AITBS
PHARMACY BOOKS

Pharmaceutical Chemistry
for Diploma in Pharmacy

Exclusively Prepared for D.Pharm First Year Students (PCI ER 2020)

Dr. Atul R. Bendale
Harshali R. Ahire
Vaishali D. Naphade
Dr. Anil G. Jadhav

AITBS PUBLISHERS, INDIA

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RECOMMENDATION TO
STUDENTS
Mob.: 9999080104

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Exclusively Prepared for D.Pharm First Year Students (PCI ER 2020)

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SYLLABUS

PHARMACEUTICAL CHEMISTRY – THEORY

Course Code: ER20-12T **75 Hours (3 Hours/Week)**

Scope: This course is designed to impart basic knowledge on the chemical structure, storage conditions and medicinal uses of organic and inorganic chemical substances used as drugs and pharmaceuticals. Also, this course discusses the impurities, quality control aspects of chemical substances used in pharmaceuticals.

Course Objectives: This course will discuss the following aspects of the chemical substances used as drugs and pharmaceuticals for various disease conditions.

1. Chemical classification, chemical name, chemical structure.
2. Pharmacological uses, doses, stability and storage conditions.
3. Different types of formulations/dosage form available and their brand names.
4. Impurity testing and basic quality control tests.

Course Outcomes: Upon successful completion of this course, the students will be able to:

1. Describe the chemical class, structure and chemical name of the commonly used drugs and pharmaceuticals of both organic and inorganic nature.
2. Discuss the pharmacological uses, dosage regimen, stability issues and storage conditions of all such chemical substances commonly used as drugs.
3. Describe the quantitative and qualitative analysis, impurity testing of the chemical substances given in the official monographs.
4. Identify the dosage form & the brand names of the drugs and pharmaceuticals popular in the marketplace.

Chapter 1: Introduction to Pharmaceutical Chemistry

Scope and Objectives

Sources and types of errors: Accuracy, precision, significant figures.

Impurities in Pharmaceuticals: Source and effect of impurities in Pharmacopoeial substances, importance of limit test, Principle and procedures of Limit tests for chlorides, sulphates, iron, heavy metals and arsenic.

Chapter 2: Volumetric Analysis

Fundamentals of volumetric analysis, Acid-base titration, non-aqueous titration, precipitation titration, complexometric titration, redox titration.

Gravimetric analysis: Principle and method.

Chapter 3: Inorganic Pharmaceuticals

Pharmaceutical formulations, market preparations, storage conditions and uses of:

- ***Haematinics:*** Ferrous sulphate, Ferrous fumarate, Ferric ammonium citrate, Ferrous ascorbate, Carbonyl iron.

- *Gastrointestinal Agents:* Antacids: Aluminium hydroxide gel, Magnesium hydroxide, Magaldrate, Sodium bicarbonate, Calcium Carbonate, Acidifying agents, Adsorbents, Protectives, Cathartics.
- *Topical agents:* Silver Nitrate, Ionic Silver, Chlorhexidine Gluconate, Hydrogen peroxide, Boric acid, Bleaching powder, Potassium permanganate.
- *Dental products:* Calcium carbonate, Sodium fluoride, Denture cleaners, Denture adhesives, Mouth washes.
- *Medicinal gases:* Carbon dioxide, nitrous oxide, oxygen.

Chapter 4: Introduction to nomenclature of organic chemical systems with particular reference to heterocyclic compounds containing up to Three rings.

Study of the following category of medicinal compounds with respect to classification, chemical name, chemical structure (compounds marked with*) uses, stability and storage conditions, different types of formulations and their popular brand names

Chapter 5: Drugs Acting on Central Nervous System

- *Anaesthetics:* Thiopental Sodium*, Ketamine Hydrochloride*, Propofol.
- *Sedatives and Hypnotics:* Diazepam*, Alprazolam*, Nitrazepam, Phenobarbital*
- *Antipsychotics:* Chlorpromazine Hydrochloride*, Haloperidol*, Risperidone*, Sulpiride*, Olanzapine, Quetiapine, Lurasidone.
- *Anticonvulsants:* Phenytoin*, Carbamazepine*, Clonazepam, Valproic Acid*, Gabapentin*, Topiramate, Vigabatrin, Lamotrigine.
- *Anti-Depressants:* Amitriptyline Hydrochloride*, Imipramine Hydrochloride*, Fluoxetine*, Venlafaxine, Duloxetine, Sertraline, Citalopram, Escitalopram, Fluvoxamine, Paroxetine.

Chapter 6: Drugs Acting on Autonomic Nervous System

- *Sympathomimetic Agents:* Direct Acting: Nor-Epinephrine*, Epinephrine, Phenylephrine, Dopamine*, Terbutaline, Salbutamol (Albuterol), Naphazoline*, Tetrahydrozoline. Indirect Acting Agents: Hydroxy Amphetamine, Pseudoephedrine. Agents with Mixed Mechanism: Ephedrine, Metaraminol.
- *Adrenergic Antagonists:* Alpha Adrenergic Blockers: Tolazoline, Phentolamine.
- *Phenoxybenzamine, Prazosin. Beta Adrenergic Blockers:* Propranolol*, Atenolol*, Carvedilol.
- Cholinergic Drugs and Related Agents: Direct Acting Agents: Acetylcholine*, Carbachol, and Pilocarpine. Cholinesterase Inhibitors: Neostigmine*, Edrophonium Chloride, Tacrine Hydrochloride, Pralidoxime Chloride, Echothiopate Iodide.

- Cholinergic Blocking Agents: Atropine Sulphate*, Ipratropium Bromide Synthetic Cholinergic Blocking Agents: Tropicamide, Cyclopentolate Hydrochloride, Clidinium Bromide, Dicyclomine Hydrochloride*.

Chapter 7: Drugs Acting on Cardiovascular System

- ***Anti-Arrhythmic Drugs:*** Quinidine Sulphate, Procainamide Hydrochloride, Verapamil, Phenytoin Sodium*, Lidocaine Hydrochloride, Lorcainide Hydrochloride, Amiodarone and Sotalol.
- ***Anti-Hypertensive Agents:*** Propranolol*, Captopril*, Ramipril, Methyldopate Hydrochloride, Clonidine Hydrochloride, Hydralazine Hydrochloride, Nifedipine,
- ***Antianginal Agents:*** Isosorbide Dinitrate.

Chapter 8: Diuretics

Acetazolamide, Frusemide*, Bumetanide, Chlorthalidone, Benzthiazide, Metolazone, Xipamide, Spironolactone.

Chapter 9: Hypoglycemic Agents.

Insulin and its Preparations, Metformin*, Glibenclamide*, Glimepiride, Pioglitazone, Repaglinide, Gliflozins, Gliptins.

Chapter 10: Analgesic and Anti-Inflammatory Agents

Morphine Analogues, Narcotic Antagonists; Non-steroidal Anti-Inflammatory Agents (NSAIDs) – Aspirin*, Diclofenac, Ibuprofen*, Piroxicam, Celecoxib, Mefenamic Acid, Paracetamol*, Aceclofenac.

Chapter 11: Anti-Infective Agents

- ***Antifungal Agents:*** Amphotericin-B, Griseofulvin, Miconazole, Ketoconazole*, Itraconazole, Fluconazole*, Naftifine Hydrochloride.
- ***Urinary Tract Anti-Infective Agents:*** Norfloxacin, Ciprofloxacin, Ofloxacin*, Moxifloxacin.
- ***Anti-Tubercular Agents:*** INH*, Ethambutol, Para Amino Salicylic Acid, Pyrazinamide, Rifampicin, Bedaquiline, Delamanid, Pretomanid*.
- ***Antiviral Agents:*** Amantadine Hydrochloride, Idoxuridine, Acyclovir*, Foscarnet, Zidovudine, Ribavirin, Remdesivir, Favipiravir.
- ***Antimalarials:*** Quinine Sulphate, Chloroquine Phosphate*, Primaquine Phosphate, Mefloquine*, Cycloguanil, Pyrimethamine, Artemisinin.
- ***Sulfonamides:*** Sulfanilamide, Sulfadiazine, Sulfamethoxazole, Sulfacetamide*, Mafenide Acetate, Cotrimoxazole, Dapsone*.

Chapter 12: Antibiotics

Penicillin G, Amoxicillin*, Cloxacillin, Streptomycin.

Tetracyclines: Doxycycline, Minocycline.

Macrolides: Erythromycin, Azithromycin, Miscellaneous: Chloramphenicol* Clindamycin.

Chapter 13: Anti-Neoplastic Agents

Cyclophosphamide*, Busulfan, Mercaptopurine, Fluorouracil*, Methotrexate, Dactinomycin, Doxorubicin Hydrochloride, Vinblastine Sulphate, Cisplatin*, Dromostanolone Propionate.

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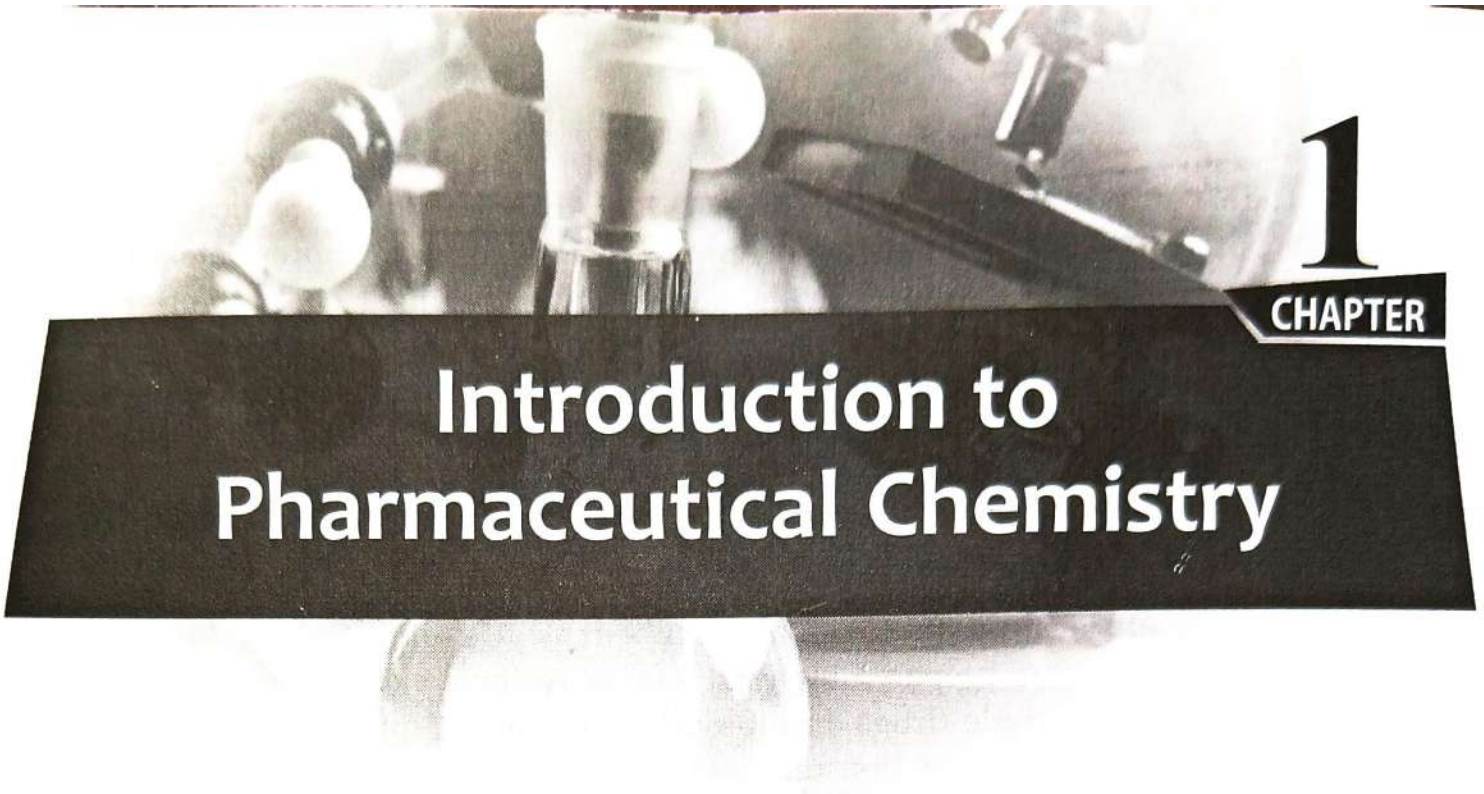


CHAPTER 1

Introduction to Pharmaceutical Chemistry

PHARMACEUTICAL CHEMISTRY

It is a division of chemistry that deals by means of the study of organic Molecules incorporated with chemical biology, structural biology and pharmacology for creating pharmaceutical drugs and medicines. In practice, it entails chemical features of identification as well as the modification of new chemical entities to make them therapeutically useful. Pharmaceutical chemistry is concerned with the quality of medications and tries to ensure their fitness for purpose by examining and assessing them in accordance with quality control standards.

It comprises drug development and the study of drugs. This includes drug discovery, metabolism, absorption and delivery. Drug is any material offered to treat, cure or prevent disease in humans or in animals.

They contain drug chemistry, quality assurance, metabolism, pharmacology and analytical techniques and cures and remedies disease.

- This discipline offers ample job openings in academic, production, research laboratories, biotechnology and medical device businesses, government organizations and various other government research laboratories. Pharmaceutical chemists are involved in wide range of activities and have the opportunity of getting excited about exploring the unknown. Pharmaceutical chemists are involved in the development, synthesis and discovery of action of novel medications, as well as the characterization and impurity profiling of existing drugs. They're in charge of creating innovative medications with better efficacy, safety and pharmacokinetic profiles.

- The expertise of Pharmaceutical Chemists and Analytical Pharmaceutical Chemists is put to good use in optimizing the process and developing appropriate ways for manufacturing pharmaceuticals, resulting in the most cost-effective and environmentally friendly procedure. They are in high demand by the pharmaceutical industry because of their ability to critically analyse and manipulate pharmacological attributes.

PHARMACOPOEIA

Pharmacopoeia appear from the Greek name "Pharmakon" (drug) and 'Poiein' (make), It is an official collection, prepared by a national or regional expert and covers list of medicinal substances, crude drugs and formulas for making formulation from them. The term 'Pharmacopoeia' was first reported in a manuscript on drug standard from Italy in 1580. There are several national and international pharmacopoeias.

In December 1820, the 1st pharmacopoeia was published in the United States. In addition to the U.S.P., a National Formulary was published later. The goal of the U.S.P. was to choose medicinally useful ingredients and transform them into appropriate preparations in order to maximise their effectiveness.

The World Health Organization produced the 1st International Pharmacopoeia in 1951 as Volume 1st and the 2nd in the year 1955 as Volume II.

The British Pharmacopoeia is the United Kingdom's national pharmacopoeia. It is a crucial constitutional component in the regulation of pharmaceuticals. It expresses the UK's pharmaceutical standards, together with the British National Formulary (BNF). The 1st volume of the British Pharmacopoeia (BP) was published in 1864.

The European Pharmacopoeia aims to provide common quality standards all over Europe. First European Pharmacopoeia was issued in 1864.

INDIAN PHARMACOPOEIA (IP)

Commission of the East Indian Company's Dispensary suggested the Publication of Pharmacopoeia in 1833. The general outline of Medicinal Plants was printed in 1844, which primarily listed normally used native medications. This was followed by IP 1868, enclosing native drugs used in India. Yet, on or after 1885 the BP was through authorized in India.

The Indian Pharmacopoeia Committee was established in 1948 with the primary purpose of publishing IP. The Indian Pharmacopoeia Commission (IPC) is an independent body within the Ministry of Health and Family Welfare that creates standards for all

medications produced that sold and utilized in India. The pharmaceuticals manufactured in India have to be characterized with the suffix I.P. (i.e., Boric Acid I.P.)

The Indian Pharmacopoeia can be summarized as follows:

Table 1.1: ***History of Indian Pharmacopoeia***

Edition	Year	Addendum/Supplement
1st	**1955**	Supplement 1960
2nd	**1966**	Supplement 1975
3rd	**1985**	Addendum 1989
		Addendum 1991
4th	**1996**	Addendum 2000
		Vet Supplement 2000
		Addendum 2002
		Addendum 2005
5th	**2007**	Addendum 2008
6th	**2010**	Addendum 2012
7th	**2014**	Addendum 2015
		Addendum 2016
8th	**2018**	Addendum 2019

In 1868, first official Pharmacopoeia of India published, which was edited by the team of Edward John Waring. In pro-independence days, British Pharmacopoeia was used in India. The foreign supplement of BP 1898 was printed in 1900 come out as Government of India version in 1901. In 1946, Government of India published "The Indian Pharmacopeial list". In 1946, "The Indian Pharmacopeial list" prepared by Sir R.N. Chopra (Chairman) together with other nine members, under Department of Health, Government of India, Delhi. In 1948, Government of India selected an Indian Pharmacopoeia committee for making "Pharmacopoeia of India" for tenure of five years

- Indian Pharmacopoeia committee in chairmanship of Dr. B.N. Ghosh Issued first edition of IP in 1955, written in English where official titles of monographs given in Latin. It contains 968 monographs. In 1960, supplement of this edition was published.

- In 1966, 2nd edition of IP was published under the Chairmanship of Dr. B. Mukherji. Official titles of monographs were given in English and dose was expressed in Metric system. 274 monographs and their supplements from previous IP were deleted and 93 new monographs were added. In 1975 its Supplement was published
- 3rd edition of IP was published in 1985; it has II volumes and 9 appendices. 261 latest monographs have been introduced and 450 monographs were removed. Its first and second addendum published in 1991 and 1989 respectively.
- In 1996 fourth IP was published under Chairmanship of Dr. Nityanand. It contains 123 appendices and 1149 monographs. It consists of 294 latest monographs and 110 monographs have been omitted. Its first and second addendum published in 2000 and 2003 respectively.
- In 2007, 5th edition of IP was published and its addendum was introduced in 2008. It was available in Three Volumes. Volume-I covers general notices and chapters; whereas Volumes II and III comprises of monographs on pharmaceutical substances, dosage forms and Pharmaceutical aids.
- 6th edition of Indian Pharmacopoeia was published in 2010 in III volumes. Volume I cover the Structure of the IPC, Notices, Preface, Acknowledgements, preface and the General Chapters, Volume II covers the Monographs on Dosage Forms, drug substances and pharmaceutical aids. Volume III covers remaining monographs.
- In 2014, 7th edition of IP was published by the IPC (Indian Pharmacopoeia Commission) for the Government of India, Ministry of Health and Family Welfare in IV volumes. It incorporates 2550 monographs of drugs from that 577 are latest monographs. 19 New Radiopharmaceutical Monographs were included in this edition. The addendums of IP 7th edition (2014) were released in 2015 and 2016 respectively.
- In 2018, 8th edition of IP was made available, it has IV volumes. It contains- 170 Chemical Monographs, 15 are Herbal, 10 are on Blood and Blood related products, 6 are Biotechnology derived therapeutic products, 3 are of Radiopharmaceuticals, 2 of Vaccines and Immunosera and 14 are of Veterinary Non-Biologicals. More precise IR, UV spectrophotometer and HPLC tests have been given. The addendums of IP 8th edition (2018) were released in 2019.

SIGNIFICANT FIGURES

These are the number of those digits that carry meaning contributing to its measurement decision. The number of significant figures is basically the number of figures that are recognized with some scale of dependability. This consist of all digits excluding:

- All leading zeros (which appears before non-zero digit in a number)
- Trailing zeros while they are only placeholders for the number's scale; and spurious digits introduced, e.g., by calculations performed to a higher precision than the unusual data or measurements reported to a higher precision than the apparatus allows.

Specifically, the policy for identifying significant figures while writing or interpreting numbers are as below:

- All non-zero digits are taken into account.

  For instance, 15 has two significant figures (1 and 5), whereas 987.65 has five (9, 8, 7, 6 and 5).
- Any zero that appears between two non-zero digits is important.

  123.0456 is an example of a seven-digit number with seven significant figures: 1 to 6.
- Leading zeros have no bearing.

  0.0098, for instance, has two significant figures: 9 and 8.
- Trailing zeros in a number containing a decimal point are significant.

  12.3400, for instance, includes six significant figures: 1, 2, 3, 4, 0 and 0. only six major figures remain in the number 0.000123400. (The zeros before the 1 are not significant).

Furthermore, because it has three trailing zeros, 504.00 has 5 significant figures.

ERROR AND ITS TYPES

The difference between the true value or standard value and observed value is called error.

