected by venlafaxine that may be unbalanced in people with depression.
- Venlafaxine is a prescription drug which is used to treat major depressive disorder, anxiety, and panic disorder.

Stability and Storage Condition

- Keep away from direct sunlight and children. It should be kept in a cool, dry place.

Types of Formulations

- Capsule,
- Tablet,

Popular Brand Name

♦ Effexor

Duloxetine

→ Duloxetine is a class of selective serotonin and norepinephrine reuptake inhibitor antidepressant (SSNRI). The chemicals in the brain get affected by Duloxetine that may be cause imbalance in people with depression.

Mechanism of Action

➲ Duloxetine inhibits the reuptake of serotonin and norepinephrine (NE) in the central nervous system.

Uses

★ Major depressive disorder in adults.
★ General anxiety disorder in adults and children of age more than 7 years

Stability and Storage Condition

- The container should be tightly closed in dry and well ventilated place. The containers should be resealed that are opened and kept upright to prevent leakage. The recommended storage temperature for Duloxetine is 20°C.

Types of Formulations

- Capsules,
- Tablets

Popular Brand Names

♦ Cymbalta,
♦ Drizalma Sprinkle,
♦ Irenka

Sertraline

→ Sertraline is a selective serotonin reuptake inhibitor (SSRI) used in the treatment of major depressive disorder, that are used social anxiety lisorder and many other psychiatric conditions.

Mechanism of Action

➢ The mechanism of action of sertraline is presumed to be linked to its **inhibition of CNS neuronal uptake of serotonin (5HT)**. Studies at clinically relevant doses in man have demonstrated that sertraline blocks the uptake of serotonin into human platelets.

Uses

♦ Major depressive disorder
♦ Obsessive-Compulsive Disorder (OCD)
♦ Panic disorder

Stability and Storage Condition

o It should be stored at 20°C to 25°C (68°F to 77°F).

Types of Formulations

- Tablets,
- Oral concentration

Popular Brand Name

- Zoloft

Citalopram

→ Citalopram is an antidepressant classified under selective Serotonin reuptake inhibitors (SSRIs).

Mechanism of Action

➢ The inhibition of CNS neuronal reuptake of serotonin (5-HT) Label leads to the mechanism of action of citalopram.

Uses

- It is most commonly used to treat depression.

Stability and Storage Condition

➢ Citalopram tablets should be stored at room temperature. This drug should be kept away from high temperatures.

Types of Formulations

- Tablets,
- Oral Solutions

Popular Brand Name

- CeleXA

Fluvoxamine

→ Fluvoxamine is a class of selective serotonin-reuptake inhibitors which is used in the treatment of obsessive- compulsive disorder.

Mechanism of Action

➲ FLV blocks reuptake of serotonin at the sodium-dependent serotonin transporter (SERT) of the neuronal membrane, enhancing actions of serotonin on 5HT1A autoreceptors

Uses

- It is a Selective Serotonin Reuptake Inhibitors (SSRI).
- It is used to treat symptoms of Obsessive Compulsive Disorder (OCD) in adults and children at least 8 years old.

Stability and Storage Condition

★ Fluvoxamine should be kept at room temperature. This drug should be kept away from light.

Types of Formulations

- Capsules,
- Tablets

Popular Brand Name

★ Luvox

Escitalopram

→ Escitalopram is a Class of selective serotonin re-uptake inhibitor which is used in the treatment of Major Depressive Disorder (MDD), Generalised Anxiety rder (GAD), and other selective psychiatric disorders like Obsessive-Co -Compulsive isorder (OCD).

Mechanism of Action

- Escitalopram increases intrasynaptic levels of the neurotransmitter serotonin by blocking the reuptake of the neurotransmitter into the presynaptic neuron.

Uses

➢ The chemicals in the brain get affected by escitalopram, which may be unbalanced in people with depression or anxiety.
➢ The major depressive disorder in adults and adolescents at least 12 years old are treated by this drug.
➢ It is also used in the treatment of anxiety in adults.

Stability and Storage Condition

- It should be stored in a closed container at room temperature.

Type of Formulation

- Tablets

Popular Brand Names

- Cipralex,
- Lexapro

Paroxetine

→ paroxetine is a class of selective serotonin reuptake Inhibitor which is used in the treatment of major. depressive disorder, panic disorder, OCD, social phobia, generalised anxiety disorder, the vasomotor symptoms of menopause and premenstrual dysphoric disorder.

Mechanism of Action

- As an SSRI class drug, paroxetine's signature mechanism of action is to block the serotonin reuptake transporter (SERT) and thus increase the concentration of synaptic serotonin.

Uses

→ Paroxetine is used to treat depression, including major depressive disorder

Stability and Storage Condition

- Tablets should be kept at room temperature.

Type of Formulation

- Tablets

Popular Brand Names

- Paxil,
- Paxil CR,
- Brisdelle,
- Pexeva

Chapter 6

Drugs Acting on Autonomic Nervous System

Topics

SYMPATHOMIMETIC AGENTS (ADRENERGIC AGONISTS)
Direct Acting Agents :

- Nor-epinephrine, *
- Phenylephrine,
- Terbutaline,
- Naphazoline, *
- Epinephrine,
- Dopamine, *
- Salbutamol,
- Tetrahydrozoline

SYMPATHOMIMETIC AGENTS (ADRENERGIC AGONISTS)
Indirect Acting Agents :

- Hydroxyamphetamine,
- Pseudoephedrine

SYMPATHOMIMETIC AGENTS (ADRENERGIC AGONISTS)
Mixed Acting Agents :

- Ephedrine,
- Metaraminol

ADRENERGIC ANTAGONISTS (SYMPATHOLYTIC AGENTS)
Alpha Adrenergic Blockers :

- Tolazoline,
- Phentolamine,
- Phenoxybenzamine,
- Prazosin.

ADRENERGIC ANTAGONISTS (SYMPATHOLYTIC AGENTS)
Beta Adrenergic Blockers :

- Propranolol, *
- Ateolol, *
- Carvedilol

CHOLINERGIC DRUGS AND RELATED AGENTS
(PARASYMPATHOMIMETRIC)
Direct Acting Agents

- Acetylcholine, *
- Carbachol,
- Pilocarpine.

Cholinesterase Inhibitors (Indirect Acting Agents)

- Neostigmine, *
- Edrophonium chloride,
- Tacrine hydrochloride,
- Echothiophate iodide.

CHOLINERGIC BLOCKING AGENTS (CHOLINERGIC ANTAGONISTS)

- Atropine sulphate, *
- Ipratropium bromide.

Synthetic Cholinergic Blocking Agents

- Tropicamide,
- Cyclopentolate hydrochloride,
- Clidinium bromide, and
- Dicyclomine hydrochloride. *

Drugs Acting on Autonomic Nervous System

SYMPATHOMIMETIC AGENTS (ADRENERGIC AGONISTS)

→ Adrenergic drugs or adrenergic agonists or sympathomimetic agents cause stimulation of the adrenergic receptors in the sympathetic nervous system.
→ They are named so as they mimic the actions of major neurotransmitters of the sympathetic nervous system, i.e., epinephrine and norepinephrine.
→ Adrenergic agents either directly or indirectly stimulate the adrenergic nerves.
→ In direct stimulation, they mimic the actions of noradrenaline; while, indirect stimulation triggers the release of noradrenalinel.
→ The therapeutic application of these drugs is in the treatment of life threatening disorders like acute attacks of bronchial asthma, cardiac arrest, shock, and allergic reactions.
→ These drugs are also used as nasal decongestants and appetite suppressants.

Direct Acting Agents

- The direct acting sympathomimetic agents directly bind and interact to activate the receptor. These agonists may have the property of receptor selectivity where in they can show selectivity (to act) either for any one particular class of receptors (like α- or β-receptors) or for any sub-class (e.g, specificity against β1 or β2 receptors).

The drugs studied below are:

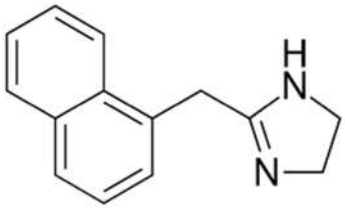
- Nor-epinephrine, *
- Phenylephrine,
- Terbutaline,
- Naphazoline, *
- Epinephrine,
- Dopamine, *
- Salbutamol,
- Tetrahydrozoline.

Naphazoline *

→ Naphazoline acts on ocular arterioles through its rapid sympathomimetic vasoconstrictor action. It decreases the congestion of conjunctiva and is present in many OTC eye drops.

Chemical Name and Structure

- 2-(naphthalen-1-ylmethyl)-4,5-dihydro-1H-imidazole



Mechanism of Action

→ Naphazoline: Naphazoline stimulates alpha-adrenergic receptors in the arterioles of the conjunctiva. Ophthalmic administration causes vasoconstriction of conjunctival blood vessels thereby decreasing conjunctival congestion.

Uses

★ Naphazoline is a decongestant that relieves redness, puffiness, and itchy/watering eyes due to colds, allergies, or eye irritations.

Stability and Storage Conditions

★ The dropper should be stored upright at room temperature between 68°-77°F (20°-25°C) and keep away from moisture and sunlight.

Types of Formulations

- Ophthalmic gel forming solution, Ophthalmic solution

Popular Brand Name

- Privine

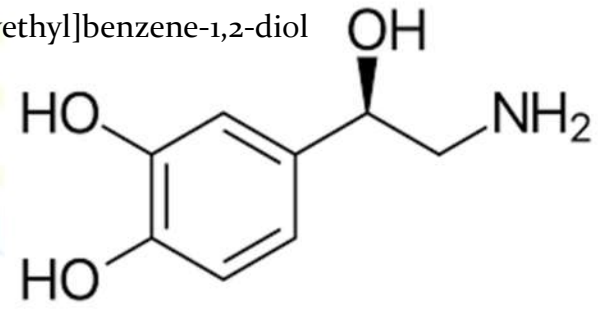
Nor-Epinephrine *

→ Nor-epinephrine (precursor of epinephrine) is a central and autonomic neurotransmitter secreted by adrenal medulla.

→ It acts as a major transmitter for the diffuse projection system which arises from the locus coeruleus of the brain and for the postganglionic sympathetic fibres.

Chemical Name and Structure

- 4-[(1R)-2-amino-1-hydroxyethyl]benzene-1,2-diol



Mechanism of Action

➢ Nor-epinephrine acts on α-adrenergic receptors for peripheral vasoconstriction and on β-adrenergic receptors for causing inotropic stimulation of heart and dilation of coronary arteries.

Uses

★ It maintains blood pressure in acute hypotensive states arising due to Surgical or non-surgical trauma, central vasomotor depression, and haemorhage.

Stability and Storage Conditions

- Solutions of norepinephrine should be stored in PVC bags at 4°C for 61 days with protection from light.

Types of Formulations

♠ Injectable solution, Intravenous solution,

Popular Brand Names

♦ Levarterenol

♦ Levophed

Epinephrine

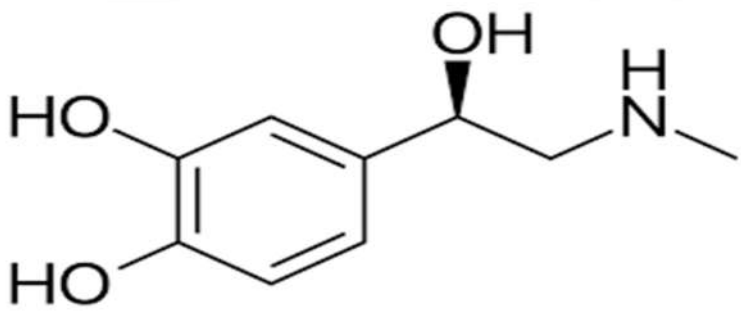
→ Epinephrine is a hormone neurotransmitter. When it is produced in the body, it contracts blood vessels, increases heart rate, dilates air passages, and contributes in the fight-or-flight response of the sympathetic nervous system.

Chemical Name and Structure

1,2-Benzenediol, 4-[(1R)-1-hydroxy-2-(methylamino)ethyl]-,

or

(-)-3,4-Dihydroxy-α-[2(methylamino)ethyl]benzyl alcohol.



Mechanism of Action

➢ Through its action on alpha-1 receptors, epinephrine induces increased vascular smooth muscle contraction, pupillary dilator muscle contraction, and intestinal sphincter muscle contraction.

Uses

- It stimulates the heart, increases heart rate and blood pressure, and relaxes the musculature of intestine and bronchi.
- It is commonly used in acute allergic disorders and histamine reactions.

Stability and Storage Conditions

♦ EpiPen and EpiPen Jr Auto-Injectors and Epinephrine Injection, USP should be stored in the carrier tube provided at a temperature of 20°-25°C (68°-77°F)

Type of Formulation

▪ Injectable solution

Popular Brand Names

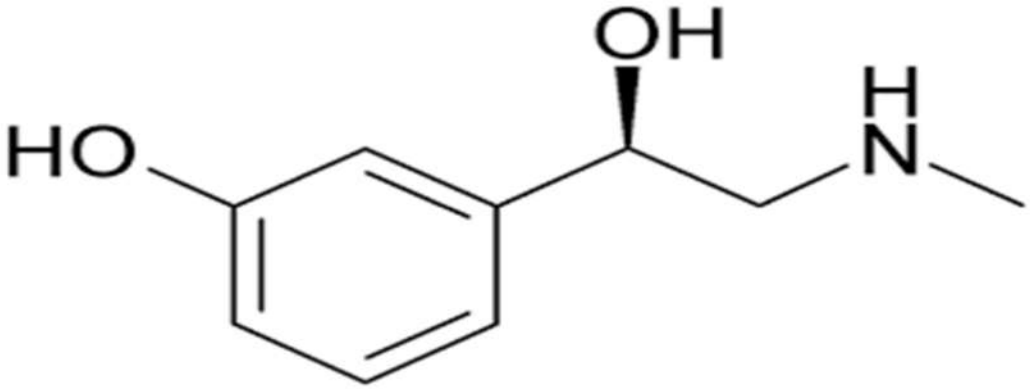
✓ Adrenalin,
✓ Epinephrinesnap-EMS,
✓ EpiPen 2-Pak,
✓ EPlsnap, Auvi-Q, Epinephrinesnap-V, EpiPen JR 2-Pak, Symjepi

Phenylephrine

→ Phenylephrine is sympathomimetic amine acting mostly on the α-adrenergic receptors. It is a vasoconstrictor and used as a nasal decongestant and cardiotonic agent.

Chemical Name and Structure

- (R)-3-[-1-hydroxy-2-(methylamino)ethyl]phenol



Mechanism

➢ Phenylephrine is an agonist of α1-adrenoceptors. Nasal decongestant action is mediated by activation of α1-adrenoceptors in the arterioles of the nasal mucosa. This causes vasoconstriction, which leads to decreased edema and increased drainage of the sinus cavities.

Uses

- Phenylephrine is used to relieve nasal discomfort caused by colds, allergies, and hay fever. It is also used to relieve sinus congestion and pressure. Phenylephrine will relieve symptoms but will not treat the cause of the symptoms or speed recovery.

Stability and Storage Conditions

♦ Protect from light.
♦ It should be store in carton until time of use.

Types of Formulations

▪ Capsules, Solution,
▪ Tablets, Granules

Popular Brand Names

✓ Neo-Synephrine,
✓ Biorphen,
✓ Sudafed PE Congestion,
✓ Suphedrine PE

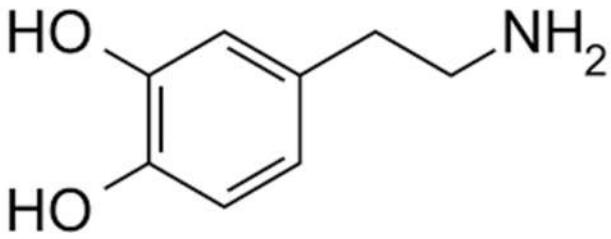
Dopamine *

→ Dopamine (a central neurotransmitter) is a metabolic precursor of nor-epinephrine and epinephrine. It does not Cross the blood brain barrier and thus has minimal effect on the CNS.

→ It acts on the receptors and produces a positive inotropic effect on heart. It increases the systolic and pulse pressures.

Chemical Name and Structure

- 4-(2-aminoethyl) benzene-1,2-diol



Mechanism of Action

➢ Dopamine is administered as a continuous intravenous infusion. At low doses, dopamine preferentially stimulates D1 and D2 receptors in the renal vasculature, which leads to vasodilation and promotes renal blood flow to preserve glomerular filtration.

Uses

- It is used in acute congestive heart failure with imminent renal failure.
- It is used in acute pancreatitis.
- It is used in septic shock and surgical shock.

Stability and Storage Conditions

♦ Dopamine HCI Injection should be stored in such a way that is should avoiding contact with alkalies (including sodium bicarbonate), oxidising agents or iron salts.

Type of Formulation

▪ Injectable solution

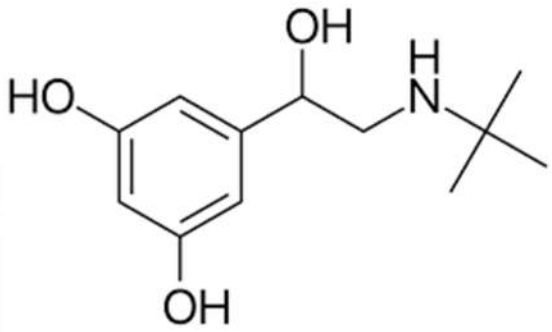
Popular Brand Names

✓ Intropin

Terbutaline

→ Terbutaline is a synthetic compound acting as a sympathomimetic amine. It is the most selective agent which stimulates β2-adrenoreceptors.

Chemical Structure



Mechanism of Action

➢ Terbutaline is a bronchodilator, a medication that dilates (expands) air passages in the lungs. It attaches to beta adrenergic receptors on muscles surrounding the air passages, causing the muscles to relax and dilate the air passages. Wider air passages allow more air to flow in and out of the lungs.

Uses

▪ It is used in breathlessness and wheezing arising from lung problems (e.g., asthma, chronic obstnuctive pulmonary disease, bronchitis, and emphysema).

Stability and Storage Conditions

♦ It should be stored at room temperature and away from light and moisture. It should not be stored in the bathroom.

Types of Formulations

- Powder,
- Solution

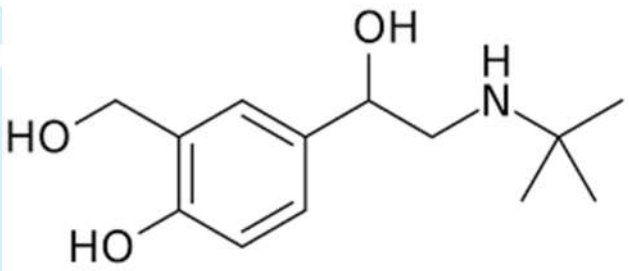
Popular Brand Names

✓ Brethine,
✓ Bricany,
✓ Brethaire

Salbutamol (Albuterol)

→ Salbutamol (INN) is also known as albuterol (USAN). It is as hort-acting β2-adrenergic receptor agonist, employed in the management of bronchospasm seen in asthma and chronic obstructive pulmonary disease.

Chemical Structure



Mechanism of Action

➢ Salbutamol relaxes the smooth muscles of all airways, from the trachea to the terminal bronchioles. Salbutamol acts as a functional antagonist to relax the airway irrespective of the spasmogen involved, thus protecting against all bronchoconstrictor challenges.

Uses

- It is used in bronchial asthma.
- It is used in peripheral vascular diseases.
- It is used in the prevention of premature labour.

Stability and Storage Conditions

- It should be stored at room temperature and keep away from light and moisture.

Types of Formulations

- Aerosol,
- Solution,
- Tablets

Popular Brand Names

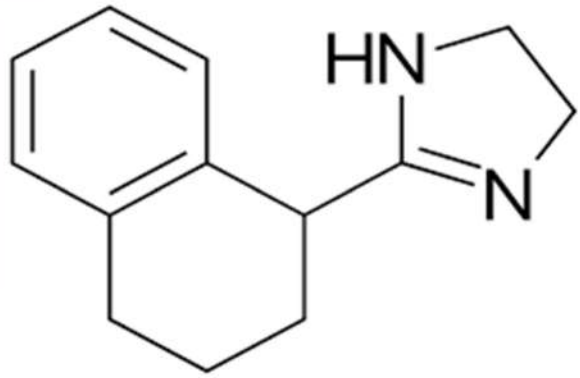
- ✓ Airomir,
- ✓ Proventil,
- ✓ Combivent,
- ✓ Xopenex,
- ✓ Ventolin

Tetrahydrozoline

→ Tetrahydrozoline is an alpha-adrenergic agonist which is used in the treatment of temporary symptomatic relief of discomfort and redness of eyes due to minor irritations, as well as it reduces nasal congestion.

Chemical Name and Structure

- (RS)-2-(1,2,3,4-tetrahydronaphthalen-1-yl)-4,5-dihydro-1H-imidazole



Mechanium of Action

➢ Adrenergic receptors are G-protein-coupled receptors (GPCR) that regulate vascular tone, i.e., vasoconstriction is caused by the stimulation of alpha-1 adrenergic receptors.

Uses

- It acts as a vasoconstrictor by narrowing swollen blood vessels in the eye for reducing eye redness.
- Its ophthalmic preparations (for the eyes) are used for providing temporary relief from minor eve redness, swelling or draining caused by minor irritants.

Stability and Storage Conditions

- It should be stored at room temperature and kept away from moisture and heat.
- The bottle should be tightly closed when it is not in use.

Type of Formulation

♦ Ophthalmic solution

Popular Brand Names

✓ Colirio Ocusan,
✓ Visine.

Indirect Acting Agents

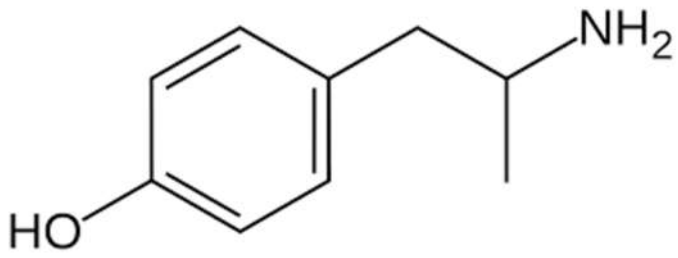
- Indirect acting sympathomimetic agents stimulate the release of a stored neurotransmitter from within the adrenergic nerve terminals. The main neurotransmitter involved here is nor-epinephrine, which on being released stimulates the adrenergic receptors on the effector organs.
- The drugs studied below are:
    1) Hydroxyamphetamine,
    2) Pseudoephedrine.

Hydroxyamphetamine

→ Hydroxyamphetamine occurs as a hydrobromide salt derived from amphetamines. It is a powerful vasoconstrictor which stimulates the α-receptors but lacks any CNS activity.

Chemical Name and Structure

- 4-(2-aminopropyl)phenol



Mechanism of Action

- Hydroxyamphetamine hydrobromide is an indirect acting sympathomimetic agent. It causes mydriasis by releasing nor-epinephrine from adrenergic nerve terminals.

Uses

- It is used in narcolepsy (sudden attack of sleep in completely inappropriate situations
- It is used in children having hyperkinetic syndrome.

Stability and Storage Conditions

- It should be stored between 20°C and 25°C. It should be protected from light and sunlight.

Type of Formulation

- Solution

Popular Brand Name

- Paremyd

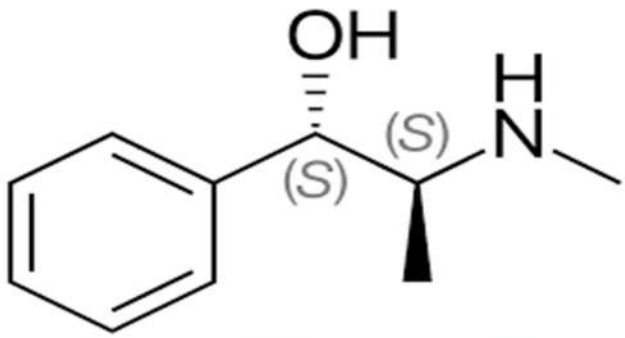
Pseudoephedrine

→ It is a α- and β-adrenergic agonist and a sympathomimetic agent which also increases nor-epinephrine release.

→ It is structurally similar to ephedrine, and relieves nasaid and Sinus congestion. It also relieves otalgia related to air travel, in aduits.

Chemical Name and Structure

- (1R,2R)-2-methylamino-1-phenylpropan-1-ol



Mechanism of Action

➢ Pseudoephedrine is a sympathomimetic with a mixed mechanism of action, direct and indirect. It indirectly stimulates alpha-adrenergic receptors, causing the release of endogenous norepinephrine (NE) from the granularity of neurons, while it directly stimulates beta-adrenergic receptors

Uses

- It is used in vasomotor rhinitis, and nasal, sinus and eustachian tube congestion. It is also used as a first line therapy in priapism.

Stability and Storage Condition

♦ It should be store at room temperature.

Types of Formulations

- Syrup,
- Tablets.

Popular Brand Names

✓ Sudafed Congestion,
✓ SudoGest,
✓ Sudafed 12-Hour,
✓ Sudafed Children's Nasal Decongestant

Agents with Mixed Mechanism

→ Some sympathomimetic agents (e-g ephedrine, metaraminol, and pseudoephedrine) have a mixed action.
→ They act by releasing a neurotransmitter, and also have a direct-agonist activity.
→ Amongst the adrenergic agonists, epinephrine and nor-epinephrine are the least specific.
→ Both α- and β-receptors can be stimulated by nor- epinephrine and epinephrine, but due to the difference in their chemical structures, nor-epinephrine has more pronounced effects at a-receptors while epinephrine has more pronounced effects at β-receptors.Also, the potency of both these drugs is different from each other.

The drugs studied below are:

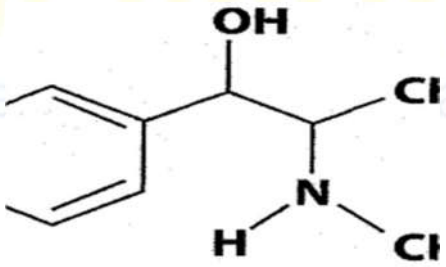
1) Ephedrine,
2) Metaraminol.

Ephedrine

→ Ephedrine acts as an agonist On α-receptor as well as on β-receptor. It also increases the release of nor-epinephrine from the sympathetic neurons Thus, it is a mixed-acting sympathomimetic drug The Structure of ephedrine involves two asymmetrical arbon atoms. The clinically used forms of ephedrine 1 - ephedrine and racemic ephedrine only.

Chemical Name and Structure

- rel-(R,S)-2-(methylamino)-1-phenylpropan-1-ol



ephedrine

Mechanism of Action

➢ Ephedrine, a sympathomimetic amine, acts on part of the sympathetic nervous system (SNS). The principal mechanism of action relies on its **indirect stimulation of the adrenergic receptor system by increasing the activity of norepinephrine at the postsynaptic α and β receptors**.

Uses

- Ephedrine and its salts are used in allergic disorders, colds, narcolepsy through oral, intravenous, intramuscular, and topical route, hypotensive conditions,

Stability and Storage Conditions

♦ This medication should be stored at room temperature.

Types of Formulations

- Tablets,
- Capsules

Popular Brand Names

- ✓ Akovaz,
- ✓ Bronkaid,
- ✓ Corphedra,
- ✓ Primatene, Rezipres, Emerphed

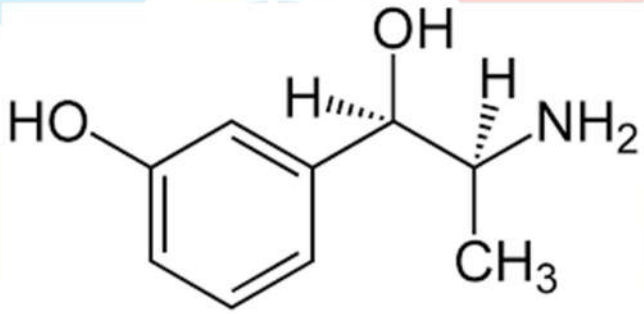
Metaraminol

→ Metaraminol (or aramine) is structurally similar to phenylephrine with the only difference that it is a primary (and not secondary) amine.

→ It directly acts on a-adrenergic receptors and has mixed mechanism of action.

Chemical Name and Structure

- (1R,2S)-3-[-2-amino-1-hydroxy-propyl]phenol



Mechanism of Action

➢ Metaraminol acts through peripheral vasoconstriction by acting as a pure alpha-1 adrenergic receptor agonist, consequently increasing systemic blood pressure (both systolic & diastolic). Its effect is thought to be associated with the inhibition of adenyl cyclase which leads to an inhibition of the production of cAMP.

Uses

- Parenterally it is used as a vasopressor for treating and preventing acute hypotensive state arising due to spinal anaesthesia.

Stability and Storage Conditions

- It should be stored between 20°C and 25°C. It should be protected from light and sunlight.

Type of Formulation

- ♦ Solution

Popular Brand Name

- ✓ Aramine

ADRENERGIC ANTAGONISTS (SYMPATHOLYTIC AGENTS)

→ Adrenoceptor antagonists or adrenergic blocking agents or anti-adrenergic drugs block the responses mediated by adrenoceptor activation. In other words, they inhibit the actions that occur by the release of adrenaline.

→ The action of sympathomimetic amines is selectively blocked by the anti-adrenergic drugs by acting either on the α- or β-receptors or on both of them. It brings about opposite effects of the catecholamines facilitated through the α-or β- receptors.

→ Based on receptor selectivity, the α-and β-adrenoceptor blocking agents are divided into primary sub-groups.

→ All of these agents have pharmacological antagonist or partial agonist property.

→ A majority of them act competitively and have reversible actions.

Classification

- α-Adrenoceptpor Blocking Drugs :
- β-Adrenoceptpor Blocking Drugs :

α-Adrenoceptpor Blocking Drugs : The effect of catecholamines facilitated via α-receptors are blocked by these agents furthermore, depending on the ability of these drugs to dissociate from the receptors, they may either be reversible or irreversible.

The drugs studied below are :

1. Tolazoline,
2. Phentolamine,
3. Phenoxybenzamine,
4. Prazosin.

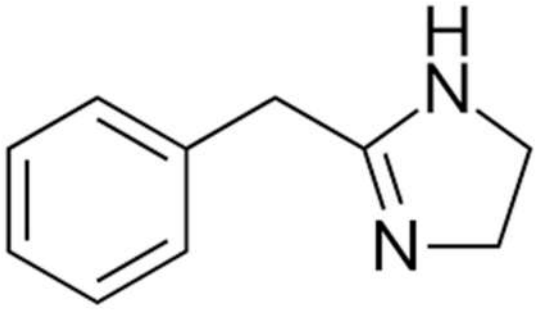
Tolazoline

→ Tolazoline (an imidazoline derivative) is a competitive α-adrenergic antagonist.

→ It possesses like affinity for both α1- and α2-receptors.

Chemical Name and Structure

- 2-Benzyl-4,5-dihydro-1H-imidazole



Mechanism of Action

- An alpha-adrenergic blocking agent, tolazoline HCl is structurally related to phentolamine. By directly relaxing vascular smooth muscle, tolazoline has peripheral vasodilating effects and decreases total peripheral resistance. Tolazoline also is a competitive alpha1 and alpha2 adrenergic blocking agent.

Uses

- ♦ It is used as a vasodilator and for stimulating heart and causing mydriasis through its sympathomimetic effect)

Stability and Storage Conditions

- ▪ It should be stored at room temperature.

Type of Formulation

- Injection solution

Popular Brand Name

- ✓ Priscoline Hydrochloride

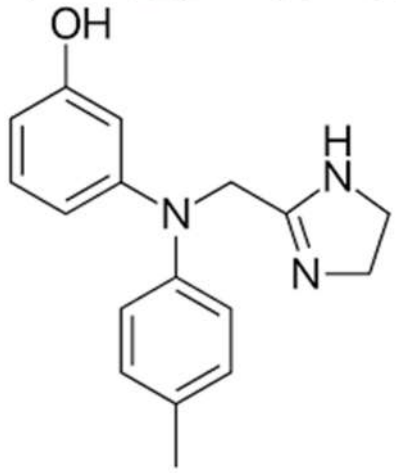
Phentolamine

→ The group attached to the imidazoline ring decides whether it will be an agonist or an antagonist.

→ Two imidazoline α-antagonists used therapeutically are tolazine (Priscoline) and phentolamine (Regitine). Both of them are competitive (reversible) blocking agents.

Chemical Name and Structure

- ▪ 3-[(4,5-Dihydro-1H-imidazol-2-ylmethyl)(4-methylphenyl)amino]phenol



Mechanism of Action

- ➢ Phentolamine produces its therapeutic actions by competitively blocking alpha-adrenergic receptors (primarily excitatory responses of smooth muscle and exocrine glands), leading to a muscle relaxation and a widening of the blood vessels. This widening of the blood vessels results in a lowering of blood pressure.

Uses

- Phentolamine is used for diagnosing pheochromocytoma (tumours of adrenal medulla).

Stability and Storage Conditions

- ▪ Phentolamine mesylate injection is stable for 48 hours at room temperature or 1 week at 2°-8 °C.

Types of Formulations

- ♦ Powder for injection,
- ♦ Injection Solution

Popular Brand Names

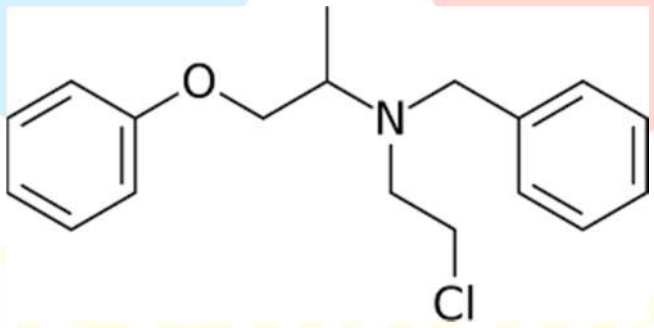
- ✓ Oraverse,
- ✓ Rogitine

Phenoxybenzamine

→ Phenoxybenzamine is α-adrenergic antagonist with long duration of action. It is used as an anti-hypertensive and as a peripheral vasodilator.