Example: If a medicine contains 10 g of active drug as standard value and after analysis the analyst observed 9.95 g of active drug in the tablet.

$$\text{ERROR} = 10.0 - 9.95 = 0.05 \text{ g}$$

$$\% \text{ Error} = \frac{0.05}{10} \times 100 = 0.5\%$$

The term error is used to describe the disparity between what is measured and what is true/standard. When a measurement is made, it is not possible to completely eliminate the error, even when the person making the measurement is an expert working with apparatus of best quality. So, different or repeated attempts are made to minimize the error.

Magnitude of error should be known to the analyst, which is the variation between the experiential value and the true/standard value.

Since true values are never known one has to made use of the most probable or standard value.

The standard value can be obtained by following method:

1. **Absolute Method:** In this method, the sample is synthesized using known quantities of the constituents and thus, a primary standard is obtained.

   Hence, the true values for the number of different constituents are recorded.

   Now, the sample is analyzed by some method and the observed values for the quantities of the constituents are recorded.

   Knowing the true and the observed values, the error of the method can be calculated.

2. **Comparative Method:** In some cases, as in the case of a mineral or an ore, it is not possible to prepare the synthetic sample. In such a case, the analytical data provided by some standard agency is obtained.

   The value provided is that data are the standard values for the quantities of the different constituents present in the sample.

   The difference in the observed and the standard value gives the error of the method used for analysis.

TYPES OF ERROR

A. Determinate or Systematic Error

Certain error whose causes, at least in principle can be known. These are usually one sided and by preplanning and careful working, these error can be avoided or kept at minimum.

Types of Determinate Error

1. **Personal Error:** As a result of the person making the decision not working properly. A person who is unable to judge the colour shift of the indicator at the titration's end point.
2. **Instrumental or Reagent Error:** As a result of a flaw in the equipment or the use of impure reagent. Assume a 10 ml pipette is used to extract a sample solution for analysis; however the pipette only extracts 9.5 ml due to a design flaw. As a result, a 0.5 ml mistake will be created, which will always be negative.

3. **Method Error:** This category includes any error that occurs during the method. Example: Decomposition of the precipitate during ignition due to complete reaction, solubility of a precipitate in gravimetric analysis.
4. **Additive Error:** In some series determinations, the degree of error is constant and irrespective of the amount of sample taken for analysis; this is referred to as additive error.

   Example: To show the colour change clearly at the end point of a titration, 0.1 mL more titrant must be applied. In other words, the end point error is 0.1 ml. As a result, if the standard value is 10 milliliters, the observed value is 10.1 milliliters.

   The standard value is 20 ml if the sample used for the titration is doubled, yet the value in the titration is 20.1 ml.
5. **Proportional Mistake:** The extent of this sort of error is determined by the sample size.

B. Indeterminate Error

These are also known as random or accidental errors. The cause of a random error may or may not be known. Indeterminate errors are not one sided and they cannot be eliminated even when the analysis is done with the great care using high quality apparatus and reagents. Random errors are due to causes over which the analyst has no control.

When the same quantity is measured several times, different observed value will not be similar and this difference is called indeterminate error.

Example: A Tablet of 1.0 g is weighed on analytical balance and we want to know its weight to the nearest of a gram, i.e., whether it is 0.8, 0.9 or 1.0 replicate result will be obtained.

But if we want to know the weight of the ball up to the fourth place of decimal, the different weight readings will vary slightly from one another and also from the standard value of the weight of the ball.

ACCURACY

The degree of agreement between the calculated and true values is known as **accuracy.** An absolute true value is seldom known. So, the term accuracy refers to how near the observed value is to true or standard value.

PRECISION

Precision is the degree of agreement among replicate measurements of the similar quantity. It is the repeatability of a result. The precision may be expressed as the standard value. So, the term precision refers to nearness between several measurements of the same quantity.

Example: There are 2 analysts A and B. who determine the percentage of the API in same tablet. The standard value for API in the tablet is 100.00%, whereas.

Two analysts obtained the following results:

Analyst A: 99.80, 99.90, 100.00, 99.30.

$$\text{Average value} = \frac{99.80 + 99.90 + 100.00 + 99.30}{4} = 99.75$$

$$\text{ERROR} = 100.00 - 99.75 = 0.25\%$$

Analyst B: 98.60, 98.65, 98.70, 98.75

$$\text{Average value} = \frac{98.60 + 98.65 + 98.70 + 98.75}{4} = 98.675$$

$$\text{ERROR} = 100.00 - 98.675 = 1.325\%$$

Because the different observed values of analyst A differ so considerably, the precision is weak but the accuracy is good.

On the other hand, the accuracy of the result of analyst B is comparatively poor (error = 1. 325 %) but his observed values do not differ much from each other hence the precision is better as compared to that in the measurement of analyst A.

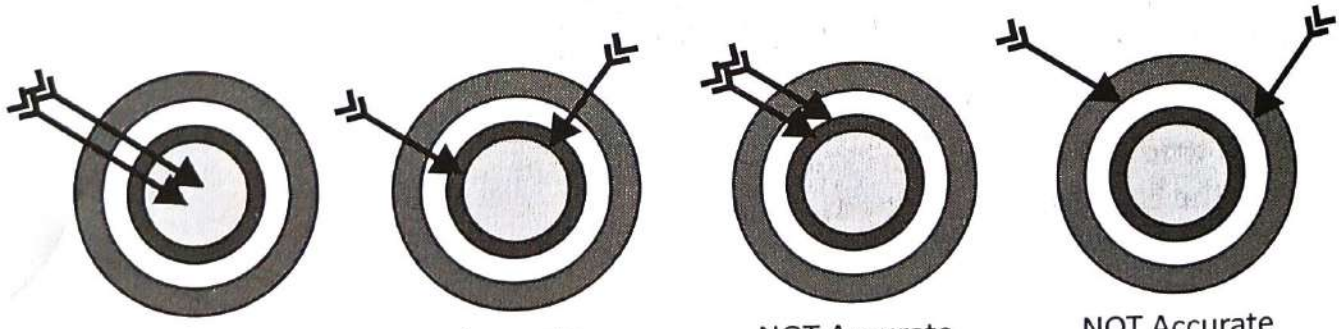
Precision can be determined by Standard deviation, lower the standard deviation value; higher will be the precision.

$$\text{Standard Deviation (s)} = \frac{\sqrt{S(X - Xi)^2}}{n - 1}$$

where s = Standard deviation,

xi = Mean/Average of the sample data,

n = number of the sample.



SOURCES OF IMPURITIES AND THEIR CONTROL

Introduction

Impurity is something that is impure or makes something else impure. In the pharmaceutical industry, an impurity is defined as any organic material other than the medication substance that results from the synthesis; inorganic contaminants, such as heavy metals or arsenic, are not considered impurities unless they are hazardous.

There may be many sources for impurities in drug products and sources are same as in reference drug substances. Impurities may arise from starting materials, by-products, residual solvents, degradation product formed and long-term storage. Impurities can be formed from heat, light, changes in pH of formulation, interaction with packaging components and other components.

Impurities can originate mainly from sources that are given below:

1. **Crystallization Related Impurities:** First goal in pharmaceutical manufacturing is to produce pure drug substance and remains in that state as long as bulk material. It is another goal in formulation of drug substance so that it remains in same state during manufacturing and during its storage. Solid properties of system may be affected by nature of structure adopted by compound on crystallization.
2. **Stereochemistry Related Impurities:** The compounds have like chemical assembly but dissimilar spatial orientation; these are regarded as impurities in the Active Pharmaceutical ingredients. The lone enantiomer of chiral compound may have superior pharmacological profile and high therapeutic index. In manufacturing of single enantiomeric drug, the undesirable stereoisomers are considered as organic impurities. Single isomeric drugs that are marketed include esomeprazole (Someprazole), levalbuterol (R-albuterol) and levofloxacin (Sofloxacin).
3. **Residual Solvents:** Commonly used solvent in drug products is water. Water is not considered as impurity most of time. When dosage form is packaged, moisture content can be important because it may be sufficient to cause the hydrolysis. Drugs products can also be affected by water from the environment. Hydrolysis due to presence of water causes chemical stability problems mainly in acetals and carboxylic acid derivatives. Even in non-aqueous liquid formulations, water can be present in sufficient amount that may cause degradation.
4. **Synthetic Intermediates and by-products:** During the synthetic process, most of the impurities in pharmaceutical compounds are generated from raw materials, solvents, intermediates and by-products. A drug substance is manufactured to much more purity requirements than Raw material.

Solvents used in synthesis may contain number of impurities from traces level to higher quantity which can react with compounds used in the synthesis to yield impurities.

5. **Formulation Related Impurities:** Excipients are also sources for generation of most impurities in drug product. The drug substance undergoes various conditions during process of formulation which may cause its degradation and some undesirable reactions. For example, when heat is used for drying, it may cause degradation. Due to hydrolysis or solvolysis, solution and suspensions are prone to degradation. In US, Fluocinonide Topical solution (USP) was recalled because of degradation or impurities production; it leads to concentration below standard level. In most cases, liquid dosage forms may undergo both degradation as well as microbial contamination.
6. **Impurities Arising during Storage:** During storage, number of impurities can be produced. For assurance of drug product safety, it is mandatory to carry out stability studies. To overcome the production of impurities, the stability characteristics can be used to store the drug substance and drug product in appropriate packaging and environmental condition. For development of best formulation, the knowledge of degradation behaviour of drug and its interaction with excipients is also useful.
7. **Method Related Impurity:** In production of parenteral dosage form of Diclofenac sodium, 1-(2, 6-dichlorophenyl) Indolin-2-one is formed as impurity when it is sterilized by autoclave. The formation of indolinone derivative and sodium hydroxide occurs due to reaction of diclofenac sodium by autoclave conditions (123+2°C).
8. **Mutual Interaction:** Due to labile nature of vitamins, over the period of time they undergo instability in liquid dosage forms. On degradation of vitamins, toxic impurities are not produced but potency of active ingredients somewhat decreases, sometimes below Pharmacopeial specifications. An example of mutual interaction is existence of nicotinamide in preparation containing vitamins like- Nicotinamide, pyridoxine, riboflavin and thiamine may cause degradation of thiamine.
9. **Functional groups Related to Degradation:**
   (a) **Ester Hydrolysis:** Impurities can be produced in esters due to presence of water in drug products as esters undergo hydrolysis. Example includes Aspirin, Benzocaine, Cefotaxime and ethyl paraben.
   (b) **Hydrolysis:** Hydrolysis means degradation of drug products or arising of impurities in presence of water. It is common in drugs having esters and liquid formulations, e.g., benzylpenicillin, oxazepam and lincomycin.

(c) **Oxidative Degradation:** It means degradation of drugs due to their oxidation. Example of drugs that are prone to oxidative degradation are hydrocortisone and methotrexate. The hydrolytic and oxidative degradation pathways were studied in drug mazipredonein 0.1 mol/lit. HCl and NaOH at 80°C.

(d) **Photolytic Cleavage**: It means degradation of products can happen in presence of light, during manufacturing as solid (or may be solution), packaging or during storage in shops or hospitals. Examples of the drugs that experience Photolytic degradation are Nifedipine, Nitroprusside, Riboflavin, Ergometrine and Phenothiazines, fluoroquinolone antibiotics. In all these compounds, free radical intermediates are formed by photochemical energy. 0.3% Eye drop preparation of ciprofloxacin is also an example of photolytic cleavage. Sunlight produces ethylene diamine derivative of ciprofloxacin by photolytic cleavage.

(e) **Decarboxylation:** It includes removal of CO_2 from carboxyl group on heated. It occurs in some carboxylic acid like, p-amino salicylic acid. Photoreaction of Rufloxacin is an example of decarboxylation.

10. **Environment Related Impurities:** Environment related factors that reduce the stability of drug substances. Exposure to unfavourable temperature Light especially UV light Humidity make such type of changes in formulations.

    (a) **Exposure to Unfavourable Temperature:** Many of drug substances are labile to heat, e.g., vitamins are heat sensitive and undergo degradation in liquid formulation that may cause decrease in potency.

    (b) **Light (UV light):** The custom-made parenteral preparation of ergometrine (0.2 mg/mL) shows degradation when kept in direct sunlight for 42 hours.

11. **Adulteration:** For increasing bulk of original compound sometimes mixed with bulkier material. This malpractice may increase weight or decrease the cost of original material. Cheaper agents of similar properties are incorporated to increase the weight and bulk of drug so as to increase revenue. This practice is punishable under the D and C Act, 1940.

12. **Humidity** For hygroscopic products, humidity may affect the formulated dosage forms. Examples of the drugs that are affected by humidity are Aspirin and Ranitidine.

ffect of Impurity on Pharmaceutical Preparations

1. **Toxic impurities:** These impurities have toxic effect on body if present beyond prescribed limit, e.g., Lead or Arsenic.
2. **Impurities which are harmless:** These may lower the potency of the substance. For example, impurities of Sodium salts in Potassium salts.

3. Impurities which affect the storage capacity of pharmaceuticals, e.g., presence of moisture beyond limit may affect the flow property of substance or decompose it.
4. Impurities causing technical difficulties, e.g., presence of carbonate impurity in ammonia solution.
5. Impurities may cause changes in odour, colour and taste thereby making the substance unethical and unhygienic.
6. Impurities may cause incompatibility with other substances.
7. Impurities may decrease the shelf life of substances.
8. Impurities, even when present in traces, may show a cumulative toxic effect after a certain period.

Test for Purity or Test for Impurity

The common impurities found in most substances are chloride, sulphate, iron, lead, heavy metals and arsenic. The permissible limit of these impurities does not vary much from compound to compound and procedure is also similar. Test for these impurities is called limit test. Limit test is a qualitative as well as semi quantitative test. Except arsenic all these limit tests are performed in a pair cylinders having, uniform diameter, i.e., Nessler cylinders as per the specification of pharmacopoeia. The limit test of arsenic is performed in a specially designed glass apparatus called "Gutzeit apparatus" in the honor of scientist "Gutzeit". The test for other impurities presents in the substance is called "Test for purity"

LIMIT TESTS

These are qualitative or semi-quantitative assessment intended to detect and limit slight amounts of impurities that are usually present in pharmaceutical substance. They are based on comparing the amount of opalescence, turbidity or colour produced by an impurity in a sample to the amount produced in a standard under the same test conditions.

Limit Test for Official Compounds

1. Limit Test for Chloride

Principle:

In the presence of dil. nitric acid, a reaction between $AgNO_3$ and soluble chlorides produces insoluble silver chloride, which is used to check chloride contamination in inorganic

substances. This silver chloride (insoluble) makes the solution opalescent and the extent of opalescence is compared to a standard opalescence in the test solution.

$$\underset{\text{(Soluble)}}{Cl^-} + AgNO_3 \longrightarrow \underset{\text{(Insoluble)}}{AgCl\downarrow} + NO_3^- \text{ (In presence of Dil. } HNO_3\text{)}$$

The material passes the limit test for chloride if the opalescence produced in the test is less intense than standard opalescence and *vice-versa.*

With silver nitrate solution, dilute nitric acid is employed to prevent the precipitation of other acid radicals.

Procedure:

Standard Solution	Test Solution
1. Add 10 ml standard chloride solution in Nessler's cylinder, Label it as "Standard".	1. Dissolve about 1 g of given unknown sample in 10 ml of distilled water. Transfer it in Nessler's cylinder and label it as "Test".
2. Add 10 ml dil.HNO_3	
3. Make up to 50 ml with distilled water.	
4. Now add 1 ml 0.1 M silver nitrate solution in it.	
5. Stir with the glass rod and set aside for 5 minutes.	
6. Compare turbidity (opalescence) of test and standard solution by observing in light.	

*Step no. 2 to 6 is common for both

Note: HNO_3 make the solution acidic and to aid silver chloride precipitation.

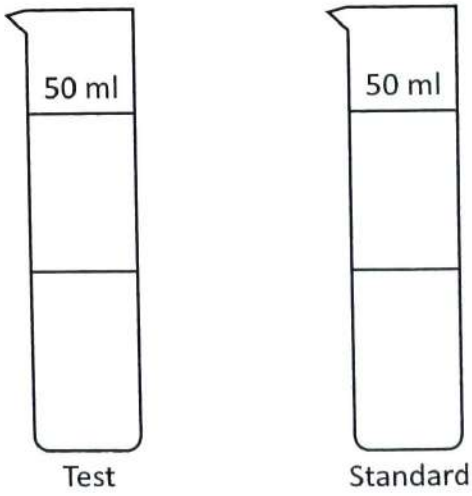


Fig. 1.1: ***Nessler Cylinder***

2. Limit Test for Sulphate

Principle:

This test is designed to control sulphate impurity primarily and found in inorganic substance and is based upon the simple reaction between barium chloride and soluble sulphate in the presence of acetic acid to give insoluble barium sulphate.

$$SO_4^{-2} + BaCl_2 \rightarrow BaSO_4 + 2Cl^-$$

Procedure:

Standard Solution	Test Solution
1. Take 1 ml Barium chloride solution (25 % w/v) in Nessler cylinder.	1. Take 1 ml barium chloride solution (25 % w/v) in Nessler's cylinder.
2. Now add 1.5 ml of sulphate standard solution (ethanolic) in it.	2. Add 1.5 ml of ethanolic sulphate standard solution (ethanolic) in it.
3. Stir well and allow standing it for 1 min.	3. Stir well and allow to stand it for 1 min.
4. Add 15 ml of standard sulphate solution (10 ppm) in it.	4. Add 15 ml solution of unknown sample in it.
5. Add 5M acetic acid (0.15 ml)	
6. Make up to 50 ml with distilled water.	
7. Stir well and keep aside for 5 minutes.	

Compare turbidity of test and standard solution by viewing in front of dark background.

*Step no. 5 to 7 is common for both

Note: Alcohol prevents super saturation

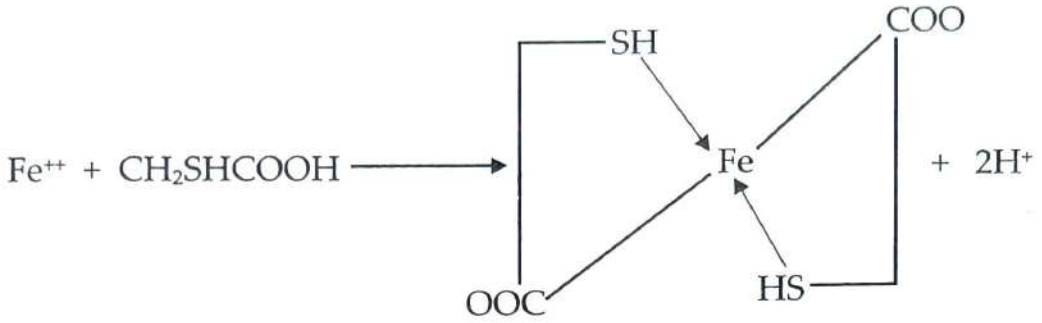
3. Limit Test for Iron

Principle:

The interaction of iron with thioglycolic acid in the presence of citric acid in an alkaline solution prepared with ammonia solution results in the creation of a pale pink to deep reddish purple colour. The colour is due to the production of ferrous thioglycolate Fe $(HSCH_2COO)_2$ a co-ordination molecule.

$$Fe^{3+} + 2CH_2^{-}SH\text{-}COOH \rightarrow Fe^{2+} + (HOOC\text{-}CH_2\text{-}S\text{-}S\text{-}CH_2\text{-}COOH)_2 + 2H^+$$

Ferric Thioglycolic acid Ferrous



The colouration formed is compared with the standard colouration having a definite quantity of iron. Citric acid is added in the official process to avoid the precipitation of iron by ammonia. Iron gets precipitated in the form of $Fe(OH)_2$ and $Fe(OH)_3$ depending upon the oxidation state of the iron, in the presence of ammonia.

Procedure:

Wash a pair of Nessler's cylinder distilled water and dry it.

Standard Solution	Test Solution
1. Add 2 ml of Standard iron solution (20 ppm Fe) in Nessler's cylinder and label it as "Standard".	1. Weigh accurately about 1 g of NaCl or sample. Dissolve it in 40 ml of distilled water.
2. Make up to 40 ml mark with distilled water.	2. Transfer the solution made in step 2 in Nessler's cylinder and label it as "Test"
3. Add 2 ml iron free citric acid solution (20% w/v).	
4. Now add 0.1 ml thioglycolic acid in it.	
5. Alkaline the solution with iron free ammonia solution.	
6. Dilute the solution up to 50 ml with distilled water.	
7. Stir well and keep aside for 5 minutes.	

Compare intensity of colour of both the solution

*Step no. 3 to 7 is common for both

Notes:

- Thioglycolic acid helps to oxidize iron (II) to iron (III).
- Ammonia to make solution alkaline

Application:

This test has been specified in IP for lactic acid, calcium lactate, dibasic calcium phosphate, potassium chloride, sodium bicarbonate, sodium chloride and many other substances.

4. Limit Test for Lead

Principle:

The development of a lead–dithionate complex when lead and diphenyl thiocarbazone (dithizone) react in an alkaline environment is the basis for the lead limit test. The lead present as a contaminant in the material is separated by extracting an alkaline solution with dithizone extraction solution. Other metal ions are eliminated from the extraction by using reagents such ammonium citrate, potassium cyanide and hydroxylamine hydrochloride to change the optimum pH.

Dithizone in chloroform has a green colour, whereas the lead-dithionate complex has a violet colour. The intensity of the complex's violet colour, which varies depending on the amount of lead in the solution, is compared to a standard colour created by treating a standard solution with a certain amount of lead.

$$2(C_6H_5.N_2H_2)_2\ CS + Pb \rightarrow (C_6H_5.N_2)_4\ C_2S_2Pb + 2H^+$$

$$Pb^{+2} + H_2S \rightarrow PbS + 2H^+$$

Method (I.P. 1996):

Procedure:

Standard Solution	Test Solution
1. Prepare a standard lead solution equal to the maximum amount of lead allowed in the sample.	1. In a separating funnel, a known quantity of sample solution is transferred.
2. Add 6 ml ammonium citrate	
3. Add 2 ml potassium cyanide and 2 ml hydroxylamine hydrochloride	
4. Add 2 drops phenol red	
5. Add ammonia solution (to make solution alkaline)	
6. Extract with 5 ml dithizone until it becomes green	
7. Combine dithizone extracts are shaken for 30 min with 30 ml of nitric acid and the chloroform layer is discarded	

Standard Solution	Test Solution
8. To the acid solution add 5 ml of standard dithizone solution	
9. Add 4 ml of ammonium cyanide	
10. Shake for 30 min.	
11. Observe the colour	

*Step no. 2 to 11 is common for both.

Notes:

- Ammonium citrate, potassium cyanide and hydroxylamine hydrochloride are used to achieve the optimal pH, removing interference and the influence of other pollutants.
- Phenol red is utilized as a colour indication at the end of the process.

5. Limit Test for Heavy Metals

This test is used to assess the number of metallic impurities coloured by H_2S under the test conditions. Iron, copper, lead, nickel, cobalt, bismuth, antimony and other heavy metals (metal impurities) are examples. The limit for heavy metals are given in ppm of lead in each specific monograph. The metal sulphides stay colloidally dispersed, resulting in a brownish colour. The colour of the test solution is compared to the colour of a standard solution containing a specific amount of lead.

Heavy metals + $H_2S/Na_2S \rightarrow$ Heavy metals sulphides (Brownish colouration)

Method:

Preparation of Test Solution	Preparation of Standard Solution
1. Take 25 ml solution of test sample in Nessler cylinder and label it as "Test".	1. Take 2 ml standard lead solution (20: ppm) in Nessler cylinder and label it as "Standard". Make up to 20 ml with distilled water.
2. Adjust pH of solution at 3.0 to 4.0 with dilute acetic acid (or add 10 ml dil. Acetic acid).	
3. Mix well with glass rod.	
4. Now add 10 ml of freshly prepared saturated solution of hydrogen sulphide.	
5. Make the volume up to 50 ml with distilled water.	
6. Stir with the glass rod and set aside for 5 minutes.	

*Step no. 2 to 6 is common for both

Note: Acetic acid and ammonia are required for maintaining pH between 3.0 and 4.0 so that the uniform precipitate formed

*Sodium sulphide can be used instead hydrogen sulphide

6. Limit Test for Arsenic

Principle:

The principle is based on a sequence of reactions that transform any arsenic impurity present in the sample to arsine gas. When arsine gas comes into contact with mercuric chloride test paper, it forms a yellow or brown stain due to mercuric arsenic production. The sample's stain is compared to a standard stain created by a standard stain. The stain used in the sample shall not be darker than the stain used in the standard

$$\underset{\text{Arsenic acid}}{H_3AsO_4} + H_2SnO_2 \longrightarrow \underset{\text{Arsenious acid}}{H_3AsO_3} + H_2SnO_3$$

$$Zn^{2+} + 2SnHCl_3 \longrightarrow ZnCl_2 + 2\,SnCl_2 + 2[H]$$

$$\underset{\text{Arsenious acid}}{H_3AsO_3} + 3H_2 \longrightarrow \underset{\text{Arsine gas}}{AsH_3} + 3H_2O$$

$$2AsH_3 + HgCl_2 \longrightarrow Hg(AsH_2)_2 + 2HCl$$

The depth of the yellow stain depends on the quantity of arsenic present in the sample. It is judge against standard stain produced from a known amount of arsenic.

Method:

Standard Solution	Test Solution
1. Take 1 ml arsenic standard solution (10 ppm).	1. Dissolve 5 g of sodium acetate in 50 ml water in the flask.
2. Dilute up to 50 ml with water in the flask.	2. To this add 15 ml stannated hydrochloric acid
3. Add 5 ml of 1 M potassium iodide.	
4. And add 10 g zinc granules, mix well.	
5. Assemble the apparatus right away and place the bottle/flask in a water bath at a temperature that allows for a uniform gas evolution.	
6. After 40 minutes check for the stain produced by sample on mercuric chloride paper.	
7. Observe the intensity of stain produce on mercuric chloride paper and compare the stain of test with stain of standard.	

*Step no. 3 to 7 is common for both

Notes:

- Stannous chloride is required for complete evolution of arsine gas.
- Zinc, stannous chloride and potassium iodide are act as a reducing agent
- HCl makes the solution acidic.
- Lead acetate papers is used to trap H_2S; which may be evolved together with arsine.

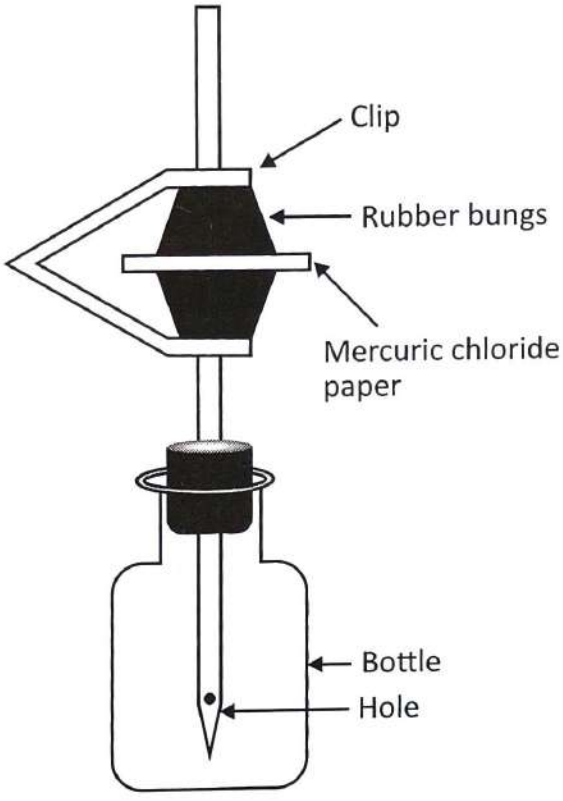


Fig. 1.2: *Gutzeit Apparatus*

Definition of Quality control

When it comes to medications and drug products, quality refers to all of the elements that contribute to the product's safety, effectiveness and dependability, whether directly or indirectly.

Importance of Quality Control in Pharmaceutical Industry

The term 'Quality Control' has assumed lots of importance in pharmaceutical field.

- The following Good Manufacturing Practices serve as the foundation for preserving a product's quality.

- Because it is critical that doctors have access to a high-quality product in order to treat patients or users, the pharmacist's and pharmaceutical industry's responsibilities have grown significantly.
- When it comes to pharmaceuticals and drug products, quality refers to all of the aspects that contribute to the product's safety, effectiveness and dependability, whether directly or indirectly.
- A quality control system is required in order for a medicine to have the features mentioned above.
- To achieve 'Quality Control,' a 'Total Quality Control' idea must be used.
- Total quality control will cover all parts of the process, from the purchase of raw materials to the finished products available in the pharmacy and until the consumer consumes it. As a result, it will cover not only GMP parameters but also storage-handling and sample preservation till final usage.
- A drug's quality is determined based on the recommendations of numerous expert bodies and these standards are published in the form of books (compendiums) such as pharmacopoeias, pharmacopeial codex and so on.
- Analyzing a medicine for quality and quantity is an important aspect of quality control.
- The official volumes detail several tests and processes for analysis, including identifying and determining contaminants.
- This is true for both the drug as a raw material and the drug as a finished product.
- This is explained in detail in the pharmacopeial monograph.
- The goal of all quality control studies and testing is to ensure that consumers and patients have access to high-quality drugs.

EXERCISE

Short Answer Type Questions

1. What is pharmacopoeia?
2. In the limit test of Iron, what is the use of citric acid, thioglycolic acid and ammonia?
3. Define:
   (a) Accuracy and precision
   (b) Pharmaceutical chemistry and quality control.
4. Explain role of acetic acid and ammonia in the limit test for heavy metals.

5. Give reason: Nitric acid used in limit test for chloride.
6. What is role of lead acetate cotton wool in arsenic limit test?
7. What is significant figure?
8. Draw neat labeled diagram of Gutzeit's apparatus.

Long Answer Type Questions

1. Describe the various sources of impurities present in pharmaceutical substances.
2. Write the principle, reactions and procedure involved in the limit test of arsenic.
3. Give principle, procedure, reactions and role of reagents involved in the limit test for Iron.
4. Give principle, procedure, reactions and role of reagents involved in the limit test for Lead
5. Write the procedure, reactions and principles for the limit tests for-
   (a) Sulphate
   (b) chloride
6. What are significant figures? Enlist the rules for retaining significant digits
7. What is error? Enlist its types
8. What is importance of Quality control in pharmaceutical industry:

Multiple Choice Questions (MCQ's)

1. Any substance that affects the purity of sample is:

(a) Poison (b) Impurity
(c) Reactant (d) Product

2. _____ is may affect by presence of impurities:

(a) Shelf life (b) Therapeutic effect
(c) Chemical properties (d) All of the above

3. Impurity in the sample can arise due to:

(a) Raw material used (b) Reagent used
(c) Solvents used (d) All of the above

4. Quantitative test to identify and control small quantity of impurity is known as:

(a) Assay (b) Titration
(c) Limit test (d) Physical constant

5. Apparatus used to perform limit test of chloride and sulphate is:

(a) Nessler cylinder (b) Round bottom flask

(c) Beakers (d) Thieles apparatus

6. Nessler cylinder made up of which type of material?

(a) Plastic (b) Borosilicate glass

(c) Toughen glass (d) Teflon

7. Limit test for chloride based on reaction between soluble chlorides and _____.

(a) HCl (b) H_2SO_4

(c) $AgNO_3$ (d) All of the above

8. Name the chemical used to perform limit test for iron:

(a) Thioglycolic acid (b) $AgNo_3$

(c) $BaSO_4$ (d) All of the above

9. In the limit test for iron, iron used as:

(a) Ferrous fumarate (b) Ferrous thioglycolate

(c) Ferrous sulphate (d) None of the above

10. Limit test for sulphate based on reaction between soluble sulphate and _____.

(a) HCl (b) H_2SO_4

(c) $BaCl_2$ (d) All of the above

11. Limit test for heavy metals based on reaction between soluble heavy metals and _____.

(a) HCl (b) H_2SO_4

(c) H_2S (d) All of the above

12. Limit test for Lead based on reaction between lead and _____.

(a) Ferrous sulphate (b) Dithizone

(c) Thioglycolic acid (d) All of the above

13. Limit test for Arsenic based on reaction between Arsine gas and _____.

(a) Hydrogen gas (b) Sulphide gas

(c) Oxygen gas (d) All of the above

14. In limit test of arsenic Yellow coloured stain was observed with _____ paper.

(a) Mercuric (b) Turmeric

(c) Lead acetate (d) None of the above

15. Apparatus used in limit test of arsenic is:

(a) Nessler's cylinder (b) Thiele's apparatus

(c) Gutzeit apparatus (d) Stark apparatus

16. What is role of stannous chloride in limit test of arsenic?

(a) Evolution of arsine (b) Trapping of arsine

(c) Conversion of arsine (d) All of the above

17. What is role of lead acetate cotton plug in limit test of arsenic?

(a) Evolution of H_2S (b) Trapping of H_2S

(c) Conversion of H_2S (d) All of the above

18. Why nitric acid used in limit test of chloride

(a) To prevent precipitation of acid radicals with $AgNO_3$

(b) To Prevent effervescence came out from reaction

(c) To produce colour (d) All of the above

19 What is the term "ppm"?

(a) 1 mg in 1 kg (b) 1 mg in 100 gm

(c) 1 mg in 10 gm (d) None of the above

20. Function of granulated zinc in limit test for arsenic is:

(a) Fast release of Nascent H_2 gas

(b) Slow and prolong release of Nascent H_2 gas

(c) To prevent release of Nascent H_2 gas

(d) None of the above

21. _____ is the degree of agreement between the measured value and the true value.

(a) Precession (b) Accuracy

(c) Robustness (d) None of the above

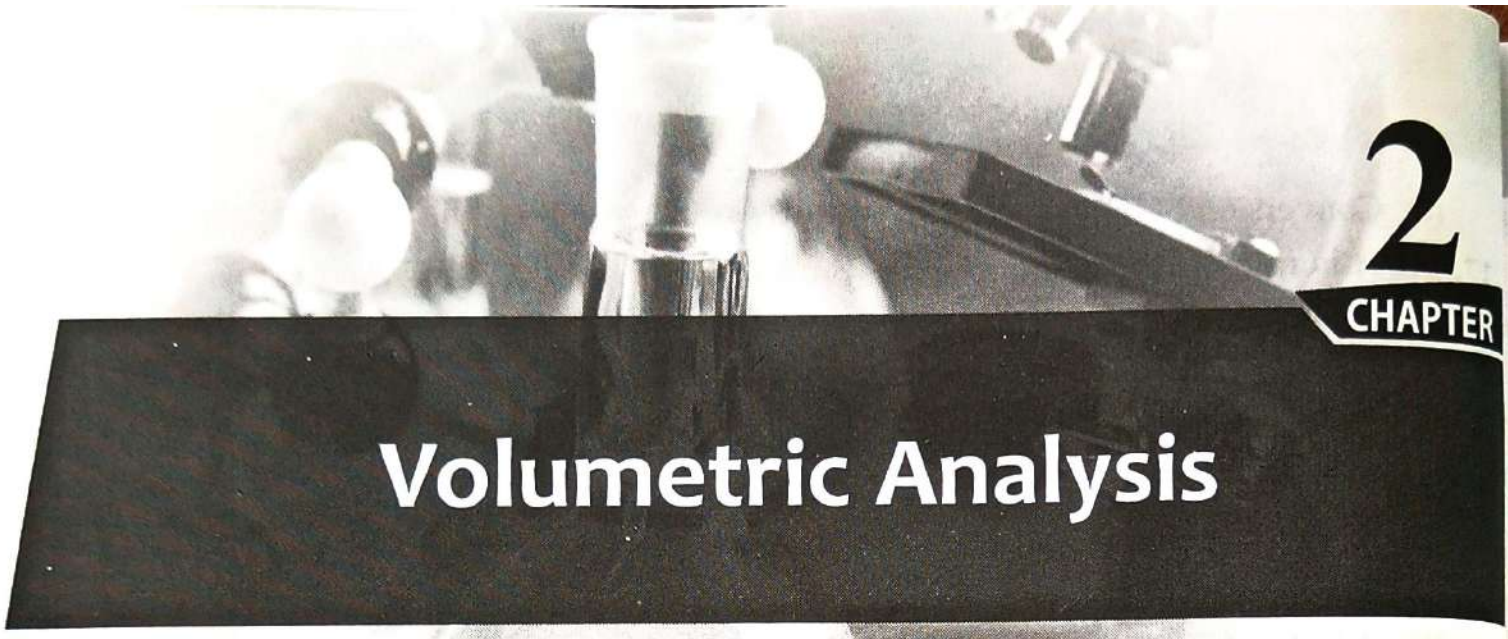
22. The difference between the true value or standard value and observed value is called as:

(a) Precession (b) Accuracy

(c) Error (d) None of the above

ANSWERS OF MULTIPLE CHOICE QUESTIONS (MCQ'S)

1. (b)	2. (d)	3. (d)	4. (c)	5. (a)	6. (b)	7. (c)
8. (a)	9. (b)	10. (c)	11. (c)	12. (b)	13. (a)	14. (a)
15. (c)	16. (a)	17. (b)	18. (a)	19. (a)	20. (b)	21. (b)
22. (c)						



CHAPTER 2

Volumetric Analysis

INTRODUCTION

Volumetric analysis (titration) is a quantitative process for determining the quantity of certain components in a sample under investigation.

Volumetric analysis is a direct chemical approach that is carried out in liquid media. Instrumental analytical methods, are utilized for quantitative determination via indirect physico-chemical measures.

METHODS OF VOLUMETRIC ANALYSIS

Titration

It is based on the precise measurement of the volume of the reagent. This reagent is added through the burette to the exact known volume of the examined sample (in the titration flask) until the quantifiable chemical reaction status is reached (point of equivalence)

Titration can be performed as:

- **Direct titration**, in which the titration reagent is directly introduced to the solution of the selected substance until both reagents' substance concentrations are equal.
- **Indirect titration**, in which the excess titration solution is first added to the solution of the specified chemical and then the generated compound is titrated.

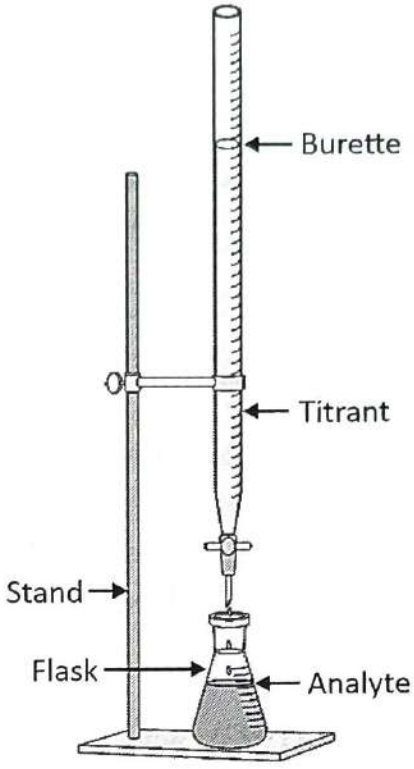


Fig. 2.1: ***Typical Titration Assembly***

- **Back titration,** in which an exact amount of titration solution is introduced in extra to a solution of a specified material, the quantitative reaction runs over and the excess titration reagent is titrated by another titration reagent.

Volumetric analysis methods are categorized according to the chemical reaction principle that the titration determination is based on:

1. ACID BASE TITRATION

Acid or alkaline compounds are determined by titration from a hydroxide (OH^-) or an acid (H^+), respectively; the principle behind acid-base titration is a neutralization reaction.

$$H_3O^+ + OH^- \rightleftharpoons 2H_2O$$

An acid-base titration is a quantitative measurement procedure that involves carefully neutralizing an acid or base with a known concentration standard solution and measuring the response using a pH indicator. The concentration of a reagent (molarity) of an analyte solution can be calculated if either pKa (acid dissociation constant) or the pKb (base dissociation constant) are known. A titration curve can be used to estimate the pKa if the concentration of solute solution is known.

Several acid-base concepts have been proposed to describe or classify acidic and basic properties of materials.

Theories of Acids and Bases

Robert Boyle was first to pronounced that reaction among acid and base yields salt and water. Based upon this assumption some theories were carrying forwarded.

Acids and bases defined on the basis of various concepts namely the Arrhenius Concept; Bronsted-Lowry Concept; Lewis Concept.

Arrhenius Concept:

According to Arrhenius, an acid is any substance that produces hydrogen ions (or protons, H^+) in aqueous solution and a base is a substance providing hydroxyl ions (OH^-) in an aqueous solution. Rendering to this, when acid and base combines, they form neutralization reaction to yield water and a salt. The above reaction may be expressed by the following general equation between an acid (HA) and a base (BOH).

$$HA + BOH \rightarrow B^+A^- + H_2O$$

Bronsted and Lowry Concept:

They established proton concept (1923), acid is a substance capable of donating a proton (H^+), while a base is a substance capable of accepting proton in a chemical reaction. This can be expressed by the equation:

$$\underset{\text{Acid}}{A} \underset{}{\overset{H^+}{\rightleftharpoons}} \underset{\text{Base}}{B}$$

Thus, Bronsted acid, which losses a proton will produce a conjugate base and base will accept a proton to produce a conjugate acid.