Chemical Name and Structure

- (RS)-N-Benzyl-N-(2-chloroethyl)-1-phenoxypropan-2-amine



Mechanism of Action

- ➢ Phenoxybenzamine widens blood vessels and relaxes muscles by blocking α-receptors. Blood pressure reduces due to widened blood vessels.

Uses

- ▪ It is used for treating pheochromocytoma and Raynaud's syndrome.

Stability and Storage Conditions

- ♦ It should be stored at 25°C (77°F)

Type of Formulation

- Capsules

Popular Brand Name

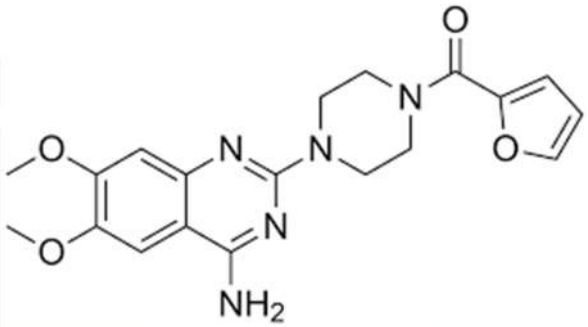
- ✓ Dibenzyline

Prazosin

→ Prazosin is derived from quinazoline and is a highly specific antagonist of α1-receptor) Structurally, it has a quinazoline ring, a piperazine ring).

Chemical Name and Structure

- [4-(4-Amino-6,7-dimethoxy-2-quinazolinyl)-1-piperazinyl](2-furyl)methanone



Mechanism of Action

➢ Prazosin **inhibits the postsynaptic alpha-1 adrenoceptors**. This inhibition blocks the vasoconstricting (narrowing) effect of catecholamines (epinephrine and norepinephrine) on the vessels, leading to peripheral blood vessel dilation.

Uses

- It is used in hypertension, symptomatic benign prostatic hyperplasia, and severe congestive heart failure.

Stability and Storage Conditions

♦ It should not be stored in the bathroom. Keep all medicines away from children.

Type of Formulation

▪ Capsules

Popular Brand Names

✓ Minipress,
✓ Prazin,
✓ Prazo

β-Adrenoceptpor Blocking Drugs : The effect of catecholamines facilitated via β-adrenoceptors are blocked by β- adrenoceptor blocking drugs. They can further be categorised as selective or non-selective β- adrenoceptor blocking drugs.

The drugs studied below are:

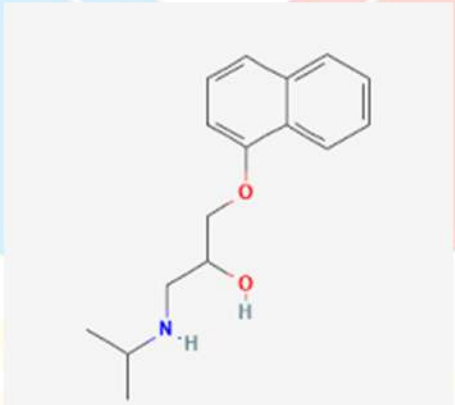
1. Propranolol, *
2. Ateolol, *
3. Carvedilol.

Propranolol *

→ Propranonol is a sympatholytic non-selective first successful β-blocker. Sympatholytics treat hypertension, anxiety, and panic.

Chemical Name and Structure

- 1-naphthalen-1-yloxy-3-(propan-2-ylamino)propan-2-ol;hydrochloride



Mechanism of Action

➢ Propranolol is a non-selective beta receptor antagonist. This means that it does not have preference to Beta-1 or Beta-2 receptors. It competes with sympathomimetic neurotransmitters for binding to receptors, which inhibits sympathetic stimulation of the heart.

Uses

▪ Tremors, angina (chest pain), hypertension (high blood pressure), heart rhythm disorders, and other heart or Circulatory conditions can be treated using propranolol

Stability and Storage Conditios

- Tablets and capsules should at a room temperature with tightly closed container

Types of Formulations

♦ Solution,
♦ Tablets

Popular Brand Name

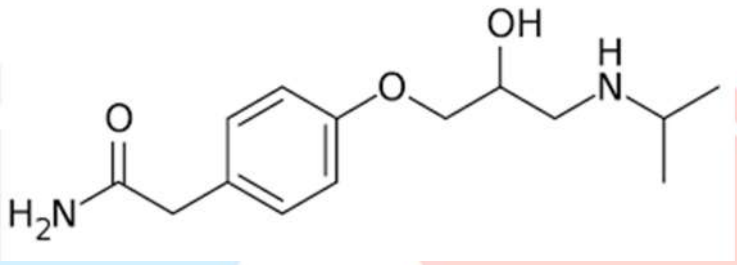
✓ Hemangeol,
✓ Hemangiol,
✓ Inderal,
✓ Innopran

Atenolol *

→ Atenolol is a cardioselective β-adrenergic blocker having potency and properties similar to propranolol, excluding the negative inotropic effect.

Chemical Name and Structure

- 2-[4-[2-hydroxy-3-(propan-2-ylamino)propoxy]phenyl]acetamide



Mechanism of Action

➢ Atenolol belongs to a class of drugs known as beta blockers. It works by blocking the action of certain natural chemicals in your body, such as epinephrine, on the heart and blood vessels. This effect lowers the heart rate, blood pressure, and strain on the heart.

Uses

♦ It is used in angina pectoris and hypertension for long-term treatment.

Stability and Storage Conditions

▪ It should be stored at room temperature between 68°F and 77°F (20°C and 25°C).

Type of Formulation

- Tablets

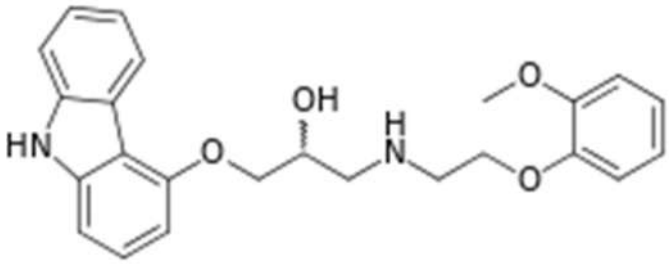
Popular Brand Name

✓ Tenormin

Carvedilol

→ Carvedilol is a non-selective β-blocker prescribed for treating mild to moderate congestive heart failure. It blocks β_1- ,β_2-, and α-adrenergic receptors.

Chemical Structure



Mechanism of Action

- Carvedilol works by blocking the action of certain natural substances in your body, such as epinephrine, on the heart and blood vessels. This effect lowers your heart rate, blood pressure, and strain on your heart. Carvedilol belongs to a class of drugs known as alpha and beta-blockers.

Uses

- It is used for treating mild to moderate heart failure of cardiomyopathic or ischemic origin

Stability and Storage Conditions

- Carvedilol tablet should be stored at 20° to 25°C (68° to 77'F). The tablets should be kept dried. The expired tablet should be safely discarded.

Type of Formulation

- Tablets

Popular Brand Name

- Coreg

CHOLINERGIC DRUGS AND RELATED AGENTS (PARASYMPATHOMIMETRIC)

→ The following two ways increase the stimulation of Acetylcholine Receptors (AChR):

→ **Binding the direct acting cholinergic agonists** to the AChR, thereby, triggering nicotinic or muscarinic effects, or both, and

→ **Binding the indirect acting cholinergic agonists** to the AChR that inhibit the hydrolysis of ACh by AChE, thereby, extending the action of available ACh.

- The hydrochloride salt of cholinergic agonist exists in the form of white crystalline powder or colourless crystals.
- It has a faint bitter taste and does not have any odour.
- It is hygroscopic and shows high solubility in water.
- Since these agents are affected by light, they are stored in tightly- closed, light-resistant containers.
- lts solutions maintained at a pH between 4 and 5 are the most stable. In the presence of Strong acids and alkalis. its solutions degrade and undergo epimerisation.

Classification

- Direct Acting Agents (Cholinergic Agonists)
- Indirect Acting Agents (Anticholinesterase)

Direct Acting Agents

→ The structure and effect of cholinergic agonists is similar to that of ACh.

→ Cholinergic agonists directly bind The bind to and activate the ACh receptors (either muscarinic or nicotinic receptors).

→ Cholinergic agents include methacholine, carbachol. bethanechol, and and pilocarpine.

The drugs studied below are

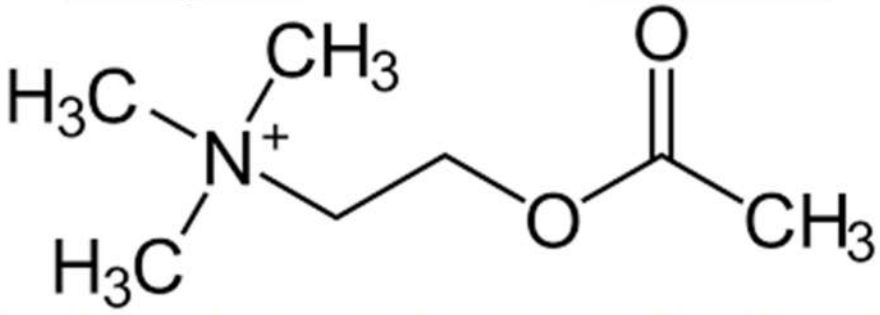
- Acetylcholine, *
- Carbachol,
- Pilocarpine.

Acetylcholine *

→ Acetylcholine is a neurotransmitter. In vertebrates, it is the major transmitter at neuromuscular junctions, parasympathetic effector junctions, autonomic ganglia, many sites in the CNS, and a subset of sympathetic effector junctions.

Chemical Name and Structure

- 2-Acetoxy-N,N,N-trimethylethanaminium



Mechanism of Action

➢ The mechanism of action of acetylcholine is as a Cholinergic Agonist. A neurotransmitter. Acetylcholine in vertebrates is the major transmitter at neuromuscular junctions, autonomic ganglia, parasympathetic effector junctions, a subset of sympathetic effector junctions, and at many sites in the central nervous system.

Uses

▪ It is used in cataract surgery, keratoplasty, iridectomy for obtaining meiosis of the iris in seconds after delivery of lens and in other anterior segment surgeries in which rapid meiosis may be required.

Stability and Storage Conditions

- It should be stored at room temperature. Away from light.

Types of Formulations

♦ Powder for injection,

♦ Gels,

♦ Lozenges

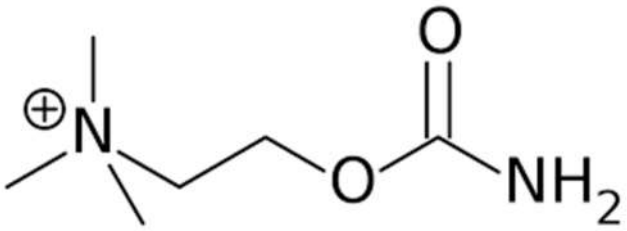
Popular Brand Name

▪ Miochol-E

Carbachol

→ Carbachol is chemically a carbamate, thus, possesses a very high potency (as opposed to esters). Another added advantage with this drug is that it undergoes slow hydrolysis. It decreases the intraocular pressure and is therefore employed in glaucoma treatment.

Chemical Structure



Mechanism of Action

➢ Mechanism : Carbachol is a potent cholinergic (parasympathomimetic) agent which produces constriction of the iris and ciliary body resulting in reduction in intraocular pressure. The exact mechanism by which carbachol lowers intraocular pressure is not precisely known.

Uses

- It is used for treating intestinal and bladder atony seen post-operatively.

Stability and Storage Conditions

- It should be stored under dry conditions.
- The product can be stored for upto 12 months.

Types of Formulations

- Tablet,
- Solution

Popular Brand Names

✓ Carbastat,
✓ Miostat

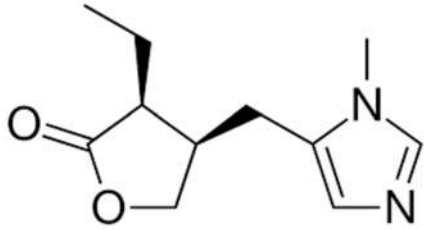
Pilocarpine

→ Pilocarpine is a parasympathomimetic alkaloid derived from the leaves of tropical American shrubs of Pilocarpus genus.

→ When applied topically in conditions of glaucoma and xerostomia, it acts therapeutically at muscarinic acetylcholine receptor M3 as it is a non-selective muscarinic receptor agonist in the parasympathetic nervous system.

Chemical Name and Structure

- (3S,4R)-3-Ethyl-4-((1-methyl-1H-imidazol-5-yl)methyl)dihydrofuran-2(3H)-one



Mechanism of Action

➢ Pilocarpine is a cholinergic parasympathomimetic agent which acts by stimulating the muscarinic receptors; thus, increases the secretions by exocrine glands, produces contraction of the iris sphincter muscle and ciliary muscle (when applied topically to the eyes).

Uses

- Pilocarpine is used for treating xerostomia occurring after head and neck radiation treatments, or in Sjorgen's syndrome (an autoimmune disorder mainly affecting females).

Stability and Storage Conditions

- All medicines should be kept out of reach and sight of children.
- It should be stored in cool, dry place and also kept away from direct heat and light.

Types of Formulations

- Tablets,
- Solution

Popular Brand Name

✓ Salagen

Cholinesterase Inhibitors (Indirect Acting Agents)

→ Acetylcholine neurotransmitter is inactivated by the enzyme cholinesterase which is inhibited by the indirect acting cholinergic agents or anticholinesterases.

→ Thus, the inactivation of ACh is prevented as a result of which the level of endogenous ACh at the neuroeffector junction of paras arasympathetic nerve endings or the neuromuscular junction increase.

→ This accumulated ACh are made available for attachment to the receptor site in order to produce cholinergic responses.

→ But in case of blockage of ACh receptors, this increased level of ACh competes with the blocking drug for the receptors, and thus reverses the blockage.

→ This results in the resumption of nerve transmission either at the parasympathetic terminal site or at the neuromuscular junction.

The drugs studied below are:

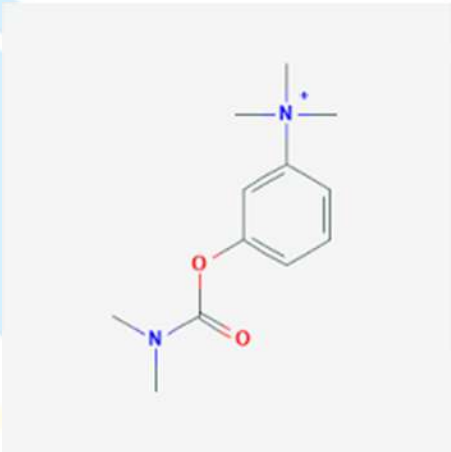
- Neostigmine, *
- Edrophonium chloride,
- Tacrine hydrochloride,
- Echothiophate iodide.

Neostigmine *

→ Neostigmine is a parasympathomimetic acting as a reversible acetylcholinesterase inhibitor.

Chemical Name and Structure

- 3-(dimethylcarbamoyloxy)phenyl]-trimethylazanium



Mechanism of Action

➢ At the neuromuscular junction neostigmine produces the concentrationof skeletal muscle by two ways:

1. By acting directly on the skeletal muscle, and
2. By inactivating the cholinesterase enzyme (as in physostigmine).

Uses

- It is used for urinary retention caused by general anaesthesia and to treat curariform drug toxicity.
- It is also used in the Ogilvie syndrome (pseudo- obstruction of colon in critically ill patients),
- It has been used as a test for early pregnancy.

Stability and Storage Conditions

- lt should be protected from light and should be stored at temperature less than 25°C.
- It should be stored in carton- until the time of use.

Type of Formulation

♦ Injectable solutions

Popular Brand Names

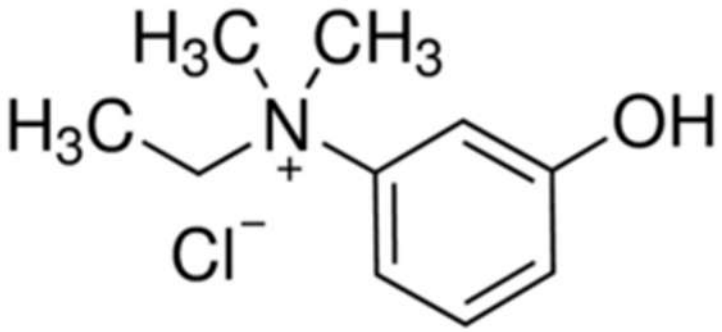
✓ Bloxiverz,
✓ Prostigmin Bromide,
✓ Prostigmin

Edrophonium Chloride

→ Edrophonium chloride is a short and rapid-acting anticholinesterase drug.

Chemical Name and Structure

- ethyl-(3-hydroxyphenyl)dimethylammonium chloride



Mechanism of Action

➢ Edrophonium chloride inhibits the acetylcholinesterase enzyme, and subsequently increases the duration of action of ACh, occurring naturally in the body. Acetylcholine stimulates nicotinic and muscarinic receptors having various effects.

Uses

▪ It is used as an adjunct for differential diagnosis of myasthenia gravis, and also for determining the treatment requirements.

Stability and Storage Conditions

♦ It should be stored at controlled room temperature 15° 30°C (59°-86°F).

Type of Formulation

- Injectable solutions

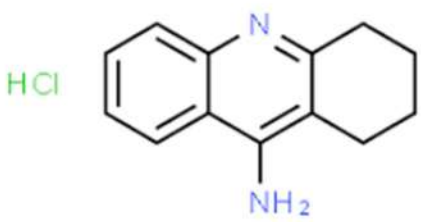
Popular Brand Names

✓ Enlon,
✓ Reversol,
✓ Tensilon

Tacrine Hydrochloride

→ Tacrine hydrochloride is a reversible cholinesterase inhibitor and a parasympathomimetic agent which is prescribed for treating mild to moderate dementia of Alzheimer's type.

Chemical Structure



Mechanism of Action

- ➢ Although the mechanism of action has not been fully elucidated, tacrine hydrochloride may bind reversibly to cholinesterase, acetylcholinesterase as well as butyrylcholinesterase, thereby decreasing the breakdown of acetylcholine, and prolonging synaptic actions as well as increased release of acetylcholine.

Uses

- ✓ It is used as a respiratory stimulant, for countering the effect of muscle relaxants, and for treating Alzheimer's disease and other CNS disorders.

Stability and Storage Conditions

- ▪ Capsules should be stored at room temperature, 15°-30° C (59°-86° F).

Type of Formulation

- ♦ Capsules

Popular Brand Name

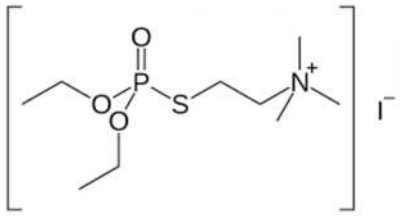
- ✓ Cognex

Echothiophate iodide

→ Echothiophate iodide is a long-acting, irreversible, potent cholinesterase inhibitor used as an ocular hypertensive for treating glaucoma.

Chemical Name and Structure

- 2-(Diethoxyphosphorylsulfanyl)ethyl-N,N,N-trimethylazanium iodide



Mechanism of Action

- ➢ Echothiophate is an indirect-acting parasympathomimetic agent. By interfering with the enzymatic destruction of acetylcholine, echothiophate potentiates the action of acetylcholine at cholinergic synapses. The pupil of the eye is constricted by contraction of the iris sphincter, producing miosis.

Uses

- → It is used for treating sub-acute or chronic angle-closure glaucoma after iridectomy or when surgery is denied or contraindicated.

Stability and Storage Conditions

- It should be stored under refrigeration between 2-8°C.

Types of Formulations

- ▪ Solution,
- ▪ Powder

Popular Brand Name

- ✓ Phospholine Iodide

Cholinesterase Reactivator – Pralidoxime Chloride

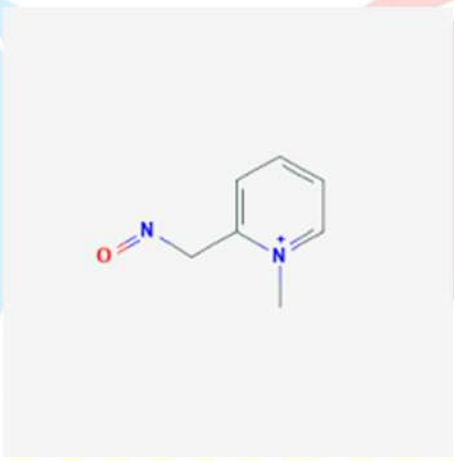
→ Cholinesterase reactivators are used for reversing the inactivation of cholinesterase by organophosphates or sulphonates.

→ They are used as a therapy in agricultural, by industrial, and military poisonings caused organophosphates and sulfonates.

→ Pralidoxime chloride is used as by an antidote in poisoning caused organophosphate pesticides and chemicals.

Chemical Name and Structure

- 2-formyl-1-methylpyridinium chloride oxime.



Mechanism of Action

➢ The principal action of pralidoxime is to reactivate cholinesterase (mainly outside of the central nervous system) which has been inactivated by phosphorylation due to an organophosphate pesticide or related compound.

Uses

- It is used for treating the poisoning caused by pesticides and chemicals organophosphates having of anticholinesterase activity.
- It is also used for controlling the overdosage of anticholinesterase drugs used for treating myasthenia gravis.

Stability and Storage Conditions

- It should be stored at 20°-25°C (68°-77°F).

Type of Formulation

♦ Injection

Popular Brand Names

✓ Atnaa,
✓ Duodote,
✓ Protopam

CHOLINERGIC BLOCKING AGENTS (CHOLINERGIC ANTAGONISTS)

→ Anticholinergic or parasympatholytic drugs are those drugs which occupy the ACh receptors (and do not allow ACh to bind to the receptors) and prevent the actions of ACh.
→ Parasympatholytic drugs are also termed as cholinergic blocking agents, cholinergic or muscarinic antagonists, anti-parasympathetic agents, anti-muscarinic agents, and antispasmodics.
→ The heart, respiratory tract, GI tract, urinary bladder, eyes, and exocrine glands are the major tissues affected by anticholinergic drugs.

Classification

Anti-Muscarinic Agents/Muscarinic Antagonists:

- These compounds exhibit high binding affinity for muscarinic receptors.
- They do not have any intrinsic activity.
- According to the proposed mechanism, binding in of an antagonist to the receptor results in a conformational change in the receptor protein.
- This change is different from that produced when an agonist binds to the receptor.
- Thus, binding of an antagonist to the receptor does not produce any response. of Examples anti-muscarinicsare atropine, scopolamine, tolterodine, homatropine, tropicamide, etc.

Anti-NicotinicAgents/NicotinicAntagonists: These chemical compounds bind to the cholinergic nicotinic receptors These agents, however, are not efficacious.

The drugs studied below are:

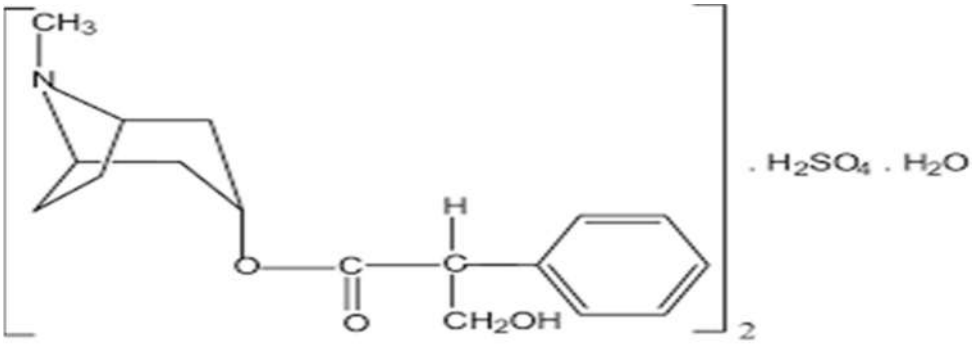
- Atropine sulphate, *
- Ipratropium bromide.

Atropine Sulphate *

→ Atropine sulphate is an alkaloid derived from Atropa belladonna and some other plants also of Solanaceae family.

Chemical Name and Structure

- (1R,3R,5S)-8-methyl-8-azabicyclo[3.2.1]octan-3-yl hydroxy-2-phenylpropanoate



Mechanism of Action

- Atropine produces a wide range of anticholinergic effects by binding to and inhibiting the muscarinic acetylcholine receptors.

Uses

- It is used for treating poisoning caused by organophosphorous nerve agents with anti-cholinesterase activity (cholinesterase inhibitors) and organophosphorous or carbamate insecticides.

Stability and Storage Conditions

- It should be stored in single or multiple-dose containers, preferably glass, at a temperature of less than 40°C (preferably between 15°-30°C). It should be protected from light and stored in airtight containers.

Type of Formulation

- Injection Solution

Popular Brand Names

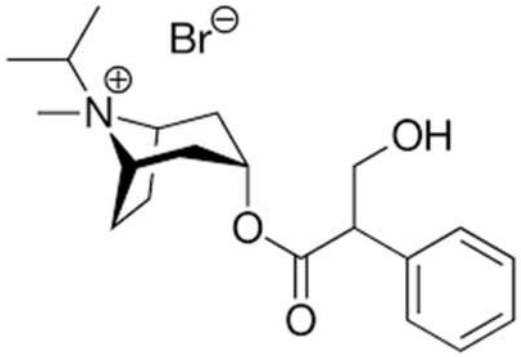
- ✓ Atnaa,
- ✓ Busulfex,
- ✓ Donnatal,
- ✓ Duodote, etc,

Ipratropium Bromide

→ Ipratropium is a muscarinic antagonist having similar structure to atropine but is considered safer and more effective for inhalational uses.

Chemical Name and Structure

- [8-methyl-8-(1-methylethyl)- 8-azoniabicyclo[3.2.1] oct-3-yl] 3-hydroxy-2-phenyl-propanoate



Mechanism of Action

- Ipratropium is an acetylcholine antagonist via blockade of muscarinic cholinergic receptors. Blocking cholinergic receptors decreases the production of cyclic guanosine monophosphate (cGMP). This decrease in the lung airways will lead to decreased contraction of the smooth muscles.

Uses

- ♦ It is used for maintenance and treatment of bronchospasm related to chronic obstructive pulmonary diseases such as chronic bronchitis and emphysema.

Stability and Storage Conditions

- It should not be stored above 25°C. It should be stored in the original package. Before using, the ampoule should be opened immediately and any solution remaining after use should be discarded.

Types of Formulations

- ▪ Spray,
- ▪ Solution

Popular Brand Names

- ✓ Atrovent,
- ✓ Ipratropium Inhalation Solution,
- ✓ Ipratropium Inhalation Aerosol

Synthetic Cholinergic Blocking Agents

→ The solanaceous alkaloids are potent parasympatholytics, but they produce a wide range of undesired effects through their non-specific blockade of autonomic functions.
→ When alkaloids are used for their antispasmodic effects they often give rise to side effects like dryness of the mouth and fluctuations in pulse rate.
→ Hence, synthesis of Compounds having specific cholinolytic actions is desirable.
→ Synthetic cholinergic blocking agents are aminoalcohols in the form of ester, ether, or alcohol.
→ These agents help to produce the effect by blocking the muscarinic action.
→ They are less potent when compared to solanaceous alkaloids.
→ Some examples are tropicamide, dicyclomine hydrochloride, and procyclidine hydrochloride.

The drugs studied below are:

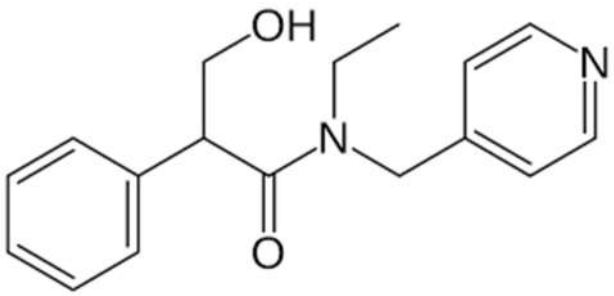
- Tropicamide,
- Cyclopentolate hydrochloride,
- Clidinium bromide, and
- Dicyclomine hydrochloride. *

Tropicamide

→ Tropicamide is a muscarinic antagonist having pnarmacological actions similar to atropine and is mainly used as an ophthalmic parasympatholytic or mydriatic.

Chemical Name and Structure

- Benzeneacetamide, N-ethyl-α-(hydroxymethyl)-N-(4-pyridinylmethyl)-.



Mechanism of Action

- ➢ Tropicamide binds with the receptors in the eye muscles (M receptors) and blocks them. It dilates the pupil and paralyses ciliary muscle by blocking the responses of iris sphincter muscle to the iris and of ciliary muscles to cholinergic stimulation.

Uses

- It is prescibed for inducing mydriasis (pupil dilation) and cycloplegia (paralysis of the ciliarymuscle of the eye) during diagnostic procedures like measurement of refractive errors and for examining the fundus of the eye.

Stability and Storage Conditions

- ✓ It should be stored at 20° to 25°C. The container should be tightly closed.

Types of Formulations

- ♦ Injection,
- ♦ Solution

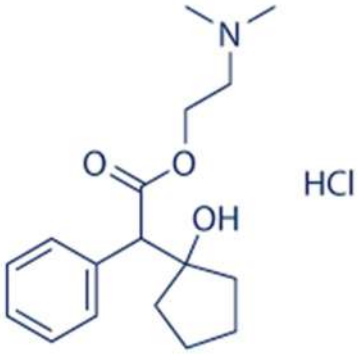
Popular Brand Names

- ✓ Minims Tropicamide,
- ✓ Mydriacyl,
- ✓ Paremyd

Cyclopentolate Hydrochloride

→ Cyclopentolate hydrochloride is a parasympatholytic anticholinergic used only for obtaining mydriasis or cycloplegia.

Chemical Structure



Mechanism of Action

- ➢ It causes mydriasis, i.e., dilates the pupil, and prevents the eye from accommodating for near vision (cycloplegia) by blocking the muscarinic receptors.

Uses

- It is used for producing mydriasis and cycloplegia during diagnostic procedures.

Stability and Storage Conditions

- ✓ A refrigerator should be used for storing some brands of cyclopentolate eye drops.

Type of Formulation

- ♦ Solution

Popular Brand Names

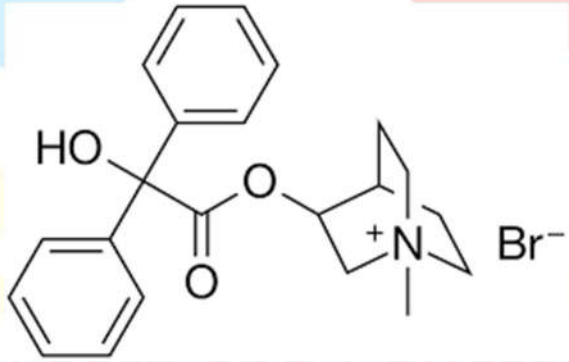
- ✓ Cyclogyl,
- ✓ AK-Pentolate

Clidinium Bromide

→ Clidinium bromide is a synthetic anticholinergic agent having a pronounced antispasmodic and anti-secretory effects on the gastrointestinal tract.

Chemical Name and Structure

- 3-[(2-hydroxy-2,2-diphenylacetyl)oxy]-1-methyl-1-azabicyclo[2.2.2]octan-1-ium bromide



Mechanism of Action

- ➢ Clidinium is a synthetic anticholinergic agent which has been shown in experimental and clinical studies to have a pronounced antispasmodic and antisecretory effect on the gastrointestinal tract. It inhibits muscarinic actions of acetylcholine at postganglionic parasympathetic neuroeffector sites.

Uses

- It is used for treating peptic ulcer diseases.

Stability and Storage Conditions

- ✓ It should be stored at a temperature of -20°C for 2 years or less than 2 years.

Types of Formulations

- ♦ Tablet,
- ♦ Capsules

Popular Brand Name

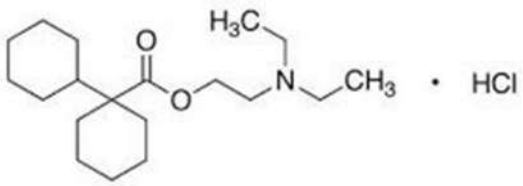
- ✓ Quarzan

Dicyclomine Hydrochloride *

→ Dicyclomine hydrochloride is a bicyclohexyl)-1-carboxylic acid 2-(diethylamino) ethyl ester hydrochloride

Chemical Name and Structure

- 2-(Diethylamino)ethyl 1-cyclohexylcyclohexane-1- carboxylate



Mechanism of Action

- **Dicyclomine hydrochloride acts by the following two mechanisms:**
  - By exerting an anticholinergic effect (anti-muscarinic. specifically) at receptor sites of ACh, and
  - By affecting the smooth muscles directly (musculotropic action).

Uses

- Dicyclomine is employed in the treatment of irritable bowel syndrome, since it decreases the symptoms of stomach and intestinal cramping. It slows down the gut movement and relaxes the muscles of stomach and intestines.

Stability and Storage Conditions

- The container should be tightly closed and should be stored in a dry, cool and well-ventilated place,

Types of Formulations

- Capsule,
- Solution,
- Syrup,
- Tablet

Popular Brand Names

- ✓ Berntyl,
- ✓ Dibent,
- ✓ Dicyclocot

Chapter 7

DRUGS ACTING ON CARDIOVASCULAR SYSTEM

Topics

Anti Arrhythmic Drugs

- Quinidine sulphate,
- Procainamide hydrochloride,
- Verapmil
- Phenytoin sodium, *
- Lidocaine hydrochloride,
- Lorcainide hydrochloride,
- Amiodarone,
- Sotalol

ANTI-HYPERTENSIVE AGENTS

- Propranolol, *
- Captopril, *
- Ramipril,
- Methyldopate hydrochloride,
- Clonidine hydrochloride,
- Hydralazi hydrochloride,
- Nifedipine

ANTI-ANGINAL AGENTS

- Isosorbide Dinitrate

DRUGS ACTING ON CARDIOVASCULAR SYSTEM

Anti Arrhythmic Drugs

→ The rhythm and normal heart rate may be affected by Some diseases and drugs. This condition is termed cardiac arrhythmia in which certain disorders affect the normal mechanical activity of heart

→ Drugs which have the ability to revert any irregular cardiac rhythm or rate to normal are known as anti-arrhythmic or anti-dysrhythmic or anti-fibrillatory drugs

properties of an ideal antiarrhythmic drug are:

1. It should be highly efficient in controlling symptoms and improving survival in both supraventricular and ventricular arrhythmias.
2. It should have no negative effect.
3. It should produce a favourable effect on myocardial Oxygen consumption.
4. It should produce both oral and intravenous activity

Examples

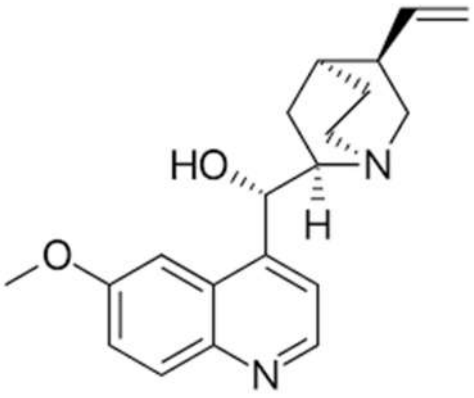
The Following anti-arrhythmic drugs are discussed below.

1. Quinidine sulphate,
2. Procainamide hydrochloride,
3. Verapmil
4. Phenytoin sodium, *
5. Lidocaine hydrochloride,
6. Lorcainide hydrochloride,
7. Amiodarone,
8. Sotalol

Quinidine Sulphate

→ Quinidine sulphate is the sulphate salt of quinidine, which is an alkaloid having antimalarial and antiarrhythmic (Class IA) properties.

Chemical Structure



Mechanism of Action

- This alkaloid dampens the excitability of cardiac and skeletal muscles by blocking sodium and potassium currents across cellular membranes. It prolongs cellular action potential, and decreases automaticity. Quinidine also blocks muscarinic and alpha-adrenergic neurotransmission.

Uses

- It is used for treating persistent, life-threatening ventricular arrhythmias, like sustained ventricular tachycardia.
- It is taken via intravenous route for treating Plasmodium falciparum malaria.

Stability and Storage Conditions

- It should be kept in a well-closed container and away from light

Types of Formulations

1. Tablet
2. Capsule

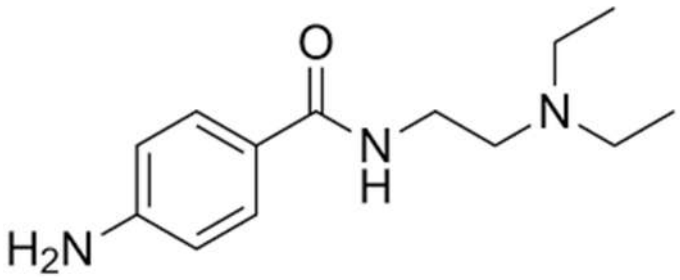
Popular Brand Names

- Quinaglute Dura-Tabs
- Quinora
- Cardioquin
- Quinidex Extentabs

Procainamide Hydrochloride

→ Procainamide hydrochloride is the hydrochloride salt of procainamide, which is a procaine analogue and an amide denvative having class IA anti-arrhythmic activity.

Chemical Structure



Mechanism of Action

- Procainamide is a class 1A anti-arrhythmic that binds to fast sodium channels inhibiting recovery after repolarization. It also prolongs the action potential and reduces the speed of impulse conduction.

Uses

- It is used to treat ventricular arhythmias, ventricular ectopy, tachycardia,supraventricular arrhythmias, atrial fibrillation, and automatic supraventricular tachycardia.

Stability and Storage Conditions

- It should be kept in a tightly closed container

Types of Formulations

1) Capsule
2) Injection

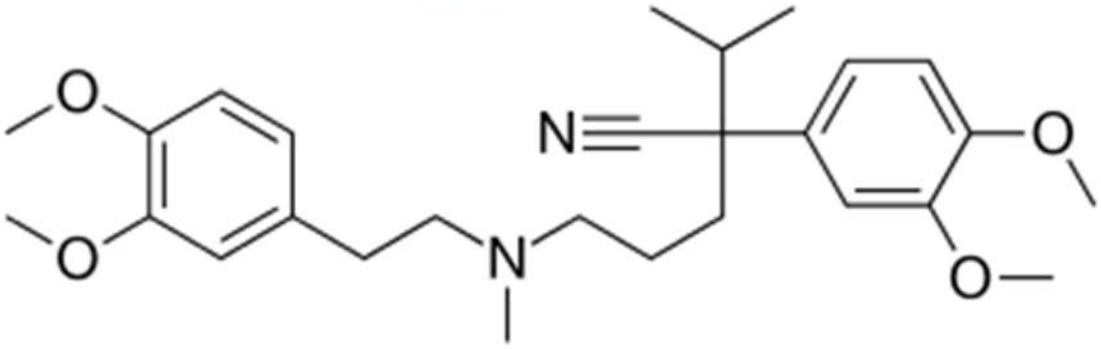
Popular Brand Names

- Pronestyl
- Procanbid
- Procan SR
- Pronestyl-SR)

Verapamil

→ Verapamil is a calcium channel blocker of class IV antiarrhythmic agent. It acts by inhibiting voltage-dependent calcium channels. Due to its effect on L-type calcium channels in the heart, ionotropy and chronotropy is reduced, which further reduces heart rate and blood pressure.

Chemical Structure



Mechanism of Action

➢ Verapamil is in a class of medications called calcium-channel blockers. It works by relaxing the blood vessels so the heart does not have to pump as hard. It also increases the supply of blood and oxygen to the heart and slows electrical activity in the heart to control the heart rate.

Uses

- It is the first generation calcium channel blocker used for treating hypertension, supraventricular tachyarrhythmias, cluster headache prophylaxis, and angina pectoris.

Storage Conditions

- It should be stored in a cool dry place and Away from light

Types of Formulation

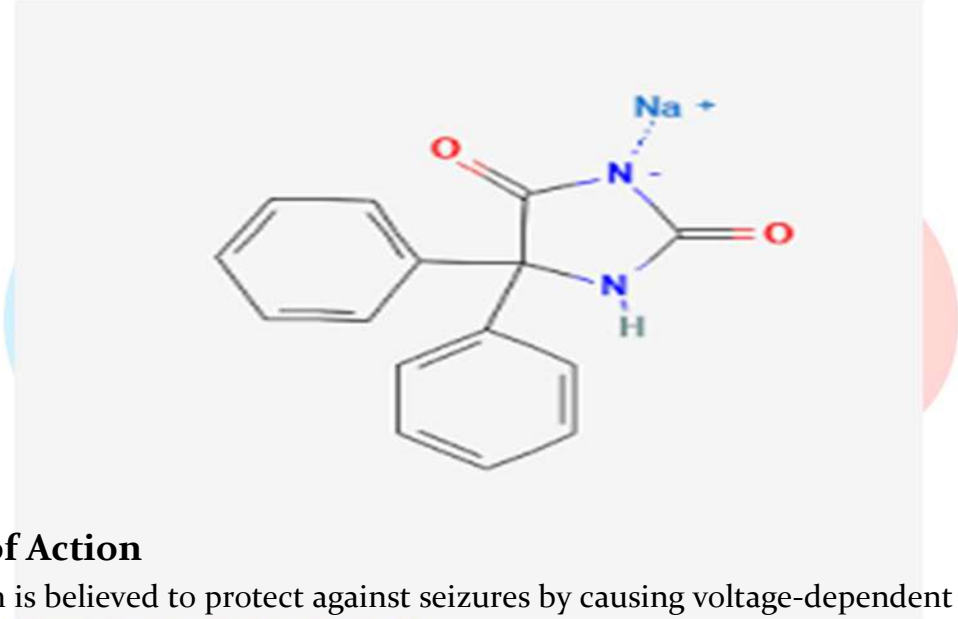
1. Tablet
2. Capsule
3. Solution

Phenytoin Sodium *

→ Phenytoin Sodium is the sodium salt of phenytoin, which is a hydantoin derivate and a non-sedative antiepileptic Having anticonvulsant activity.

Chemical Name And Structure

sodium 5,5-diphenyl-2, 4-imidazolidinedione,



Mechanism of Action

➢ Phenytoin is believed to protect against seizures by causing voltage-dependent block of voltage gated sodium channels. This blocks sustained high frequency repetitive firing of action potentials.

Uses

- It is used in the prophylactic management of tonic- clonic seizures with complex symptomatology.
- It provides protection against the development of focal seizures with complex symptomatology.
- It is used for treating ventricular tachycardia and sudden episodes of atrial tachycardia when the patients do not respond to other antiarrhythmic medications or cardioversion.

Stability and Storage Conditions

- It should be stored at room temperature and away from light and moisture.

Types of Formulations

1. Capsue
2. Injection

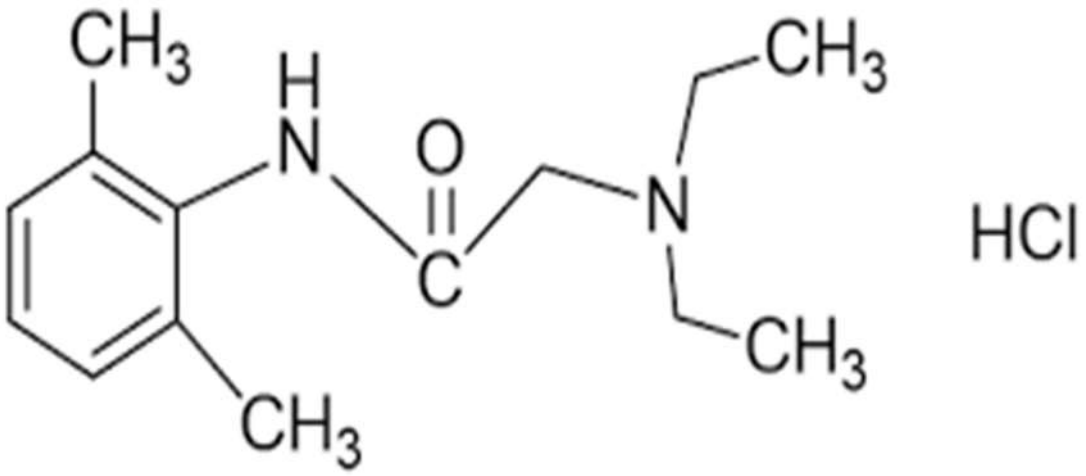
Popular Brand

- Dilantin
- Phenytek

Lidocaine Hydrochloride

→ Lidocaine hydrochloride is the hydrochloride Salt of lidocaine, which is an aminoethylamide and a prototypical member of the amide class anaesthetics having anti-arrhythmia activity

Chemical Structure



Mechanism of Action

➢ Lidocaine is an antiarrhythmic medication of the class Ib type. This means it works by blocking sodium channels and thus decreasing the rate of contractions of the heart. When injected near nerves, the nerves cannot conduct signals to or from the brain.

Uses

- This medication is used to prevent and relieve pain during certain medical procedures (such as inserting a tube into the urinary tract). It is also used to numb the lining of the mouth, throat, or nose before certain medical procedures (such as intubation).

Stability and Storage Conditions

- Its solution should be stored at controlled room temperature 15-30°C (59-86°F).

Type of Formulation

1. Solution

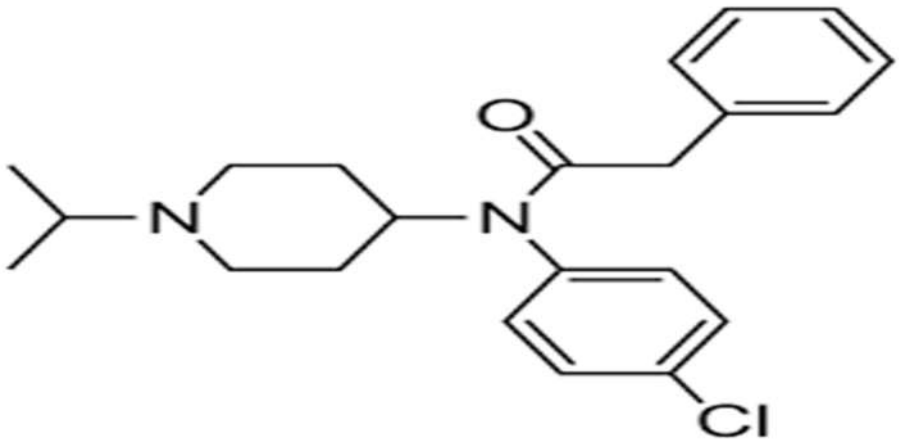
Popular Brand Name

♦ Xylocaine Viscous

Lorcainide Hydrochloride

→ Lorcainide hydrochloride is a Class IC antiarrhythmic agent. It helps in restoring the normal heart rhythm and conduction in patients having premature ventricular contractions, ventricular tachycardiac, and Wolff Parkinson-White syndrome.

Chemical Structure



Mechanism of Action

➢ Lorcainide is a class Ic antiarrhythmic medication. It was reported to be highly efficient for the treatment of ventricular arrhythmias, ventricular fibrillation, and tachycardia. The drug was used under the name Remivox. The mechanism of lorcainide action involves the blockage of sodium channels.

Used

- Uses It is for treating premature ventricular contractions, ventricular tachycardiac, and Wolff-Parkinson-White syndrome.

Stability and Storage Conditions

- It should be stored and dispensed at room temperature for up to 1 year or it should be stored at -20°C for up to 3 months

Type of Formulation

1. Tablets

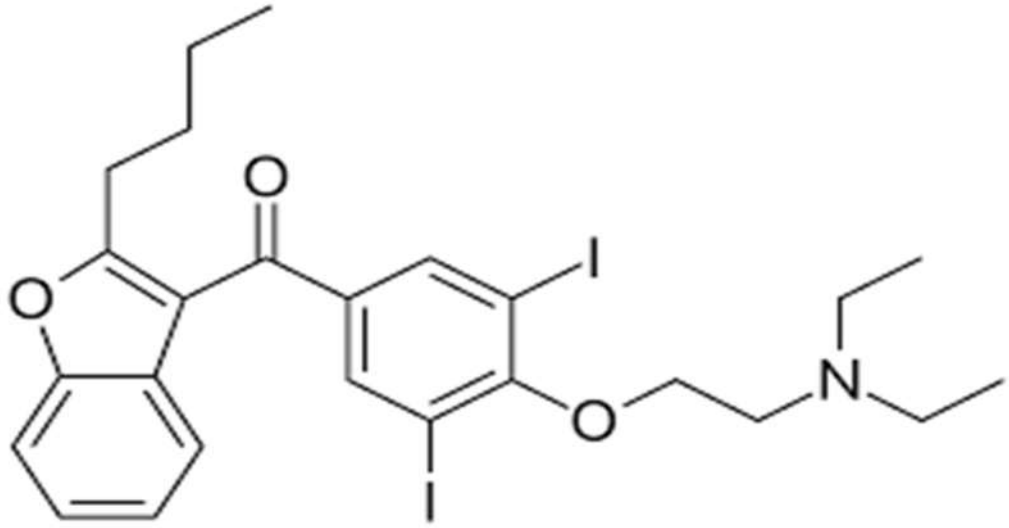
Popular Brand Names

- Lerka
- Larpin
- Aristo Larpin
- Landip

Amiodarone

→ Amiodarone is an anti-anginal and anti-arrhythmic drug, which increases the duration of ventricular and atrial muscle action by blocking the Na-K-activated myocardial adenosine triphosphatase. This reduces the heart rate and vascular resistance.

Chemical Structure



Mechanism of Action

➢ Amiodarone is considered a class III anti-arrhythmic drug. It blocks potassium currents that cause repolarization of the heart muscle during the third phase of the cardiac action potential.

Uses

- Amiodarone is used to treat life-threatening heart rhythm problems called ventricular arrhythmias.

Stability and Storage Conditions

- Store at room Temperature

Type of Formulation

1. Tablets

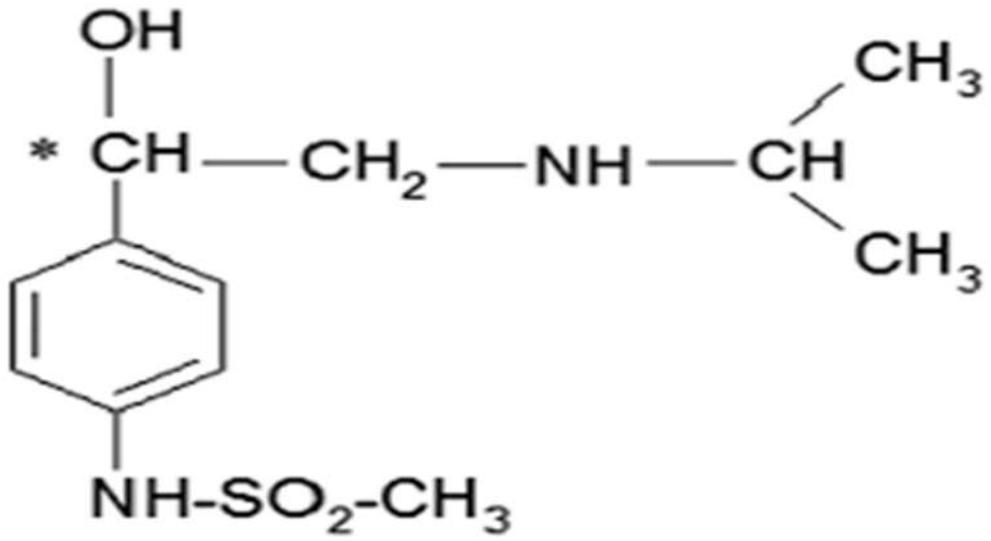
Popular Brand Names

- Pacerone
- Cordarone
- Cordarone IV
- Nexterone

Sotalol

→ Sotalol is an ethanolamine derivative having Class III anti-arrhythmic and anti-hypertensive activities. It is a non-selective B-adrenergic receptor and potassIum channel antagonist.

Chemical Structure



Mechanism of Action

➢ Sotalol inhibits beta-1 adrenoceptors in the myocardium as well as rapid potassium channels to slow repolarization, lengthen the QT interval, and slow and shorten conduction of action potentials through the atria.

Uses

- It is used for maintaining the normal sinus
- It also used for treating documented life-threatening ventricular arrhythmias.

Stability and Storage Conditions

▪ It Should be stored in room temperature.

Types of Formulations

1) Solution
2) Tablets

Popular Brand Names

♦ Betapace
♦ Betapace AF
♦ Sorine
♦ Sotalol Hydrochloride AF
♦ Sotylize

ANTI-HYPERTENSIVE AGENTS

→ A condition in which the blood pressure of systemic artery increases beyond the normal pressure is known as hypertension. Therefore to deliver blood to tissues, the heart works harder to overcome the increased systemic pressure. This increased systemic arterial pressure puts

→ Strain on heart and other arteries thus Resulting in high blood pressure

Examples

The following anti-hypertensive agents are- below

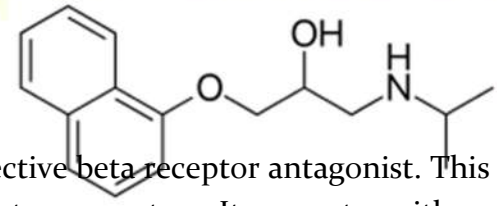
- Propranolol, *
- Captopril, *
- Ramipril,
- Methyldopate hydrochloride,
- Clonidine hydrochloride,
- Hydralazi hydrochloride,
- Nifedipine

Propranolol *

→ Propranolol Propranonol is a sympatholytic non-selective first successful B-blocker. Sympatholytics treat hypertension, anxiety, and panic.

Chemical Name and Structure

(RS)-1-(1-methylethylamino)-3-(1-naphthyloxy)propan-2-ol



Mechanism of Action

➢ Propranolol is a non-selective beta receptor antagonist. This means that it does not have preference to Beta-1 or Beta-2 receptors. It competes with sympathomimetic neurotransmitters for binding to receptors, which inhibits sympathetic stimulation of the heart.

Uses

- Tremors, angina (chest pain), hypertension (high blood pressure), heart rhythm disorders, and other heart or circulatory conditions can be treated using propranolol.

Stability and Storage Condition

▪ Tablets and capsules of propranolol should be stored at room temperature, and in a tightly closed container.

Types of Formulations

Capsule, Solution, Tablet

Popular Brand Names

♦ Hemangeol, Hemangiol

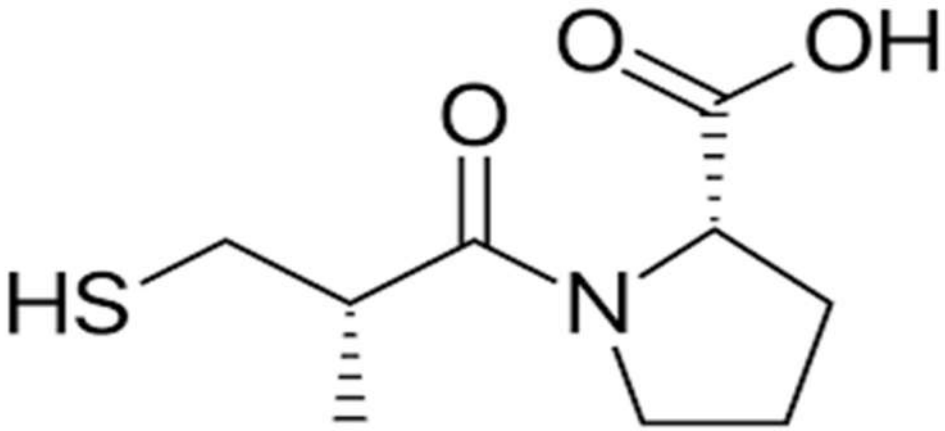
♦ Inderal, Innopran

Captopril *

→ Captopril is a potent competitive inhibitor of Angiotensin-Converting Enzyme (ACE), which is responsible for converting Angiotensin I (ATI) to Angiotensin II (ATII). ATII controls the blood pressure and is a major component of the Renin-Angiotensin- Aldosterone System (RAAS).)

Chemical name And Structure

(2S)-1-[(2S)-2-methyl-3-sulfanylpropanoyl]pyrrolidine-2-carboxylic acid



Mechanism of Action

- Captopril blocks the conversion of angiotensin I to angiotensin II and prevents the degradation of vasodilatory prostaglandins, thereby inhibiting vasoconstriction and promoting systemic vasodilation.

Uses

- Captopril is used alone or together with other medicines to treat high blood pressure (hypertension).

Stability and Storage Conditions

- It should be stored at room temperature and away from light and moisture

Types of Formulations

1) Tablet

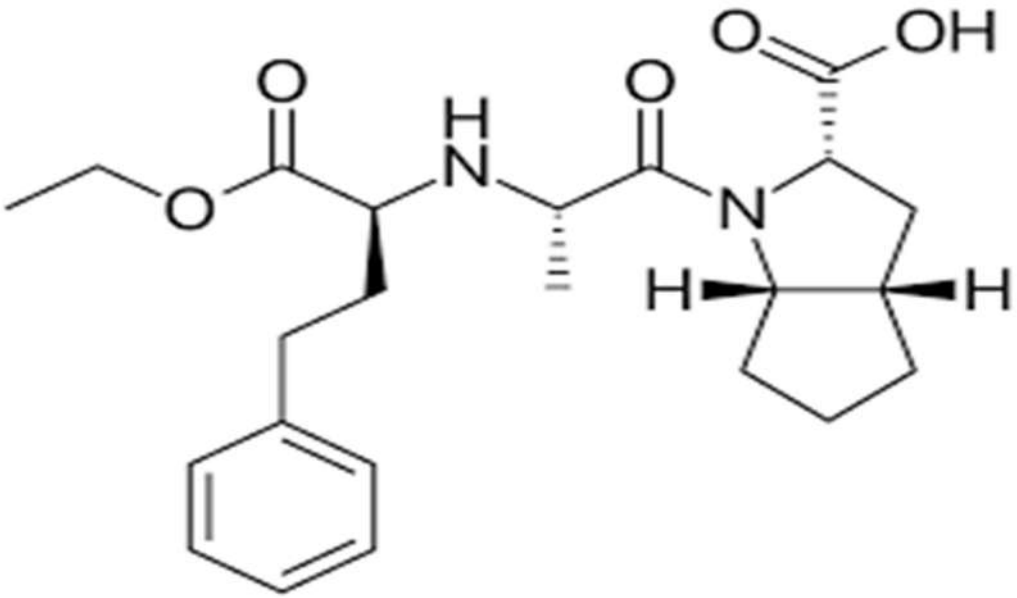
Popular Brand Name

- Capoten

Ramipril

→ Rampril is an ACE inhibitor that is used for the treatment of hypertension and reduction of cardiovascular mortality which may result myocardial infraction in hemodynamically stable patients having symptoms of congestive heart failure

Chemical Structure



Mechanism of Action

➢ Ramipril inhibits angiotensin-converting enzyme and decreases angiotensin II formation. As a result, sympathetic activity goes down, sodium and water reabsorption from the kidneys reduces, smooth muscles in the arterioles also relax. As a result, blood pressure decreases.

Uses

- Ramipril is used alone or together with other medicines to treat high blood pressure (hypertension).

Storage and Stability Condition

▪ It should be stored at room temperature and away from light and moisture.

Types of Formulations

1) Tablet
2) Capsule

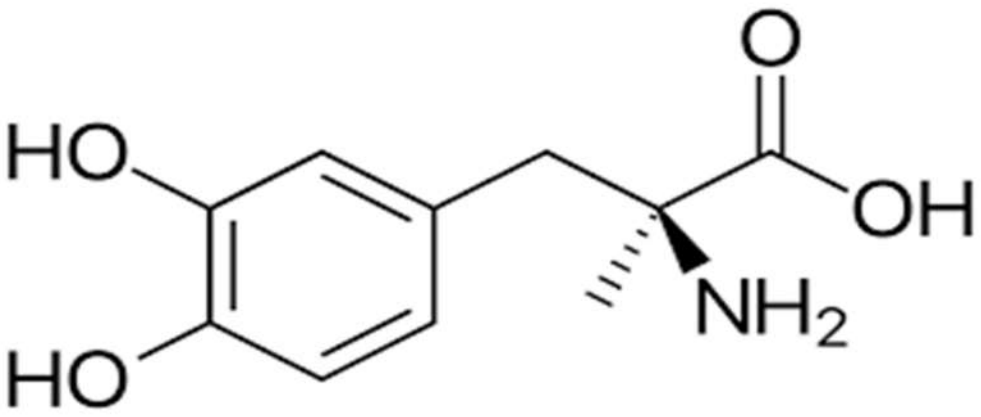
Popular Brand Name

♦ Altace

Methyldopate Hydrochloride

→ Methyldopate hydrochloride is the hydrochloride salt of methyldopa, which is a derivate of phenylalanine and inhibitor of aromatic amino acid decarboxylase.It also exhibits antihypertensive activity

Chemical Structure



Mechanism of Action

- Although the mechanism of action has yet to be conclusively demonstrated, the antihypertensive effect of methyldopa probably is due to its metabolism to alpha-methyl-norepinephrine, which then lowers arterial pressure by stimulation of central inhibitory alpha-adrenergic receptors, false neurotransmission, and/or reduction of plasma renin activity.

Uses

- It is used for treating hypertension.
- It also used for treating gestational hypertension (or pregnancy-induced hypertension) and pre eclampsia.

Stability and Storage condition

- It Should be stored in a well-closed container at controlled room temperature.

Type of Formulation

1) Tablet
2) Popular

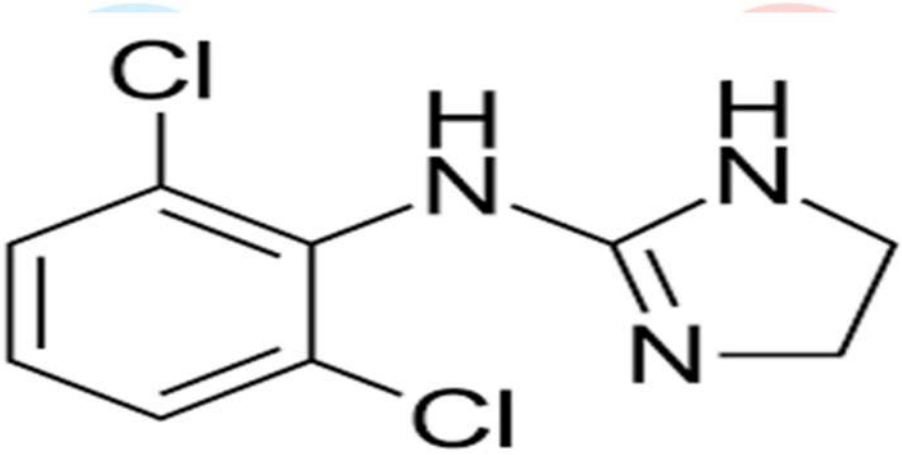
Brand Name

- Aldoril

Clonidine Hydrochloride

→ Clonidine hydrochloride is the hydrochloride salt of clonidine, Which is an imidazoline derivative, and centrally-acting alphaadrenergic agonist and antagonist having antihypertensive activity.

Chemical Structure



Mechanism of Action

➢ Clonidine has an alpha-antagonist effect in the posterior hypothalamus and medulla. The final response is reduced sympathetic outflow from the central nervous system (CNS), which clinically causes a decrease in arterial blood pressure.

Uses

- It is used as an adjunct in hypertension, as an epidural infusion as an adjunct treatment in severe cancer pain (not relieved by opiate analgesics alone), and for differential diagnosis of pheochromocytoma in hypertensive patients.

Stability and Storage Conditions

- It should be stored in a well-ventilated place at the temperature of -20°C

Type of Formulation

1) Tablets

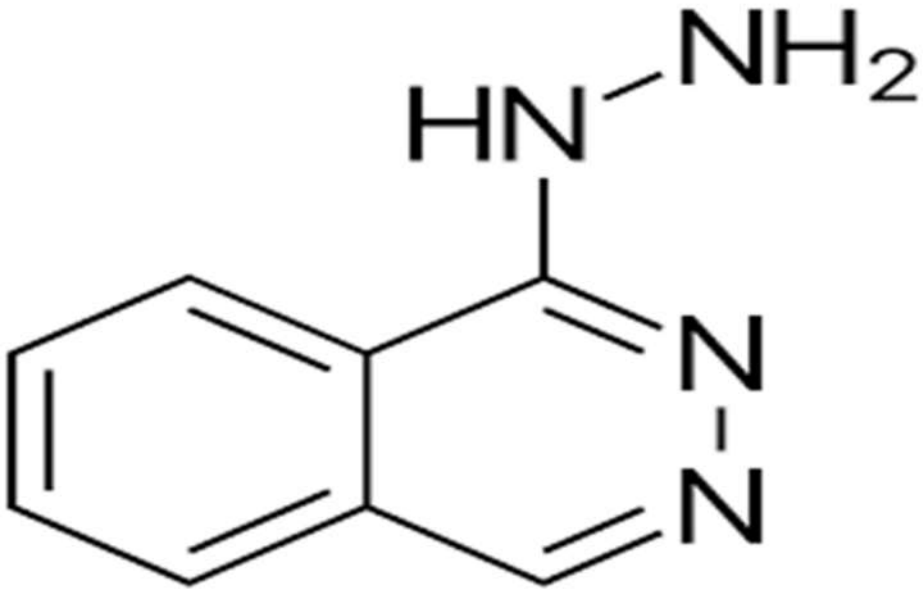
Popular Brand Names

- Catapres
- Kapvay
- Nexiclon

Hydralazine Hydrochloride

→ Hydralazine hydrochloride is the hydrochloride salt of hydralazine, which is a phthalazine derivative having antihypertensive and potential antineoplastic activities.

Chemical Structure



Mechanism of Action

➢ Hydralazine is a drug that conducts the blood pressure lowering effects by vasoconstrictive repression. It is a direct-acting smooth muscle relaxant and acts as a vasodilator primarily in resistance arterioles, also known as the smooth muscle of the arterial bed.

Uses

- It is used either as an adjunct or as a monotherapy to treat essential hypertension.
- It is also used to treat severe hypertension in cases when oral administration of the drug is not possible or when an immediate decrease in blood pressure is desired

Stability and Storage Conditions

- It should be stored in dry and tightly closed container.

Types of Formulations

1) Tablets
2) Solution

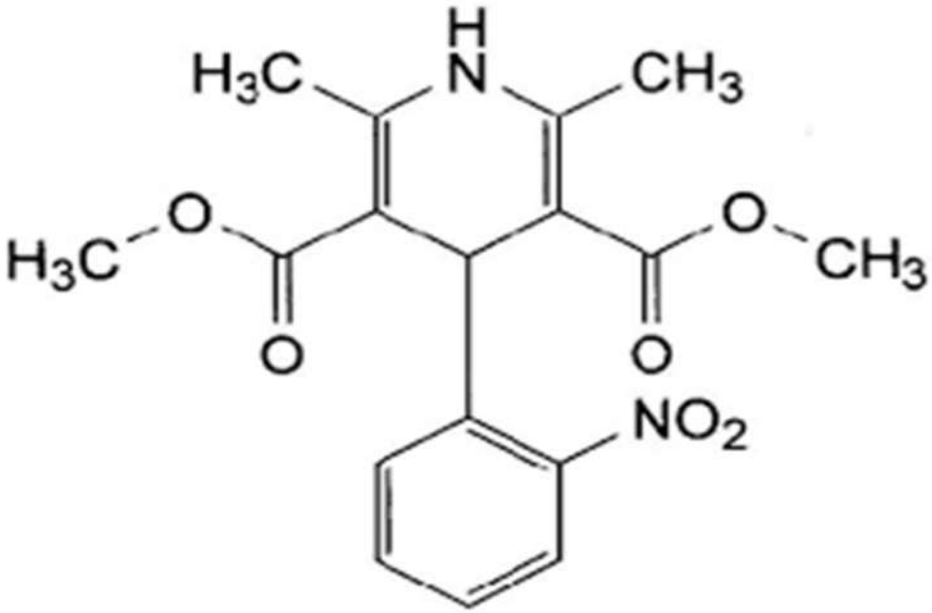
Brand Names Popular.

- Bidil
- Apresoline

Nifedipine

→ Nifedipine is a calcium channel blocker that relaxes the Nilessels (veins and arteries) so that the heart easily pumps blood and its workload is reduced.

Chemical Structure



Mechanism of Action

➢ Nifedipine is a peripheral arterial vasodilator which acts directly on vascular smooth muscle. The binding of nifedipine to voltage-dependent and possibly receptor-operated channels in vascular smooth muscle results in an inhibition of calcium influx through these channels.