$HCl \rightarrow H^+ + Cl^-$ (HCl is acid & Cl^- is conjugate base of HCl)

$HCl + H_2O \rightarrow Cl^- + H_3O^+$

$CH_3COOH + H_2O \rightarrow CH_3COO^- + H_3O^+$

According to Bronsted and Lowry theory a strong acid has tendency to lose proton while a strong base has tendency to accept the proton. If an acid is strong its conjugate base will be weak and if a base is strong, its conjugate acid will be weak.

Lewis Acid-Base Concept:

Lewis put forwarded the postulate that "All compounds considered as bases in Lowry Bronsted concept contain at least one lone pair of electrons". It is the lone pair of electrons which runs the acid base reaction. On this concept Lowry defines the acid and base as: "Acid is acceptor of a pair of electrons and base donates a pair of electrons". This concept also known as "electron-pair concept". Lewis's acids and bases may interact to give a **donor-acceptor complex.**

Summary of Acid-Base Theories

Name of Theory	Acid	Base
1. Arrhenius theory	Proton donor	Hydroxide ion donor
2. Bronsted-Lowry theory	Proton donor	Proton acceptor
3. Lewis's theory	Electron pair acceptor	Electron pair donor

Principle of Acid-Base Titration

The concept of acid-base titration, as mentioned in the principle, requires calculating the concentration of an acid or basic with a burette and pipette, as well as a pH indicator. An indicator dissolved in the sample solution and is commonly used to determine the titration's endpoint.

2. COMPLEX-FORMING TITRATION

Here, the determined metal's cation is bonded to a soluble compound ion, causing the free cation to leave the solution. Chelatometry is alternative name for complexometric titration. Complexometric titrations are volumetric titrations or analyses in which the endpoints are specified by coloured substances. In complexometric titrations, an indicator is added to specify the titration's equivalence point (or endpoint) which is determined by the creation of a complex between the analyte and the titrant. It's ideal for defining the concentration of a metal ion combination in a sample solution.

Finding out water hardness using EDTA and Eriochrome black-T as the indicator, is a common example of complexometric titration.

Principle Behind Complexometric Titration

The indicator Eriochrome Black T turns wine-red when it binds to metal ions, but it remains blue when it is not coupled to metal ions. Regardless of whether it is coupled to a metal ion or not, Ethylene Diamine Tetra Acetic Acid (EDTA) is colourless. Because Eriochrome black T (EBT) binds to different metal ions, adding an EBT indicator to the sample turns it wine-red coloured. EDTA binds to metal ions firmly, whereas Eriochrome Black T binds to metal ions gently. As a result, the EBT indicator in the trial solution remains unbound after all of the metal ions have been coupled to EDTA and the solution appears blue.

Types of Complexometric Titration

EDTA can be utilized in a variety of ways as a chelating titrant. As a result, EDTA titrations may be accomplished in a variety of ways. Here are a few of them:

1. **Direct Titration Method:** This method is easy and convenient and it is again similar with the acid-base titration technique. The standard EDTA solution is slowly added to the metal ion solution using a burette until the anticipated endpoint is attained in this procedure. Copper, zinc, mercury, barium, chromium, aluminum and lead, among other metal ions, are measured via direct titration.
2. **Back Titration Method:** A back titration is a complexometric titration that uses a known quantity of surplus reagent to determine the analyte concentration. Those metal ions that can't be directly titrated with EDTA are calculated using this method.
3. **Replacement Titration Method:** The replacement titration method is employed when back titration or direct titration fail to provide sharp endpoints. The metal ion is measured by replacing zinc or magnesium ions in an EDTA complex with an equivalent quantity of metal ions, then titrating the released Zn or Mg ion with a standard EDTA solution.
4. **Indirect Titration Method:** This method is widely employed when traditional titrations are slow or the endpoint is tough to determine, as well as in other applications such as the weak acid-weak base reaction. When Some anions like barium, come into contact with metal cations, they precipitate and these ions does not react with EDTA. As a result, these compounds can be identified by indirect titration with EDTA.

Applications of Complexometric Titrations

(a) It is used to quantify the amount of metal ions present in test solution.

(b) It's being used to determine amount of calcium is present in various diets.

(c) It helps calculate the exact hardness of water.

(d) It is usually used in the pharma industry to assess the metal concentration in a formulation.

(e) In chemical analysis, it is used to execute the assay.

(f) It is used to determine hazardous metals in environmental analysis.

(g) Cosmetic items are usually subjected to complexometric titration.

3. PRECIPITATION TITRATION

The formation of marginally soluble compounds is required for titration; the titrated ingredient precipitates and leaves the solution. For example, argentometry uses the cation Ag^+ to form insoluble salts; the titration substance is $AgNO_3$; and it can be used to detect Cl^-, Br^-, I^-, CN^-, SCN^- and other ions.

It is a type of titration in which a precipitate forms during the process of titration. The argentometric method refers to precipitating titration employing silver nitrate ($AgNO_3$) as precipitating agent, whereas precipitation titration denotes to volumetric approaches based on the generation of a slightly soluble precipitate. It's an important technique for detecting halogens and certain metal ions.

Example: We need to titrate a sample against a known quantity of $AgNO_3$ solution to estimate the chloride ion concentration. The chemical reaction that occurs is as follows (we studied same reaction in limit test of chloride):

$$Ag^+(aq) + Cl^-(aq) \rightarrow AgCl(s)$$

AgCl settles at the bottom of the flask as a white precipitate during the titration.

The quantity of silver ion used to achieve the equivalence point is similar as the initial amount of chloride ion.

4. REDOX TITRATION

Redox titration is an oxidation-reduction titration. When an oxidising and reducing material interact, an redox reaction occurs. Here, electrons are transferred to the reactant ions of aqueous solutions, causing a chemical reaction. In this technique, an oxidising agent is titrated against a standard solution of a reducing agent or *vice-versa.*

It's used to check for organic solutes and determine chlorination levels in general. In redox titration, the potentiometer or the redox indicator is commonly utilised.

Principle of Redox Titration

According to the oxidation-reduction (Redox titration) concept, the oxidation phase involves electron loss, whereas the reduction phase involves electron gain.

The following are the key features of redox reactions, which include both oxidation and reduction reactions:

- **Oxidation reaction:** The following are examples of how a solute can undergo oxidation reaction:
  - Oxygen atom addition, Hydrogen atom removal, Electron donation or loss, an overall enhance in the substance's oxidation state.

- **Reduction reaction:** The following are examples of how a solute can undergo reduction reaction:
  - Hydrogen atom addition, Oxygen atom removal, Accepting electrons, Reduction in the oxidation state of the analyte.

5. NON-AQUEOUS TITRATION

It is the titration of weakly acidic (or basic) analytes in a solvent that doesn't contain water. The solute is dissolved in a non-aqueous solvent before being titrated using an acid or base titrant. Non-aqueous titration works on the same principles as acid-base titration.

The Theory behind Non-aqueous Titrations:

Water can be act as a weak acid and a weak base at the same time. It effectively competes in proton receiving and donation where other weak acids or bases may dissolve in water. Titrating, on the other hand, could not give you the results you want. This necessitates the use of a non-aqueous titration method. This approach benefits from the non-aqueous solvent's ability to dissolve organic molecules, as well as precision titration of weak acids and bases.

The Lowry-Bronsted theory's concepts may used in understanding the reactions that occur in various non-aqueous titrations. As a result, an acid functions as a proton donor while a base functions as a proton acceptor.

Indicators Used in to Detect Endpoints:

- **Visual indication:** Colour change, precipitate development and fluorescence were all subjectively detected changes in the appearance of the titration solution. In the titration solution, the most frequent way is to employ a suitable organic reagent as an indicator. Just when the point of equivalence is achieved, the colour changes.
- **Instrumental indication:** The titration curve is produced by measuring the physical properties of the titration solution (for example, conductivity, pH and so on) in relation to the volume of titration reagent applied. The quantity is chosen so that at the point of equivalent, the critical titration curve change (e.g., a turning point or break) occurs. From a certain point in the change, the amount of titration reagent consumed is computed.

Indicators:

Chemicals that react with the reagents being tested or excess titration reagent are known as indicators. Before and after the reaction, the indicator forms have different colours. One form transforms into the other at the endpoint. The titration reagent or the

titrated substance are usually the same sort of chemical as the indicator. Depending on the type of titration, there are a variety of indicators.

(a) **Acid-base indicators** (Acids and hydroxides are commonly titrated with this method.) These are organic acids or bases that aren't very strong. Examples of acid-base indicators are: Methyl orange, Methyl red, Phenol red, Phenolphthalein

(b) **Indicators of complexometric titrations:** Compounds that form complexes with the required metal ion are metallochromic indicators of complexometric titrations. Complexometric indicators include eriochrome black T, xylenol orange and murexide.

(c) **Indicators of precipitation titrations:** They produce coloured precipitation and then soluble coloured complexes when there is a surplus of titration reagent just before the endpoint. As a result of adsorption or desorption on precipitate or solution particles in the endpoint, these indicators can affect the colour of precipitation.

(d) **Indicators of redox reactions:** In their reduced and oxidized states, these chemicals have a distinct colour. The reduced form of the indicator is converted to the oxidized form just before the endpoint by the first surplus of oxidized titration reagent (examples: benzidine or diphenylamine– colourless to blue conversion). Many redox indicators have an irreversible behaviour, such as some colour compounds (such as methyl red), which get oxidized after a first surplus of oxidized reagent, then decolorize and breakdown. The colour of the reduced form cannot be regained through reduction.

GRAVIMETRIC ANALYSIS

It is a method for calculating the amount of analyte based on the mass of a solid in analytical chemistry. *Example:* The suspended particles in the water sample are weighed. After an indicated volume of water has been filtered, the solids recovered are weighed.

The Principle of Gravimetric Analysis

The idea behind gravimetric analysis is that it can be used to calculate the mass of an ion in a pure substance. It was afterwards used to calculate the mass % of the same ion in a known amount of impure substance.

Steps followed in the Gravimetric Analysis

1. Preparation of the solution

2. Precipitation
3. Digestion
4. Filtration
5. Washing
6. Drying or ignition
7. Weighing
8. Calculation

Types of Gravimetric Analysis

Gravimetric analysis can be divided into four categories. There are two main methods, both of which involve changing the phase of the analyte to separate it from the rest of the mixture, resulting in a mass change.

Gravimetry of Volatilization: We can separate components of mixture using gravimetry by heating or physically decomposing the sample. The analyte is volatilized (dried) before being collected and weighed in this procedure. (Or, otherwise, the mass of the volatilize product is indirectly dictated by the sample's mass loss).

At a proper temperature, the analyte products are volatilized. The volatile product is then weighed, resulting in an indirect determination of the product's mass based on the sample's mass loss. Ignition, for example, may separate water from most inorganic substances.

Precipitation Gravimetry: A precipitation reaction is used to turn one or more components of a solution into solids. Precipitation with a suitable reagent is required to convert the analyte to a solid (precipitate). The solution's precipitates are filtered, washed, purified (if needed) and weighed.

By precipitating calcium oxalate and igniting the oxalate ion to calcium oxide, calcium can be measured gravimetrically.

$$Ca^{2+} + C_2O_4^{2-} \rightarrow CaO + CO_2 + CO$$

The resulting precipitate is weighed and the quantity of calcium oxide is calculated.

Electrogravimetry: It's a method for isolating and measuring ions in a substance, most commonly a metal.

Thermogravimetry: This is a type of thermal analysis that assesses changes in chemical and physical properties of materials as a function of temperature or time.

Advantages of Gravimetric Analysis

- Gravimetric analysis is more precise and accurate than volumetric analysis.
- Temperature variations, calibration mistakes and other issues related with volumetric analysis are avoided with gravimetric analysis.

- It is an ABSOLUTE method, i.e., it involves direct measurements without any form of calibration.
- Relatively low-cost

Disadvantages of Gravimetric Analysis

- You can only analyze a single element or a small group of elements at a time.
- It's crucial to use proper lab procedure.
- Time-consuming and meticulous.
- Very clean glassware is required.

EXERCISE

Short Answer Type Questions

1. Give the principle behind:

(a) Acid-base titration
(b) Non-aqueous titration
(c) Precipitation titration
(d) Complexometric titration
(e) Redox titration

2. Define:

(a) Arrhenius acid and base
(b) Bronsted-Lowry acid and base
(c) Lewis's acid and base
(d) Indicator

Long Answer Type Questions

1. Discuss the principle and methods of gravimetric analysis.
2. Explain different types of titrations with example.
3. Discuss different theories of acids and bases.
4. Discuss different indicators used in titration.

Multiple Choice Questions (MCQ's)

1. Acid is a substance which dissociates in water to produce hydrogen ions, this theory given by which scientist?

(a) Arrhenius theory
(b) Lewis theory

(c) Bronsted theory (d) Lowry theory

2. Substance capable of oxidization or reduction and that will produce different colours in the individual oxidized and reduced forms:

(a) Redox indicators (b) Redox potential

(c) Redox number (d) Redox state

3. The Oxidation & Reduction type of titration is also known as:

(a) Gravimetric titration (b) Complexometric titration

(c) Redox titration (d) Gasometrical titration

4. Find out the chelating agent from following:

(a) Salicylic acid (b) EDTA

(c) Benzoic acid (d) Glycerol

5. Which of the following compound used as titrant in non-aqueous titration?

(a) EDTA (b) Perchloric acid

(c) Sodium nitrite (d) Silver nitrite

6. The method of addition of known concentration of sample until till completion of reaction with known volume is called as _____.

(a) Titrant (b) Analysis

(c) Titration (d) Titrend

7. Which one of the following is used to change the colour at end point in titration?

(a) Measuring cylinder (b) Burette

(c) Instrument (d) Indicator

8. What is the Arrhenius acid?

(a) It is a proton donor

(b) It is a proton acceptor

(c) It produces hydrogen ions in solution

(d) It produces hydroxide ions in solution

9. What is an Arrhenius base?

(a) A compound that accepts OH^- in solution

(b) A compound that releases OH^- in solution

(c) A compound that accepts protons in solution

(d) A compound that donates protons in solution

10. What is a Lowry-Bronsted acid?

(a) A substance that releases H^+ (aq)

(b) A substance that releases OH^- (aq)

(c) A substance that accepts proton in solution

(d) A substance that donates proton in solution

11. In which cases non aqueous titration is carried out?

(a) For water insoluble drug (b) For weakly acidic drug

(c) For weakly basic drug (d) All of the above

12. Which one of the following is used as an indicator in complexometric titration?

(a) Xylenol orange (b) Eriochrome black T

(c) Mordant black II (d) All of the above

13. In which technique, analyte is separated from a solution of the sample as a precipitate and is converted into a compound of known composition?

(a) Volatilization gravimetry (b) Precipitation gravimetry

(c) Electrogravimetry (d) Precipitation point

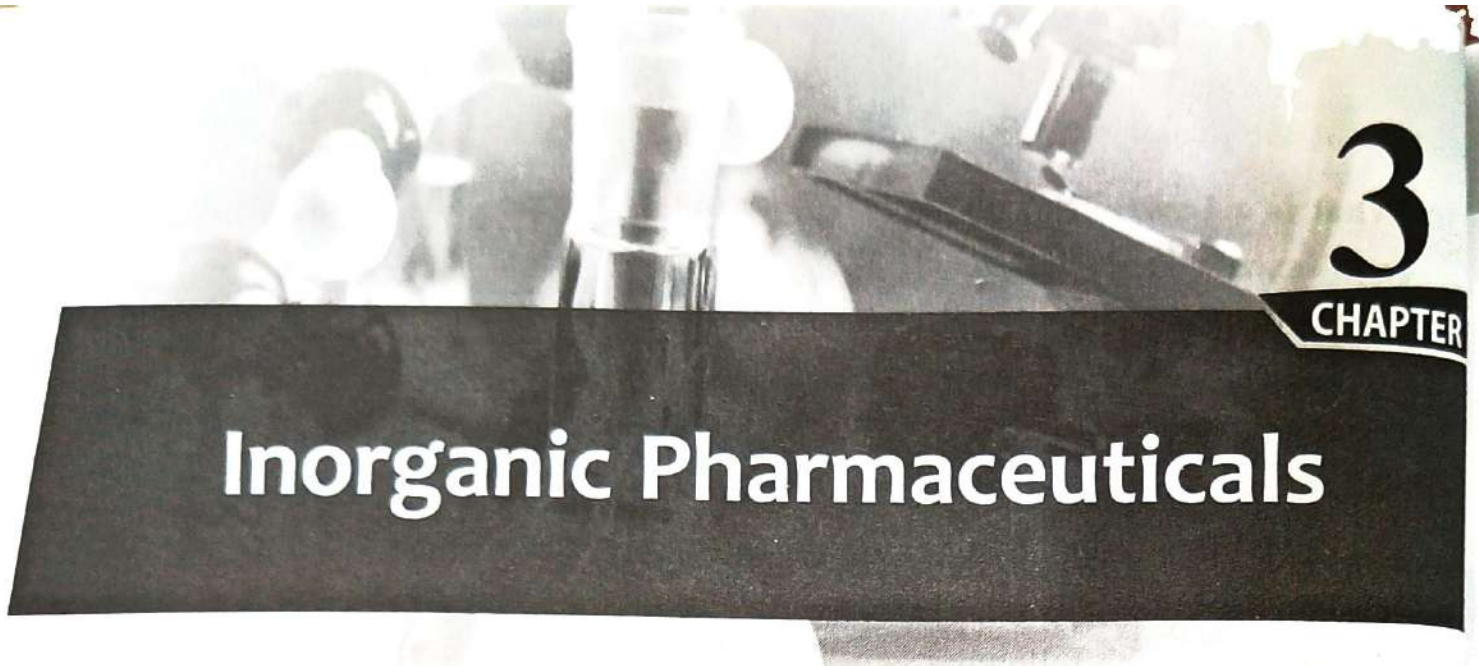
14. How hydrogen acts as a reducing agent?

(a) By taking oxygen (b) By giving electron

(c) By taking hydrogen (d) Both (a) and (b)

ANSWERS OF MULTIPLE CHOICE QUESTIONS (MCQ'S)

1. (a)	2. (a)	3. (c)	4. (b)	5. (b)	6. (c)	7. (d)
8. (c)	9. (b)	10. (d)	11. (d)	12. (d)	13. (b)	14. (d)



CHAPTER 3

Inorganic Pharmaceuticals

HAEMATINICS

Introduction

These are the substances used for the expansion of blood and helpful in treatment of anemias. The examples of popular haematinics include Vitamin B_{12}, iron and folic acid.

Iron plays important role in physiological processes such as synthesis of haemoglobin and myoglobin. Meat, eggs and vegetables are rich sources of iron. Generally, human absorbs about 10% of the iron after taking food containing it. Body starts increased absorption of iron through food to complete body's demand; when there is decrease in the store of iron. Erythropoiesis plays important role in storage and release of iron. The requirement of iron for adult males is 1mg/day; but adult females require 2 mg/day of iron to fulfill body's demand. For pregnant women, the requirement of iron is more to encounter the increased requirements in pregnancy (3-3.5 mg/day).

Iron Distribution in a Body

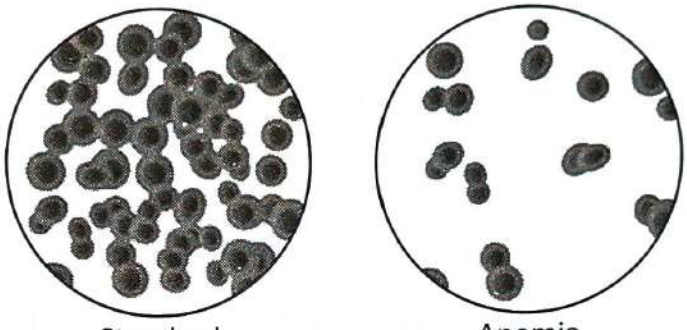
Total iron present in body of healthy person is 2.5-5 g (approximately 3.5 g). It is more in men (50 mg/kg) than in women (38 mg/kg). Iron is distributed as Haemoglobin (66%); Iron stored as hemosiderin and ferritin (25%); myoglobin (3%); and parenchymal iron about 6%. Haemoglobin is protoporphyrin containing 4 irons containing haeme units. Iron is stored as ferric form in combination with large protein apoferritin.

Sources of Iron

Food sources of iron are as follows: Liver, egg yolk, dry beans, wheat germ, dry fruits, yeast, spinach, chicken, fish banana, apple, milk products and root vegetables.

Anaemia

Anemia is a condition in where the amount of red blood cells (RBCs) or a hemoglobin concentration within RBCs is lower than standard level.



According to the WHO, anemia affects 42% of kids below the age of five and 40% of pregnant women globally. When the balance between the creation and destruction of RBCs is disrupted, anemia develops due to:

(a) Blood loss;

(b) Decreased red cell formation due to factors such as iron, Vitamin B_{12}, folic acid, bone marrow depression (hypoplastic anemia) and erythropoietin deficiency;

(c) Increased destruction of RBCs in hemolytic anemia.