Uses

- It is used in the treatment of vasospastic angina, chronic stable angina, hypertension, and Raynaud's phenomenon.
- It is also used as a first line agent for left ventricular hypertrophy and for isolated systolic hypertension (long-acting agents)

Stability and Storage Conditions

▪ It should be stored at room temperature and away from light and moisture. After each use it should be stored in a tightly close container.

Types of Formulations

1) Capsules
2) Tablets

Popular Brand Names

♦ Adalat
♦ Nifediac
♦ Afeditab CR
♦ Nifedical

ANTI-ANGINAL AGENTS

→ Angina pectoris, usually referred to as angina, denotes severe chest pain which may be caused by ischemia (lack of blood, and hence lack of oxygen supply) of heart muscle. This ischemia is the result of obstruction or spasm of coronary artery (vessels supplying blood to heart).Thus, the main cause of angina is coronary artery disease which results from atherosclerosis of the cardiac arteries.

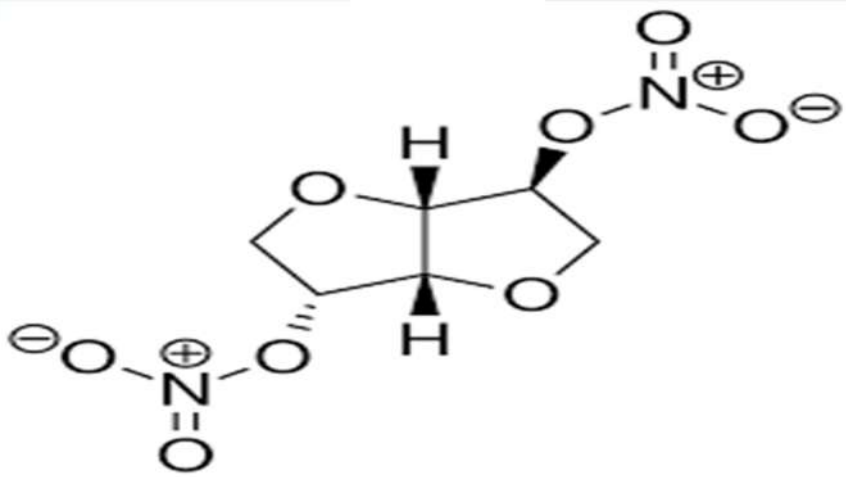
Example

- Isosorbide Dinitrate

Isosorbide dinitrate

→ Isosorbide dinitrate is a vasodilator. It is used for treating angina pectoris. It has actions similar to nitroglycerine, however it has a slower onset of action.

Chemical Structure



Mechanism of Action

➢ sosorbide Dinitrate is a moderate to long acting oral organic nitrate used for the relief and prophylactic management of angina pectoris. It relaxes the vascular smooth muscle and consequent dilatation of peripheral arteries and veins, especially the latter.

Used

- It is used for treating angina, congestive heart failure and oesophageal spasms.
- It is also used for treating or preventing the angina attacks.
- It dilates the blood vessels so that the blood flow easily through them and the heart also pumps blood easily.

Stability and Storage Conditions

- It should be stored at room temperature.

Types of Formulations

Tablets, Capsules

Popular Brand Names

Bidil, Dilatrate, Isordil

Chapter 8

DIURETICS

Topics

DIURETICS

- Acetazolamide
- Furosemide *
- Bumetanide
- Benzthiazide
- Xipamide
- Chlorthalidone
- Metolazone
- Spironolactone

DIURETICS

→ Drugs promoting urine output are known as diuretic drugs, which refer only to those agents that act directly on the kidneys.
→ These drugs primarily increase the excretion of water and ions like sodium (Na+), chloride (CI-), or bicarbonates HCO_3-) from the body.
→ Glomerular filtration, tubular reabsorption, and tubular secretion in kidneys determine the excretion of substances.
→ It is also employed in the treatment of various disorders like diabetes insipidus, nephrotic syndrome, hypertension, nutritional oedema, oedema of pregnancy, and liver cirrhosis.
→ They also decrease the intracellular and cerebrospinal fluid pressure.

Examples

Examples of diuretics are given below:

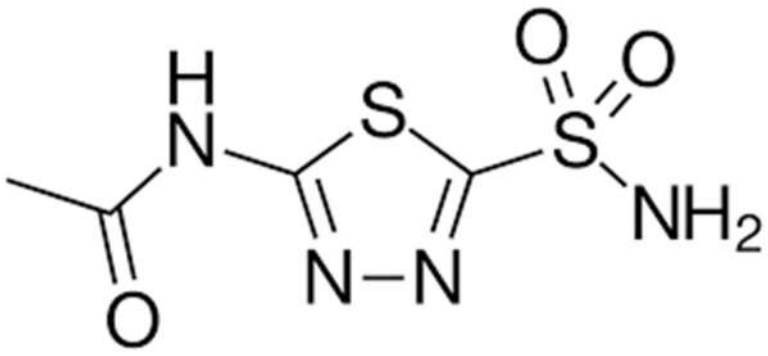
- Acetazolamide
- Furosemide
- Bumetanide
- Benzthiazide
- Xipamide
- Chlorthalidone
- Metolazone
- Spironolactone

Acetazolamide

→ Acetazolamide is the prototype carbonic anhydrase inhibitor.

→ This type of diuretics inhibit carbonic anhydrase enzyme in the membrane and cytoplasm of epithelial cell.

Chemical Structure



Mechanism of Action

➢ Acetazolamide is a carbonic anhydrase inhibitor. That means this drug works to cause an accumulation of carbonic acid by preventing its breakdown. The result is lower blood pH (i.e., more acidic), given the increased carbonic acid, which has a reversible reaction into bicarbonate and a hydrogen ion.

Uses

- Acetazolamide is self-limiting in nature.
- It produces adverse effects like acidosis and hypokalaemia.
- Thus, it is not used as a diuretic anymore; instead, it is currently being employed in the treatment of
    - ♦ Glaucoma
    - ♦ Alkalinising Urine
    - ♦ Epilepsy
    - ♦ Acute Mountain Sickness

Stability and Storage Conditions

- It can be stored up to 48 months.
- It should not be stored above 25°C.
- It should be stored in the original pack in order to protect from light and moisture.

Types of Formulations

1. Capsules
2. Tablets

Popular Brand Names

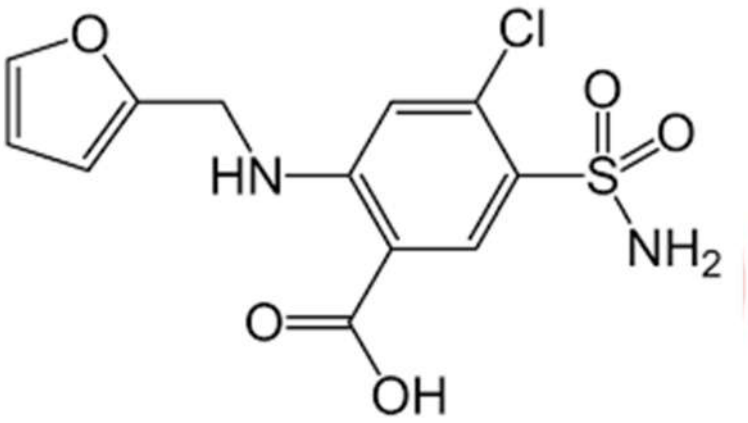
♦ Diamox

♦ Diamox Sequels

Furosemide *

→ Furosemide is a benzoic-sulfonamide-furan with fast onset and short duration of action. It is used for treating oedema and chronic renal insufficiency.

Chemical Structure



Mechanism of Action

➢ Furosemide, an anthranilic acid derivative, is a rapid acting, highly efficacious diuretic Rankin (2002). Its mechanism of action is inhibition of the sodium-potassium-2 chloride (Na+-K+-2 Cl–) co-transporter (symporter) located in the thick ascending limb of the loop of Henle in the renal tubule Jackson (1996).

Uses

- It is used for the treatment of oedema related to congestive heart failure, liver cirrhosis, and renal disease.
- It is also used either alone or with other antihypertensive agents for the management of hypertension.

Stability and Storage Conditions

- It should be kept at room temperature from 59°F (15°C) and 86°F (30°C).
- This drug should be kept away from light.
- This medication should not be stored in moist or damp areas like bathrooms.

Types of Formulations

1. Tablet
2. Solution

Popular Brand Names

- Lasix,
- Diaqua-2,
- Lo-Aqua

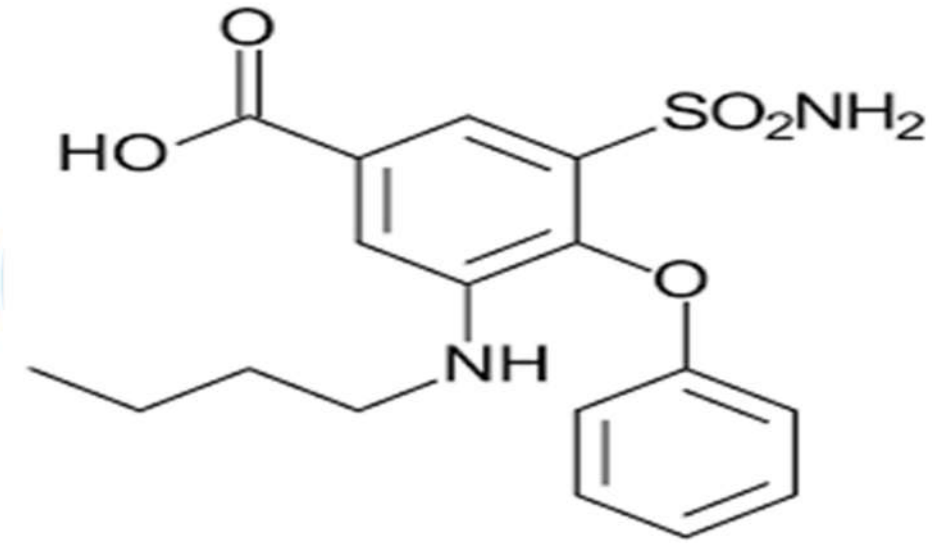
Bumetanide

→ Bumetanide is a loop diuretic of sulfamyl category.

→ It is used for treating heart failure.

→ It is used by the people who are not responding to high doses of furosemide or other diuretics.

Chemical Structure



Mechanism of Action

➢ The mechanism of action and effects of bumetanide are similar to those of furosemide. The drug increases urinary excretion of water, sodium, and chloride by inhibiting reabsorption of sodium and chloride through interference with the chloride-binding cotransport system in the ascending loop of Henle.

Uses

- It is used for treating oedema related to congestive heart failure, hepatic and renal disease including nephrotic syndrome.

Stability and Storage Conditions

- It should be stored at room temperature between 68°F and 77°F (20°C and 25°C), and should be kept away from light.

Type of Formulation

1. Tablets

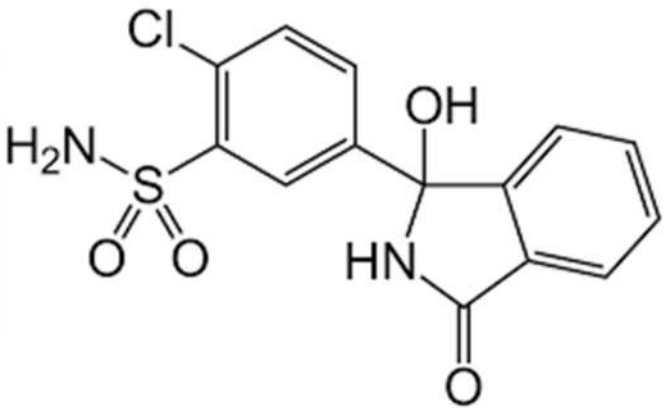
Popular Brand Names

- Bumex,
- Burinex

Chlorthalidone

→ Chlorthalidoneis a diuretic which is used in the treatment of hypertension or odema caused by heart failure, renal failure, hepatic cirrhosis, estrogen therapy, and other conditions.

Chemical Structure



Mechanism of Action

➢ Chlorthalidone inhibits sodium reabsorption at the level of the distal convoluted tubule and thus chloride via inhibition of the Na/Cl symporter. By removing sodium reabsorption at this location, the distal convoluted tubule of the nephron retains a higher sodium content.

Uses

- Chlorthalidone is used alone or together with other medicines to treat high blood pressure (hypertension).

Stability and Storage Conditions

- It should It should be dispensed in a tight, light-resistant container as defined in USP using a child-resistant closure.
- This medication should be kept away from reach of children.

Type of Formulation

1. Tablets

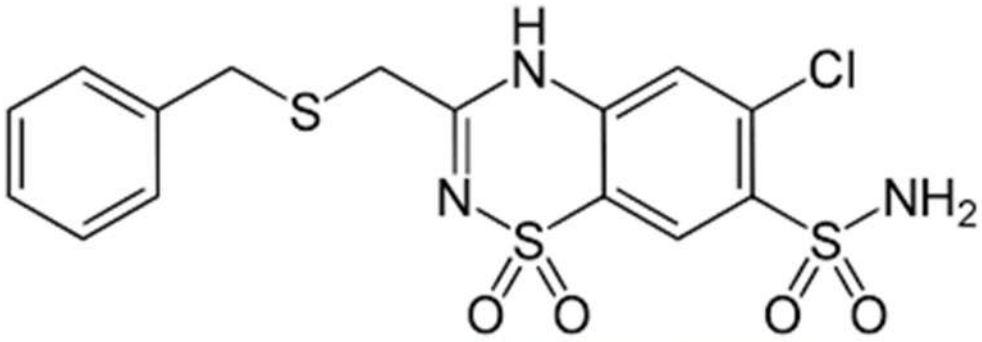
Popular Brand Names

- Hygroton
- Thalitone
- Chlorthalid

Benzthiazide

→ Benzthiazide is a class of thiazide diuretics which has an intermediate acting agent. Benzthiazide is also known as benzothiazide.

Chemical Structure



Mechanism of Action

- Benzthiazide is used to treat hypertension and edema. Like other thiazides, benzthiazide promotes water loss from the body (diuretics). They inhibit Na+/Cl- reabsorption from the distal convoluted tubules in the kidneys. Thiazides also cause loss of potassium and an increase in serum uric acid.

Uses

- It is used in the treatment of High blood presure (hypertension).
- The build-up of fluid in your body ocdema.

Stability and Storage Conditions

- It should be stored at room temperature in a well closed container and should be protected from light.

Type of Formulation

1. Tablets

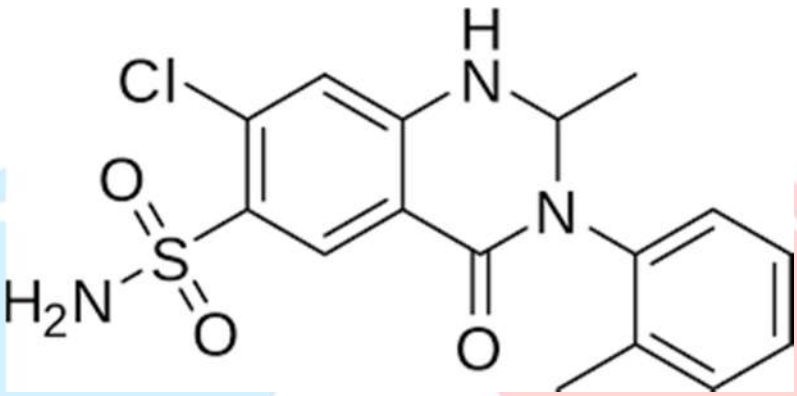
Popular Brand Names

- Exna

Metolazone

→ Metolazone is a thiazide like diuretic which is used in the treatment of hypertension.

Chemical Structure



Mechanism of Action

- Metolazone works by inhibiting sodium transport across the epithelium of the renal tubules (mostly in the distal tubules), decreasing sodium reabsorption, and increasing sodium, chloride, and water excretion.

Uses

- Prevent body from absortbing too much salt that can cause fluid retention.
- Treat fluid retention (edema) in peuplewth congestiveheart failure, or a kicney disorder such nephrotic syndrome.

Stability and Storage Conditions

- It should be stored at room temperature (77°F or 25°C) away from light and moisture.

Type of Formulation

1. Tablets

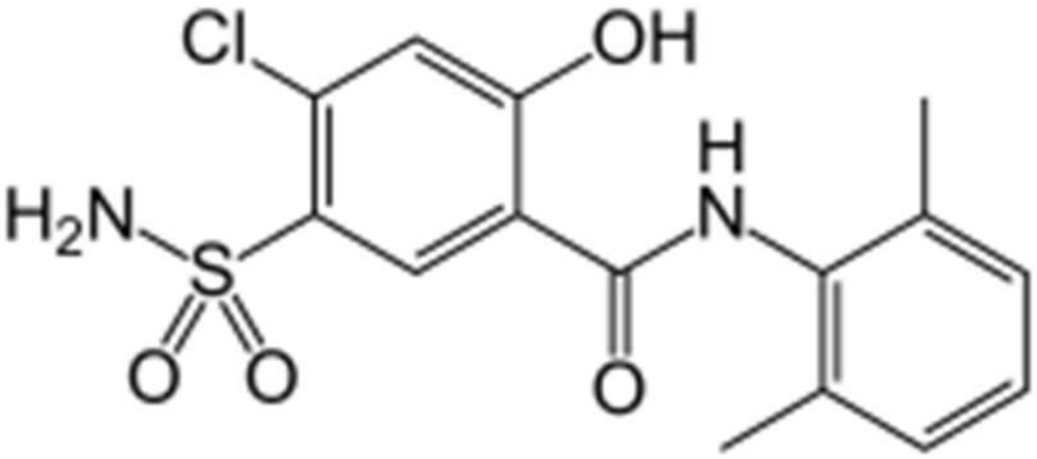
Popular Brand Names

- Zaroxolyn
- MykrOx

Xipamide

→ Xipamide is a diuretic which is used for the treatment of oedema.

Chemical Structure



Mechanism of Action

➢ Xipamide leads to an increase of K+ and Mg2+ excretion, but to a decrease of Ca2+ excretion in urine, a charactaristical feature of the thiazide-like diuretics.

Uses

- Xipamide is used for:
- Treating hypertension (high blood pressure)
- Treating oedema

Stability and Storage Conditions

▪ It should be stored in cool and dry place and should be kept away from direct heat and light.

Type of Formulation

1. Tablets

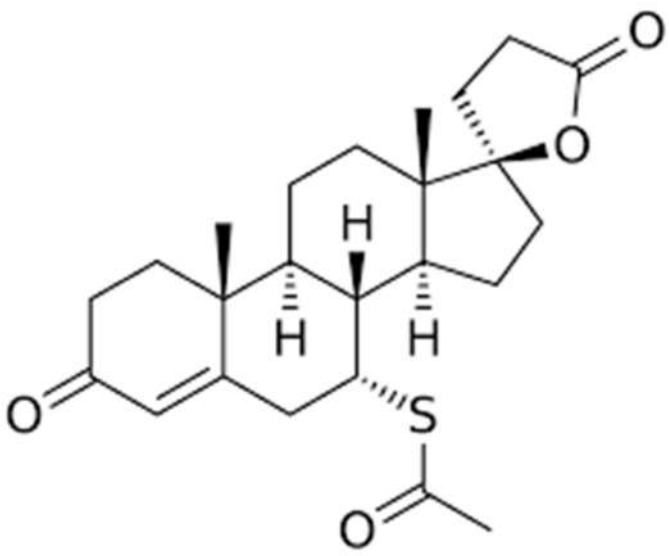
Popular Brand Names

♦ Aquaphoril
♦ Aquaphor

Spironolactone

→ Spironolactone is a potassium sparing diuretic which acts by antagonising aldosterone in the distal renal tubules.

Chemical Structure



Mechanism of Action

➢ Aldactone (spironolactone) is a specific pharmacologic antagonist of aldosterone, acting primarily through competitive binding of receptors at the aldosterone-dependent sodium-potassium exchange site in the distal convoluted renal tubule.

Uses

- It is used for treating refractory oedema in patients having failure, nephrotic syndrome, or hepatic cirrhosis.
- It is also used for treating hypokalaemia, Conn's syndrome, and low-renin hypertension.

Stability and Storage Conditions

- Spironolactone should be kept at room temperature between 68°F and 77°F (20°C and 25°C).
- It should be kept away from light and high temperature.

Types of Formulations

1. Tablet
2. Capsule

Popular Brand Names

- Aldactazide
- Aldactone
- Carospir

Chapter 9

HYPOGLYCEMIC AGENTS

Topics

HYPOGLYCEMIC AGENTS

- Metformin *
- Glybenclamide *
- Glimepiride
- Pioglitazone
- Repaglinide
- Gliflozin
- Gliptins

HYPOGLYCEMIC AGENTS

→ Hypoglycaemic agents are used in the treatment of diabetes mellitus by lowering the blood glucose levels.
→ With the exceptions of insulin, exenatide, liraglutide and pramlintide, all the other hypoglycaemic agents are administered orally and are therefore known as oral hypoglycaemic agents or oral anti-hyperglycaemic agents.

Insulin

→ Paul Langerhans (a German medical student) in 1869 studied that the pancreas has two different groups of cells, i.e., the acimer cells that secrete digestive enzymes, and islets (cells clustered in islands) that serve a second function.
→ Banting, Macleod, Bert, and Collip isolated insulin from bovine pancreas and used it for treating diabetes mellitus.
→ Insulin is a hormone produced in pancreas and permits the body to utilise sugar (glucose) from carbohydrates in the food.
→ Insulin restricts the blood sugar levels from getting too high (hyperglycaemia) or too low (hypoglycaemia).
→ Insulin occurs as a white or almost white coloured crystalline powder.
→ It is faintly soluble in water; soluble in dilute solution of mineral acids and with degradation in solutions of alkali hydroxide; and almost insoluble in alcohol, chloroform, and ether.

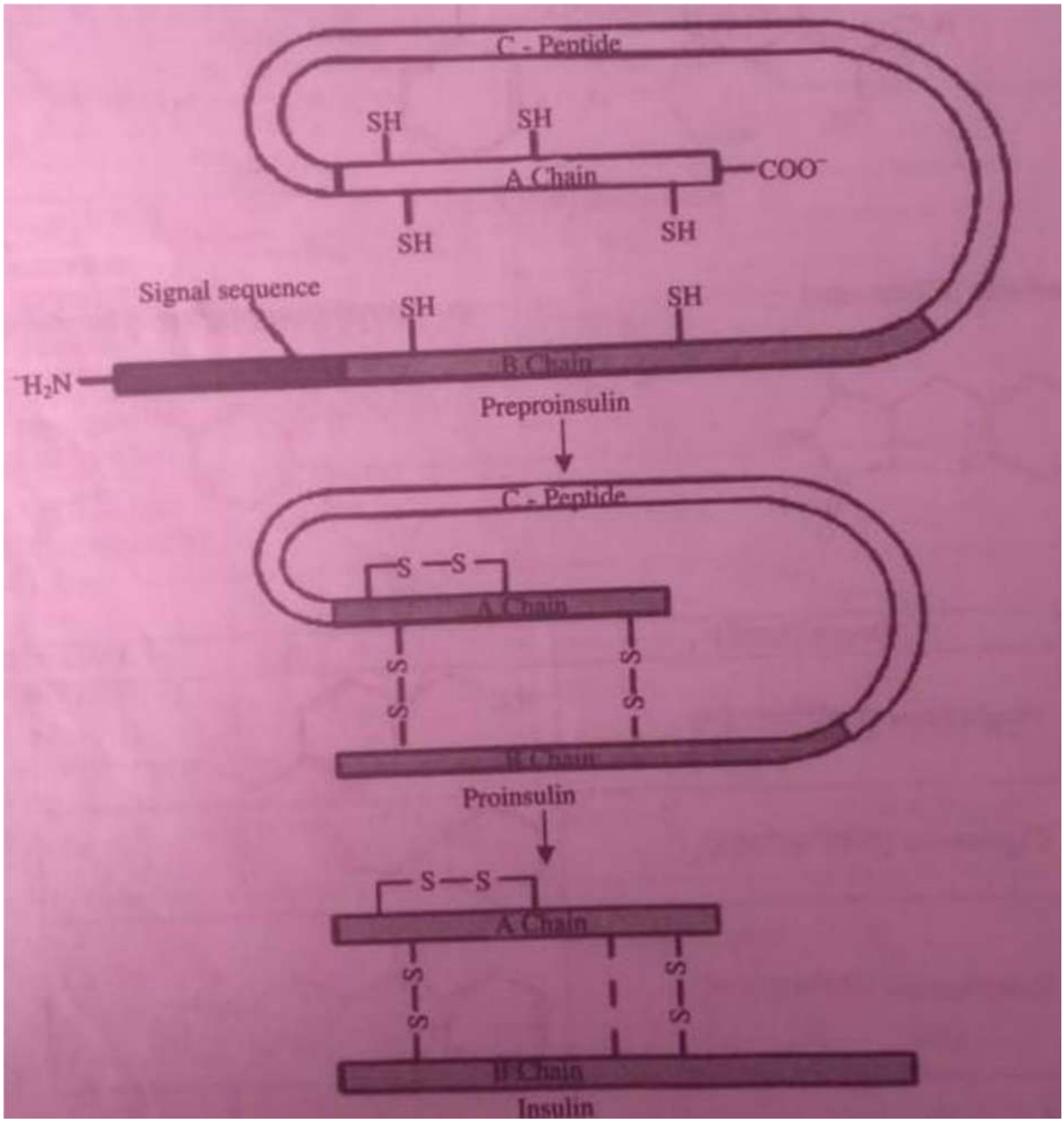
Synthesis

- Synthesis Significant quantity of insulin is synthesised in the pancreatic beta cells. The insulin mRNA is translated as a single chain precursor known as pre-pro-insulin, and removal of its signal peptide during insertion into the endoplasmic reticulum produces pro-insulin.

- Pro-insulin contains three domains, ie, an amino terminal B chain, a carboxy-terminal A chain, and a C peptide (connecting peptide in the middle). Pro-insulin, in the endoplasmic reticulum, is exposed to some specific endopeptidases that excise the C peptide and generates the mature form of insulin.

- Insulin and free C peptide are packaged in the Golgi into secretory granules accumulating collect in the cytoplasm.

- Insulin is secreted from the pancreatic B-cells by exocytosis when these cells are stimulated. After its release, the insulin diffuses into islet capillary blood. C peptide is also secreted into bloodstream; however it is not biologically active.



Uses

Insulin has the following uses:

- ✓ It is used for controlling diabetes mellitus (uncontrollable by diet alone) or for treating insulin dependent diabetes mellitus,
- ✓ It is used for regulating carbohydrate metabolism.
- ✓ It is used for treating hyperkalemia.
- ✓ It is used for treating severe ketoacidosis or diabetic coma.

Examples

Examples of hypoglycaemic agents are as follows :

- Metformin *
- Glybenclamide *
- Glimepiride
- Pioglitazone
- Repaglinide
- Gliflozin
- Gliptins

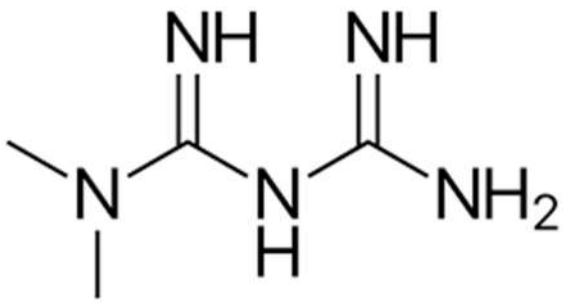
Metformin *

→ Metformin is a biguanide antihypertensive agent.

→ It improves glycaemic control by decreasing hepatic glucose production and glucose absorption, and also by increasing insulin-mediated glucose uptake.

Chemical Name and Structure

N,N-Dimethylimidodicarbonimidic diamide



Mechanism of Action

➢ Metformin reduces the blood glucose levels by decreasing hepatic glucose production (gluconeogenesis), decreasing the intestinal absorption of glucose, and increasing insulin sensitivity by increasing the glucose uptake and utilisation by the peripheral tissues.

Uses

- It is used as an adjunct to diet and exercise in NIDDM patients older than 18 years.
- It can also be used for managing metabolic and reproductive abnormalities related to polycystic ovary syndrome.
- It can also be used with a sulphonylurea or insulin to improve glycaemic control in adults.

Stability and Storage Conditions

- This medication should be kept in the tightly closed container and out of reach of children.
- It should be stored at room temperature and kept away from light, excess heat and moisture.

- It should not be stored in the bathroom.

Types of Formulations

a. Suspension
b. Tablet
c. Solution

Popular Brand Names

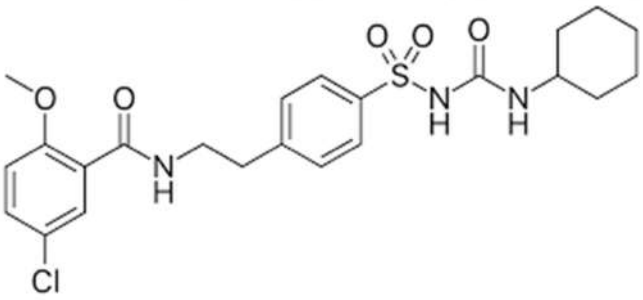
- Fortamet
- Glucophage
- Glucophage
- Glumetza
- Riomet

Glibenclamide *

→ Glybenclamide is an oral antihyperglycaemic drug of sulfonylurea class.
→ Glybenclamide is a white to silver crystalline compound with molecular formula C23H28ClN3O5S and molecular weight 494.00.

Chemical Name and Structure

1-[[p-[2-[5-chloro-o-anisamido) ethyl] phenyl] sulfonyl]-3-cyclo-hexylurea



Mechanism of Action

- Glibenclamide is an oral hypoglycaemic agent of the sulfonylurea group.
- It acts by lowering the blood glucose level acutely by stimulating the release of insulin from the pancreas.
- This is an effect dependent upon functioning B-cells in the pancreatic islets.

- Extrapancreatic effects may play a part in the mechanism of action of oral sulfonylurea hypoglycaemic drugs,

Uses

- It is used to treat patients with impairment of hepatic function.
- It acts as a hypoglycaemia and hematologic agent

Stability and Storage Conditions

- It can be stored at a temperature of more than 40 C or at 40° C for at least 90 days.

Type of Formulation

1. Tablets

Popular Brand Names

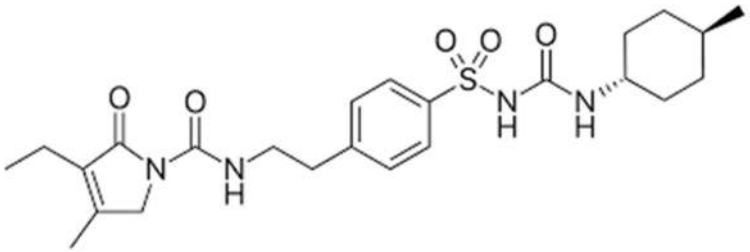
- Diabeta
- Flycron
- Glyburide

Glimepiride

→ Glimepiride is the first III generation sulphonylurea.

→ It is a highly potent sulphonylurea having long duration of action.

Chemical Structure



Mechanism of Action

- Glimepiride decreases blood glucose levels by stimulating insulin release from the functioning pancreatic B-cells, and by increasing the sensitivity of peripheral tissues to insulin
- Glimepiride binds to ATP-sensitive potassium channels present on the pancreatic cell surface, thus depolarises the membrane and reduces potassium conductance.

Uses

- It is used with insulin for treating the non-insulin dependent (type 2) diabetes mellitus

Stability and Storage Conditions

- It should be stored at room temperature.

Type of Formulation

1. Tablets

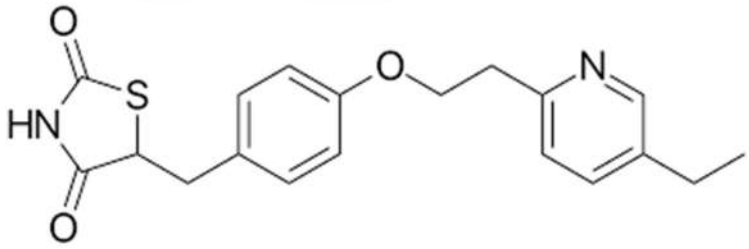
Popular Brand Name

- Amaryl

Pioglitazone

→ Pioglitazone is used as an adjunct to diet, exercise, and other anti-diabetic drugs to control type diabetes mellitus.

Chemical Structure



Mechanism of Action

- Pioglitazone improves glycaemic control in people with Type 2 diabetes by improving insulin sensitivity through its action at PPAR gamma 1 and PPAR gamma 2, and affects lipid metabolism through action at PPAR alpha.

Uses

- It is used as an adjunct to diet and exercise for improving glycaemic control in individuals having type 2 diabetes mellitus.

Stability and Storage Conditions

- It should be stored at a temperature of 25°C (77°F) and Container should be tightly closed and protected from light, moisture and humidity.

Type of Formulation

1. Tablets

Popular Brand Name

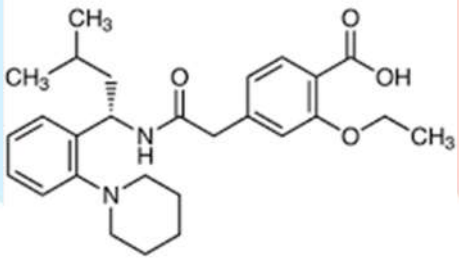
- Actos

Repaglinide

→ Repaglinide is used for treating NIDDM.

→ It is an oral anti hyperglycaemic drug of meglitinide class having short acting insulin secretagogues that bind to pancreatic B-cells for stimulating insulin release.

Chemical Structure



Mechanism of Action

➢ Repaglinide is an insulin secretagogue, meaning it binds to receptors on pancreatic beta cells and stimulates insulin release. Repaglinide binds to an ATP-dependent potassium channel on beta cells, known as SUR1, bringing about its closure.

Uses

- It is used as an adjunct to diet and exercise for improving glycaemic regulation in individuals having type 2 diabetes mellitus

Stability and Storage Conditions

- It should be stored at room temperature and kept away from light and moisture.
- It should not be stored in the bathroom.
- All medicines should be kept away from the reach of children and pets.
- Medications should not be flushed down in the toilet or poured into a drain unless instructed to do so.