Treatment of Iron Deficiency Anemia

(a) Oral formulations used to treat anemias include inorganic salts to recover from deficiency of iron such as ferrous gluconate, ferrous sulphate and ferrous fumarate.

(b) Parenteral therapy for treatment of iron deficiency anemias includes iron dextran, iron sucrose and sodium ferric gluconate complex.

FERROUS SULPHATE OR IRON (II) SULPHATE

Chemical Formula: $FeSO_4.7H_2O$

Molecular Weight: 278.02

Synonyms: Green vitriol, Iron vitriol and Copperas

Properties: It appears as blue green crystals (heptahydrate), white crystals when anhydrous and white yellow crystals as monohydrate form. Crystal structures present as orthorhombic in anhydrous form and monoclinic for heptahydrate form. It is odourless compound with astringents and metallic taste.

Storage: Keep in a tightly closed container away from moisture.

Uses:

1. Ferrous sulphate is a hematinic used to treat and prevent iron deficiency anemias.
2. Ferrous sulphate is also used in manufacture of iron gall ink.
3. In horticulture, iron sulphate is used for treating iron chlorosis.
4. Green vitriol is used in gold refining.

Official Preparation:

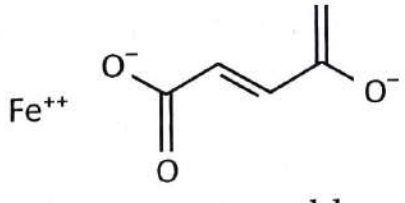
1. Ferrous Sulphate Tablet
2. Ferrous Sulphate Syrups

Brand Name: Feton-Z-TR, Fer-In-Sol, Feratab, Iron, Mol-Iron, Feosol, MyKidz Iron 10

FERROUS FUMARATE

Molecular Formula: $C_2H_4\ FeO_4$

Molecular Weight: 169.9



Properties: It appears as a reddish orange to red-brown in colour, odourless powde which may hold soft lumps that create a yellow coloured streak when crushed. It slightly soluble in water and very slightly in alcohol.

Storage: Keep in a tightly sealed container away from moisture.

Use: It is used as Haematinic.

Official preparation: Ferrous Fumarate Tablet

Brand name: Ferretts, Hemocyte

FERRIC AMMONIUM CITRATE

Molecular Formula: $C_6H_8FeNO_7$

Molecular Weight: 261.98

Properties: It is a solid that is yellowish brown to red in colour and has a faint ammonia odour. It is water soluble.

Storage: Store in well closed container protected from moisture

Uses:

1. It is used to control phosphorus levels in case of chronic kidney disease or dialysis.
2. Ferric ammonium citrate is also used to treat iron deficiency anemia

Official Preparation:

1. Ferric Ammonium Citrate Suspension
2. Ferric Ammonium Citrate Capsule
3. Ferric Ammonium Citrate Syrup

Brand Name: Auryxia, Intavital syrup, Pons Suspension

FERROUS ASCORBATE

Molecular Formula: $C_{12}H_{14}FeO_{12}$

Molecular Weight: 406.08

Properties: It is white or slightly yellowish crystalline powder; it is water soluble

Storage: Store in well closed container protected from moisture

Uses:

1. It is a combination of iron and vitamin C.
2. It is used to treat-anaemia due to iron deficiency and anaemia due to chronic kidney disease.
3. Iron works by replenishing the iron stores in your body and corrects iron deficiency anaemia.

Official preparation: Ferrous Ascorbate Tablet.

Brand name: Ferikind, Feronia-Xt, Ferox-Xt, Irozorb, Ferox-Xt.

CARBONYL IRON

Molecular Formula: Fe (CO)5

Molecular Weight: 195.9

It is a highly pure iron that is made by decomposing refined iron pentacarbonyl in a chemical reaction. It typically appears as a grey powder made up of spherical microparticles.

This drug is an iron supplement used to treat or prevent iron deficiency in the blood (as in anemia or pregnancy). Iron is a most essential mineral for the body's production of red blood cells and overall health.

Properties: It is grayish to black colour power, insoluble in water and organic solvent.

Brand name: Feosol Caplet, Arion Forte, Super Fe, Nokifer Tab, Mumfer-XT, Herfem

GASTROINTESTINAL DRUGS

Overview of the Gastrointestinal (GI) System

The oral cavity, pharynx, oesophagus, stomach, small intestine, large intestine, rectum and anus are all part of the GI System, which is a tube measuring 25 to 32 feet long. The liver, pancreas, appendix and gallbladder, which generate and discharge digestive enzymes and acids, aid the system's function.

This system is involved in digesting and absorbing nutrients and fluids, eliminating and detoxifying wastes and is an integral part of the body s immune system.

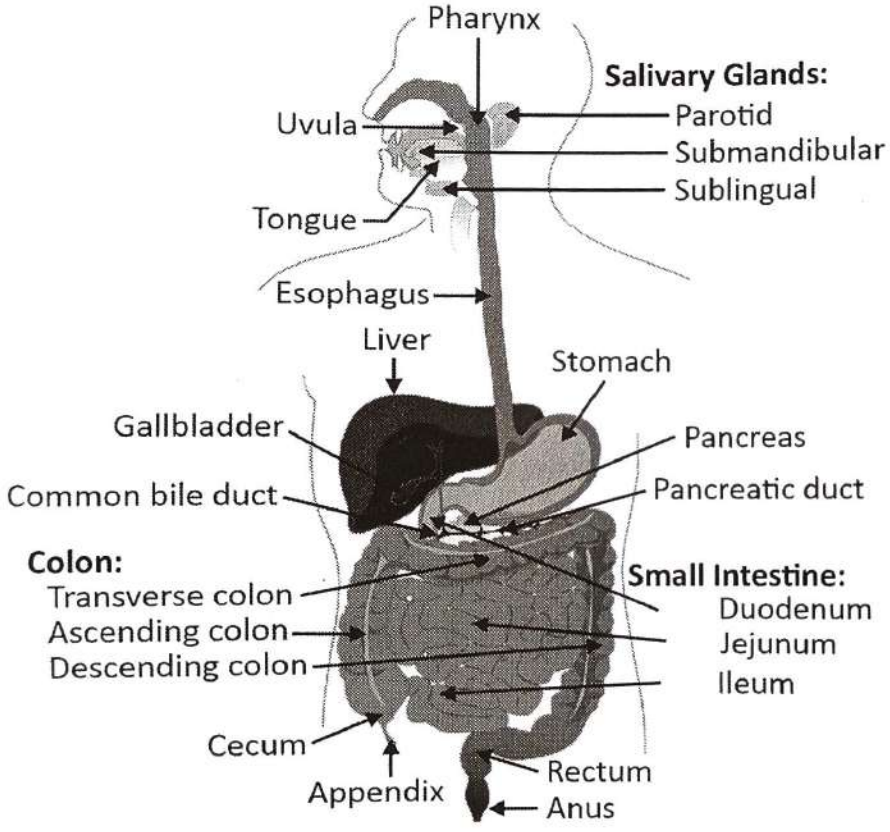


Fig. 3.1: ***Gastrointestinal (GI) System***

A well-functioning Gastrointestinal (GI) System is critical for good overall health.

GI-System Problems & Related Disorders

Problems associated with a compromised GI System include: gastritis, colitis, leaky gut, Crohn's disease, irritable bowel (IBS), ulcers, constipation, diarrhoea and haemorrhoids. Each disorder has its own underlying causative factors, but common to all are usually poor diet/nutrition and inflammation.

Classification of Gastrointestinal Agents

1. **Gastric acidifiers/Acidifying agent:** Dilute Hydrochloric Acid
2. **Antacid:**
   (i) Systemic Antacid- Sodium Bicarbonate
   (ii) Non systemic Antacid- Aluminium Hydroxide, Aluminium Phosphate, Basic aluminium carbonate, Magnesium carbonate, Magnesium oxide, Magnesium hydroxide, Magnesium trisilicate, Calcium carbonate, Calcium Phosphate, Sodium bi-carbonate etc.
3. **Protective and Adsorbent:** Bismuth Sub carbonate, Bismuth sub nitrate, kaolin, Milk of bismuth etc
4. **Cathartics:** It is also classified as:
   (a) Stimulant
   (b) Bulk purgative
   (c) Lubricants
   (d) Saline cathartics

For example, Methyl cellulose, Castor oil, liquid paraffin, Magnesium sulphate, Isapgol, etc.

ANTACIDS

Antacids are used to prevent and relieve pain in the characteristic controlling of gastric and duodenal ulcers and reflux esophagitis. These are alkaline substances used to neutralize the surplus gastric HCl associated with gastric and peptic affecting the stomach which are not always related to hyperacidity.

An ideal antacid should have the following characteristics:

(a) It should not be absorbable or cause systemic alkalosis.

(b) It should cause neither diarrhoea nor constipation.

(c) It should have a quick and long-lasting effect.

(d) Its reaction with gastric acid should not cause a large evolution of gas.

(e) It should inhibit pepsin.

The important side effects associated with antacid therapy are acid rebound secretion, systemic alkalosis; increases blood sodium levels (for sodium containing products) and local effects in the gastrointestinal tract. Calcium and aluminium salt tend to be constipating while magnesium salt may have a laxative effect.

Classifications

A. **Systemic/Absorbable antacids:** Sodium Bicarbonate

B. **Non-systemic/non-absorbable antacids:**

(a) ***Aluminium containing antacids:*** Aluminium Hydroxide, Aluminium Phosphate, Basic aluminium carbonate.

(b) ***Calcium containing antacids:*** Calcium carbonate, Calcium Phosphate.

(c) ***Magnesium containing antacids:*** Magnesium carbonate, Magnesium oxide, Magnesium hydroxide, Magnesium trisilicate.

(d) ***Combination antacids:*** Aluminium Hydroxide and Magnesium hydroxide, Aluminium Hydroxide gel and Magnesium trisilicate.

ALUMINIUM HYDROXIDE GEL

Aluminium hydroxide is official in I.P. in three forms:

(a) Aluminium Hydroxide Gel.

(b) Dried Aluminium Hydroxide gel.

(c) Aluminium Hydroxide Tablets.

Description: It is an aqueous suspension of hydrated aluminium oxide composed with variable quantities of basic aluminium carbonate and bicarbonate.

It contains 3.5 to 4.4 % w/w of Al_2O_3

Properties: Aluminium hydroxide gel is a white viscous suspension from which small amounts of clear liquid may separate on standing.

Storage: store in well closed container protected from moisture

Uses:

1. The aluminium – containing antacids are widely used.
2. They are nonabsorbable and produce practically no systemic effects.

3. The aluminium hydroxide gels buffer in pH 3-5 regions by virtue of their amphoteric character.

Reaction with hydrochloric acid gives the water-soluble astringent salt, aluminium chloride. Hence, it may cause constipation and nausea. It eventually forms the insoluble aluminium phosphate in the intestines leading to increased faecal phosphate excretion.

Official Preparations: Aluminium hydroxide gel

Aluminium, Magnesium and Simethicone oral suspension and chewable tablet.

Brand Name: Digen, gelusil, Happicid

MAGNESIUM HYDROXIDE I.P.

Description: It contains 95.0 to 100.5 % of Mg $(OH)_2$.

Properties:

1. It is a bulky, white, odourless powder.
2. It is practically insoluble in water and in ethanol.
3. It dissolves in dilute acids.

Storage: store in well closed container protected from moisture

Use: Antacid, osmotic laxative

Dose: As antacid- 0.5 to 0.75 gm.

Official Preparations:

1. Magnesium Tablet
2. Magnesium and Alumina Tablet
3. Magnesium and Alumina oral suspension

Brand Name: Digen, gelusil, Happicid

MAGALDRATE (HYDRATED MAGNESIUM ALUMINATE, MONALIUM HYDRATE)

Formula: $Al_{12}H_{14}Mg_4O_{14}.\ 2H_2O$

Molecular Weight: 425.3

Description:

Magaldrate is a chemical combination of aluminium hydroxide and magnesium hydroxide.

It is superior to the simple admixture.

Magaldrate contains the equivalent of 28 to 39 % magnesium oxide and 17 to 25 % of aluminium oxide.

It occurs as white, odourless, crystalline powder which is insoluble in water and alcohol but soluble in dilute mineral acids.

Storage: Store in well closed container protected from moisture

Use: Antacid

Official Preparations:

1. Magaldrate Oral Suspension
2. Magaldrate Tablet
3. Magaldrate and simethicone chewable Tablet
4. Magaldrate and simethicone oral suspension

Brand Name: Rantac MPS, Ulgel, Chilkep, Omac, Megacaine, Jecaine, Ulgel-A (Syrups)

SODIUM BICARBONATE

Synonym: Baking Soda

Chemical Formula: $NaHCO_3$

Molecular Weight: 84.01

Properties:

1. Sodium bicarbonate occurs as white crystalline powder or opaque crystals.
2. It is odourless and has saline taste.
3. It is freely soluble in water and is practically insoluble in alcohol.

Storage: Store in well closed container protected from moisture

Uses:

1. It is categorized as an electrolyte replenisher and systemic alkaliser.
2. It is an antacid with a rapid onset but short duration of action.
3. It reacts with acid causing evolution of carbon dioxide. This may lead to bleaching and flatulence.

$$NaHCO_3 + HCl \rightleftharpoons NaCl + CO_2 + H_2O$$

4. It is readily absorbed and prolonged administration can lead to sodium retention. It inhibits the absorption of tetracyclines from the gastrointestinal tract.
5. It is advisable in treatment of crystalluria.

Official Preparations:

1. Sodium Bicarbonate Injection
2. Sodium Bicarbonate Tablet

Brand Name: Rabium Fast, Riflux Forte, Urisoda, Acigon

CALCIUM CARBONATE

Synonym: Precipitated Chalk

Chemical Formula: $CaCO_3$

Molecular Weight: 100.09

Properties:

1. It is a fine, white, microcrystalline powder.
2. It is odourless and tasteless.
3. It is insoluble in water and alcohol

Storage: Store in well closed container protected from moisture

Uses:

1. It is used as an antacid and adsorbent
2. It reduces gastric hyperacidity and pain in gastric and duodenal ulcers.
3. It is used as emulsifying agent.
4. The major difference between the activities of calcium carbonate and aluminium antacids is that the action of the former depends on its basic properties while that of the latter depends on amphoteric nature. Calcium carbonate is rapidly acting and largely non-systemic.

$$CaCO_3 + 2HCl \longrightarrow CaCl_2 + H_2CO_3$$

$$H_2CO_3 \longrightarrow H_2O + CO_2$$

Calcium carbonate causes constipation and is therefore given in combination with a magnesium antacid. Other side effects observed are hypercalcaemia and alkalosis.

Official Preparations:

1. Calcium carbonate Chewable tablet
2. Calcium carbonate tablet

Brand Name: Calcium Sandoz, Coral Calcium, Intacal

COMBINATION PREPARATION OF ANTACIDS

No single antacid may be considered ideal. Many of the marketed products contain two antacids to approach the ideal behaviour. The combination commonly attempts to balance the constitutive effect of calcium and aluminium with the laxative effect of magnesium.

Some products combine one antacid with a rapid onset of action and another with the long duration of action. The important combinations used are:

(i) **Aluminium hydroxide gel-magnesium hydroxide:** The combination tends remove the constipation and laxative effects of the individual antacids. In suspension, 2-4 % of each agent is used.

(ii) **Magaldrate (hydrated Magnesium aluminate, monalium hydrate)**

Formula: $Al_{12}H_{14}Mg_4O_{14}.\ 2H_2O$

Molecular Weight: 425.3

Description: The chemical compound magaldrate is made up of aluminium hydroxide and magnesium hydroxide.

It is more effective than simple mixing.

Magaldrate is made up of the magnesium oxide equivalent of 28 to 39 percent and the aluminium oxide equivalent of 17 to 25 percent.

It's a crystalline white powder with no odour that's insoluble in water and alcohol but soluble in dilute mineral acids.

Dose: 0.4-0.8 gm.

(iii) **Aluminium hydroxide gel-magnesium trisilicate:** The combination gives additional of the protective effect of magnesium trisilicate.

(iv) **Combinations containing calcium carbonate:** Calcium carbonate is combined with aluminium hydroxide gel to yield products with rapid onset and prolonged action. It is also combined with the magnesium antacid to balance the constipative effect of calcium with the laxative effect of magnesium.

(v) **Combinations containing alginic acid:** Preparation containing the hydrophilic colloid alginic acid along with sodium bicarbonate, aluminium hydroxide gel and magnesium trisilicate have been marketed. These are useful to provide relief in reflux esophagitis. While passing to the stomach, alginic acid reacts with sodium bicarbonate forming sodium alginate and carbon dioxide. Alginic acid is precipitated which floats on the top of the foam along with the antacids.

(vi) **Products containing simethicone:** Simethicone is a defoaming agent. It is added to some antacids to give relief from flatulence.

ACIDIFYING AGENTS

The condition in which hydrochloric acid is absent in gastric secretion is termed **achlorhydria**. It is also called gastric acidity. It is a result of gastric mucosal atrophy.

Gastric hydrochloric acid acts by killing the bacteria in ingested food, softening fibrous and promoting formation of pepsin. The proteolytic enzyme pepsin is formed from pepsinogen at acidic pH. The symptoms of achlorhydria include mild diarrhoea, epigastric pain and sensitivity to spicy food, patients with achlorhydria may also suffer from pemicious anaemia due to the lack of intrinsic factor, a protein essential for Vitamin B_2 absorption.

DILUTE HYDROCHLORIC ACID I.P.

Chemical Formula: HCl

Molecular Weight: 36.46

Descriptions:

1. It appears as a colourless liquid with pungent odour. It is water soluble.
2. It is a strong acid & attacks metals forming their hydrochlorides with the evolution of hydrogen gas.

Storage: It is stored in glass-stoppered containers at a temperature not exceeding 30°C.

Uses of Hydrochloric Acid:

1. Hydrochloric acid as such cannot be used as medicine.
2. The dilute hydrochloric acid is used as acidifying agent.
3. It is also utilised as a laboratory reagent and as a solvent in a variety of industries.

AMMONIUM CHLORIDE

Chemical Formula: NH_4Cl

Molecular Weight: 53.49

Description:

1. It occurs as white crystals, odourless, cooling or saline taste.
2. Slightly hygroscopic, soluble in water, sparingly soluble in alcohol but freely soluble in glycerine.
3. It sublimes on heating.
4. Its aqueous solution is acidic to litmus.
5. It shows reactions of ammonium and chloride radicals.

Storage: Store in well closed container protected from moisture.

Uses:

1. Expectorant
2. Replaces chloride lost during vomiting.
3. Systemic acidifier (treatment of metabolic alkalosis).
4. It is also used in the treatment of urinary tract infections.
5. It is used as an expectorant in cough medicines, systemic acidifying agent for the treatment of alkalosis.

GASTROINTESTINAL PROTECTIVES AND ADSORBENTS

The agents are commonly used in the treatment of mild diarrhoea. Diarrhoea is symptom resulting from impaired digestion and/or absorption which increases the intestinal bulk causing increased peristalsis and evacuation. Diarrhoea may be acute or chronic. Chronic diarrhoea can result from gastrointestinal surgery, carcinomas and absorptive defects.

In the very young and elderly patients, diarrhoea may prove hazardous. The loss of fluids and electrolytes can lead to dehydration and electrolyte imbalances. The antidiarrheal agents treat only the symptoms but not the disease. Most antidiarrheal products contain an adsorbent-protective, an antispasmodic and possibly an antibacterial agent by coating on the intestinal mucosa. They include bismuth salts, kaolin and activated charcoal. These agents can adsorb many drugs and are therefore used in the treatment of acute poisoning. Polymeric and adsorbents are used in hemoperfusion systems and in various manufacturing processes.

Ideal Properties of the Protective and Adsorbents

1. It must be physiologically inactive: Chemically inert compounds are required to avoid interactions between the protective substance and the tissue.
2. It should have a good adsorbent effect, which is important for adsorbing moisture from the skin as well as toxins and other dangerous chemicals in the G.I.T.
3. It should have fine particle size since adsorbent action is increased as particle size decreases. The surface area of small particles is greater.
4. It should be insoluble in water.

BISMUTH SUBCARBONATE (BASIC BISMUTH CARBONATE)

Bismuth and its salts were previously widely used in the treatment of syphilis and yaws. Some insoluble salts of bismuth have been given orally for their protective and antacid

action, for their mildly astringent action in diarrhoea and for their supposed antiseptic effect, some bismuth salts have been used topically for their protective action on mucous membranes. The salts used include bismuth subnitrate, sub carbonate and subsalicylate.