Types of Formulation

1. Tablets
2. Capsules

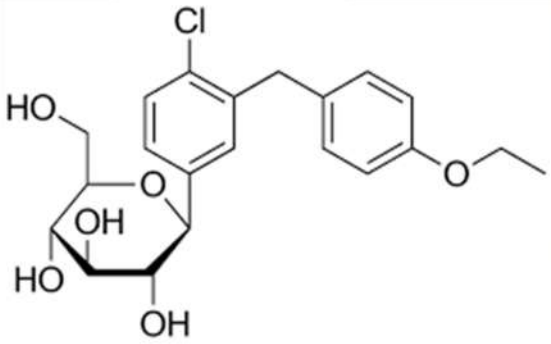
Popular Brand Names

- Enyglid
- Gluconomi
- Prandin

Gliflozins

→ Gliflozin drugs, ie, newly developed class of oral hypoglycaemic agent is the sodium-glucose co transporter which is used in the treatment of type- 2 diabetes mellitus.

Chemical Structure



Mechanism of Action

➢ SGLT-2 protein gets blocked by this class of drugs from the site of the proximal convoluted tubule (PCT) in the kidney which result in preventing reabsorption of glucose molecule and allow excretion of glucose in urine. The blood glucose level in the body gets lowered by this mechanism.

Uses

- It is used to treat
- 1) Type 2 diabetes. 2) Type 1 diabetes.

Stability and Storage Condition

▪ It should be stored at room temperature and should kept away from light and moisture.

Type of Formulation

1. Tablets

Popular Brand Names

♦ Canaglifiorin

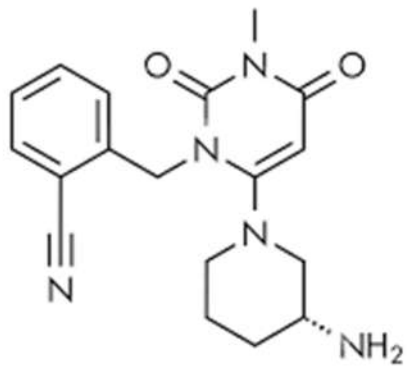
- Dapaglifiotin
- Empagliflozin

Gliptins

→ Gliptins, is a DPP-4 inhibitors that is a recently introduced class of oral drugs intended for the treatment of type 2 diabetes.

→ It block the metabolism by the DPP-4 enzyme of incretin hormones, including GLP-1 and glucose dependent insulinotropic polypeptide (GIP), which are secreted by the intestine in response to food.

Chemical Structure



Mechanism of A

➢ DPP-4 inhibitors work by blocking the action of DPP-4, an enzyme which destroys the hormone incretin. Incretins help the body produce more insulin only when it is needed and reduce the amount of glucose being produced by the liver when it is not needed.

Uses

- Gliptins, i.e., DPP-4 inhibitors are a group of medications which is used in the treatment of type 2 diabetes.

Stability and Storage Condition

- Medicines may get damaged in direct contact with heat, air and light.
- The medicine should be kept in a safe place and out of children's reach.
- Mainly the drug should be kept at room temperature.

Type of Formulation

1. Tablets

Popular Brand Names

- Januvia (Sitagliptin)
- Galvus (Vildagliptin)
- Onglyza (Saxagliptin)
- Tradjenta

Chapter 10

Analgestic and Anti-Inflammatory Agents

Topics
Analgestic and Anti-Inflammatory Agents
Morphine Analogues
Narcotic Antagonists
NON-STEROIDAL ANTI INFLAMMATORY AGENTS (NSAIDS)
• Aspirin, * • Diclofenac • Ibuprofen, * • Piroxicam • Celecoxib, • Mefenamic acid, • Paracetamol, * and • Aceclofenac

Morphine Analogues

→ Morphine analogues are closely related to morphine structure and are even synthesised from it. They may be agonists [eg.. morphine, dimorphine (heroin) and codcine], partial agonists (e.g. nalorphine and levorphan). or antagonists (e.g., naloxone).

1. Morphine: It is a psychoactive opiate analgesic drug. It is regarded as the archetypal opioid. It is the gold standard of analgesics in clinical practice, and it is used to relieve severe pain and suffering.
2. Codeine: It has lower analgesic potency thun morphine. Within the body, it is partially metabolised to morphine. Codeine has a central effect.
3. Diamorphine: It is an opioid analgesic used to treat severe pain caused by surgical procedures, myocardial infarction, or agony in the terminally ill, as well as dyspnea caused by acute pulmonary, edoema.

Narcotic Antagonists

→ When taken alone, narcotic antagonists have little effect, but they prevent the effects of opiates.

→ Naloxone: It was the first pure opioid antagonist and having affinity for all three opioid receptors. It is most commonly used to treat respiratory depression induced by opiate overdose.

NON-STEROIDAL ANTI INFLAMMATORY AGENTS (NSAIDS)

→ NSAIDs are used to treat inflammation, mild to moderate discomfort and fever, Headaches, arthritis, sports injuries, and menstrual cramps are among the conditions for which it is used.

→ In high-risk people, aspirin is used to reduce blood clotting, and prevent strokes and heart attacks.

→ NSAIDs are also found in a variety of cold and allergy medications.

→ The use of NSAIDs is linked to a variety of negative effects.

Classification

1) Non-Selective COX Inhibitors (Conventional NSAID)

I. Salicylates: (Aspirin) Diflunisal Salsalate, Sodium Salicylate (Salol) Salicylamide, Benorilate, Choline salicylate.
II. ii) Pyrazolone Derivatives: Phenylbutazone,Oxyphenbutazone.
III. iii) Indole Derivatives: Indomethacin, Sulindac,
IV. iv) Propionic Acid Derivatives: Tbuprofen. Naproxen, Ketoprofen, Flurbiprofen
V. V) Anthranilic Acid Derivatives: Mephenamic acid.

2) Preferential COX-2 Inhibitors : Nimesulide, Meloxicam, Nabumetone.

3) Selective COX-2 Inhibitors : Celecoxib, Rofecoxib, Valdecoxib.)

Examples

1. Aspirin, *
2. Diclofenac
3. Ibuprofen, *
4. Piroxicam
5. Celecoxib,
6. Mefenamic acid,
7. Paracetamol, *and
8. Aceclofenac

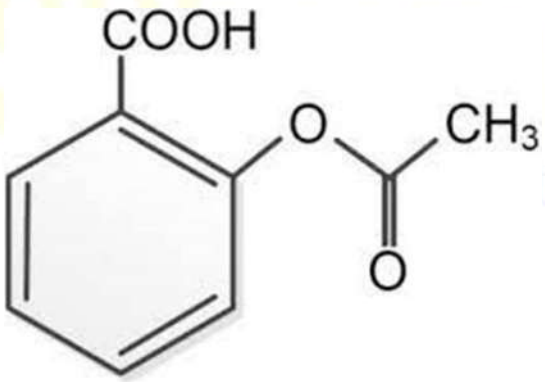
Aspirin *

→ Aspirin is made by acetylating salicylic acid with acetic anhydride.

→ The crude product can be recrystallised using benzene, an acetic acid-water (1:1) mixture, or other non-aqueous solvents. Chemically, it is 2-acetoxy benzoic acid.

Chemical Name and Structure

Aspirin



Mechanism of Action

- Aspirin's effects and respective mechanisms of action vary with dose: Low doses (typically 75 to 81 mg/day) are sufficient to irreversibly acetylate serine 530 of cyclooxygenase (COX)-1. This effect inhibits platelet generation of thromboxane A2, resulting in an antithrombotic effect

Uses

- Aspirin is used to treat fevers and mild to moderate discomfort associated with muscle aches, toothaches, the common cold, and headaches. It can also be used to treat pain and swelling associated with arthritis.

Stability and Storage Conditions

- It should be kept at room temperature, between 20" and 25 C (68" and 77 F), in a well-sealed container away from moisture.

Type of Formulation

1. Tablet

Popular Brand Names

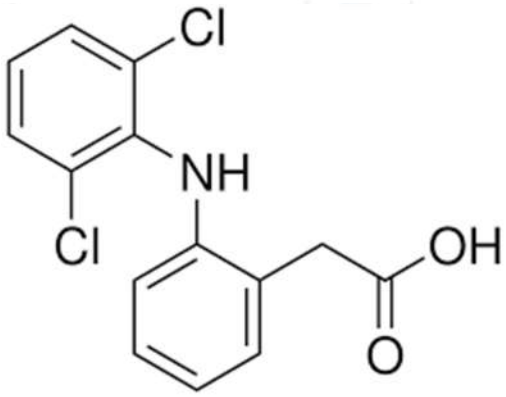
- Arthritis Pain,
- Aspi-Cor, Aspir-Low,
- Bufferin, Ecotrin,
- Miniprin, Aspir, Bayer Plus, Durlaza

Diclofenac

→ Diclofenac is an analgesic and antipyretic acetic acid NSAID medication.

→ It is helpful in treating pain, ocular inflammation, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and actinic dysmenorrhea, ocular keratosis.

Chemical Structure



Mechanism of Action

- As with all NSAIDs, diclofenac exerts its action via inhibition of prostaglandin synthesis by inhibiting cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) with relative equipotency.

USES

- Diclofenac is a commonly used NSAID for
- Rheumatoid and osteoarthritis
- Burnsitis

- Ankylosing spondylitis
- Dysmenorrheal
- Post-trnuitmatic inflammatory conditions
- Post-operative inflammatory conditions

Stability and Storage Conditions

- This suspension should be stored at room temperature.

Types of Formulations

1. Capsule
2. Powder
3. Tablet

Popular Brand Names

- Cambia
- Voltaren
- Zipsor
- Canflam
- Voltaren-XR
- Zarvolex

Ibuprofen *

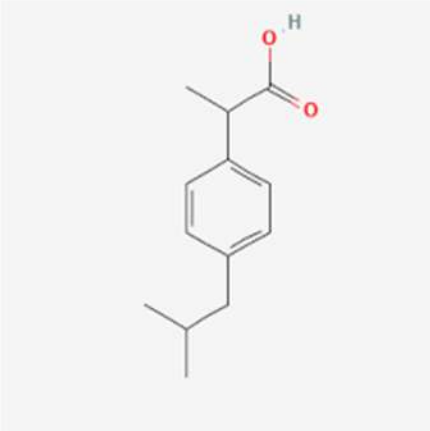
→ Ibuprofen, sometimes known as brufen, is a non steroidal anti-inflammatory medication (NSAID).

→ It is used to treat arthritis, primary dysmenorrtica, fever, and as an analgesic, especially in cases of inflammation When compared to aspirin or other well-known antiplatelet medicines, its antiplatelet impact is moderate and short-lived.

→ Ibuprofen has also been proven to be a broad vasodilator.

Chemical Name and Structure

(RS)-2-(4-2-Methylpropy)phenyl)propanoic acid,



Mechanism of Action

- The main mechanism of action of ibuprofen is the non-selective, reversible inhibition of the cyclooxygenase enzymes COX-1 and COX-2

Uses

- It is used to treat rheumatoid arthritis, juvenile theumatoid arthritis, and osteoarthritis symptoms.
- It can be used to treat mild to severe pain as well as control dysmenorrhea
- It can be used as anti-pyretic
- It has been used to treat antikylosing spondylitis, goat. and psoriatic arthritis.
- It may help in reducing pericarditis discomfort, fever, and inflammation.

Stability and Storage Conditions

- It should be kept away from light, moisture and bathroom. It should be stored at room temperature in a dry place away from the light.

Types of Formulations

1. Tablet
2. Suspension
3. Capsule

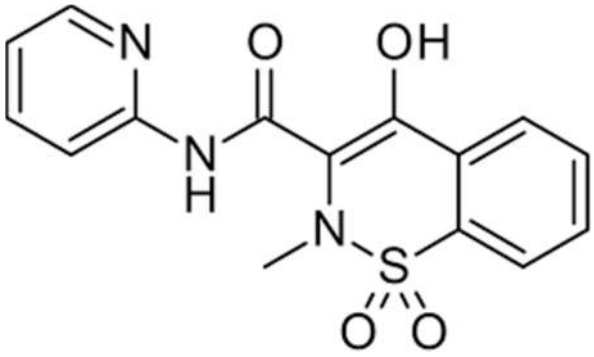
Popular Brand Names

- Advil
- Motrin
- Mourin IB
- IBU

Piroxicam

→ Piroxicam is a NSAID that is used to treat the indication of osteoarthritis and rheumatoid arthritis.

Chemical Structure



Mechanism of Action.

➢ Piroxicam is a potent inhibitor of prostaglandin (PG) synthesis in vitro. Piroxicam concentrations reached during therapy have produced in vivo effects. Prostaglandins sensitize afferent nerves and potentiate the action of bradykinin in inducing pain in animal models.

Uses

- Its used to treat osteoarthritis and rheumatoid arthritis pain and inflammation.

Stability and Storage Conditions

- The drug should be stored at a temperature not more than 25°C and should be kept in a tightly closed tube.

Type of Formulation

1. Capsules

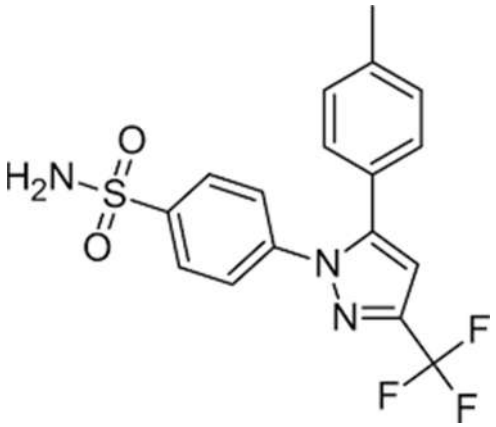
Popular Brand Name

♦ Feldene

Celecoxib

→ Celecoxib is a sulphonamide NSAID and selective COX-2 Inhibitor used to treat osteoarthritis, rheumatoid arthritis, acute pain, painful menstruation and menstrual symptoms, and to reduce the number of polyps in the colon and rectum in patients with familial adenomatous polyposis

Chemical Structure



Mechanism of Action

- The mechanism of action of celecoxib is due to selective inhibition of cyclooxygenase-2 (COX-2), which is responsible for prostaglandin synthesis, an integral part of the pain and inflammation pathway. [4] This pharmacologic activity gives celecoxib its analgesic, anti-inflammatory, and antipyretic effects.

Uses

- It is used to relief of the signs and symptoms of Osteoarthritis and rheumatoid arthritis in adults.
- It is also been allowed to help people with familial adenomatous polyposis reduce the number of polyps in their intestines.
- It is also used in:
- Acute pain and primary dysmenorrhoea,
- Osteoarthritis,
- Rheumatoid arthritis,
- Ankylosing spondylitis,
- Juvenile idiopathic arthritis, and
- Acute pain and dysmenorrhoea.)

Stability and Storage Conditions

- Store at room temperature between 20°C and 25°C

Type of Formulation

1. Capsule

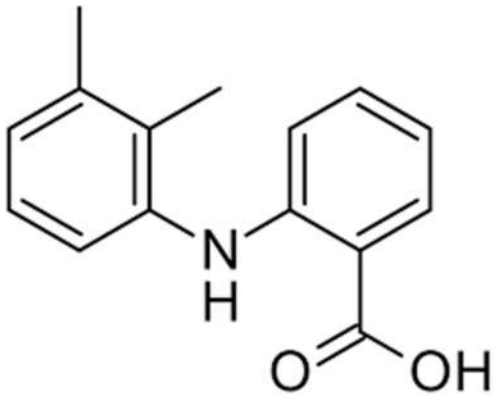
Popular Brand Names

- Celebrex
- Elyxyb

Mefenamic Acid

→ It is a derivative of anthranillic acid, 2-(2,3. dimethylphenyl) aminobenzoic acid is its chemical name.

Chemical Structure



Mechanism of Action

- It binds to the COX-1 and COX-2 prostaglandin synthetase receptors, decreasing prostaglandin synthetase activity.

Uses

- It is used to relieve mild to moderate pain caused by a variety of disorders in the short term.
- It can also be used to reduce menstruation pain and blood loss.
- It is a nonsteroidal anti-inflammatory medication (NSAID).

Stability and Storage Conditions

- It should be stored between 68°F and 77°F (20°C and 25°C) at room temperature. It should not be kept in a moist or damp environment, such as a bathroom,

Types of Formulations

1. Capsules
2. Tablets

Popular Brand Names

- Ponstel
- Mefenamic

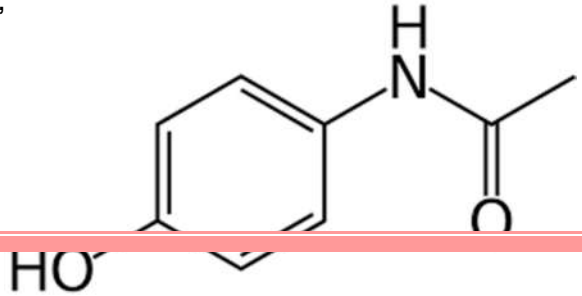
Paracetamol *

→ It exhibits analgesic and antipyretic properties similar to acetanilide, in addition to the same toxicities; however, these toxicities occur less often and are milder than those seen in other derivatives.

→ As a result, it is said to be safer for use. It has analgesic properties similar to aspirin except the anti-inflammatory properties.

Chemical Name and Structure

N-(4-hydroxyphenyl)acetamide,



Mechanism of Action

- Paracetamol has a central analgesic effect that is mediated through activation of descending serotonergic pathways. Debate exists about its primary site of action, which may be inhibition of prostaglandin (PG) synthesis or through an active metabolite influencing cannabinoid receptors.

Uses

- It is an over-the-counter analgesic and antipyretic used extensively.
- It is a traditional remedy for headaches and other mild aches and pains, and a key element in many cold and flu cures.
- It can be used in combination with opioid analgesics to treat more severe pain, like post-surgical pain and palliative care in advanced cancer patients.
- Stability and Storage Conditions
- When the temperature is mised from 25 to 45°C.) paracetamol tablets exhibit an increase in disintegration tine ranging from 9.1 to 65.5% (200 mg tablets) und 1.2 to 1.50.0 % (500mg tablets) (75 % RHD.

Stability and Storage Conditions

- It should be stored between 68°F and 77°F (20°C and 25°C) at room temperature. It should not be kept in a moist or damp environment, such as a bathroom,

Type of Formulation

1. Tablets

Popular Brand Names

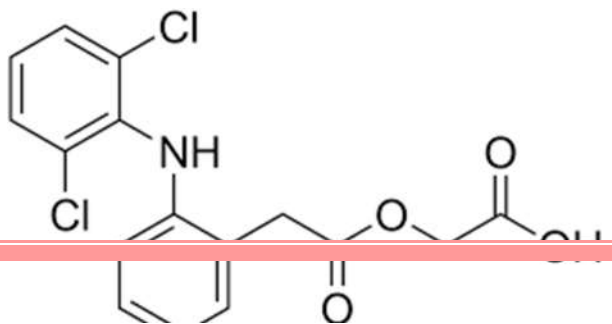
- Tylenol
- Calpol
- Excedrin
- Panadol

Aceclofenac

→ Aceclofenac is an anti-inflammatory, analgesic and con-steroidal anti-inflammatory medication used to treat osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis.

Chemical Name and Structure

2-[(2-{2-[(2.6 dichlorophenyl)amino]phenyl}acetyl)oxylacetic acid



Mechanism of Action

- The mode of action of aceclofenac is largely based on the inhibition to prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins. After oral administration, aceclofenac is rapidly and completely absorbed as unchanged drug.

Uses

- It is an anti-inflammatory drug that is used to treat pain. Therefore it is used in rheumatoid arthritis, ankylosing spondylitis, and osteoarthritis to reduce pain and inflammation. 1
- It is an NSAID (Non-Steroidal Anti-Inflammatory Drug). Stability and Storage Conditions
- Stability and Storage Conditions
- It should be stored in a cool and dry place in an airtight container. It should be kept away from the sunlight and children's reach and sight.

Stability and Storage Conditions

- It should be stored between 68°F and 77°F (20°C and 25°C) at room temperature. It should not be kept in a moist or damp environment, such as a bathroom,

Type of Formulation

1. Tablets

Popular Brand Names

- Abate
- Aclonac-SR
- Abdal
- Acec

Chapter 11

ANTI-INFECTIVE AGENTS

Topics

ANTIFUNGAL AGENTS

- Amphotericin B,
- Griscofulvin.
- Miconazole,
- Ketoconazole, *
- Itraconazole,
- Fluconazole, * and

- Naftifine hydrochloride.

URINARY TRACT ANTI INFECTIVE AGENTS

- Norfloxacin,
- Ciprofloxacin,
- Ofloxacin, *
- Moxifloxacin.

ANTI – TUBERCULAR AGENTS

- INH (Isoninzid), *
- Ethambutol,
- Para- amino salicylic acid,
- Pyrazinamide,
- Rifampicin,
- Bedaquiline,
- Delamanid, and
- Pretomanid. *

ANTIVIRAL AGENTS

- Amantadine hydrochloride,
- Idoxuridine,
- Acyclovir, *
- Zidovudine,
- Ribavirin,
- Favipiravir,

ANTIMALARIALS

- Quinine sulphate,
- Chloroquine phosphate, *
- Primaquine phosphate,
- Mefloquine, *
- Cycloguanil,
- Artemisinin
- Pyrimethamine,

SULFONAMIDES

- Sulfanilamide,
- Sulfadiazine
- Sulfamethoxazole,
- Sulfacetamide, *
- Mafenide acetate,
- Dapsone, *
- Cotrimoxazole,

ANTIFUNGAL AGENTS

→ Fungi are neither plants nor animals, and are classified as their own kingdom.
→ Fungi grow either as yeasts (single round cells) or as molds (many cells forming long, thin threads called hyphae.
→ Some fungi even go through both the forms during their life cycle.
→ Many fungi, including bread molds and mushrooms, can be seen with the naked eye.
→ Fungal infections are often caused by fungi present in the environment.
→ Most fungi are not dangerous, but some of them can be harmful Fungal spores are present in the air or in soil, thus fungal infections begin mostly in the lungs or on the skin.
→ These infections progress slowly and are not serious, unless they weaken the immune system.
→ Antifungal agents used to treat fungal infections are either applied topically on the infected site or are taken orally or injected in case the infection is serious.

Classification

The antifungal drugs are classified as follows:

1) Antibiotics

i) Polyenes : Amphotericin B (AMB), Nystatin. Hamycin, and Natamycin (Pinaricin).

ii) Heterocyclic Benzofuran : Griseofulvin.

2) Antimetabolite: Flucytosine (5-FC).

3) Azoles

Imidazoles (Topical): Clotrimazole, Econazole, and Miconazole. (Systemic): Ketoconazole.

Triazoles (Systemic): Fluconazole and Itraconazole.

4)Allylaminer : Terbinafine.

5) Other Topical Agents : Tolnaftate, Undecylenic acid, Benzoic acid, Quiniodochlor, Ciclopirox olamine, and Sodium thiosulfate.

Examples

The following drugs are studied in detail:

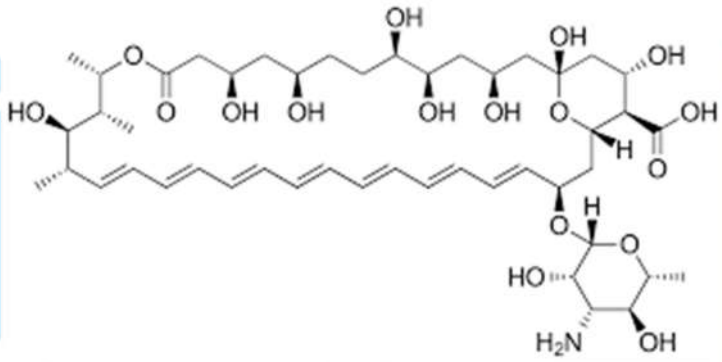
- Amphotericin B,
- Griscofulvin.
- Miconazole,
- Ketoconazole, *
- Itraconazole,

- Fluconazole, * and
- Naftifine hydrochloride.

Amphotericin B

→ Amphotericin B injection is used to treat serious and potentially life-threatening fungal infections. Amphotericin B injection is in a class of medications called antifungals. It works by slowing the growth of fungi that cause infection.

Chemical Structure



Mechanism of Action

➢ Amphotericin B binds to ergosterol in the fungal cell membrane, which leads to the formation of pores, ion leakage and ultimately fungal cell death.

Uses

- It is used for treating many serious fungal Infections.
- It is useful in severe mycotic infections such as candidiasis, blastomycosis, aspergillosis, coccidioidomycosis, phycomycosis (algae like fungi),) sporotrichosis and
- It is used for treating mucocutaneous and cutaneous leishmaniasis and candidiasis, primary amoebic meningoencephalitis, and Cryptococcal meningitis in combination with flucytosine.
- It is also used for suppressing oral or intestinal candidiasis.

Stability and Storage Conditions

- Amphotericin B should be stored in the refrigerator and protected against exposure to light before rehabilitation.
- The rehabilitated solution should be stored in the dark at room temperature for 24 hours or at refrigerator

Type of Formulation

1. Powder for injections

Popular Brand Names

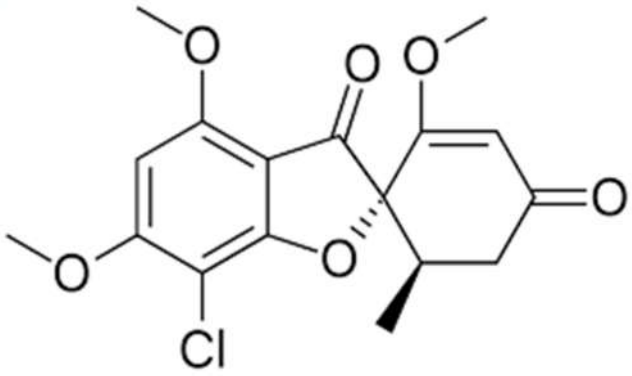
- Abelcet, Amphoted
- Ambisome, Fungizone

Griseofulvin

→ Griseofulvin is an antifungal agent used for treating infections related to skin, nails, scalp, feet, groin, and other body parts.

→ Mostly it is used for treating infections occurring from tinea strains of fungi.

Chemical Structure



Mechanism of Action

➢ Griseofulvin is fungistatic, however the exact mechanism by which it inhibits the growth of dermatophytes is not clear. It is thought to inhibit fungal cell mitosis and nuclear acid synthesis. It also binds to and interferes with the function of spindle and cytoplasmic microtubules by binding to alpha and beta tubulin.

Uses

- Griseofulvin used for treating infections hair, skin, and ie, tinea corporis, tinea pedis, tinea barbae, tinea cruris, cradle conditions caused by Microsporum or Trichophyton fungi.

Stability and Storage Conditions

- It should stored room temperature.
- All medicines should be kept away from children and Medications should not be flushed down toilet or poured into drains unless instructed to do

Types Formulations

1) Tablet
2) Suspension

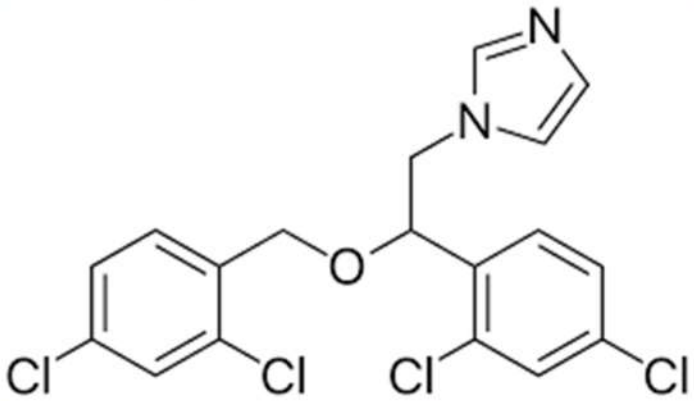
Popular Brand Names

- Grifulvin
- Griseofulicin
- Gris-PEG
- Griseofulvic

Miconazole

→ Miconazole is imidazole antifungal agent that used topically and intravenous infusion

Chemical Structure



Mechanism of Action

➢ Miconazole inhibits the synthesis of ergosterol, a major component of fungal cell membranes. This interferes with the barrier function of the membrane and with membrane-bound enzymes.

Uses

- Topical miconazole is used to treat tinea corporis(ringworm; fungal skin infection that causes a red scaly rash on different parts of the body), tinea cruris (jock itch; fungal infection of the skin in the groin or buttocks), and tinea pedis (athlete's foot; fungal infection of the skin on the feet and between the toes

Stability and Storage Conditions

- Miconazole tablets should stored room temperature 68°F 77°F (20°C 25°C).

Types of Formulations

1. Tincture
2. Spray
3. Tablet
4. Cream
5. Gel/jelly
6. Ointment

Popular Brand Names

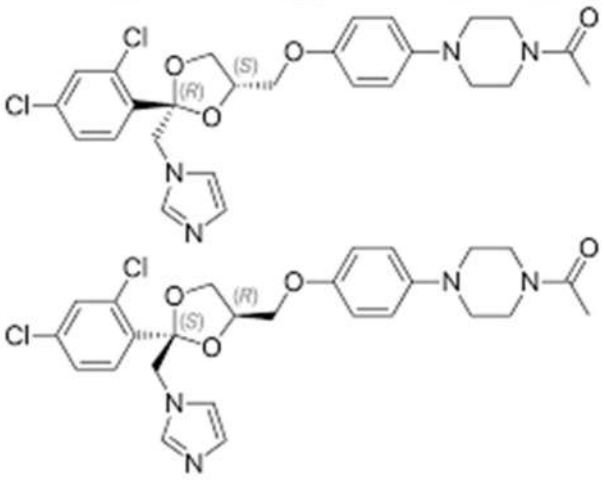
- Oravig
- Aloe Vesta Antifungal
- Baza Antifungal
- Carrington Antifunga

Ketoconazole *

→ Ketoconazole is a broad spectrum antifungal agent that is used in high doses for long periods in immune suppressed patients. It is a racemade comprising of equimolar amounts of (2R4S) und (2S4R) ketoconazole with the chiral centers on acetal ring.

Chemical Name and Structure

1-[4-[4-[2-(2,4-dichlorophenyl)-2 (imidazol-1-ylmethyl); 1,3-dioxolan-4-yl]methoxy]phenyl]piperazin-1-yl]ethanone



Mechanism of Action

➢ Ketoconazole blocks the synthesis of ergosterol, a key component of the fungal cell membrane, through the inhibition of cytochrome P-450 dependent enzyme lanosterol 14α-demethylase responsible for the conversion of lanosterol to ergosterol in the fungal cell membrane.

Uses

- Ketoconazole in used in a wide range of systemic fungal infections, like candidiasis, chronic mucocutaneous Candidiasis, oral thrush, candiduria, blastomycosis, coccidioidomycosis, histoplasmosis, chromomycosis, and paracoccidioidomycosis

Stability and Storage Conditions

- Ketoconazole topical cream should not be stored at a temperature less than 25°C

Types of Formulations

1. Shampoo Foam
2. Cream
3. Gel

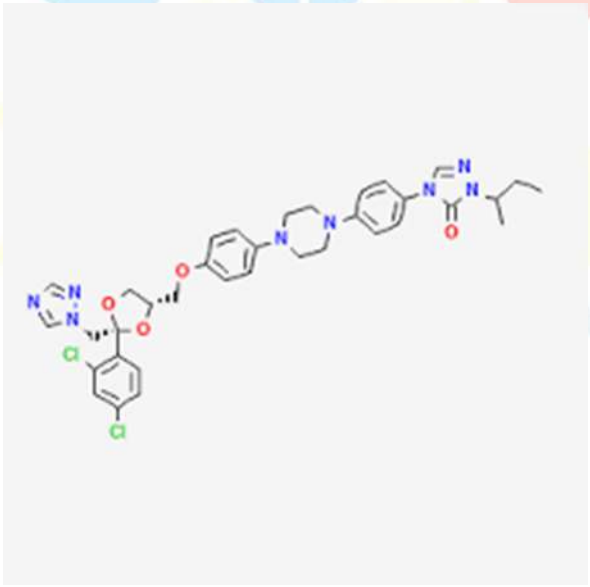
Popular Brand Names

- Extina
- Kuric
- Nizoral

Itraconazole

→ Itraconazole is used to treat a variety of fungal infections. It belongs to a class of drugs known as azole antifungals.

Chemical Structure



Mechanism of Action

➢ The drug is metabolized extensively via the CYP450 system; specifically, itraconazole is a CYP3A4 substrate. It has a half-life of 34 to 42 hours. The drug is excreted in the urine (35%) feces (between 3 and 18%)

Uses

- Fluconazole is used for the treatment and prophylaxis of fungal infections when other antifungals have failed or are not tolerated due to adverse effects, including candidiasis caused by susceptible strains of Candida, tinea corporis, tinea cruris or tines [pedia, anychomycosis, and cryptococcal meningitis.

Stability and Storage Conditions

- Reconstituted fluconazole oral suspension remain stable in both the products, ie, original plastic bottles and in amber polyethylene oral syringes for at least 70 days when stored at 22-25 degrees C

Types of Formulations

1. Capsule
2. Oral suspension

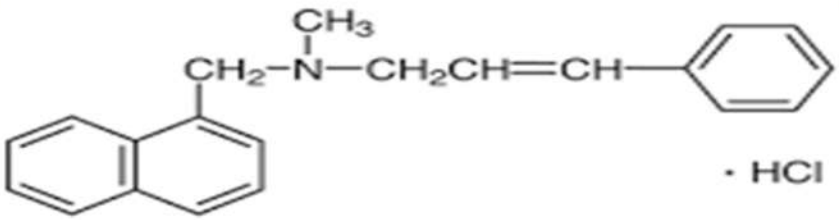
Popular Brand Names

- Diflucan
- Fluconeo
- Fluconazole Omega

Naftifine Hydrochloride

→ Naftifine is a synthetic, broad spectrum, antifungal and allylamine derivative that is used topically in tinea pedis, tinea cruris, and tinea corporis caused by Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum.

Chemical Structure



Mechanism of Action

➢ Naftifine exerts its antifungal effect by selective inhibition of the enzyme squalene 2,3-epoxidase, a key enzyme in ergosterol biosynthesis in fungi. Typically, squalene is transformed into ergosterol in the fungus.

Uses

- Naftifine is used topically for the treatment of tinea pedis, tinea cruris, and tinea corporis caused by Trichophyton nubrum, Trichophyton mentagrophytes Trichophyton fonsurans and Epidermophyton floccosum.

Stability and Storage Conditions

- This medicine should be stored in a closed container at room temperature and kept away from heat, moisture and direct light. It should not be frozen. It should be kept out of reach of children. Outdated medicine or medicine which is no longer needed should not be kept.

Types of Formulations

1. Capsule
2. Solution

Popular Brand Names

- Onmel
- Sporanox

URINARY TRACT ANTI INFECTIVE AGENTS

→ Urinary tract infections are among most common bacterial infections of human.

→ These infections range from asymptomatic bacteriuria on one hand to acute pyelonephritis and [gram-negative septicaemia (only in men) on the other hand.

→ Females are mostly at risk of developing UTIs because of their short urethra, and certain behavioural factors which include delay in micturition, sexual activity, and the use of diaphragms and spermicides.

→ A symptomatic bacterial infection of the urinary tract is termed Urinary Tract Infection (UTT).

→ It includes a lower urinary tract infection, eg. cystitis (symptomatic infection of bladder), urethritis (infection in (urethra), prostatitis (infection in prostate gland), or an upper urinary tract infection, eg, pyelonephritis (symptomatic infection of kidney).

→ In UTIs, many drugs are used for killing or inhibiting the growth of pathogenic organisms in the urinary tract.

→ These agents are retained in the renal tubules.

→ They are effective antiseptics due to their localised actions in the urinary bladder, ureters, and kidneys.

→ Some important urinary antiseptics include mandelic acid, methenamine mandelate, nitrofurantoin, nalidixic acid, and hexylresorcinol.

Examples

The following drugs are studied in detail:

- Norfloxacin,
- Ciprofloxacin,
- Ofloxacin, *

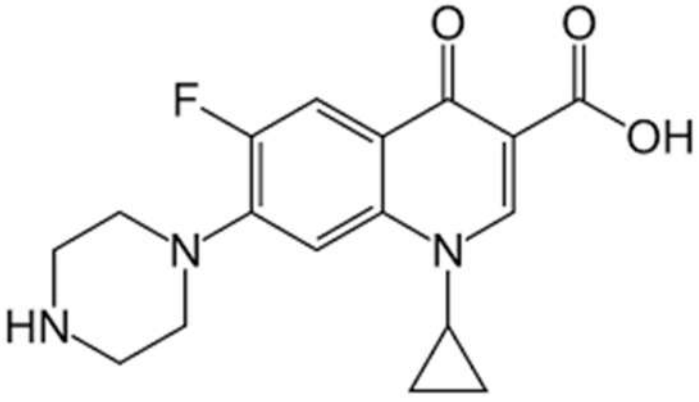
- Moxifloxacin.

Ciprofloxacin

→ Ciprofloxacin is a synthetic chemotherapeutic antibiotic of fluoroquinolone class. It is a second generation fluoroquinolone antibacterial.

→ It is a bactericidal and interferes with the enzymes that cause DNA to rewind after being copied, thus blocks DNA and protein synthesis

Chemical Structure



Mechanism of Action

- Ciprofloxacin acts on bacterial topsomerase II (DNA gyrane) und topoisomeruse IV.
- Ciprofloxacin's targeting of the alpha subunits of DNA gyrase prevents it from supercoiling the bacterial DNA that prevents DNA replication

Uses

- Ciprofloxacin is used to treat infections of bones and joints, endocarditis, gastroenteritis, malignant cutis externa, respiratory tract infections, cellulitis, and urinary tract infections

- It has an important role in treatment guidelines issued by major medical societies for the treatment of serious infections caused by gram-negative bacteria. including Pseudomonas aeruginosa.

Stability and Storage Conditions

- Ciprofloxacin tablets should be stored at room temperature

Types of Formulations

1. Tablet
2. Suspension
3. Suoluyion

Popular Brand Names

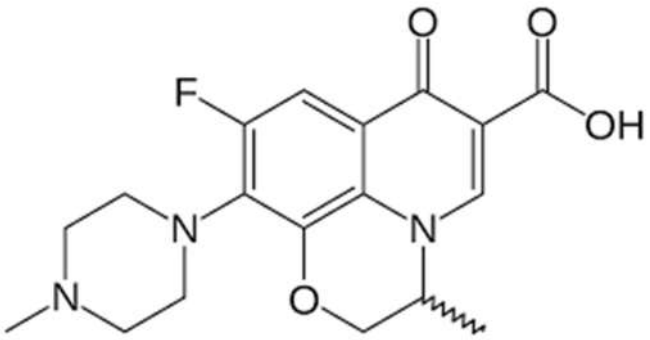
- Cipro
- Cipro XR
- ProQuin XR

Ofloxacin *

→ Ofloxacin is a synthetic chemotherapeutic antibiotic of fluoroquinolone class. It is a second generation fluoroquinolone

Chemical Name and Structure

(RS)-7-fluoro-2-methyl-6-(4-methylpiperazin-1-yl)-10-oxo-4-oxa-1-azatricyclo[7.3.1.05,13]trideca-5(13),6,8,11-tetraene-11-carboxylic acid.



Mechanism of Action

➢ Ofloxacin acts on DNA gyrase and topoisomerase IV. enzymes, which (like human topoisomerase) prevents

Uses

- infections skin, urinary bladder, urinary tract, reproductive organs, and gland.
- It is used to treat various bacterial infections

Stability and Storage Conditions

- should be stored room 77°F (15°C-25°C) and kept away from and moisture

Types of Formulations

1. Tablets

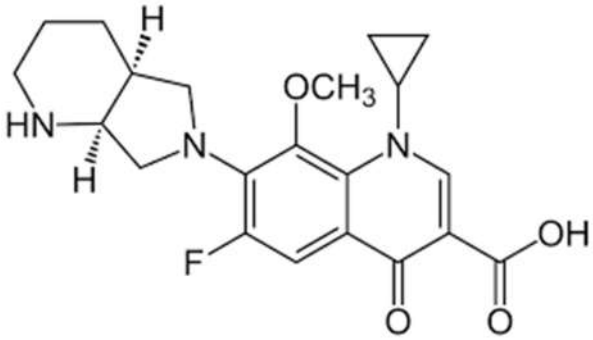
Popular Brand Names

- Floxin
- Floxin IV

Moxifloxacin

→ Moxifloxacin synthetic developed by Bayer marketed in hydrochloride form oral treatment.

Chemical Structure



Mechanism Action

➢ Moxifloxacin is a bactericidal, concentration dependent, anti-infective. It interferes with bacterial survival by binding to DNA gyrase (topoisomerase II) and topoisomerase IV, essential

bacterial enzymes involved in the replication, translation, repair and recombination of deoxyribonucleic acid.

Uses

- Moxifloxacin is used to treat certain infections caused by bacteria such as pneumonia, and skin, and abdominal (stomach area) infections. Moxifloxacin is also used to prevent and treat plague (a serious infection that may be spread on purpose as part of a bioterror attack.

Stability and storage conditions

- It should be stored 2°C-25°C.

Type Formulation

1. Solution

Popular Brand Name

- Moxeza
- Vigamus

ANTI – TUBERCULAR AGENTS

→ Taberculosis (TB) is an infective diseases most commonly affecting the lungs, and caused by Mycobacterium tuberculosis and Mycobacterium bovis.

→ Since TB is an it spreads via air in the form of small droplets Patients infected with pulmonary TB or laryngeal TB may the infection by sneezing, coughing, singing, or even while talking.

→ The infective droplets, once released into the air in there for a few hours due to their very small size.

→ Tuberculosis can be treated in a long-term, i.e.. 8 months to 3 years

→ Tuberculosis infection can be cured it proper treatment is given within time. Non tuberculosis mycobacterial infections are known as M. arium complex (MAC) as they are caused by M. alam, M. kansali, M. murinum, and M. scrofulaceum. These organisms are resistant the commonly used anti-tuberculosis drugs; thus along with the standard Jugh some newer agents like fluoroquinolones. amikacin clarithromycin, azithromycin, or rifabutin are used.

Classification

Anti-tubercular drugs are classified as follows:

1) First Line Drugs

Isoniazid (H), Rifampin (R), Exhambutol (E), and Pyrazinamide(Z), Streptomycin (S).

2) Second Line Drugs

Thiacetuzone (Tzn), Paru aminosalicylic acid (PAS), Ethionamide (Em), Cycloserine (Cys), Kanamycin (Kmc), Amikacin (Am), and Capreomycin (Cpr).

3) Newer Drugs

Ciprofloxacin, Clarithromycin, Ofloxacin, Azithromycin, and Rifabutin

Examples

The following drugs are studied detail:

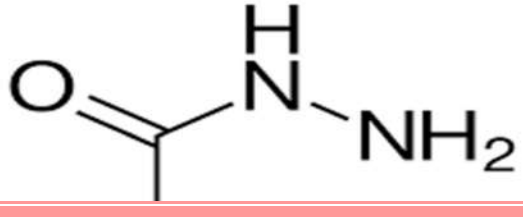
- INH (Isoninzid), *
- Ethambutol,
- Para- amino salicylic acid,
- Pyrazinamide,
- Rifampicin,
- Bedaquiline,
- Delamanid, and
- Pretomanid. *

Isoniazid *

→ Isoniazid (or isonicotinylhydrazine, INH) an organic compound used the first line drug for preventing and treating tuberculosis.

Chemical Name and Structure

Pyridine-4-carbohydrazide



Mechanism of Action

- The antimicrobial activity of INH is selective for mycobacteria, likely due to its ability to inhibit mycolic acid synthesis, which interferes with cell wall synthesis, thereby producing a bactericidal effect

Uses

- It is used with other drugs in the treatment of active tuberculosis (TB) infection.

Stability Storage Conditions

- It should be stored in room temperature.

Types ofFormulations

1. Tablet
2. Solution

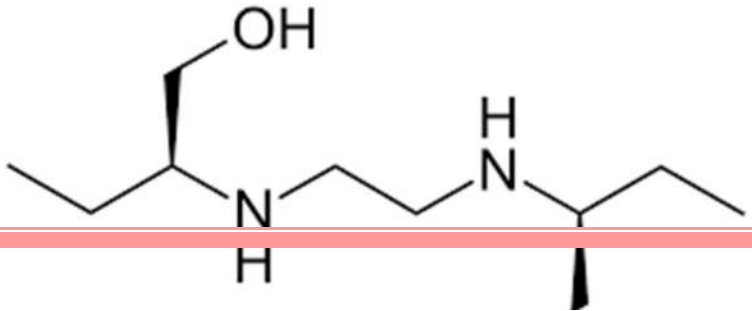
Popular Brand Names

- Nydrazid
- Pms-Isoniazid

Ethambutol

→ Ethambutol is used with other medications to treat tuberculosis (TB). Ethambutol is an antibiotic and works by stopping the growth of bacteria.

Chemical Structure



Mechanism Action

- The mechanism of action of ethambutol is not completely known. There is evidence that the drug exerts its bacteriostatic activity by virtue of inhibition of arabinosyl transferase, an enzyme that polymerizes arabinose into arabinan and then arabinogalactan, a mycobacterial cell wall constituent.

Uses

- It is used along with other drugs in the treatment of tuberculosis.
- It is also used treat MAC (Mycobacterium avium complex).

Stability and Storage Conditions

- Ethambutol should be stored at room temperature (below 25°C) in the original pack. It should be kept in PP bottle with PP child resistant closure. There should be pack sizes of 28 or 56 tablets.

Type of Formulation

1. Tablets

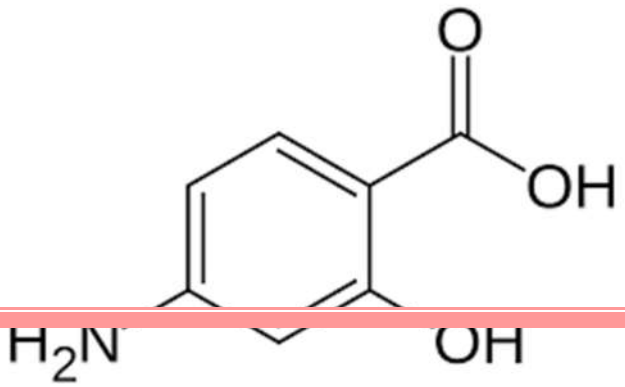
Popular Brand Names

- Etihi
- Myambiutol

Para-Amino Salicylic Acid (PAS)

→ PAS is an antibiotic which is being used since 1940s for treating inflammatory bowel diseases. It shows greater patency the treatment of ulcerative colitis and Crohn's disease

Chemical Structure



Mechanism of Action

- It inhibits the onset of bacterial resistance to streptomycin and isoniazid. The mechanism of action has been postulated to be inhibition of folic acid synthesis (but without potentiation with antifolic compounds) and/or inhibition of synthesis of the cell wall component, mycobactin, thus reducing iron uptake by M.

Uses

- After streptomycin, it was the second antibiotic that was effective in tuberculosis treatment. It was a part of the standard treatment for tuberculosis before rifampicin and pyrazinamide were introduced.

Stability and Storage Conditions

It should be stored below 59°F (15°C) in a refrigerator or freezer.

Type of Formulation

1. Tablets

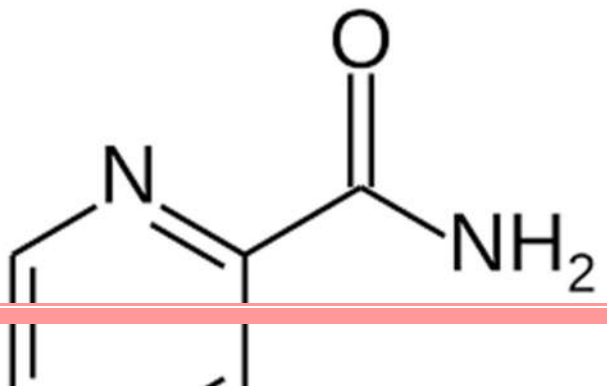
Popular Brand Names

- Granupas,
- Paser,

Pyrazinamide

→ Pyrazinamide is a synthetic pyrazinoic acid amide derivative having bactericidal properties. It is specifically active against slowly multiplying intracellular bacilli.

Chemical Structure



Mechanism of Action

- The parent compound enters the bacterium passively and is metabolized via pyrazinamidase (PZase) within the cytoplasm to pyrazinoic acid; pyrazinoic acid is the active form of the drug [4]. PZA and its analog, 5-chloro-PZA, may inhibit the fatty acid synthetase I enzyme of M. tuberculosis

Uses

- Pyrazinamide is used alone or along with other drugs for the treatment of the following diseases:
- It is used along with isoniazid and rifampicin for treating Mycobacterium tuberculosis.
- It is used along with rifampin for treating latent tuberculosis.
- It is a potent anti-uricosuric drug and is used for diagnosing the causes of hyperuricemia and hyperuricosuria.

Stability and Storage Conditions

- It should be stored in a well-closed container at controlled temperature between 15°C to 30°C (59°F to 86°F) I should be dispensed in a well-closed container with a child resistant container.

Types of Formulations

1. Tablets
2. Liquid

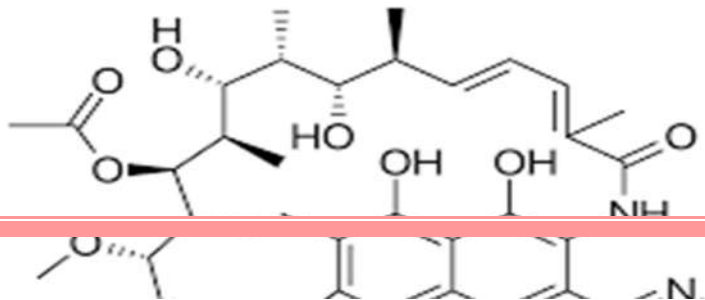
Popular Brand Name

- Zinamide

Rifampicin

→ Rifampicin is a semi-synthetic antibiotic derived from Streptomyces mediterranei. It has a broad antibacterial activity, and is also active against several Mycobacterium.

Chemical Structure



Mechanism of Action.

- Rifampicin inhibits the DNA-dependent RNA polymerase, and thus suppresses RNA synthesis and cause cell death.

Uses

- It is used to treat Mycobacterium infections, including tuberculosis and Hansen's disease.
- With multidrug therapy used as the standard treatment of Hansen's disease, it is used along with dapsone and clofazimine to avoid eliciting drug resistance.
- Along with fusidic acid, it is useful in Methicillin Resistant Staphylococcus aureus (MRSA)
- It shows some effectiveness against vaccinia virus.

Stability and Storage Conditions

- Rifampicin was found to be chemically stable in each suspension for 56 days at room temperature.

Types of Formulations

1. Capsules
2. Powders

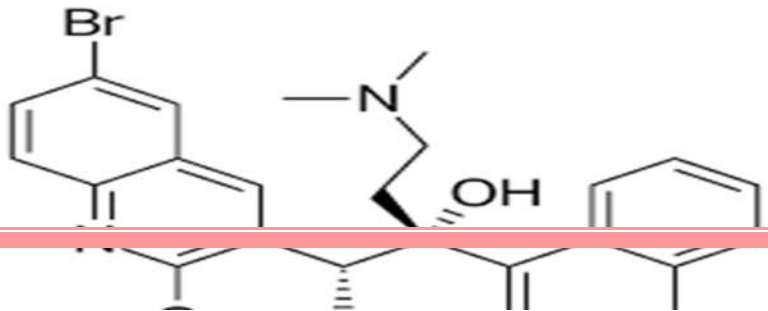
Popular Brand Names

- Rifadin
- Rimactane

Bedaquillne

→ Bedaquiline is a class of diarylquinoline antimycobacterial which is used in combination with other antibacterials for the treatment of pulmonary multidrug resistant tuberculosis (MDR-TB)

Chemical Structure



Mechanism of Action

- Bedaquiline (BDQ) inhibits ATP generation in Mycobacterium tuberculosis by interfering with the F-ATP synthase activity

Uses

- It is used alone or along with other drugs for the treatment of the following diseases:
- It is used for treating active multi drug-resistant tuberculosis (TB) of lungs in patient having limited treatment options.
- It acts by stopping the growth of bacteria which This antibiotic is used only for bacterial infections.
- It is not used for viral infections like common cold,flu

Stability and Storage Conditions

- It should be stored below 25°C. It should be stored at room temperature and kept away from light and moisture

Type of Formulation

1. Tablets

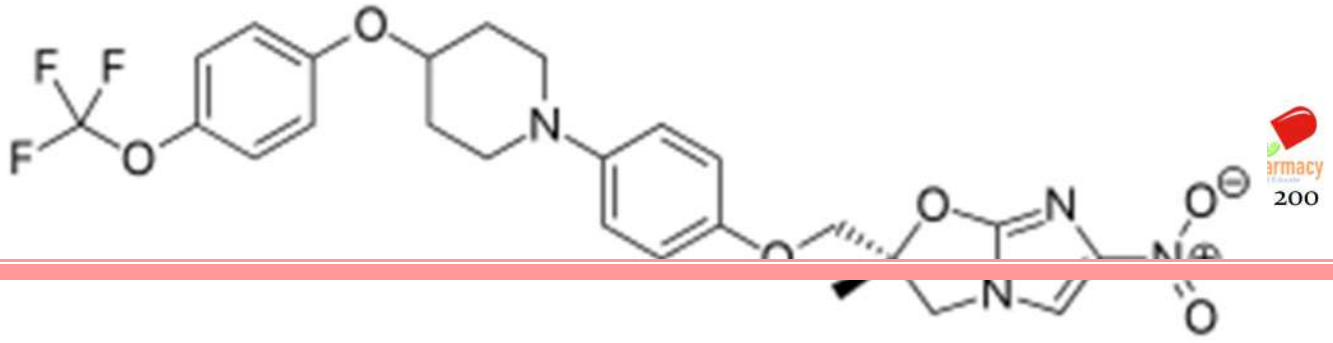
Popular Brand Name

- Sirturo

Delamanid

→ Delamanid is an antibiotic which is used in the treatment of resistant tuberculosis.

Chemical Structure



Mechanism of Action

- Delamanid is a dihydro-nitroimidazooxazole derivative. It acts by inhibiting the synthesis of mycobacterial cell wall components, methoxy mycolic acid and ketomycolic acid. Delamanid is a pro-drug which gets activated by the enzyme deazaflavin dependent nitroreductase

Uses

- It is used to treat tuberculosis.

Stability and Storage Conditions

- It should be stored in the original container at room temperature below 25 C. It should be kept away from excess heat, moisture and children.

Type of Formulation

1. Tablet

Popular Brand Name

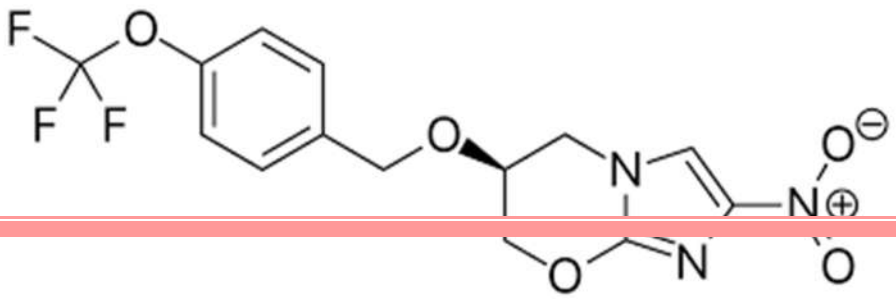
- Deltyba

Pretomanid *

→ Pretomanid is a part of three-drug regimen which is used widely in the treatment of drug-resistant and multidrug resistant pulmonary tuberculosis.

Chemical Name and Structure

(6S)-2-Nitro-6-{[4-(trifluoromethoxy)betury|]oxy}-6,7-dihydro-5H-imidazo[2,1-b][1,3]oxazine



Mechanism of Action

- Pretomanid inhibits cell wall biosynthesis via blockage of the oxidation of hydroxymycolate to ketomycolate. Under anaerobic conditions, pretomanid causes respiratory poisoning of the bacterial cell through the release of reactive nitrogen species.

Uses

- It is an antibiotic which is used in the treatment of multi-drug-resistant tuberculosis affecting the lungs.
- It is commonly used along with bedaquiline and linezolid and administered orally

Stability and Storage Conditions

- Pretomanid Tablets, bedaquiline, and linezolid should be stored at room temperature below 86°F (30°C).

Type of Formulation

1. Tablets

Popular Brand Name

- Dovprela

ANTIVIRAL AGENTS

→ Antiviral agents are used for treating viral infections.
→ Similar to antibiotics for bacteria, specific antivirals are effective against specific viruses.
→ Antiviral drugs, instead of destroying their target pathogen, inhibit their development.
→ Since antiviral drugs are harmless to the host, they can be used to treat infections.
→ They should be distinguished from viricides that are not medications but destroy virus particles outside the body.

→ The available antivirals are mostly designed to help against HIV, herpes viruses (that mainly causes cold sores and genital herpes; however, can cause various other diseases), hepatitis B and C viruses (that cause liver cancer), and influenza A and B viruses.

→ Since the viruses replicate within the host cells, it is difficult to find targets for the drug that would interfere with the virus without harming the host cells.

→ Due to this reason, designing safe and effective antiviral drugs is a difficult task.

Classification

Antiviral drugs are classified into the following classes on the basis of mechanism of action:

1) Anti-Herpes Virus: Idoxuridine Acyclovir, Pamciclovir, Ganciclovir, and Foscarmet.

2) Anti-Retrovirus

i) Nucleoside Reverse Transcriptase Inhibitors (NRTIs): Zidovudine (AZT), Didanosine, Zalcitabine, and Stavudine.

ii) Non- Nucleoside Reverse Transcriptase Inhibitors (NNRTis): Efavirens and Delavirdine.

Examples

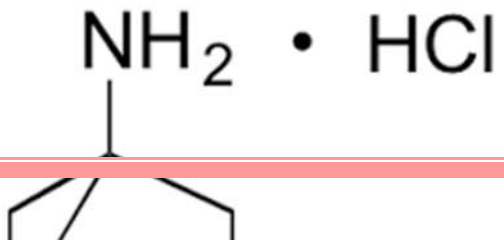
The following drugs

- Amantadine hydrochloride,
- Idoxuridine,
- Acyclovir, *
- Zidovudine,
- Ribavirin,
- Favipiravir,

Amantadine Hydrochloride

→ This medication is used to treat Parkinson's disease. It is also used to treat certain movement disorders caused by some drugs (extrapyramidal reactions).

Chemical Structure



Mechanism of Action

- Amantadine interferes with the release of infectious viral nucleic acid into the host cell through interaction with the transmembrane domain of the M2 protein of the virus. It also appears to prevent virus assembly during replication in some cases.

Uses

- Amantadine is an antidyskinetic medicine. It is used to treat Parkinson's disease (sometimes called "paralysis agitans" or "shaking palsy") and its symptoms, including dyskinesia (sudden uncontrolled movements). It may be given alone or in combination with other medicines (eg, levodopa) for Parkinson's disease.

Stability and Storage Condition

- It should be stored below 25°C. It should be stored at room temperature and kept away from light and moisture

Type of Formulation

1. Tablet
2. Capsule

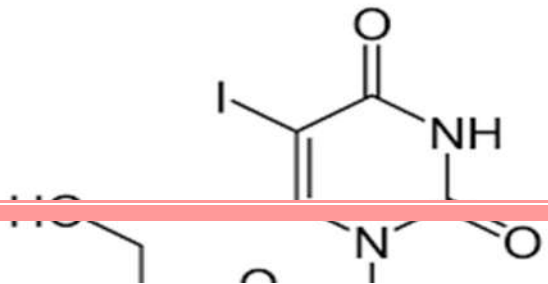
Popular Brand Names

- Parkitidin
- Comantrel

Idoxuridine

→ Idoxuridine is a pyrimidine analog antiviral used for the treatment of viral eye infections, including herpes simplex keratitis.

Chemical Structure



Mechanism of Action

- Idoxuridine acts as an antiviral agent by inhibiting viral replication by substituting itself for thymidine in viral DNA. This in turn inhibits thymidylate phosphorylase and viral DNA polymerases from properly functioning.

Uses

- Idoxuridine is used in keratoconjunctivitis and keratitis caused by herpes simplex virus.

Stability and Storage Conditions

- It should be kept in a well closed container and should be protected from light.

Type of Formulation

1. Solution

Popular Brand Names

- Dendrid
- Herplex

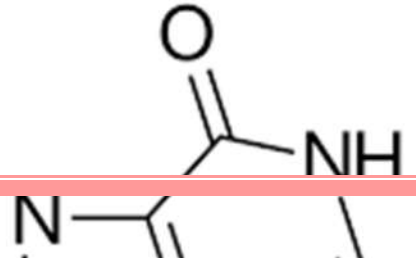
Acyclovir *

→ Acyclovir is a nucleotide analog antiviral that is used for treating infections like herpes simplex, herpes zoster, herpes labialis, and acute herpetic keratitis.

→ It is the first line drug to be used in the treatment of infections caused by these viruses.

Chemical Name and Structure

2-Amino-1,9-dihydro-9-((2-hydroxyethoxy)methyl)-3H-purin-6-one



Mechanism of Action

- Acyclovir triphosphate competitively inhibits viral DNA polymerase by acting as an analog to deoxyguanosine triphosphate (dGTP). Incorporation of acyclovir triphosphate into DNA results in chain termination since the absence of a 3' hydroxyl group prevents the attachment of additional nucleosides.

Uses

- Acyclovir cream with hydrocortisone is used in recurrent herpes labialis, and shortening lesion healing time in 6 years and older patients.
- Acyclovir ophthalmic ointment is used in acute herpetic keratitis.
- Acyclovir oral tablets, capsules, and suspensions are used in herpes zoster, genital herpes, and chickenpox.
- Acyclovir buccal tablet is used in recurrent herpes labialis.

Stability and Storage Conditions

- Acyclovir suspension should be stored at 59°F to 77°F (15°C to 25°C) and kept away from light.

Types of Formulations

1. Capsules
2. Tablets
3. Suspensions

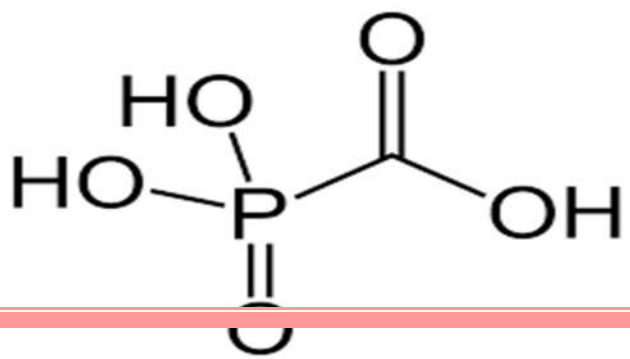
Popular Brand Name

- Zovirax

Foscarnet

→ Foscarnet is an antiviral drug which is used in the treatment of CMV,HIV and HSV infection.

Chemical Structure



Mechanism of Action

- Foscarnet is an analog of inorganic pyrophosphate that functions as a noncompetitive inhibitor of herpesvirus DNA polymerase. Foscarnet blocks the pyrophosphate binding site, preventing cleavage of pyrophosphate from deoxynucleotide triphosphates.

Uses

- It is an antiviral drug that inhibits the growth of viruses in body.
- It is used for the treatment of cytomegalovirus (CMV) retinitis in patient having AIDS.
- It is also used in the treatment of herpes simplex virus (HSV) in patient with a weak immune system.

Stability and Storage Conditions

- should be kept in glass bottles
- It should be stared below 30°C and should not be refrigerated.

Type of Formulation

1. Solution

Popular Brand Name

- Foscavir

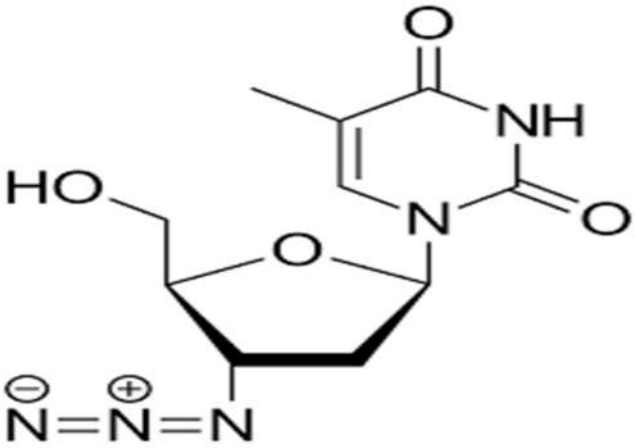
Zidovudine

→ Zidovudine is a dideoxynucleoside compound whose 3-hydroxy group on the sugar moiety has been replaced with an azido group.

→ This replacement prevents the formation of phosphodiester linkages required for the completion of nucleic acid chains.

→ Zidovudine is a potent inhibitor of HIV replication that acts as a chain-terminator of viral DNA during reverse transcription.

Chemical Structure



Mechanism of Action

- Zidovudine is phosphorylated to active metabolites that compete for incorporation into viral DNA. They inhibit the HIV reverse transcriptase enzyme competitively and act as a chain terminator of DNA synthesis.

Uses

- It is used with other HIV medications to control HIV infection.
- It decreases the amount of HIV in body to improve the functioning of immune system.
- It can also be used in pregnant women to prevent the virus from spreading to the foetus.

Stability and Storage Conditions

- Zidovudine tablets should be stored at room temperature between 68°F to 77 F (20°C to 25°C). Zidovudine capsules and oral solution should be stored between 59°F and 77°F (15°C to 25°C).

Type of Formulation

1. Capsules

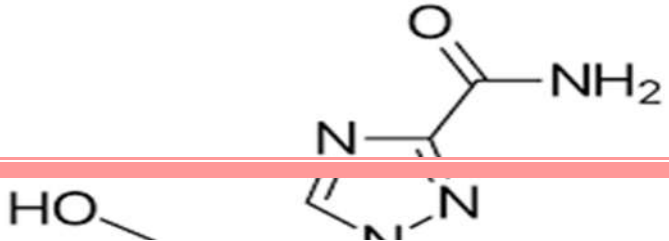
Popular Brand Name

- Retrovir

Ribavirin

→ Ribavirin is a class of guanosine nucleoside which is used in the treatment of some forms of Hepatitis C

Chemical Structure



Mechanism of Action

- Since ribavirin is a nucleoside analogue of guanosine, the most straightforward possible mechanism of action would be that ribavirin acts as an inhibitor of the viral polymerase.

Uses

- It is also known as tribavirin.
- It is antiviral drug which is used treatment RSV infection, hepatitis and some viral hemorrhagic fevers.

Stability and Storage Conditions

- Ribavirin tablets capsules should be stored at room temperature between 68° 77°F
- Ribavirin oral Solution should be stored at room temperature between 68F and 77°F (20°C to 25°C).

Types of Formulations

1. Solution
2. Tablet
3. Capsule

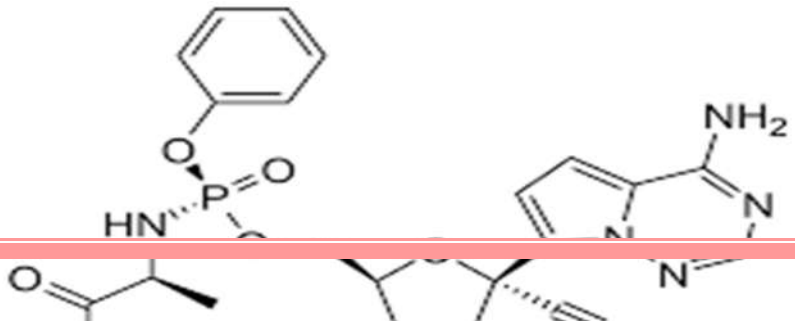
Popular Brand Names

- Rebetol
- Ibuvyr
- Virazole

Remdesivir

→ Remdesivir is nucleoside analog which is used in the treatment of RNA virus infection including COVID 19

Chemical Structure



Mechanism of Action

- The active form of remdesivir acts as a nucleoside analog and inhibits the RNA-dependent RNA polymerase (RdRp) of coronaviruses including SARS-CoV-2. Remdesivir is incorporated by the RdRp into the growing RNA product and allows for addition of three more nucleotides before RNA synthesis stalls.