Bismuth sub carbonate is basic salt of varying composition approximating to $(BiO)_2CO_3 . ½ H_2O$. It contains the equivalent of 80% to 82.5% of Bi.

Properties: It is a white or creamy, odourless, tasteless powder. It is practically insoluble in water and alcohol. It dissolves in mineral acids with effervescence. It should be protected from light.

Uses: Milk of bismuth, an astringent and antacid preparation is a suspension of bismuth hydroxide and bismuth sub carbonate in water. Bismuth sub carbonate is rarely used now.

KAOLIN

Kaolin is purified native hydrated aluminium silicate of variable composition. It is recognized in two forms. Heavy Kaolin and light kaolin.

Properties:

Kaolin is practically insoluble in water, mineral acid and solution of alkali hydroxide. It is sterilized by heating at a temperature of 160°C for less than one hour. Light Kaolin may contain a suitable dispersing agent.

Uses:

1. It is used in mixtures intended for treatment in dysentery, diarrhoea and for symptomatic treatment of colitis, cholera etc.
2. It is employed in the treatment of food and alkaloidal poisoning as it adsorbs toxins.
3. It also finds use in dusting powder, cosmetic preparations and is an ingredient of Kaolin poultice.
4. For the internal use, it is mainly the light Kaolin which is employed.
5. It is used as a drying agent for moist sores and infections, e.g., weeping eczema, as weeping ulcers.
6. It is also used as a clarifying agent.

CATHARTICS

Catharsis is the emptying, cleansing, purging or evacuation of the bowels (intestines). Cathartics increase the motility of the intestine or increase the bulk of feces or accelerate

defecation, more specifically used for softening feces. The defecation or expulsion of waste from body is cause of peristalsis movement of muscles. The abnormality in the movement of these muscles can cause constipation. The term laxative is used for mild cathartics while **purgative** is used for strong cathartics.

Classification

Cathartics may be broken down into several different categories:

Bulk cathartics stimulate evacuation of the bowel by increasing the bulk of the feces (stool). Examples include psyllium husk, methylcellulose and dietary fibre such as wheat and oat bran.

Lubricant or **emollient cathartics** soften the feces and reduce friction between the stool and the intestinal wall. Examples include mineral oil, docusate sodium and glycerine (as suppositories).

Osmotic cathartics increase the water content and weight of the feces using the principle of osmosis. Osmotic cathartics have the potential to cause hypernatremic dehydration, because both the ileum and colon have the ability to absorb sodium against the large concentration gradient. These can be further subdivided into two categories:

- **Saline cathartics:** They act by increasing the osmotic load of intestine by absorbing large quantity of water and ultimately stimulating peristalsis. Examples include magnesium citrate, magnesium sulphate, sodium sulphate and magnesium hydroxide (Milk of Magnesia)
- **Disaccharides:** An example is sorbitol which increases stool bulk through fermentation in the bowel.

Stimulant cathartics cause wave like muscular contractions around the intestines (peristalsis) that expel the contents. A currently available example is bisacodyl (the active ingredient in Dulcolax). Stimulants are much faster acting, harsher and more likely to cause laxative dependency than the other types of laxatives.

MAGNESIUM SULPHATE (HEPTAHYDRATE)

Chemical Formula: $MgSO_4 . 7H_2O$ (Epsom Salt)

Molecular Weight: 246.47

Description: Magnesium sulphate is a small colourless (White) crystal. Magnesium aspartate dihydrate is one of the most absorbable forms of magnesium.

Properties: When magnesium sulphate heptahydrate is gently heated, it loses most of its water and converted to monohydrate (white powder).

$$\underset{\text{Heptahydrate}}{MgSO_4.7H_2O} \longrightarrow \underset{\text{Monohydrate}}{MgSO_4.H_2O}$$

Storage: Store in well closed container protected from moisture

Uses: It's used to treat magnesium deficiencies, especially in cases of acute hypomagnesemia accompanied by tetany symptoms comparable to hypercalcemia.

Official Preparation: Magnesium Sulphate tablet.

Brand name: M-Cal 500, Richlyte, vimita cap.

SODIUM POTASSIUM TARTRATE (ROCHELLE SALT, SEIGNETTE SALT)

Chemical Formula: $C_4H_4KNaO_6.\ 4H_2O$

Properties: It occurs as odourless, colourless crystals or white crystalline powder with a cooling saline taste. It effloresces in warm dry air. It is freely soluble in water and practically insoluble in alcohol. It is incompatible with acids, calcium salts, magnesium sulphate and silver nitrate.

Storage: Store in well closed container protected from moisture.

Uses: Sodium potassium tartrate is poorly absorbed from the gut and retains water in the intestinal lumen. When a dilute solution is administered orally, it acts as a saline cathartic and produces a watery evacuation of the bowel. It is also used in the food industry as a stabilizer.

Dose: As cathartic 7.5-15 gm

BENTONITE

Chemical Name: Hydrous silicate of alumina

Chemical Formula: $Al_2H_2Na_2O_{13}Si_4$

Description: Swelling bentonite contains a high concentration of sodium ions and will substantially increase in volume when it is wetted with water

Properties: The clay with montmorillonite contains a small portion of other mineral matter, usually quartz, feldspar, volcanic glass, organic matter, gypsum or pyrite. Structurally, montmorillonite is made of two basic building blocks, the aluminium octahedral sheet and the silica tetrahedral sheet.

Storage: Store in well closed container protected from moisture

Bentonite as cathartics: The clay has negative charged molecules, which gives adsorptive properties to it and makes it medicinally useful. It also has the ability to pass through the intestinal tract and attract the toxins which are positively charged.

Uses:

1. It is used for removal of toxic positively charged ions.
2. It can be used as cathartics, because of swelling properties.
3. It is used for liver detoxification.
4. It is used for the removal of intestinal parasites from GIT.

ANTIMICROBIALS

Topical Agents

Topical agents are substances or preparations that are applied topically to the skin or mucous membranes.

OR

Topical agents are substances that are placed to the body's surface, including bodily cavities that are open to the outside. Oral, vaginal, colonic, nasal, ear, rectum

Classifications

1. **Protectives and Adsorbents,** e.g., Talc, Zinc oxide, calamine, zinc stearate, titanium dioxide, silicon polymers etc.
2. **Antimicrobial Agents:**
   (a) **Compounds acting by oxidation,** e.g., hydrogen peroxide, potassium permanganate, chlorinated lime.
   (b) **Compounds acting by halogenation,** e.g., iodine preparations, e.g., iodine, povidone iodine, chlorinated lime, sodium hypochlorite.
   (c) **Compounds acting by protein precipitation,** e.g., silver nitrate, mild silver protein, mercury and mercury compounds like yellow mercuric oxide, ammoniated mercury, boric acid, borax.
3. **Sulfur and its compounds,** e.g., sublimed sulfur, precipitated sulfur, selenium sulphide.
4. **Astringents,** e.g., Alum, zinc sulphate, Aluminum chloride, etc.

The compounds employed against microorganisms are called antimicrobial agents. They exhibit their action either by killing the microbes (bactericidal) or by inhibiting growth and multiplication of microbes (bacteriostatic). Some basic terminologies regarding their specific action are discussed below:

A. **Antiseptic:** Agents which opposes sepsis; kills or inhibit the growth and multiplication of microorganism.

B. **Germicidal:** Agents which kills the microorganism.

C. **Disinfectant:** Agent shows same action that of germicidal, but they are applied to nonliving system rather than body parts especially for sanitation purpose. Disinfection is the process of destruction of infectious agents.

D. **Sterilization:** The process involves complete destruction of microorganism by using disinfectants and other chemical or mechanical process. The sterile object is said to be free from living organisms.

Antimicrobial Agents

Antimicrobial is a broad terminology describing activity against microbes. Specific terminology describes exact mode or mechanism of action, e.g., antiseptics, disinfectant, germicide (bactericide against bacteria), fungicide (against fungi), virucide (against virus) etc. denotes exact action), bacteriostatic.

Mechanism for Antimicrobial Action

Inorganic antimicrobial agents exhibit their action by one of following mechanism:

1. **Oxidation:** Inorganic antimicrobial agents which are capable of oxidization may irreversibly oxidize and thus inactivates the essential metabolic compounds like proteins with sulfhydryl group. Many compounds exert their inhibitory effect by interfering with cellular oxidation process. They oxidize functional group of proteins or enzymes which are needed for survival or growth of the microorganism.

   Example: The free sulfhydryl group of protein is altered to form disulfide bond by oxidation.

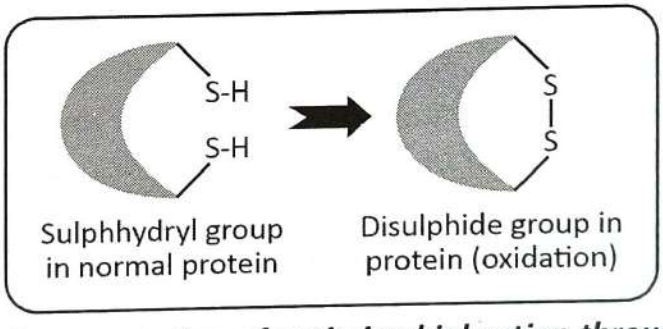


Fig. 3.2: ***Diagrammatic presentation of antimicrobial action through oxidation process***

2. **Halogenation:** All or most of the enzymes are proteinous in nature. The protein molecules are connected with each other through peptide linkage. The peptide linkage undergoes chlorination which modifies the shape/conformation of protein and thereby leading to destruction of protein.

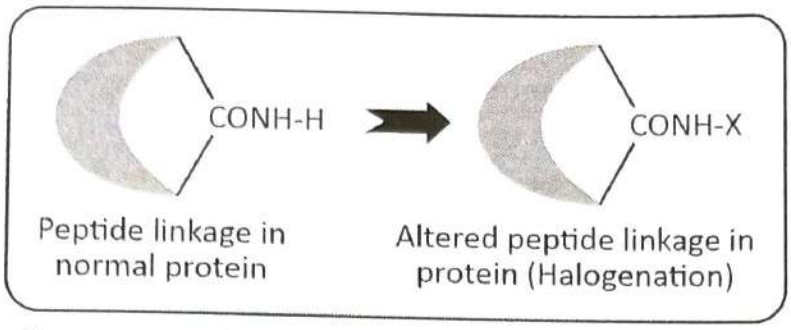


Fig. 3.3: ***Diagrammatic presentation of antimicrobial action through halogenation process***

3. **Protein denaturation (precipitation):** Astringents are the compound which shows protein denaturation. Some metal ions have affinity towards particular enzymes. The metal ions forms complex with the functional group of enzymes, which ultimately changes the structural properties of enzyme, results into deactivation of them.

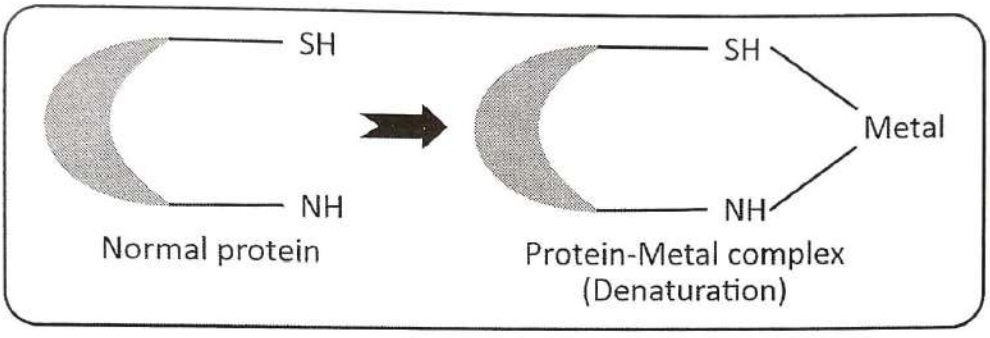


Fig. 3.4: ***Diagrammatic presentation of antimicrobial action through denaturation of protein***

SILVER NITRATE

Formula: $AgNO_3$

Molecular Weight: 169.9

Description: Colourless or white crystals; odourless; bitter in taste. Soluble in 0.4 part of water in slightly more than 0.1 part of boiling water, in 30 parts of alcohol and in about 6.5 parts of boiling alcohol; slightly soluble in solvent ether

Storage: Store in amber colour container protected from light

Category: Local anti-infective.

Official Preparations:

1. Silver Nitrate topical ointment 10%
2. Silver Nitrate topical solution

Brand Name: Silniwyn, Silverex Ionic, Silverex Ionic Cream, Silverex Ionic Gel

IONIC SILVER

Ionic silver has been used for countless years as the "ultimate" antibiotic, antifungal and antiviral alternative. This natural ingredient is thought to inhibit bacteria's respiratory metabolism. Viruses are rendered useless when silver particles prevent them from infecting others and preventing them from replicating.

Uses: It is use as Antifungal, Antibacterial and antiviral.

Brand Name: Cosilarc Gel, Hydroheal Am Gel, Megahea Gel, Silverex Heal Cream

CHLORHEXIDINE GLUCONATE

Molecular Formula: $C_{34}H_{54}Cl_2N_{10}O_{14}$

Molecular Weight: 897.8

Description: It is the gluconate salt version of the biguanide chemical chlorhexidine, which is used as an antiseptic having topical antibacterial action.

The positively charged chlorhexidine gluconate reacts with the negatively charged microbial cell surface, damaging the cell membrane's integrity.

Chlorhexidine gluconate then penetrates the cell, causing intracellular component leakage and ultimately cell death. Gram-positive bacteria are more sensitive to this chemical because they are more negatively charged.

Storage: Store in well closed container protected from moisture

Uses:

1. The mouthwash chlorhexidine gluconate is a germicidal mouthwash that kills germs in the mouth.
2. Gingivitis is treated with chlorhexidine gluconate oral rinse (swelling, redness, bleeding gums).
3. A dentist will usually prescribe chlorhexidine gluconate.

Official Preparation: Chlorhexidine gluconate Mouth wash

Brand Name: Hexi Gel, Rexidin, TpHexid Mouth Wash, Orahex Oral Rinse, TpHexid Mouth Wash, Nitra Hex, Clohex, Microshield

HYDROGEN PEROXIDE SOLUTION

Chemical Formula: H_2O_2

Molecular Weight: 34.016 g/mol

Descriptions:

1. Colourless and odourless liquid with slight acidic taste.
2. Soluble in water, alcohol and ether.
3. Decomposes in contact with oxidizable matter, reducing agents, on making alkaline,
4. Or on standing $2\ H_2O_2 \longrightarrow 2\ H_2O + O_2$
5. It acts as an oxidizing or reducing agent depending upon the chemical environment

Category: Antiseptic, Topical anti-infective agent.

Storage: store in well closed container protected from light

Uses:

1. Antiseptic and Disinfectant- For cleaning of wounds.
2. 1.6% solution is used as Deodourant, gargle and mouth wash.
3. Used for bleaching the hair.
4. As an antidote in phosphorous and cyanide poisoning.

Official Preparation: Hydrogen peroxide solution

Brand Name: Hydroxyl mouth wash, Listerine mouth wash

BORIC ACID

Chemical Formula: H_3BO_3

Molecular Weight: 61.8 g/mol

Descriptions:

1. It is a white, colourless crystalline powder, odourless, unctuous to touch.
2. It has bitter, sweetish after taste
3. It is soluble in alcohol, freely soluble in glycerin, propylene glycol and boiling water
4. Stable in air.

Chemical Properties:

1. When heated above 100°C, it dehydrates, forming metaboric acid (HBO_2):

$$H_3BO_3 \longrightarrow HBO_2 + H_2O$$

2. Boric acid melts at about 160°C, forming tetraboric acid or pyroboric acid ($H_2B_4O_7$):

$$4HBO_2 \longrightarrow H_2B_4O_7 + H_2O$$

3. When heated above 160°C further dehydrates, forming boron trioxide.

$$H_2B_4O_7 \longrightarrow 2\ B_2O_3 + H_2O$$

Solubility: Soluble in glycerin and partially soluble in water and alcohol.

Storage: It should be stored in air-tight, well closed container. Store in well closed container protected from moisture.

Category: Anti-infective, Antiseptic, Bacteriostatic, Fungi static.

Uses:

1. It is used as a local anti-infective medicine in the form of cream, ointment and lotion
2. It is used as a buffer in topical treatments
3. It is used as a carrier for ophthalmic solution
4. Boric acid is used as a base for suppositories
5. It is also used to soak surgical dressings.

Official Preparations:

1. Boric acid Capsule, eyedrop
2. Boric acid powder

Brand Name: Eskata, Orajel Mouth Sore Rinse, Eco Whitening

BLEACHING POWDER

Synonym: Calcium hypochlorite, Chlorinated Lime

Chemical Formula: $CaOCl_2$

Molecular Weight: 136.98 g/mol

Description: A dull white powder having characteristic odour. Gradually decomposes in contact with air by absorbing moisture.

Uses:

1. It is used as disinfectant & bleaching agent.
2. It shows bactericidal action.
3. It is used to disinfect faeces, urine, sputum & other organic material.
4. It is employed for disinfecting drainages.
5. It is a powerful bleaching agent. Its powerful bleaching action must be considered while disinfecting coloured materials.
6. It is used as one to two grams per liter for sterilization of water. The treated water should be exposed to air and allowed to settle before use.

7. Chlorinated lime is used in the preparation of surgical chlorinated soda solution, employed as a wound disinfectant.

Category: Antiseptic, Disinfectant.

Official Preparation: Bleaching powder Granules.

Brand Name: Calcium hypochloride granules

POTASSIUM PERMANGANATE

Chemical formula: $KMnO_4$

Molecular Weight: 158.0 g/mol

Properties:

1. Potassium permanganate occurs in the form of dark purple-coloured monoclinic prisms, almost opaque with a blue metallic luster.
2. It is odourless. An aqueous solution has sweetish astringent taste.
3. It is water soluble and more soluble in boiling water.
4. When heated, it decrepitates.
5. Potassium permanganate is a powerful oxidizing agent.
6. In acidic solution potassium permanganate is reduced form Mn^{+7} to manganous ion Mn^{+2} with evolution of oxygen.
7. In neutral or alkaline media also, oxygen is liberated

Uses:

1. Topical anti-infective.
2. Antiseptic & Antibacterial.
3. Antidote in barbiturate poisoning.
4. Oxidizing agent.
5. 1:5000-1:15,000 solutions are used in cleaning wounds and ulcers.

Category: Antiseptic, Anti-infective, Antibacterial, Antifungal

Official Preparations:

1. Potassium Permanganate Solution
2. Potassium Permanganate Granules

Brand Name: Koimedtricho-ex Permsol, Permitabs

INTRODUCTION

Study and maintenance of dental hygiene has been considered as important part of pharmaceutical science since long time. A wide range of dental products are available on the market to help maintain dental cleanliness. A variety of chemicals are used in both their preparation and dentistry. Although it is common knowledge that clean teeth are healthy and do not decay, it is impossible to clean teeth continually after each meal. Dental decay is caused by a variety of reasons, including poor oral hygiene.

There are numerous inorganic compounds and their formulations that are used in the treatment of dental and oral problems. They are compared to other medications and pharmaceuticals since they come into contact with the human body.

ANATOMY OF HEALTHY TOOTH

Enamel: Crystalline calcium salts (hydroxyapatite) covering the crown to protect the tooth.

Dentin: Largest part of the tooth beneath an enamel and protect pulp.

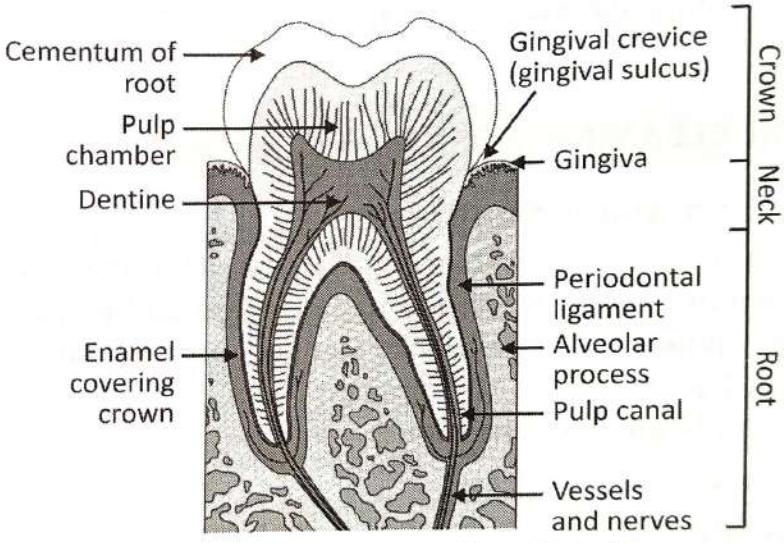


Fig. 3.5: ***Transverse section of Tooth.***

Cementum: Bone-like structure, covering root and provide the attachment of tooth with periodontal ligaments. These are hard connective tissue covering tooth root, giving attachment to the periodontal ligament.