Uses

- It is used for the treatment of coronavirus disease 2019 (COVID-19). It approved use in adults and children of at least 12 years age having at least 88 pounds (40 kilograms) of weight.

Stability and Storage Conditions

- Stored at Room Temperature

Types of Formulation

1. Power for injection
2. Solution

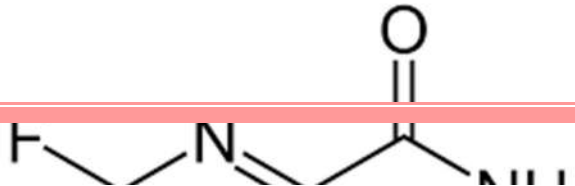
Popular Brand Names

- Veklury

Favipiravir

→ Favigiravir is an antiviral drug which is used in managing influenza and has a potential to target other viral infections

Chemical Structure



Mechanism of Action

- This mechanism of action of favipiravir is quite unique, since marketed influenza drugs inhibit either entry or release of the virus.

Uses

- It is used to treat influenza.
- It is only used for novel influenza (strains that cause more severe disease rather than seasonal influenza

Stability and Storage Conditions

- It should be store at -20°C

Type of Formulation

1. Tablet

Popular Brand Names

- Avigan
- Avifavir
- Areplivir
- FabiFlu
- Favipira

ANTIMALARIALS

→ Malaria is an infectious disease affecting humans and other animals.
→ It is a mosquito-borne infectious disease caused by parasitic protozoans (group of single-celled microorganisms) of Planodium type.
→ The symptoms of this disease include fever, vomiting, fatigue, and headache.
→ The symptoms usually begin 10-15 days after being bitten by mosquitoes.
→ In severe cases, the skin becomes yellow, the patient experiences seizures, goes to coma, or finally dies

→ Malaria is transmitted by an infected female Anopheles mosquito,
→ which introduces the parasites from its saliva into the person's blood.
→ The parasites reach the liver to mature and reproduce there.
→ Five species of Plasmodiun can infect humans, P. falciparum causes most of the deaths; while P. vivax, Poyale, and P. malariae cause milder forms of malaria: P. knowlesi rarely cause a disease in humans.
→ The risks can be reduced by the prevention of mosquito bites by using mosquito nets, repellents, spraying insecticides, and draining standing water

Classification Antimalarial drugs are classified as follows:

1) Based on the Affected Plasmodial Stage:

I. **Primary Tissue Schizonticides:** They destroy the primary tissue schizonts in the liver. immediately after the infection. e.g..Primaquine.
II. **Blood Schizonticides**: They suppress the symptoms by destroying the schizonts and merozoites in the erythrocytes, elem Chloroquine, Amodiaquine, Mefloquine, and Quinine.
III. **Gametocides:** They prevent the spread of infection by destroying the gametocytes in the blood, e.g., Primaquine for P. falciparum, and Chloroquine for P. vivax, P. malariae, and P. Kovale.
IV. **Sporonticides:** They eraulicate malaria by preventing sporogony in the mosquito, e.g. Chloroguanide and Pyrimethamine.
V. **Secondary Tissue Schizonticides:** They cure chronic relapsing fevers due to infection by P vivat, P. malariae, and P. ovale. They do so by destroying the secondary exoerythrocytic tissue schizonts developing in the liver (eg, Primaquine).

2) Based on their Chemical Structure:

i. **Quinoline Derivatives:** Cinchona alkaloids, 4 Amino quinolines, 8-Amino quinolines, and Mefloquine.
ii. **9-Amino Acridines:** Quinacrine and Acriquine
iii. **2,4-Diaminopyrimidines:** Pyrimethamine.
iv. **Biguanides:** Proguanil and Chlorproguanil.
v. **Pyrimidine Analogue:** Pyrimethamine and Trimethoprim.
vi. **Suphone and Sulphonamides:** Sulfadoxine and Dapsonc.
vii. **New Antimalarial Drug:** Artemisinin.

Examples

The following drugs are studied in detail:

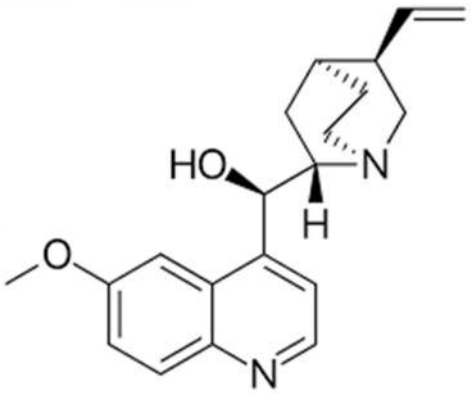
- Quinine sulphate,

- Chloroquine phosphate, *
- Primaquine phosphate,
- Mefloquine, *
- Cycloguanil,
- Artemisinin
- Pyrimethamine,

Quinine Sulphate

→ Quinine is an alkaloid derived from Cinchona bark. It is an antimalarial agent and an active ingredient in extracts of cinchona used before 1633.

Chemical Structure



Mechanism of Action

➢ Quinine inhibits nucleic acid synthesis, protein synthesis, and glycolysis in Plasmodium falciparum and can bind with hemazoin in parasitized erythrocytes. However, the precise mechanism of the antimalarial activity of quinine sulfate is not completely understood.

Uses

- Quinine is used for treating malaria.
- It is a mild antipyretic and analgesic and has been used in common cold preparations.
- It was used as a bitter and flavouring agent.
- It is still used in the treatment of babesiosis.

Stability and Storage Conditions

▪ It should be stored at 20°C to 25°C (68° 16 77°F).

Type of Formulation

1. Capsules

Popular Brand Names

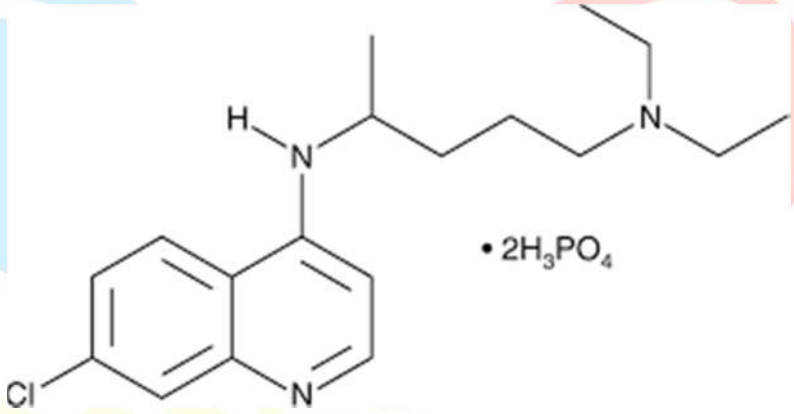
♦ Qualaquin
♦ OM-260
♦ Quinamm

Chloroquine Phosphate *

→ Chloroquine is the precedent antimalarial drug. It is used for treating all types of malaria, excluding the one caused by chloroquine-resistant Plasmodium falciparum.

Chemical Name and Structure

(RS)-N-(7-chloroquinolin-4-yl)-N,N-diethyl-pentane-1,4-diamine



Mechanism of Action

➢ The drug chloroquine is bactericidal for Bacillus megaterium; it inhibits DNA and RNA biosynthesis and produces rapid degradation of ribosomes and dissimilation of ribosomal RNA. Inhibition of protein synthesis is also observed, evidently as a secondary effect.

Uses

- Chloroquine is used for acute malarial attacks caused by P. vivax, P.malariae, P. ovale, and susceptible strains of P. falciparum.
- It is also used for suppressive treatment of malaria.

Stability and Storage Conditions

- It should be stored at room temperature between 15-25°C.
- It should be protected from light.
- Product in powder form is stable for 6 months at room temperature when it is properly stored.

Type of Formulation

1. Tablets

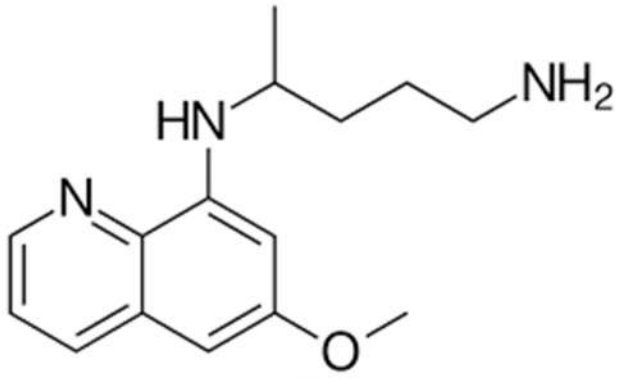
Popular Brand Names

- Aralen Phosphate
- Aralen Hydrochloride

Primaquine Phosphate

→ Primaquine is an aminoquinoline which is indicated orally for radically curing and preventing relapse of vivax, and ovale malaria after treatment with blood schizontocide.

Chemical Structure



Mechanism of Action

➢ The mechanism of action of primaquine is not well understood. It is assumed to generate reactive oxygen species, interfere with the electron transport in the parasite, or bind to and alter the properties of protozoal DNA.

Uses

- Primaquine is used for treating malaria caused by P. ovale and P viwar

Stability and Storage Conditions

▪ Primaquine phosphate tablets should be stored in well closed and light-resistant containers at a temperature less than 40 °C, ideally between 15-30°C.

Type of Formulation

1. Tablets

Popular Brand Name

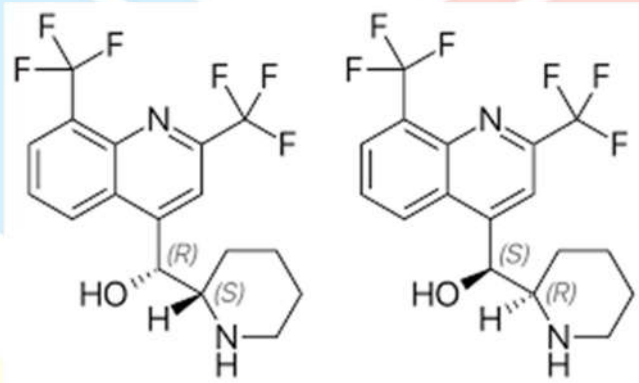
♦ Primaquine

Mefloquine *

→ Mefloquine is a phospholipid-interacting antimalarial that is very effective against Plasmodium falciparum und has very few side effects.

Chemical Name and Structure

[(R*, S*)-2, 8-Bis(trifluoromethyl) quinolin-4-yl]-(2-piperidyl)methanol



Mechanism of Action

➢ The mechanism of action of mefloquine is not completely understood. Some studies suggest that mefloquine specifically targets the 80S ribosome of the Plasmodium falciparum, inhibiting protein synthesis and causing subsequent schizonticidal effects.

Uses

- Mefloquine is used in the treatment of mild to moderate acute malaria caused by mefloquine susceptible strains of Plasmodium falciparum or by Plasmodium vivax.

Stability and Storage Conditions

- It should be kept away from children and direct sunlight.
- It should be kept in a cool and dry place.

Type of Formulation

1. Tablets

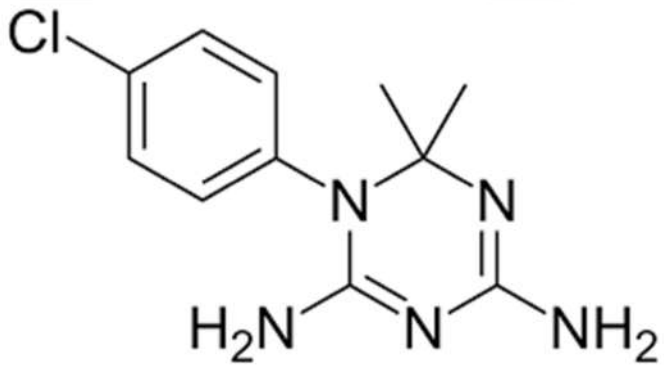
Popular Brand Name

♦ Lariam

Cycloguanil

→ Cycloguanil is the active metabolite of proguanil.

Chemical Structure



Mechanism of Action

- mainly through cycloguanil, its active metabolite, which inhibits folate production in both pre-erythrocytic and erythrocytic parasites. It is often used for malarial prophylaxis alone or in combination with chloroquine. It can also be used in the prophylaxis and treatment of P.

Uses

- Cycloguanil is a dihydrofolate reductase inhibitor and is used for suppression of malaria. However, it failed to achieve a wide acceptance.

Stability and Storage Condition

- It should be stored at-20°C

Types of Formulations

1. Suspension
2. Tablet
3. Capsule

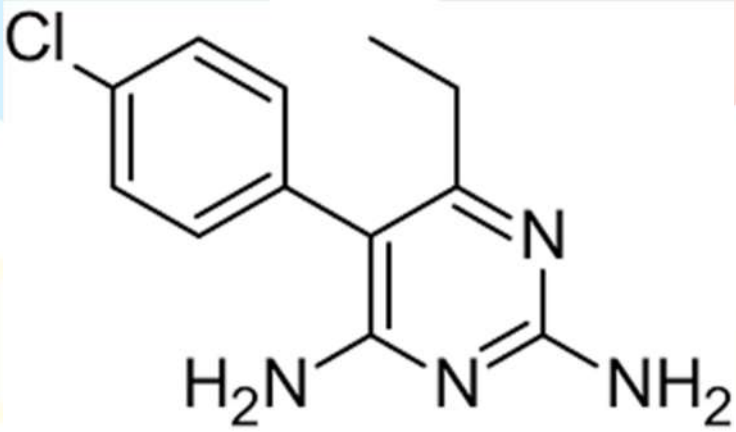
Popular Brand Names

- Alendronate tablet,
- Fosarmax
- Zovirat
- Diphenoxylate hydrochloride

Pyrimethamine

→ Pyrimethamine is a synthetic derivative of ethyl pyrimidine. It has potent antimalarial properties and also inhibits Dihydrofolate Reductase (DHFR)

Chemical Structure



Mechanism of Action

➢ Pyrimethamine selectively inhibits the plasmodial form of dihydrofolate reductase, reducing the production of folic acid required for nucleic acid synthesis in the malarial parasite

Uses

- Pyrimethamine is used for treating toxoplasmosis and acute malaria.
- It is used for preventing malaria in areas Don-resistant to pyrimethamine.
- It is used for treating malaria and prophylaxis as it is a primary tissue schizonticide and slow blood schizonticide.

Storage and Stability Conditions

▪ The stability of pyrimethamine is a liquid dosage formulation stored for up to the months was studies

Type of Formulation

1. Tablets

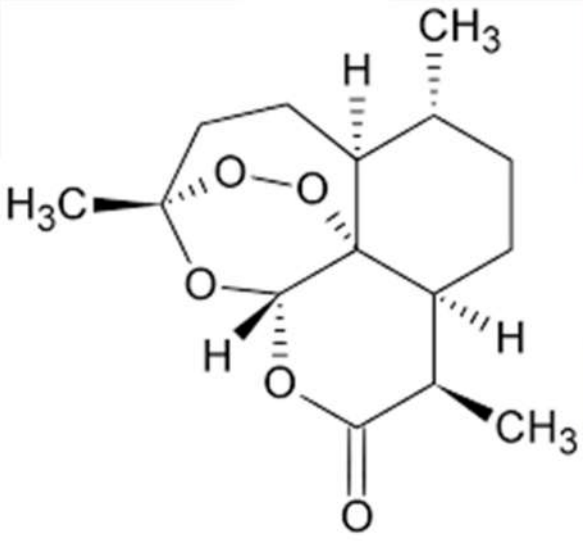
Popular Brand Name

♦ Daraprim

Artemisinin

→ Artemisinin is a drug intended for the treatment of malaria

Chemical Structure



Mechanism of Action

- Artemisinin is believed to act via a two-step mechanism. Artemisinin is first activated by intraparasitic heme-iron which catalyzes the cleavage of this endoperoxide. A resulting free radical intermediate may then kill the parasite by alkylating and poisoning one or more essential malarial protein(s).

Uses

- Its derivatives are at basis of current treatment against malaria because of their high potency, rapid clinical and parasitological response, efficiency against various pactite stages and low toxicity

Stability and Storage Conditions

- It should be kept in a well-closed container, and protected from light. It should be stored in cool place.

Types of Formulations

1. Injection

2. Tablets
3. Suppository

Popular Brand Names

- Dimisines
- Amiqin
- Artequik
- Alaxin

SULFONAMIDES

→ Several Groups of drugs are derived from sulphonamides (or sulpha drugs). These are synthetic antimicrobial agents containing sulphonamide group

Classification

Based on their Pharmacological Action:

- **Used in systemic infections,** eg Sulphadiazine.
- **Used in eye infections,** eg, Sulphacetamide.
- **Used in intestinal infections,** eg, Sulphapyridine.
- **Used in urinary tract infections,** eg, Sulphamethoxazole.

Examples

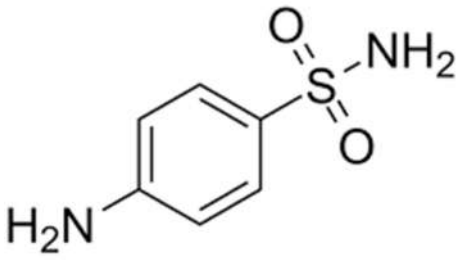
The following drugs are studied in detail:

- Sulfanilamide, *
- Sulfadiazine
- Sulfamethoxazole,
- Sulfacetamide,
- Mafenide acetate,
- Dapsone, *
- Cotrimoxazole,

Sulfanilamide *

→ Sulfanilamide is a class of sulfonamide anti-infective drug which is used in the treatment of vulvovaginal candidiasis caused by Candida albicans.

Chemical Structure



Mechanism of Action

- As a sulfonamide antibiotic, sulfanilamide functions by competitively inhibiting (that is, by acting as a substrate analogue) enzymatic reactions involving para-aminobenzoic acid (PABA). Specifically, it competitively inhibits the enzyme dihydropteroate synthase.

Uses

- It is used to treat vaginal infections.

Stability and Storage Conditions

- It should be stored in a closed container at room temperature.
- It should be kept away from heat, moisture,direct light and children's reach

Types of fromulation

1. Cream

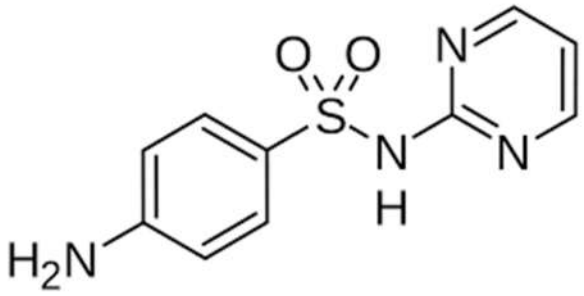
Popular Brand Names

- AVC Vaginal

Sulfadiazine

→ Sulfadiazine is a short-acting bacteriostatic and a synthetic pyrimidinyl sulfonamide derivative.

Chemical Structure



Mechanism of Action

- Sulfadiazine is a competitive inhibitor of the bacterial enzyme dihydropteroate synthetase. This enzyme is needed for the proper processing of para-aminobenzoic acid (PABA) which is essential for folic acid synthesis. The inhibited reaction is necessary in these organisms for the synthesis of folic acid.

Uses

- Sulphadiazine can be used for the treatment of upper respiratory tract infections, otitis media, Meningococcal meningitis, boils carbuncle, puerperal fever, urinary tract infections, acute dysentery, etc.

Stability and Storage Conditions

- Sulfadiazine tablets should be stored at room temperature. and should be protected from light. container should be tightly closed.

Type of Formulation

1. Tablets

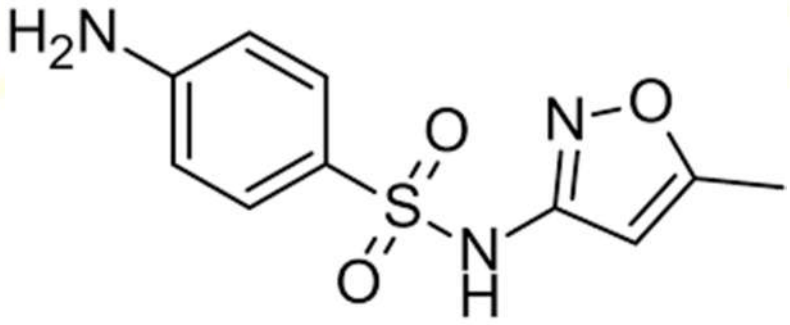
Popular Brand Names

- Lantrisul
- Neotrizine
- Sulfadiazine
- Sulfaloid
- Sulfonamides Duplex

Sulfamethoxazole

→ Sulfamethoxazole is a bacteriostatic antibacterial agent that interferes with folic acid synthesis in susceptible bacteria. Its broad spectrum of activity has been limited by the development of resistance.

Chemical Structure



Mechanism of Action

➢ Sulfamethoxazole is hepatically metabolized by the CYP450 system; it is a CYP2C9 inhibitor. Its half-life is 6 to 12 hours, increasing to between 20 and 50 hours in renal failure.

Uses

- Sulfamethoxazole used the treatment of bacterial infections

Stability and Storage Conditions

- Sulfamethoxazole/trimethoprim tablets should be stored at room temperature

Types of Formulations

1. Suspension

Popular Brand Names

- Bactrim,

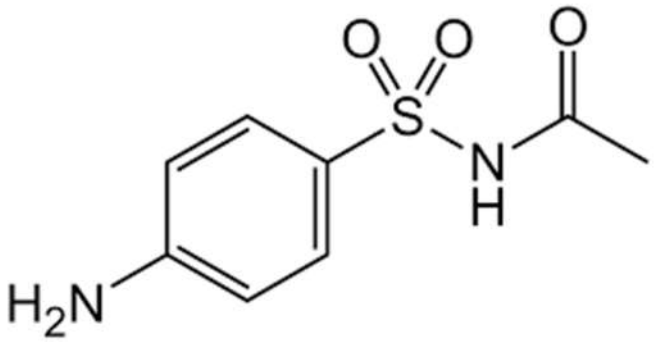
- Septra,
- Bactrim DS,
- Septra,

Sulfacetamide

→ Sulfacetamide is a sulphonamide antibacterial agent that is topically used for treating skin infection and orally used for treating urinary tract infection.

Chemical Name and Structure

N-[(4-aminophenyl)sulfonyl]acetamide



Mechanism of Action

➢ Sulfacetamide is a sulfonamide antibiotic. Sulfonamides are synthetic bacteriostatic antibiotics, that are active against gram-positive and gram-negative bacteria. It blocks the synthesis of dihydrofolic acid by inhibiting the enzyme dihydropteroate synthase.

Uses

- Sulfacetamide is used for treating bacterial vaginitis, keratitis, acute conjunctivitis, blepharitis.

Stability and Storage Condition

- It stored in a room temperature

Types of Formulations

1. Solution
2. Suspension
3. Emulsion

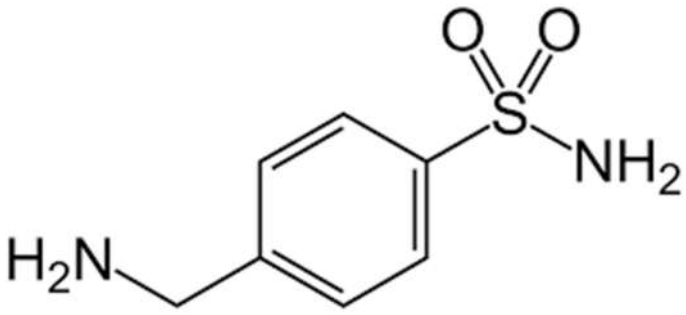
Popular Brand Names

- Avar
- Bleph-10
- Bp Cleansing Wash
- Isopto Cetantide
- Blephamide
- Cetumide, EML-S

Mafenide Acetate

→ Maleride is a sulfonamide-type antimicrobial agent that is used to treat severe burn. It reduces bacterial population in the burn tissue and promotes healing of deep burns.

Chemical Structure



Mechanism of Action

➢ Mafenide displays bacteriostatic activity against a number of gram-negative and gram-positive bacteria including Pseudomonas aeruginosa and certain anaerobic strains. The antibacterial action is not affected by the presence of pus, tissue exudate, or serum nor by the acidity of the application site.

Uses

- Mafenide is used as an adjunctive topical antimicrobial agent to control bacterial infection when used under moist dressings over meshed autografts on excised barn wounds.

Stability and Storage Conditions

- Solution may be stored in unopened containers

Type of Formulation

1. Solution

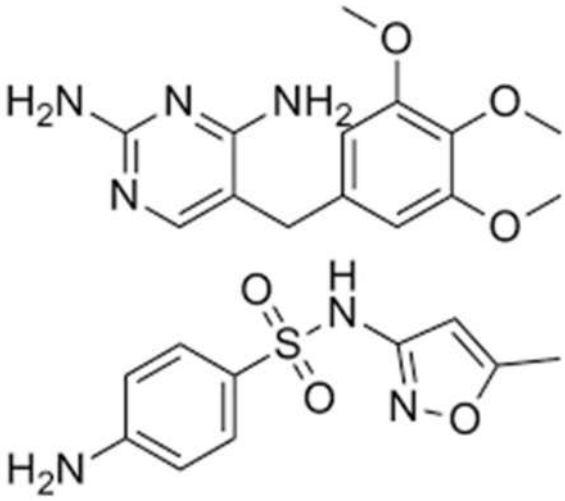
Popular Brand Name

- Sulfamylon

Cotrimoxazole

→ Cotrimoxazole is a synthetic antibacterial, and combination of sulfamethoxazole and trimethoprim.

Chemical Structure



Mechanism of Action

➢ Co-trimoxazole is a combination of trimethoprim and sulfamethoxazole and is in a class of medications called sulfonamides. It works by stopping the growth of bacteria. Antibiotics will not kill viruses that can cause colds, flu, or other viral infections.

Uses

- Cotrimoxazole is effective against Escherichia coli,Klebsiella, Enterobacter, Proteus mirabilis, Haemophilus bfluencot Streptococcus precamonise, Sanjaylococca aureus, Acinetobacter, Salmonella, Shigella, and P. carinii.

Stability and Storage Conditions

- It should be stored at controlled room temperature between 15-25°C and should be protected from light.

Types of Formulations

1. Tablets
2. Suspension
3. Syrup

Popular Brand Names

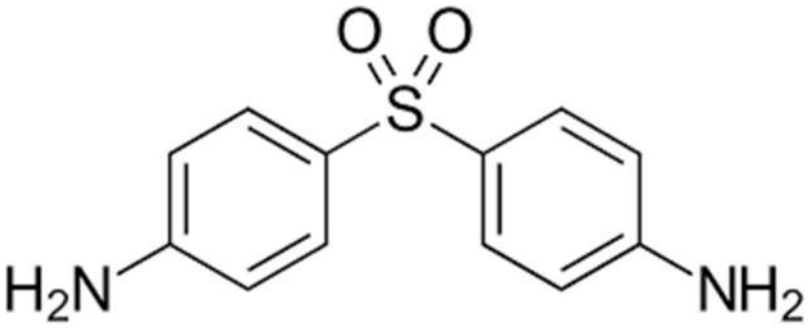
- Cotrimox
- Orprim
- Trimox
- Wypal

Dapsone *

→ Dapsone is a nearly water-insoluble agent that is very weakly basic (pK, 1.0). In lack of solubility is somewhat responsible for the occurrence of gastrointestinal irritation. Even if dapsone is poorly soluble, it gets efficiently absorbed from the GIT. Although dapsonic bound to plasma protein (-70%), it is distributed throughout the body,

Chemical Name and Structure

4-[(4-aminobenzene)sulfonyl]aniline |



Mechanism of Action

- As an antimicrobial agent, dapsone is bacteriostatic in action. It inhibits the synthesis of dihydrofolic acid through by competing with para-aminobenzoic acid for the active site of dihydropteroate synthetase thus resembling the action of sulphonamides.

Uses

- Dapsone is used to control dermatologic symptoms of dermatitis herpetiformis

- It is used alone or with other anti-leprosy drugs for leprosy

Stability and Storage Conditions

- The medicine should be kept in a safe place and out of children's reach. Mainly the drug should be kept at room temperature between 68°F and 77°F (20°C and 29°C).

Type of Formulation

1. Gel

Popular Brand Name

- Aczone

Chapter 12

ANTIBIOTICS

Topics

ANTIBIOTICS

- Amoxicillin,
- Penicillin,
- Cloxacillin,

AMINOGLYCOSIDES

- Streptomycin

TETRACYCLINES

- Doxycycline
- Minocycline

MACROLIDE

- Erythromycin
- Azithromycin

MISCELLANEOUS

- Chloramphenicol,
- Clindamycin.

ANTIBIOTICS

→ The word antibiotic was derived from the word antibiosis which means against life.

→ Historically, antibiotics were believed to be organic compounds produced by a microorganism toxic other microorganisms.

→ Due to this belief, an antibiotic was initially defined as a substance produced by a microorganism, which can prevent the growth of, or are fatal to other microorganisms even at low concentrations But this definition has been modified at the present time for including antimicrobials produced by synthetic means either partially or wholly.

→ Antibiotics can either kill other bacteria or inhibit their growth.

→ Those antibiotics which kill bacteria are termed as bactericidal and those which inhibit bacterial growth are termed bacteriostatic.

→ Even though antibiotics are referred to as antibacterial agents, still they are differentiated as antibacterials; antifungals, and antivirals to indicate the type of microorganisms against which they act.

Classification

Antibiotics can be classified as follows:

1) Based on their Chemical Structure

1. **β - Lactam Antibiotics:** Penicillins, Monobactams, Cephalosporins.Carbapenems, etc.
2. **Aminoglycosides:** Streptomycin, Gentamycin, Framyeetin, Neomycin, etc.
3. **Macrolides:** Erythromycin, Roxithromycin, Clarithromycin, Azithromycin, etc.
4. **Tetracyclinest:** Oxytetracycline, Doxycycline, Minocycline, etc.
5. **Nitrobenzene Derivatives:** Chloramphenicol, etc.

B-LACTAM ANTIBIOTICS

→ The B-lactam antibiotics belong to a broad category, in which all the antibiotics have a B-lactam nucleus in their molecular structure, i.e., members of this antibiotic class possess a highly reactive 3-carbon and 1-nitrogen ring.

→ The B-lactam antibiotics include penicillin derivatives (penams), monobactams, carbapenems and cephalosporins (cephems). They are the most widely used among all the antibiotics and act by inhibiting the cell wall synthesis of the bacterial organism.

→ The B-lactam antibiotics are generally given with lactamase inhibitors (e.g., clavulanic acid) because the bacteria obtain resistance to B-lactam antibiotics by producing B-lactamase enzyme which attacks the -lactam ring.

Examples

The following drugs are studied detail

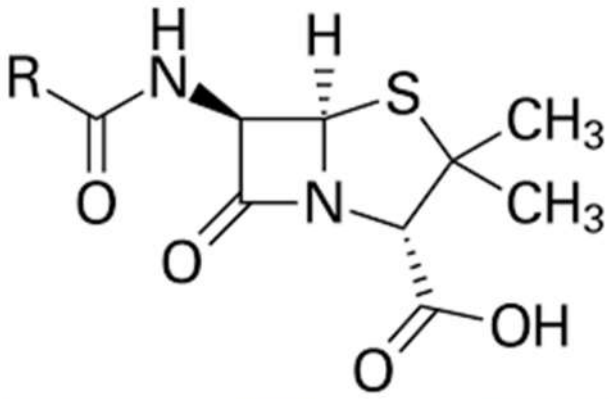
- Amoxicillin,
- Penicillin,
- Cloxacillin,

Penicillin G (Benzyl Penicillin)

→ Benzylpenicillin a narrow spectrum natural penicillin antibiotic. It is used treating infections caused by susceptible bacteria

→ It shows poor oral absorption, thus administered intravenously or intramuscularly.

Chemical Structure



Mechanism of Action

➢ Penicillin G exerts a bactericidal action against penicillin-susceptible microorganisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell-wall peptidoglycan, rendering the cell wall osmotically unstable.

Uses

- Penicillin G benzathine injection is used to treat bacterial infections (eg, mild to moderate infections of the upper respiratory tract, syphilis, yaws, bejel, pinta). It is also used to prevent rheumatic fever, chorea, rheumatic heart disease, or acute glomerulonephritis. This medicine is an antibiotic.

Stability and Storage

- All solutions should be stored in a refrigerator at 2º to 8ºC

Types of Formulation

1. Injection Powder
2. Solutions

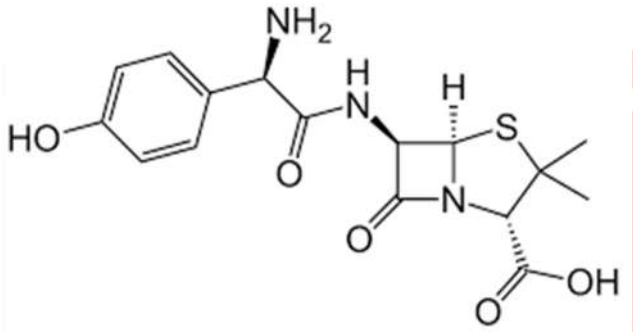
Popular Brand

♦ Pfizerpen

Amoxicillin

→ Amoxicillin is a penicillin derivative used to treat infections produced gram-positive bacteria, particularly in the upper respiratory tract infections caused by streptococcal bacteria

Chemical Structure



Mechanism of Action

➢ Amoxicillin is similar to penicillin in its bactericidal action against susceptible bacteria during the stage of active multiplication. It acts through the inhibition of cell wall biosynthesis that leads to the death of the bacteria.

Uses

- It is a bacteria fighting penicillin antibiotic.
- It is used for a variety of bacterial infections, including tonsillitis, bronchitis, pneumonia, infections of the ear, nose, throat, skin, and urinary tract.

Stability and Storage Conditions

▪ Capsules and pills should be kept at room temperature, away from heat and moisture (not in the bathroom).

Types of Formulations

1. Suspensions
2. Tablets

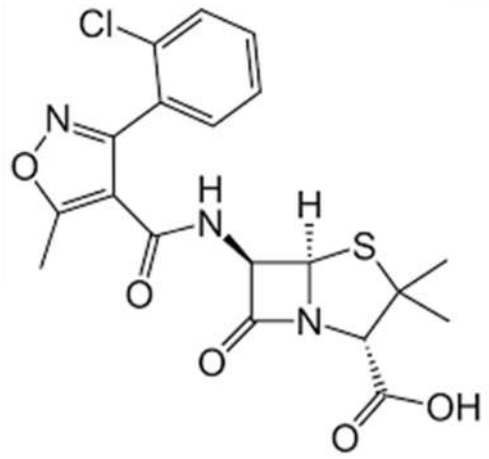
Popular Brand Names

♦ Amoxil
♦ Trimox
♦ Maxatag

Cloxacillin

→ Cloxacillin is an antibiotic that is used to treat infections Caused by beta-hemolytic streptococcal, pneumococcal, and staphylococcal infections.