Pulp: Consists of free nerve endings.

Neck: The area where the crown joins the root.

Alveolar Bone (Jawbone): The part of a jaw that surround the root of the tooth.

Root Canal: The portion of a pulp cavity inside the root of tooth; the chamber within the root of the tooth that contains the pulp.

Root: Embedded in the socket are one to three roots.

CLASSIFICATION OF DENTAL PRODUCTS

1. **Anticaries Agents:** Dental caries is a disease of teeth caused by acids formed by action of microorganism on carbohydrate and it is characterized by decalcification of tooth and foul mouth odour.

   Anticaries agents help in the prevention of dental caries.

   Example: Sodium fluoride, Stannous fluoride.
2. **Cleaning Agents**: It helps to remove stains from teeth and gives abrasiveness.

   Example: Calcium phosphate dibasic, sodium metaphosphate.
3. **Polishing Agents**: It gives whiteness to the teeth.

   Example: Calcium carbonate, Calcium pyrophosphate.
4. **Desensitizing Agents:** It reduces the sensitivity of teeth to hot and cold.

   Example: Zinc chloride, Strontium chloride.

DENTIFRICES OR CLEANING AGENTS

General Information about Dentifrices

Dentifrices are a French word for toothpastes. These are cleaning and polishing solutions that are used in combination with a toothbrush to clean and polish the teeth. They are available as a paste, powder, gel or liquid. Dentists prescribe toothpaste as the most important dentifrice. These are used in conjunction with a toothbrush to aid in the removal of food particles and plaque from the mouth.

Dentifrices are broadly classified as:

1. **Cosmetic Dentifrices:** It is used to clean and polish the teeth.
2. **Therapeutic Dentifrices:** It is used to reduce some disease process in mouth such as caries, gingivitis, calculus, sensitivity.

Anti-caries Agents

Dental caries, often known as tooth decay, is a condition of the teeth caused by acids created by microbes acting on carbohydrates. Acids produced by bacterial fermentation of carbohydrates affects the teeth, causing sores where bacteria can colonise and eventually cause dental caries.

Decalcification of the teeth is a symptom of this condition, as is a bad mouth odour. It is impossible to pinpoint the exact cause and process of dental caries. However, it is widely known that dental caries begins on the tooth's surface.

Dentifrices are required to prevent dental cavities and to keep a clean and healthy mouth.

The primary purpose of dentifrices is to clean the teeth's exposed surfaces. There are chemicals that have been proven to have therapeutic efficacy. As a result, dentifrices have included ammoniated dental pastes, urea ammonia-containing powders, antibiotic-containing combinations and antienzyme chemicals. These chemicals each have their own set of benefits and drawbacks.

ROLE OF FLUORIDE IN THE TREATMENT OF DENTAL CARIES

Fluoride's role in preventing dental cavities is widely known. The administration of tiny amounts of fluoride salts or their usage as a topical application on teeth has yielded positive benefits.

Fluoride ion is a trace element that naturally occurs in human bodies. It can usually be gotten in sufficient amounts through food and water. Ground water in various places of the world is completely devoid of fluoride. Dental caries cases arose in frightening proportions in certain places. Fluoridation is the process of adding fluoride to municipal water supplies. Fluoridation can aid in the reduction and prevention of dental cavities. Those who consume fluoride over time experience mottling of teeth, increased bone density, gastrointestinal problems, muscular weakness, convulsions and even heart failure.

Due to beneficial effects in treating dental caries and osteoporosis; fluoride ions find application in dental practice.

When a fluoride containing preparations are taken orally, it is readily absorbed, transported and deposited in the bone or developing teeth. Remaining is gets excreted through kidneys. The deposition fluoride over surface of teeth prevents the action of acids or enzymes in producing lesions. A small quantity (1 ppm) of fluoride is vitally important to prevent caries. However, if more quantity of fluoride (>2-3 ppm) is ingested; it is carried to bones and teeth causing mottled enamel known as dental fluorosis.

Fluoride formulations can be administered by two routes:

(a) Orally;

(b) Topically

One of the most popular and effective methods of oral delivery is fluoridation of public water supplies. To avoid dental caries, a water source with roughly 0.5-1ppm fluoride is provided. It can also be provided in a concentration of about 1ppm/day in drinking water or fruit juice. In dental practise, sodium fluoride tablets or solutions with a daily dose of 2.2 mg are also utilised. On teeth, a 2 percent solution of sodium fluoride is commonly utilised for topical treatment.

DENTURE CLEANERS

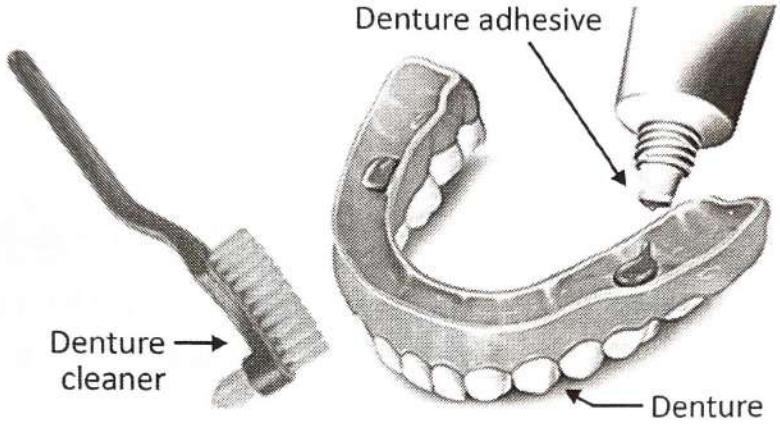


Fig. 3.6: Denture Adhesive and Denture Cleaner

CALCIUM CARBONATE I.P.

Precipitated chalk is fine powdery texture used in dentifrices. It is ingredients of both powders and pastes. It produces abrasive and antacid effect in the mouth. It is common ingredient of tooth powder and toothpaste.

Molecular Formula: $CaCO_3$

Molecular Weight: 100 g/mol

Calcium carbonate occurs in nature as limestone, marble, calcite, vaterite, aragonite and shell of sea animals.

Properties: It occurs as a white, odourless, tasteless microcrystalline powder, stable in air. It exists in two crystal form such as aragonite and calcite.

Uses:

1. Calcium carbonate is a moderate abrasive that facilitates the removal of plaque and softly polishes away surface stains while brushing.
2. In addition to raising dental calcium levels and neutralising plaque acids, calcium carbonate has further benefits.

Official Preparations:

1. Calcium Carbonate Tablet
2. Calcium Carbonate oral suspension

Brand name: Shelcal-os, Calvimax forte, Calcigel

SODIUM FLUORIDE

Molecular Formula: NaF

Molecular Weight: 41.99 g/mol

Description: It is colourless, odourless crystals and appeared as white powder.

Properties: It is soluble in water but insoluble in alcohol. Aqueous solution of sodium fluoride is able to corrode ordinary glass bottles. Hence, the sodium fluoride solution should be prepared in distilled water and stored in dark Pyrex bottles.

On acidification of salt solution, hydrofluoric acid is produced. It is weakly acidic and poisonous. Aqueous solution of salt produces alkaline reaction.

Action and uses:

(a) Sodium fluoride due to its fluoride content is an important ingredient in dentifrices to retard or prevent formation of dental caries.

(b) 2% aqueous solution of sodium fluoride is used topically and applied over surface of dry teeth at regular intervals over several times to produce therapeutic effects. Fluoride ion enters in enamel of teeth and becomes part of enamel structure to show effectiveness.

(c) 2.2 mg of sodium fluoride contains 1 mg of fluoride ion approximately. Each gm of sodium fluoride is equivalent to 23.8 mmol of sodium and fluoride.

(d) Sodium fluoride and other soluble fluorides are readily absorbed from gastrointestinal tract. Fluoride gets absorbed slowly from gums when applied as paste or powder and incorporated into the teeth. Fluoridised teeth have been resistant to microorganisms causing dental caries. These preparations are able to decrease microbial acid production.

(e) Sodium fluoride can be used as solution, tablet, oral gel or varnish for systemic use or orally as a mouth wash.

Official Preparation:

1. Sodium Fluoride Tablet
2. Sodium Fluoride Gel

Brand name: Nunaf, Duraflor, Clinpro-500

DENTURE ADHESIVE

Denture adhesives, which are non-toxic, soluble products that are applied between the denture and the mucosal surface with the goal of improving the retention, stability and function of complete dentures, are widely available. When used appropriately, adhesives can provide accurate estimates of the dental doctor's ability to apply methods of retention precisely and they can also be an important element of the patient's dental treatment. Adhesives create a temporary connection between a denture and the underlying tissues. They become a requirement for the patient, since they improve that connection.

The ideal requirements of a denture adhesive are:

1. It should be in the form of a powder, gel or cream on the physical level.
2. It must be non-toxic, irritant-free and biocompatible.
3. It should have a low odour and no flavour.
4. It needs to be simple to put to the denture's tissue surface.
5. It must not encourage the growth of microorganisms.
6. It should possess retentive adhesive qualities for longer period (12-16 hours).
7. It should provide comfort, retention and stability during functions.

Composition

The major constituents of denture adhesives can be broadly divided in to three groups:

Group 1: Materials responsible for adhesive properties such as: Karaya gum, Tragacanth, Acacia, Pectin, Gelatin, Methyl-cellulose, Hydroxyl methyl cellulose, Sodium carboxy-methyl cellulose and Synthetic polymers (Polyethylene oxide, Acrylamides, Acetic poly- vinyl).

Group 2: Anti-microbial agents such as Hexachlorophene, Sodium borate, Sodium tetraborate and ethanol.

Group 3: Additives, Plasticizers, wetting agents and flavouring agents such as oil of wintergreen, oil of peppermint, etc.

Currently the Denture Adhesives can be divided as:

1. **Soluble Group:** That includes Creams, Pastes, Powders. They have active ingredients like Carboxymethyl Cellulose (CMC) and Polyvinyl ether methyl methacrylate (PVM-MA). When compared to the PVM-MA combination, the CMC compound has a strong initial grip but dissolves quickly due to its high solubility and loses its effectiveness soon.
2. **Insoluble Group:** Include Pads and synthetic wafers. A laminated fabric with water active component like sodium alginate or ethylene oxide polymer impregnated within fabric's mesh. It is reported in literature the use of dentifrices as denture adhesives in emergencies, but the retentive qualities are poor and short acting.

Advantages of Denture Adhesives:

1. Increased stability.
2. Increased retention.
3. Reduction in denture mediolateral movement and dislodgement

Disadvantages of Denture Adhesives:

1. Prevent from recognizing that denture was not fit properly.
2. Using denture adhesive can give the patient a false sense of security.
3. Can cause candidiasis, denture stomatitis, an imbalance of oral flora as a result of microbial contamination and alveolar bone resorption.
4. If used for partial dentures, denture adhesive containing Karaya gum will generate a solution with a pH below 5.5-6.5, which can cause enamel decalcification.

MOUTH WASHES

A mouthwash is a flavoured, typically antiseptic solution that is used to refresh the breath and clean the mouth. Mouthwash, often known as mouth rinse, is an antiseptic solution that patients can use at home to improve their oral hygiene. Antiseptic and anti-plaque mouthwashes, according to some mouthwash makers, eliminate the bacteria that cause cavities, gingivitis and foul breath. Fluoride is used in anti-cavity mouth rinses to prevent tooth decay. However, it is well acknowledged that using mouthwash does not negate the requirement for brushing and flossing.

In today's world, there are two sorts of mouthwashes, each of which might assist you in distinct ways.

Therapeutic mouthwash: This rinse has more potential to help your oral health than you may realize. It can help to minimize plaque buildup in your mouth, lower your risk of gum disease and prevent tooth decay. This rinse also contains fluoride, which can help to clean your teeth and strengthen your chomper.

Cosmetic mouthwash: This rinse will brighten your smile and provide you with new results. Some mouthwashes effectively whiten teeth over time, while others freshen your breath and leave you with a nice flavor.

Main ingredients of mouthwashes are: Alcohol, Benzydamine (analgesic), Cetylpyridinium chloride (antiseptic), Chlorhexidine digluconate and hexetidine (antiseptic), Essential oils, Fluoride (anticavity), Hydrogen peroxide, Povidone/iodine, Sodium bicarbonate (baking soda), Sodium lauryl sulphate (foaming agent), Zinc

MEDICINAL GASES

INTRODUCTION

We are surrounded by atmosphere which composed by various gases. There are many gases which are of vital therapeutic significance. Therapy with oxygen is useful or necessary for life in several diseases and intoxication that interfere with normal oxygenation of the blood or tissues. Various gases are incorporated in different treatments for humans.

INHALANTS

The drugs or chemicals, in the vapour from are inhaled or administered through respiratory system in the body are known as inhalants.

When gases are inhaled, they bring about various physiological changes and bring pharmacological actions. Some inhalant can act as anaesthetics when it is administered by inhalation by closed-mask method. Such effects of gases depend upon its nature, concentration and condition in which it is used, that mean effect of gases will be different at different conditions.

Gases like oxygen, carbon-dioxide and nitrogen occur in blood in dissolved form. Out of this maximum concentration of oxygen is found in blood, as it rapidly attaches to haemoglobin (to form oxyhaemoglobin), so only a small portion of oxygen remains in blood. Thus, the body is having very small store of oxygen which can be used upon the several physiological conditions like anoxia. The total store is about 1500 ml of oxygen enough to maintain life for 6 minutes. Similarly, carbon-dioxide from tissue gets rapidly converted to carbonic acid and to sodium bicarbonate, so very few quantities remain in free form in blood.

Properties of Inhalants

The properties of Ideal inhalation anaesthetics are as follows:

1. It should be free from toxic effects;
2. It should have a wide margin of safety;
3. It should be non-irritant;
4. It should be free from unpleasant taste and smell;
5. It should act rapidly and produce pleasant induction with smooth recovery without unpleasant symptoms of nausea;
6. The potency should be high so that adequate amounts of oxygen can be administered with the anaesthetics;
7. For control of depth of anaesthesia, the agent should be rapidly acting and rapidly eliminated from the body;
8. From the surgeon's viewpoint the agent should produce complete muscle relaxation and should not increase capillary bleeding and
9. The agent should be cheap and stable on storage because no single agent fulfils all these requirements.

Carbon dioxide	Grey
Nitrogen	Black
Nitrous Oxide	Blue
Oxygen	White

Fig. 3.7: ***Colour Codes for Medical Gases***

CARBON DIOXIDE

Formula: CO_2

Molecular Weight: 44.01

Properties: Carbon dioxide is a heavy, colourless, odourless gas having a faintly acidic taste. It can be liquefied under water. It is soluble in water. Carbon dioxide does not support Combustion.

Storage and Labelling: It should be stored under compression in metal cylinder. The shoulder of cylinder is painted grey and has the name and symbol of "CO_2" stencilled in paint on the shoulder.

Uses:

1. Regulation of acid-base balance.
2. Rarely used as respiratory stimulant.
3. Along with oxygen it is used in the treatment of Carbon monoxide poisoning.
4. Liq. CO_2 promote the absorption of liquid by mucous membrane.
5. Frozen CO_2/dry ice is used in the treatment of eczema, acne, psoriasis and also used in minor surgical operation for destroying tissue.

NITROUS OXIDE (IP 1996)

Formula: N_2O

Molecular Weight: 44.01

Description: Colourless gas; odourless.

Properties: It is a colourless gas having a characteristic odour and taste. It dissolves in about 2 volumes of water and is soluble in solvent ether and alcohol. It gets decomposed at high temperature (500°C).

Storage and Labeling:

1. The gas is stored in metal cylinder under compression and at a temperature not exceeding 37°C.
2. The cylinder is painted blue and carries a label stating the name of gas and symbol N_2O stenciled in paint.

Uses:

1. It is used as anaesthetic.
2. It is used as an inhalant. A mixture of Oxygen and Nitrous oxide (50:50) can safely be used for the relief of pain in child birth.
3. A mixture of Oxygen and Nitrous oxide (65:35) is used in myocardial infarction.
4. Also used as a good analgesic. Small amount of Nitrous oxide dulls the sensitivity of pain.
5. As a laughing gas large amounts of nitrous oxide have a stimulating effect on the nervous system.

OXYGEN (IP 1996)

Symbol: O

Atomic Weight: 16.00

Formula: O_2

Molecular Weight: 32.0

Oxygen is the vital constituent of air and constitutes about 21 percent by volume of Atmosphere. Oxygen as per IP contains not less than 99.0 per cent v/v of O_2. Argon with traces of nitrogen or hydrogen may be present as a residue. It is supplied and made available in metallic cylinders in compressed form. For oxygen white colour code is there which is present on the neck of metallic cylinder (filled with O_2 gas).

Properties:

1. It is colourless, odourless, tasteless gas.
2. It is heavier than air with density 1.105
3. Oxygen dissolves in about 32 volumes of water, 36 volumes of alcohol.
4. Oxygen readily dissolves in some molten metal like silver.
5. It is a paramagnetic in nature.
6. Oxygen supports combustion.
7. Chemically oxygen is strong oxidizing agent.

Storage and Labelling: It should be stored under compression in metal cylinder. It should be stored in a special storage room which should be cool and free from inflammable materials. The shoulder of the metal cylinder is painted WHITE and remainder is painted BLACK. The cylinder carries a label stating the name of the gas and in addition, the symbol "O_2" is stencilled in paint on the shoulder

Uses:

1. It is used in the treatment of hypoxia.
2. It is used in the anaesthesia.
3. It is used in asthma as well as in-circulatory failure, respiratory depression/failure.
4. It is used in treatment of carbon monoxide poisoning, respiratory depression or respiratory failure.
5. It is used in the management of abdominal distension, intestinal gas-filled cysts and to persons working in pressurized spaces.
6. It is used as diluents of volatile and gaseous anaesthetics.

EXERCISE

Short Answer Type Questions

1. Preparation and medicinal uses of calcium carbonate.

2. What are dental products? Classify them with examples.
3. What are mouthwashes? Give example.
4. **Give properties and uses of:**
   (a) $FeSO_4$
   (b) Ferrous fumarate
   (b) Aluminium hydroxide gel
   (c) Magnesium hydroxide
   (d) Boric acid
   (e) Bleaching powder
   (f) Calcium carbonate
5. **Give storage and labelling for:**
   (a) Oxygen
   (b) Carbon dioxide
6. **Define the following terms:**
   (a) Haematinics
   (b) Adsorbents
   (c) Protectives
   (d) Cathartics
   (e) Dentifrices
7. **Write the molecular formula and uses of the following:**
   (a) Aluminium hydroxide gel
   (b) Magnesium hydroxide
   (c) Sodium bicarbonate
   (d) Calcium Carbonate
   (e) Silver Nitrate
   (f) Hydrogen peroxide
   (g) Boric acid
   (h) Bleaching powder
   (i) Potassium permanganate

Long Answer Type Questions

1. Classify gastrointestinal agents with examples.
2. Define antimicrobial agents and explain their mechanism of action. Give properties of potassium permanganate.
3. Define cathartics. Classify with examples. Give synonym and molecular formula of sodium potassium tartrate.
4. Define achlorhydria. Give properties, uses and molecular formula of agent used to treat achlorhydria.
5. Classify gastrointestinal agents with examples.
6. What are adsorbents and protectives? Give examples.
7. What are dental products? Discuss the role of fluorides in dental caries.
8. Classify cathartic agents with examples.
9. Explain combination preparation of antacids.