Chemical Structure



Mechanism of Action

➢ Cloxacillin is for use against staphylococci that produce beta-lactamase. By binding to specific penicillin-binding proteins (PBPs) located inside the bacterial cell wall, cloxacillin inhibits the third and last stage of bacterial cell wall synthesis.

Uses

- It is used to treat bacterial infections

Stability and Storage Conditions

- The capsules should be kept away from light and moisture at room temperature, between 59 and 86" F (15° and 30°C).
- The liquid solution should be refrigerated until it reaches a temperature of 36-46 F. (2-8 C)

Types of Formulations

1. Powder
2. Liquid

Popular Brand Name

♦ Amclo AHPL

AMINOGLYCOSIDES

→ Aminoglycoside is a molecule or a portion of a molecule composed of amino-modified sugars.

→ It has a hexose ring, either streptidine (in streptomycin) or 2- deoxystreptamine (other aminoglycosides), and various amino sugars are attached to this ring by glycosidic linkages. It is water-soluble, stable in solution, and more active at alkaline pH.

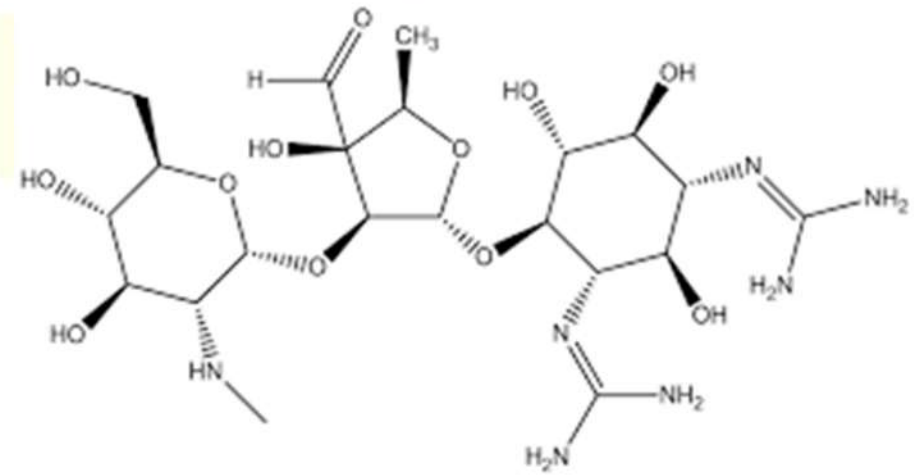
→ Some of the aminoglycosides (e.g., amikacin, arbekacin, gentamicin kanamycin. [neomycin, netilmicin paromomycin, rhodostreptomycin, streptomycin,

Example

Streptomycin

→ Streptomycin is an antibiotic produced by Streptomyces griseus (a soil actinomycete). It is an aminoglycoside antibacterial and anti-mycobacterial.

Chemical Structure



Mechanism of Action

➢ It binds to the small 16S rRNA of the 30S ribosomal subunit irreversibly, interfering with the binding of formyl-methionyl-tRNA to the 30S subunit.

Uses

- Streptomycin is used for treating tuberculosis..
- In combination with other drugs, it is used for treating.

Stability and Storage Conditions

▪ It can be stored at room temperature before being reconstituted.

Type of Formulation

1. Powder for injection

Popular Brand Name

- Brucella

TETRACYCLINES

→ Tetracycline is a potent, broad-spectrum antibacterial agent with activity against a host of gram-positive and gram-negative acrobic and anaerobic bacteria.

→ Therefore, they are the drugs of choice or well-accepted alternatives for various infectious diseases.

→ They are also used in the treatment of sexually transmitted and Gonococcal diseases, urinary tract infections, bronchitis, and sinusitis, Most of the marketed tetracyclines (tetracycline, chlortetracycline oxytetracyeline, and demeclocycline) occur naturally and are obtained by the fermentation of Streptomyces spp, broths.

→ The duration of antibacterial [action of semi-synthetic tetracyclines (methacycline, daxycycline, and minocycline) is longer.

→ They also have a similar profile in terms of antibacterial potency.

Examples

1) Doxycycline
2) Minocycline.

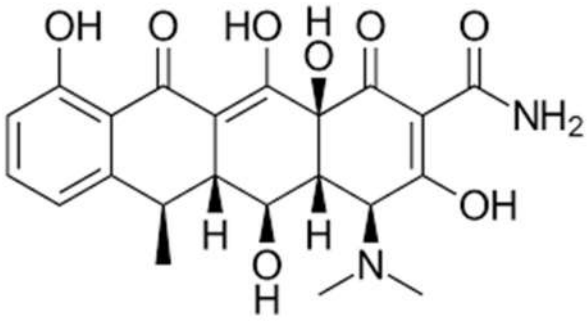
Doxycycline

→ Doxycycline is a broad-spectrum antibiotic and a synthetic derivative of oxytetracycline.

→ It is a second-generation tetracycline with lesser toxicity than first-generation tetracyclines.

→ It may be used for treating various bacterial infections, depending on the results of antibiotic susceptibility testing

Chemical Structure



Mechanism of Action

➢ The bacteriostatic action of tetracyclines, like doxycycline hyclate, is intended to stop the growth of bacteria by allosterically binding to the 30S prokaryotic ribosomal unit during protein synthesis.

Uses

- Rocky mountain spotted fever, typhus fever. Q fever. rickettsial pox, and tick fevers caused by Rickettside.
- Respiratory tract infections caused by Mycoplasma preumonic.

Stability and Storage Conditions

- Tablets, capsules, and syrup should be stored at room temperature between 15° and 30°C (59h and 86°F) In airtight, and light-resistant containers.

Types of Formulations

1. Powder for Suspension
2. Capsule
3. Tablet

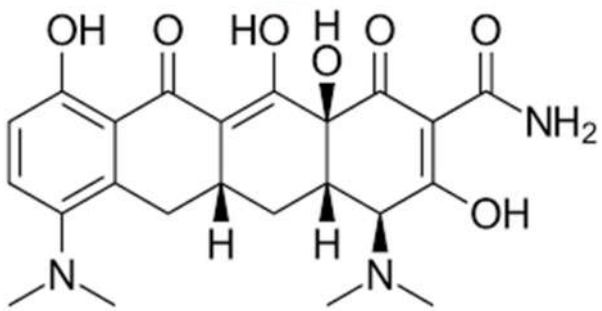
Popular Brand Names

- Adoxa TT
- Monodox
- Periostat
- Vibra-Tabs

Minocycline

→ Minocycline is a tetracycline analogue, 7-dimethylamino but lacking 5-methyl and hydroxyl groups. It is effective against tetracycline-resistant Staphylococcus infections)

Chemical Structure



Mechanism of Action

➢ As with other tetracyclines, the mechanism of action of minocycline involves attaching to the bacterial 30S ribosomal subunit and preventing protein synthesis.

Uses

- Minocycline is used in infections caused by susceptible strains of microorganisms, such as Rocky Mountain spotted fever, typhus fever, Q fever, rickettsial pox and tick fevers caused by Rickettsiae, upper respiratory tract infections caused by Streptococcus pneumonia and asymptomatic carriers of Neisseria meningitidis.

Stability and Storage Conditions

- should be stored at room temperature between 15° and 30°C (59h and 86°F) In airtight, and light-resistant containers.

Types of Formulations

1. Tablets
2. Capsules

3. Injection

Popular Brand Names

- Dynacin
- Minocin
- Solodyn
- Ximina

MACROLIDE

→ Macrolides are compounds with a macrocyclic lactonering (containing 14 or 16 atoms) with attached deoxy sugars.

→ Erythromycin is the prototype drug which was obtained in 1952 from Streptomyces erythreus.

→ Macrolides are orally administered, but can be taken via parenteral route They LATE used to treat pharyngitis and pneumonia caused by Streptococcus in individuals allergic to penicillin.

→ They are used in pneumonia caused by Mycoplasma species or Legionella pneumophila (organism causing Legionnaire disease).

→ They are also used in pharyngeal carriers of Corynebacterium diphtherine (bacillus causing diphtheria).

Examples:

- Erythromycin
- Azithromycin

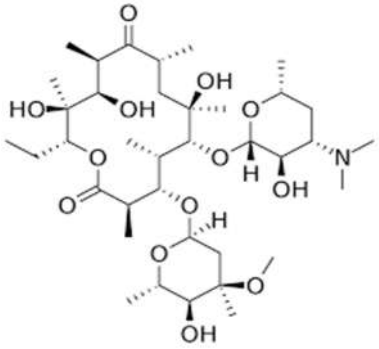
Erythromycin

→ Erythromycin is a bacteriostatic macrolide antibiotic produced by a strain of Saccharopolyspora erythraea in 1952.

→ It is widely used in various Infections caused by gram-positive and gram-negative bacteria.

→ It can be administered in various forms, like Intravenous, topical preparations, and eye drops

Chemical Structure



Mechanism of Action

➢ Erythromycin acts by inhibition of protein synthesis by binding to the 23S ribosomal RNA molecule in the 50S subunit of ribosomes in susceptible bacterial organisms.

Uses

- It is also used in STDs, like syphilis,
- It is used to treat ear, Intestine, gynaecologic, urinary tract, and skin infections,
- It prevents recurrent rheumatic fever.

Stability and Storage Conditions

- It should be kept at temperatures below 86°F (30°C). It is critical to keep tablets safe from moisture and extreme heat

Types of Formulations

1) Tablet
2) Capsules
3) Powder

Popular Brand Names

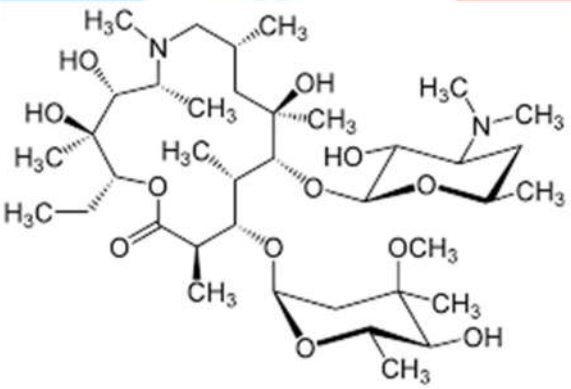
- Erythrocia
- B-Mycin
- EES Granites
- losshe

Azithromycin

→ Arithromycin is a broad-spectrum macrolide antibiotic with a long, half-life and a high degree of tissue penetration.

→ It is a part of the azalide sub-class of macrolides, and has a 15-membered ring with a methyl substituted nitrogen (and not a carbonyl group) at C-9a on the aglycone ring to prevent its metabolism.

Chemical Structure



Mechanism of Action

➢ Azithromycin is a macrolide antibiotic which inhibits bacterial protein synthesis, quorum-sensing and reduces the formation of biofilm.

Uses

- Community acquired pneumotia caused by Chlamydia pneumonia, Haemophilus influenzae, or S. pneumonia,
- Chronic obstructive pulmonary disease complications related to M. catarrhalis or S. pneumonia,
- Skin infections related to Staphylococcus or Streptococaureits, Streptococcus pyogenes, agalactiae,
- Tonsillitis caused by S. pyogenes,

Stability and Storage Conditions

- Azithromycin pills, suspension, and extended-release suspension are kept at room temperature, away from heat, and moisture (not in the bathroom).

Types of Formulations

1. Tablet
2. Solution

3. Powder

Popular Brand Names

- Azasite
- Zithromax
- Zmax

MISCELLANEOUS

Some other antibiotics commonly in use are:

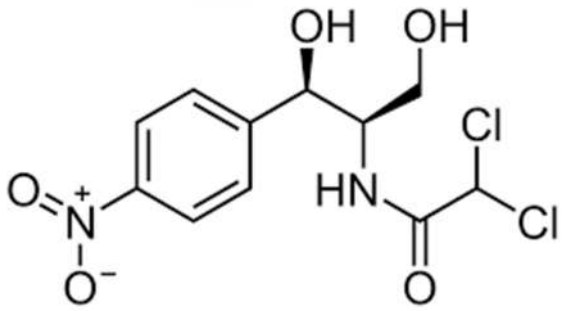
- Chloramphenicol,
- Clindamycin.

Chloramphenicol

→ Chloramphenicol is bacteriostatic in nature, and is a prototypical broad-spectrum antibiotic along with the tetracyclines. Chloramphenicol is active against many gram-positive and gram-negative organisms. It occurs as fine, white to greyish, white or yellowish white needle-like crystals or elongated plates. It is slightly soluble in water; and freely soluble in acetone, alcohol, ethyl acetate, and propylene glycol.

Chemical Name and Structure

2,2-dichloro-N-[(1R,2R)-1,3-dihydroxy-1-(4- nitrophenyl)propan-2-yl]acetamide



Mechanism of Action

➢ Chloramphenicol is an antibacterial with a broad spectrum of activity against gram-positive bacteria, gram-negative bacteria, and Rickettsia. Its mechanism of action is by inhibition of bacterial protein synthesis by binding with ribosomes. The major toxicity of chloramphenicol is hematologic.

Uses

- Chloramphenicol is used to treat serious infections in different parts of the body. It is sometimes given with other antibiotics. However, chloramphenicol should not be used for colds, flu, other virus infections, sore throats or other minor infections, or to prevent infections.

Stability and Storage Conditions

▪ This showed that chloramphenicol in eyedrops will be most stable if stored in refrigerator temperature. The temperature of refrigerator used in this study is 3–7 °C, and included into cold temperature. The lower the temperature, the slower the reaction rate will be.

Type of Formulation

1. Powder for Solution

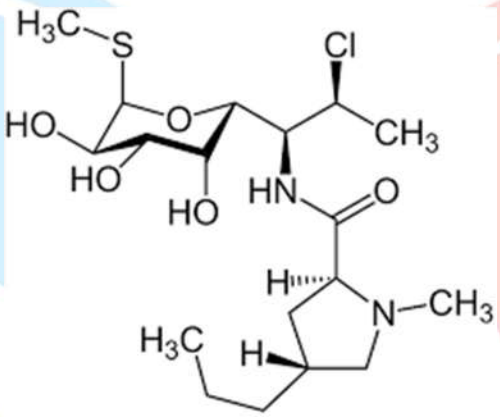
Popular Brand Name

- Chloromycetin cetin

Clindamycin

→ Clindamycin is a semi-synthetic lincosamide antibiotic that has replaced lincomycin due to its improved side effect profile. It binds to bacterial 50S ribosomal subunit and inhibits bacterial protein synthesis. It may be bacteriostatic or bactericidal depending on the organism and drug concentration.

Chemical Structure



Mechanism of Action

➢ Clindamycin given via systemic or vaginal route binds to 50S bacterial ribosomal subunits and inhibits bacterial protein synthesis.

Uses

- It is useful in polymicrobial infections, like intra- abdominal or pelvic infections, osteomyelitis, diabetic foot ulcers, aspiration pneumonia, and dental infections.
- It is also used in the treatment of MSSA and respiratory infections caused by S. pneumoniae and S. pyogenes in patients intolerant to other indicated antibiotics or infected with resistant organisms.

Stability and Storage Conditions

▪ Keep this medication tightly wrapped in its container and out of the reach of children. It should be kept at room temperature, free from heat and moisture (not in the bathroom). Its liquid preparation should not be refrigerated because it might get thicken and viscous.

Types of Formulations

1. Powder for Solution
2. Foam Solution
3. Lotion Gel/Jelly

Popular Brand Names

- Cleocin

- Cleocin Phosphate
- Cleocin Pediatric
- Capsule
- Cleocin HCI

Chapter 13

Anti-Neoplastic Agents

Topics

Anti-Neoplastic Agents

- Cyclophosphamide,
- Busulfan,
- Mercaptopurine,
- Fluorouracil,
- Methotrexate,
- Dactinomycin,
- Doxorubicin hydrochloride,
- Vinblastine sulphate,
- Cisplatin, and
- Dromostanolone propionate.

Anti-Neoplastic Agents

→ Cancer is a disease characterised by abnormal and uncontrolled cell division attacking the surrounding tissues and organs, and also the distant body parts by circulating with blood and lymph.

→ Cancer is classified into the following categories

- **Carcinoma :** This type of cancer starts in the skin or tissues lining the internal organs. There are many sub types of carcinoma, like adenocarcinoma, basal cell carcinoma, squamous cell carcinoma, and transitional cell carcinoma.
- **Sarcoma :** This type of cancer starts in the bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissues.
- **Leukaemia :** This type of cancer starts in the blood forming tissues (i.e., the bone marrow) and produces numerous abnormal blood cells.
- **Lymphoma and Myeloma :** This type of cancer starts in the cells of immune system.
- **Central Nervous System Cancers :** This type of cancer starts in the brain and spinal cord tissues.

→ Antineoplastic or anticancer drugs are used for treating malignancies or cancerous growths. Either these drugs are used alone (chemotherapy) or in combination with surgery or radiation therapy.)

Examples

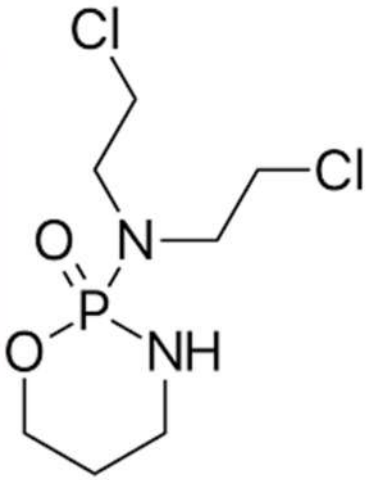
The following alkylating agents are discussed

- Cyclophosphamide,
- Busulfan,
- Mercaptopurine,
- Fluorouracil,
- Methotrexate,
- Dactinomycin,
- Doxorubicin hydrochloride,
- Vinblastine sulphate,
- Cisplatin, and
- Dromostanolone propionate.

Cyclophosphamide

→ Cyclophosphamide is a precursor of alkylating nitrogen mustard antineoplastic and immunosuppressive agent. It activates in the aldophosphamide.) liver to form the active

Chemical Structure



Mechanism of Action

➢ Aldophosphamide is cleaved to the active alkylating agent phosphoramide mustard and acrolein. The phosphoramide metabolite forms cross-linkages within and between adjacent DNA strands at the guanine N-7 position. These modifications are permanent and eventually lead to programmed cell death.

Uses

- It is used in the treatment of malignant lymphomas, multiple myeloma, leukaemia, mycosis fungoides, neuroblastoma, adenocarcinoma of the ovary, retinoblastoma, and carcinoma of breast.
- It is also used in biopsy-proven minimal change nephrotic syndrome in paediatrics.

Stability and Storage Conditions

▪ These preparations should be refrigerated in glass containers for up to 14 days before using.

Types of Formulations

1. Injection
2. Powder for solution

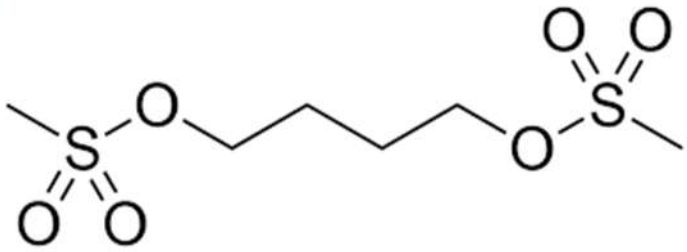
Popular Brand Name

♦ Procytox

Busulfan

→ Busulfan is a bifunctional alkylating agent. It exerts a selective immunosuppressive effect on bone marrow. It is not a structural analogue of nitrogen mustards. It is used in the treatment of chronic myeloid leukaemia; however, it provides only symptomatic relief and no permanent cure.

Chemical Structure



Mechanism of Action

➢ Busulfan is a bifunctional alkylating agent and cell cycle- non-specific. It interacts with the thiol groups of proteins and nucleic acids and forms DNA-protein and DNA-DNA cross-links. These cross-linkages prevent the synthesis and function of DNA.

Uses

- It is used with cyclophosphamide as a conditioning regimen before allogeneic hematopoietic progenitor cell transplantation for chronic myelogenous (myeloid, myelocytic, and granulocytic) leukaemia.
- It is also a component of pre-transplant conditioning regimen in bone marrow transplantation for acute myeloid leukaemia and non-malignant diseases.

Stability and Storage Conditions

- Refrigerate intact vials between 2°C and 8°C (36°F and 46°F).

Types of Formulations

1. Tablet
2. Solution

Popular Brand Names

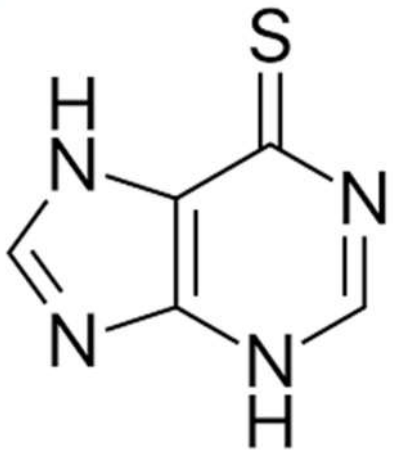
♦ Busulfex

- Myleran

Mercaptopurine

→ Mercaptopurine is an antimetabolite antineoplastic drug having immunosuppressant properties. It prevents purine metabolism, thus inhibits nucleic acid synthesis. It is used with other drugs for the treatment of or in remission maintenance programs for leukaemia.

Chemical Structure



Mechanism of Action

➢ The anticancer drug 6-mercaptopurine (6-MP) inhibits de novo purine synthesis and acts as an antiproliferative agent by interfering with protein, DNA and RNA synthesis and promoting apoptosis.

Uses

- It is used for remission induction and maintenance therapy of acute lymphatic leukaemia.

Stability and Storage Conditions

- It should be kept at room temperature, free from heat and moisture (not in the bathroom). After the opening of the bottle, the mercaptopurine suspension can be kept at room temperature for up to 6 weeks)

Types of Formulations

1. Tablet
2. Suspension

Popular Brand Name

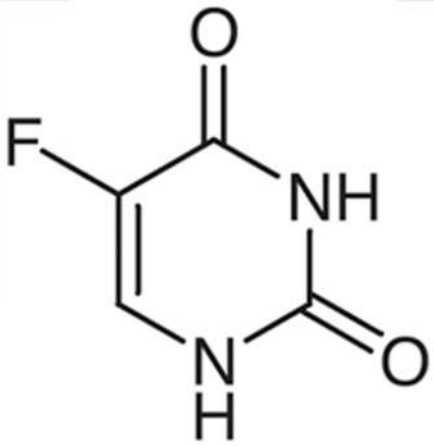
- Purixan

Fluorouracil

→ Fluorouracil is a pyrimidine analogue which is an antineoplastic antimetabolite. It inhibits DNA synthesis by preventing the conversion of thymidylate synthetase of deoxyuridylic acid into thymidylic acid.

Chemical Name and Structure

5-Fluoro-1H, 3H-pyrimidine-2,4-dione



Mechanism of Action

➢ Fluorouracil blocks an enzyme which converts the cytosine nucleotide into the deoxy derivative. In addition, DNA synthesis is further inhibited because Fluorouracil blocks the incorporation of the thymidine nucleotide into the DNA strand.

Uses

- It is used in acute lymphocytic leukaemia, Crohn's disease, and ulcerative colitis
- It is used for treating the slowly growing solid tumours (e.g., colorectal, breast, ovarian, pancreatic, and gastric carcinomas).
- It is used with levamisole (a veterinary anthelmintic agent) in patients having colon cancer.
- On topical application, it is effective in superficial basal cell carcinomas.

Stability and Storage Conditions

▪ 5-fluorouracil's stability has been evaluated in a variety of liquids and containers at temperatures ranging from 4°C to 35°C. When 5-fluorouracil was synthesised in NS and stored in polyolefin bags at 5°C 3°C for 28 days, it remained stable.

Types of Formulations

1. Injections
2. Solutions

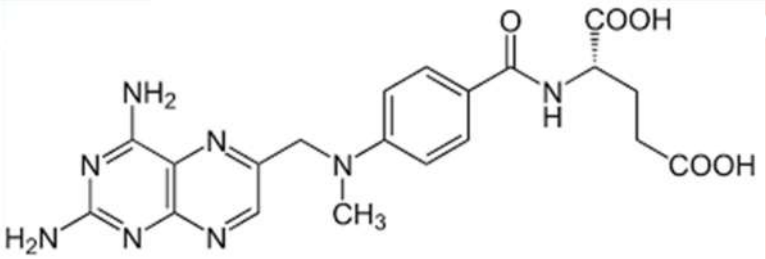
Popular Brand Names

- Actikeral
- Fluoroplex
- Carac
- Tolak

Methotrexate

→ Methotrexate (MTX) is an antineoplastic antimetabolite with immunosuppressant properties. It inhibits the formation of tetrahydrofolate dehydrogenase, which is required for the synthesis of thymidylate (an important DNA component

Chemical Structure



Mechanism of Action

➢ The mechanisms of action of methotrexate are complex. Developed as a folic acid analogue, methotrexate inhibits purine and pyrimidine synthesis, which accounts for its efficacy in the therapy of cancer as well as for some of its toxicities.

Uses

- It is effectively used with other drugs in acute lymphocytic leukaemia, choriocarcinoma, Burkitt lymphoma in children, breast cancer, and head and neck carcinomas.
- It is alone effective in low doses against certaininflammatory diseases (e.g., severe psoriasis)

Stability and Storage Conditions

▪ Multidose vials of methotrexate injection USP (with benzyl alcohol as a preservative) should be stored at temperatures between 15°C and 25°C. The vials should be stored between 2°C and 8°C for a maximum of four weeks after being punctured (30 days). It should be protected from light and freezing.

Types of Formulations

1. Injectable solution
2. Powder for injection

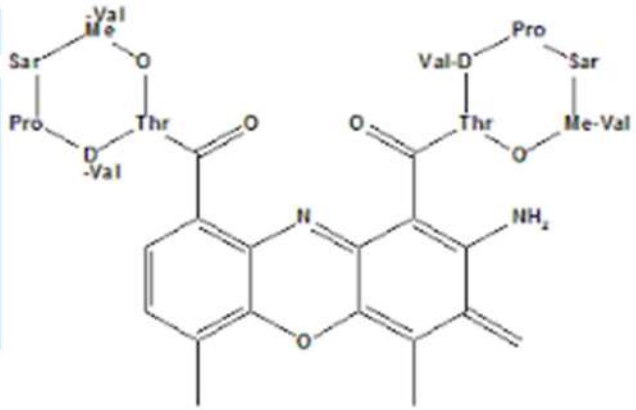
Popular Brand Names

- Trexall
- Xatmep

Dactinomycin

→ Dactinomycin is a high molecular weight antineoplastic antibiotic, which is isolated from Streptomyces parvulus.

Chemical Structure



Dactinomycin

Mechanism of Action

➢ Dactinomycin binds to DNA and blocks the RNA transcription with chain elongation more sensitive than initiation, termination, or release. This impaired mRNA production also declines the protein synthesis.

Uses

- It is used as a part of combination chemotherapy and/or multi-modality treatment regimen for treating Wilms' tumour, childhood rhabdomyosarcoma, Ewing's sarcoma and metastatic, non-seminomatous testicular cancer.

Stability and Storage Conditions

- Temperatures should be kept between 20° and 25° Celsius (68° and 77 °F) and away from light and humidity. It is caustic to the skin, irritating to the eyes and mucous membranes of the respiratory tract, and highly poisonous when taken orally, according to animal studies.

Type of Formulation

1. Powder for injection

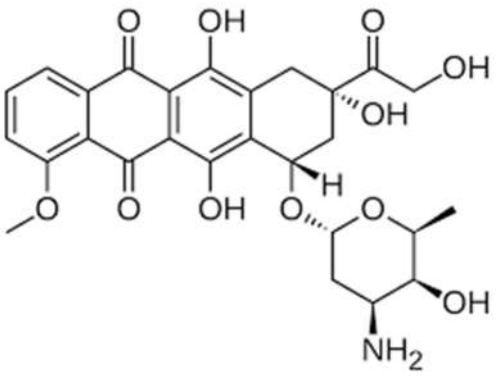
Popular Brand Name

♦ Cosmegen

Doxorubicin Hydrochloride

→ Doxorubicin is a cytotoxic anthracycline antibiotic. It is obtained from cultures of Streptomyces peucetius var. caesius. It binds to nucleic acids by intercalation of the planar anthracycline nucleus with the DNA double helix.

Chemical Structure



Mechanism of Action

➢ Doxorubicin exerts its antimitotic and cytotoxic activity by forming complexes with DNA through intercalation between base pairs. It blocks the activity of topoisomerase II by stabilising DNA-topoisomerase II complex, inhibiting the religation portion of the ligation-religation reaction catalysed by topoisomerase II.

Uses

- It is used for producing regression in disseminated neoplastic conditions such as acute lymphoblastic
- It is also used as a part of adjuvant therapy in women showing signs of axillary lymph node involvement after the resection of primary breast cancer.

Stability and Storage Conditions

- It should be stored at a temperature of 2° to 8°C.

Types of Formulations

1. Powder for injection
2. Solution

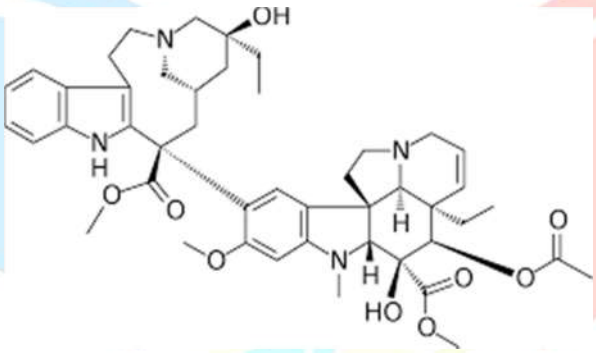
Popular Brand Names

- Adriamycin
- Rubex
- Adriamyc
- Adriamyc

Vinblastine Sulphate

→ Vinblastine sulphate is the sulphate salt of vinblastine, which is a natural alkaloid, obtained from Catharanthus roseus (Madagascar periwinkle). This plant possesses antineoplastic properties.

Chemical Structure



Mechanism of Action

➢ Vinblastine sulphate exerts its antitumour activity by interacting with tubulin and inhibiting mitosis at metaphase. Vinblastine binds to the microtubular proteins of the mitotic spindle and causes crystallisation of the microtubule and mitotic arrest or cell death.

Uses

- It is used in the treatment of breast cancer, testicular cancer, lymphomas, neuroblastoma, Hodgkin's and non- Hodgkin's lymphomas, mycosis fungoides, histiocytosis, and Kaposi's sarcoma.

Stability and Storage Conditions

▪ It is should be refrigerated between 20 and 8 °C. The vial should be kept in the outer carton to ensure safety from light

Types of Formulations

1. Injection solution
2. Powder

Popular Brand Name

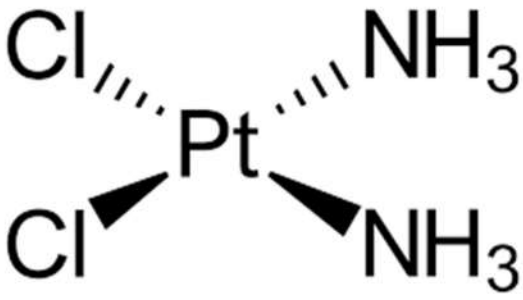
♦ Velban

Cisplatin

→ Cisplatin, cisplatinum or cis-diamminedichloroplatinum (II) (CDDP) is a platinum based chemotherapy drug. It isused for treating many types of cancers, such as sarcomas, some carcinomas (e.g., small cell lung cancer and ovarian cancer), lymphomas, and germ cell tumours.

Chemical Name and Structure

(SP-4-2)-diamminedichloroplatinum(II)



Mechanism of Action

➢ cisplatin mechanism of action is that the drug induces its cytotoxic properties through binding to nuclear DNA and subsequent interference with normal transcription, and/or DNA replication mechanisms.

Uses

- It is used for treating metastatic testicular tumours, metastatic ovarian tumours, and advanced bladder cancer.

Stability and Storage Conditions

▪ It is physically and chemically stable, when stored in glass containers or diluted with 0.9 % sodium chloride in PE bags at a concentration of 10 mg/ml at room temperature (15-25°C) for at least 30 days.

Types of Formulations

1. Injection
2. Solution

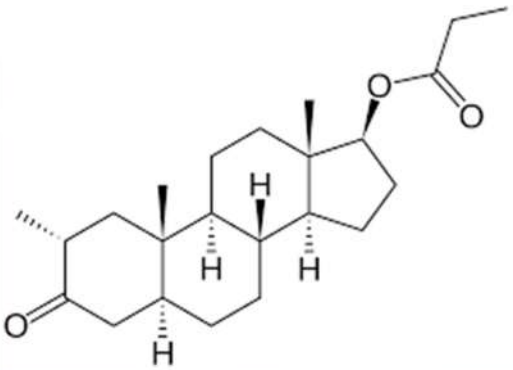
Popular Brand Names

♦ Platinol

Dromostanolone Propionate

→ Dromostanolone, like testosterone, is a synthetic androgen, or male hormone. Dromostanolone acts by binding to androgen receptors, which allows it to interact with cell components involved in protein synthesis.

Chemical Structure



Mechanism of Action

➢ Like testosterone and other androgenic hormones, dromostanolone binds to the androgen receptor. This causes downstream genetic transcriptional changes. This ultimately causes retention of nitrogen, potassium, and phosphorus; increases protein anabolism; and decreases amino acid catabolism.

Uses

- It is prescribed for the treatment of breast cancer in women, but it has been withdrawn from the market. It can also be used as to administer injection in the muscle.

Stability and Storage Conditions

▪ It should be stored at 0°- 4°C for short-term (days toweeks) or at -20°C for long-term (months to years) in dry and dark places.

Types of Formulations

1. Injection
2. Solutions

Popular Brand Names

♦ Drolban
♦ Masteril

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