Multiple Choice Questions (MCQ's)

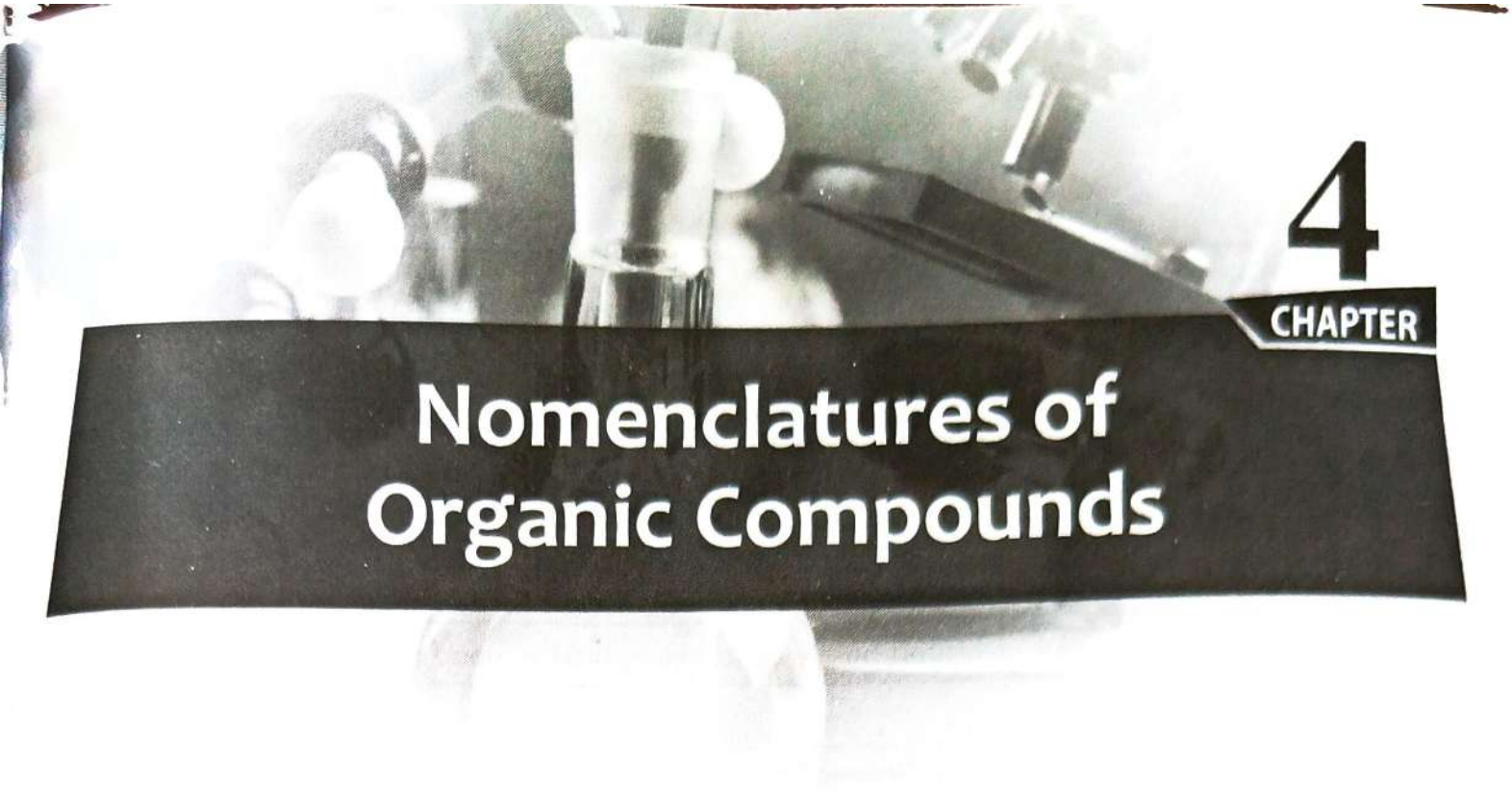
1. **Desensitizing agent are used for _____.**
   (a) Dental carries (b) Sensitivity in teeth
   (b) Dentifrices (b) None of the above
2. **Dentifrices include _____.**
   (b) $CaCO_3$ (b) $SrCl_2$
   (b) NaF (b) All of the above
3. **Calcium carbonate can't be used in toothpastes containing NaF due to formation of:**
   (b) Soluble complex (b) Insoluble complex
   (c) Both (a) & (b) (d) None of the above
4. **Excess of Fluoride in teeth may lead to:**
   (a) Dental Fluorosis (b) Mottling
   (c) Both (a) & (b) (d) None of the above
5. **Which of the following is used as anticaries agent/agents?**
   (b) $CaCO_3$ (b) SnF_2
   (b) NaF (d) Both (a) and (b)
6. **_____ are the agents used for the formation of blood and helpful in treatment of various types of anaemia?**
   (a) Acidifying agents (b) Medicinal gases
   (c) Haematinics (d) Anti-microbial agent
7. **_____ are used to prevent and relieve pain in the symptomatic management of gastric and duodenal ulcers.**
   (a) Acidifying agents (b) Medicinal gases
   (c) Antacids (d) Anti-microbial agent
8. **Rochelle Salt is synonym of:**
   (a) Sodium potassium tartrate (b) Bleaching powder
   (c) Potassium permanganate (d) Calcium Carbonate
9. **Baking Soda is synonym for:**
   (a) Sodium bicarbonate (b) Bleaching powder
   (c) Potassium permanganate (d) Calcium Carbonate

10. The Chlorinated Lime is synonym for:

(a) Sodium bicarbonate
(b) Bleaching powder
(c) Potassium permanganate
(d) Calcium carbonate

ANSWERS OF MULTIPLE CHOICE QUESTIONS (MCQ'S)

1. (b)	2. (a)	3. (b)	4. (a)	5. (d)	6. (c)	7. (c)
8. (a)	9. (a)	10. (b)				



4

CHAPTER

Nomenclatures of Organic Compounds

CLASSIFICATION OF ORGANIC COMPOUNDS

It is basically based on the functional group. The chemical properties of compound depend on the properties of the functional group present in it. The rest of the molecule simply affects the physical properties, e.g., M.P., B.P., density etc., and has very little effect on its chemical properties.

TYPES OF NOMENCLATURE

1. Trivial or Common Names

Because IUPAC designations were not available in the past, the names of compounds were determined by the source from which they were obtained. Despite the IUPAC nomenclature, several of the common names are still in use today. We prefer to use common names in some cases where the IUPAC term is too long, such as lactic acid and sucrose.

S.No.	Common Name	Source	Structure
1.	Formic acid	Formica (red ant)	HCOOH
2.	Acetic acid	Acetum (vinegar)	CH_3COOH
3.	Propionic acid	Protopion (first fat)	CH_3CH_2COOH
4.	Butyric acid	Butyrum (butter)	$CH_3CH_2CH_2COOH$

Table contd...

Table contd...

S.No.	Common Name	Source	Structure
5.	Valeric acid	Valerian (shrub)	$CH_3(CH_2)_3COOH$
6.	Caproic acid	Caper (Goat)	$CH_3(CH_2)_4COOH$
7.	Urea	Urine	NH_2CONH_2
8.	Malic acid	Malum (apple)	CH_2COOH | $CH(OH)COOH$
9.	Methyl alcohol	Methu hule (Mehtu-wine, hule = wood)	CH_3OH

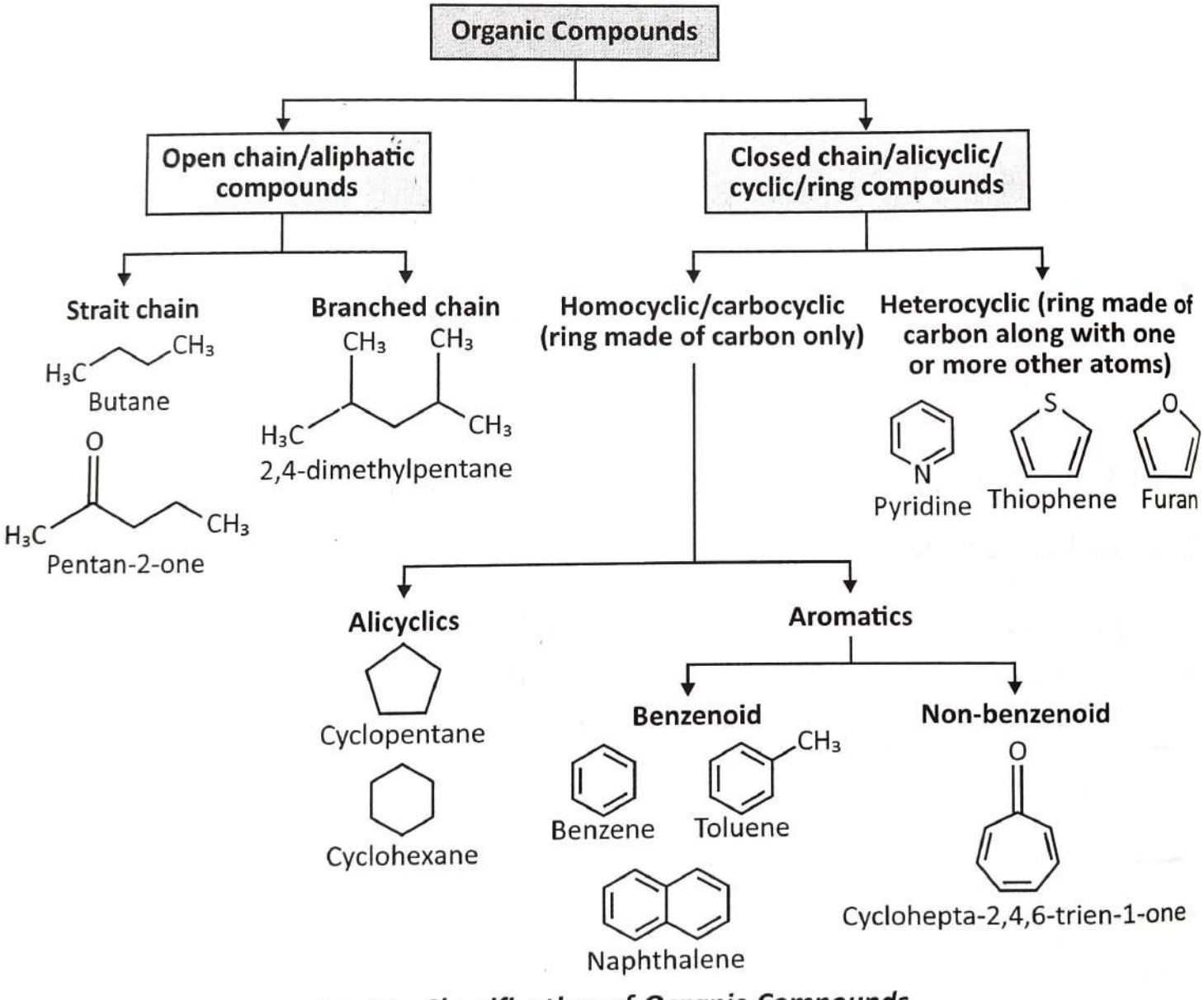


Fig. 4.1: ***Classification of Organic Compounds***

2. IUPAC Nomenclature

The nomenclature of organic compounds used by the International Union of Pure and Applied Chemistry (IUPAC) is a systematic method of naming organic molecules.

Systematic IUPAC Name Format

The systematic IUPAC name of an organic compound consists of four parts:

1. Root word
2. Suffix(es)
3. Prefix(es) and
4. Infix

Prefix(es) + infix + root word + 1° suffix + 2° suffix

The suffix is separated into two categories: Primary and secondary. As a result, the entire systemic IUPAC name can be represented as:

Prefix(es) + infix + [root word + 1° suffix] + 2° suffix

Base Name

*The "word root" and "1° suffix" composed is known as base name.

*The Prefix, infix and 2° suffix may or may not be required always.

A base name is made up of the "word root" and the "1° suffix."

The prefix(es), infix and 2° suffix are not usually necessary.

1. Root Word:

The number of carbon atoms in the longest continuous carbon chain, also known as the parent chain, as determined by a set of rules, is indicated by the word root of the IUPAC name. The word roots used for different length of carbon chain are shown below (up to 12)

Number of carbon atoms in the parent chain	1	2	3	4	5	6	7	8	9	10	11	12
Root word	Meth	Eth	Prop	But	Pent	Hex	Hept	Oct	Non	Dec	Undec	Dodec

2. Suffix:

It is again divided into two types:

A. Primary Suffix: It's a metric that shows how saturated or unsaturated the main chain is. It is placed right after the IUPAC name's word root.

Type of carbon chain	Primary suffix
Saturated (all C-C bonds)	-ane
Unsaturated: One C=C	-ene
Unsaturated: Two C=C	-diene
Unsaturated: One C≡C	-yne
Unsaturated: Two C≡C	-diyne
Unsaturated: One C=C & one C≡C	-enyne

B. Secondary Suffix: It is put soon after the 1° suffix in the IUPAC name to denote the primary functional group in the chemical molecule.

Note: If a compound has two or more functional groups, the functional group with the highest priority is chosen as the 1° operational group, which must be denoted by a secondary suffix. Prefixes are used to designate the remaining functional groups with lesser concern.

In the table below, the suffixes and prefixes used for certain significant functional groupings are listed in decreasing order of priority.

Also, when the functional group's carbon atom is not part of the main chain, a separate suffix is used.

Name of Functional group	Representation	Suffix (When carbon of the functional group is part of the parent chain)	Suffix (When carbon of the functional group is NOT part of the parent chain)	Prefix
Carboxylic acid	-COOH	-oic acid	-carboxylic acid	carboxy-
Acid anhydride	$-O-\overset{O}{\overset{\|\|}{C}}-O-\overset{O}{\overset{\|\|}{C}}-O-$	-oicanyhydride	-carboxylic anhydride	—
Ester	-COOR	alkyl -oate	alkyl -carboxylate	alkoxycarbonyl-
Acid halide	-COX	-oyl halide	-carbonyl halide	halocarbonyl-

Table contd...

Table contd...

Name of Functional group	Representation	Suffix (When carbon of the functional group is part of the parent chain)	Suffix (When carbon of the functional group is NOT part of the parent chain)	Prefix
Acid amide	$-CONH_2$	-amide	-carboxamide	carbamoyl-
Nitrile	$-CN$	-nitrile	-carbonitrile	cyano-
Aldehyde	$-CHO$	-al	-carbaldehyde	oxo-
Ketone	$-CO-$	-one	—	oxo-
Alcohol	$-OH$	-ol	—	hydroxy
Thiol	$-SH$	-thiol	—	mercapto
Amine	$-NH_2$	-amine	—	amino-
Imine	$=NH$	-imine	—	imino-
Alkene	$C=C$	-ene	—	—
Alkyne	$C\equiv C$	-yne	—	—

3. Prefix:

Side chains, substituents and low priority functional groups are indicated by the prefix (which are taken as substituents). The prefix may come before the word root or the IUPAC name infix.

Prefixes for certain commonly used side chains and substituents are listed below. (Functional group prefixes are already provided).

Side chain or Substituent	Prefix
$-CH_3$	methyl-
$-CH_2CH_3$ (or) $-C_2H_5$	ethyl-
$-CH_2CH_2CH_3$	propyl-
$H_3C-\overset{\vert}{C}H-CH_3$	isopropyl-
$-CH_2CH_2CH_2CH_3$	butyl
$H_3C-CH_2-\overset{\vert}{C}H-CH_3$	sec-butyl (or) (1-methyl)propyl

Table contd...

Table contd...

Side chain or Substituent	Prefix
$H_3C-\underset{}{\overset{CH_3}{\overset{\vert}{C}H}}-CH_2-$	Isobutyl(or)(2-methyl)propyl
$H_3C-\overset{CH_3}{\overset{\vert}{C}}-CH_3$	tert-butyl(or)(1,1-dimethyl)ethyl
-X	halo-
-OR	alkoxy-
$-NO_2$	-nitro

The alkyl groups along with halo, nitro and alkoxy have the same preference. They have lower priority than double and triple bonds.

4. Infix:

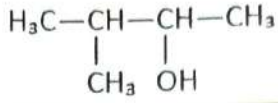
The infixes, like cyclo (indicate the cyclic structure of the parent chain), spiro (indicate the spiro compound.), bicyclo (indicate the bicyclic nature of the parent chain), are added amid the prefix(es) and root word in the IUPAC name to designate the type of parent chain.

The infixes are sometimes called as primary prefixes.

STEPS INVOLVED IN WRITING IUPAC NAME

1. Selecting the parent chain and assigning a word root is the first stage in giving an organic compound an IUPAC name.
2. The root word must then be suffixed with the appropriate primary suffix(es) to signify saturation or unsaturation.
3. A secondary suffix must be appended to designate the principal functional group if the molecule comprises one or more functional groups. If the molecule does not include any functional groups, this step is optional.
4. If the parent chain is cyclic, prefix the root word with "cyclo".
5. Finally add the prefix(es) to the IUPAC name, if there are side chains or substituents on the parent chain.

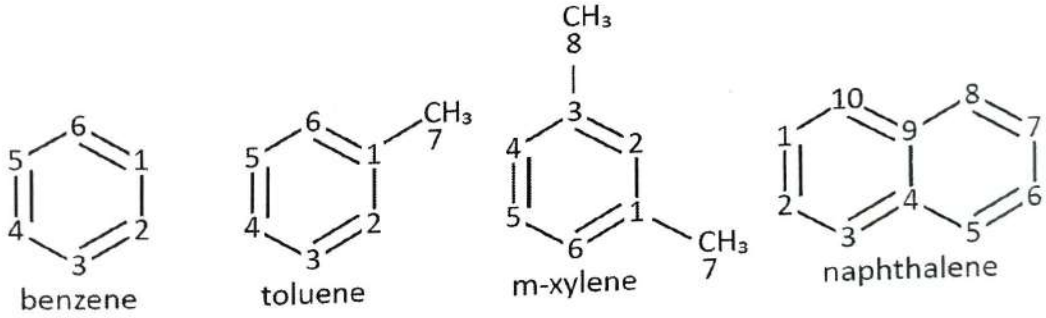
For example, the IUPAC name of the following compound (3-methylbutan-2-ol) is arrived in steps mentioned below:



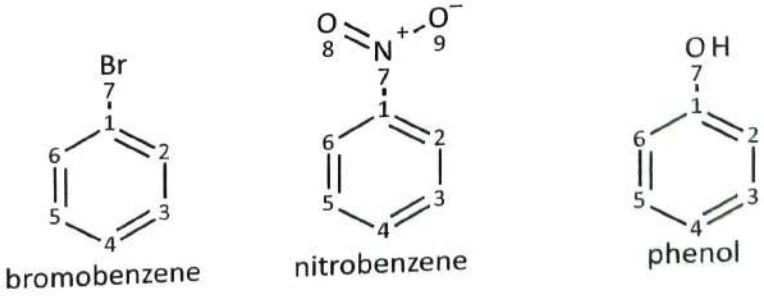
3-Methyl	+	but	+	ane	+	2-ol
Prefix		Root word		1° suffix		2° suffix

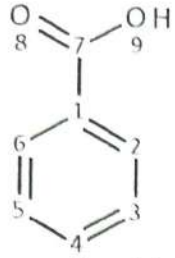
Step-1	How many carbons are there in the parent chain?	4	Root word = "but"
Step-2	Saturated or Unsaturated?	Saturated	1°suffix = "ane"
Step-3	Is there any functional group?	Yes. There is an alcohol group on 2nd carbon.	2°suffix = "2-ol"
Step-4	Are there any side chains or substituents?	Yes. There is a methyl group on 3rd carbon.	2°prefix = "3-methyl"

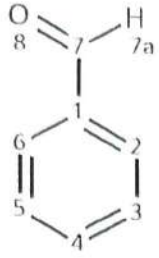
Examples of Aromatic Hydrocarbons

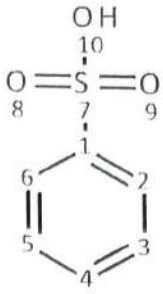


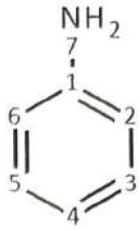
Examples of Aromatic Hydrocarbons (C, H and other Elements)

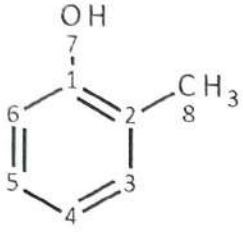


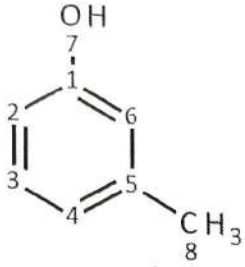

benzoic acid


benzaldehyde


benzenesulfonic acid


aniline


o-cresol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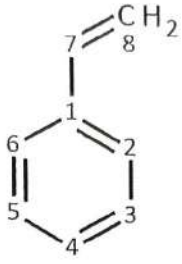
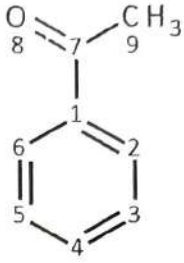
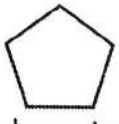
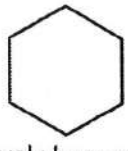

styrene


1-phenylethanone

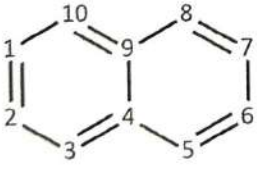
Examples of Cyclic Compounds (Cycloalkanes)

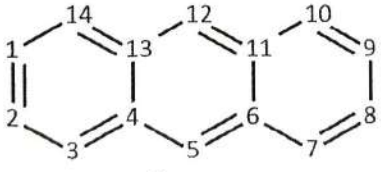
Cycloalkaneshave one or more rings of carbon atoms. The general formula for a cycloalkane composed of n carbons is CnH_2n

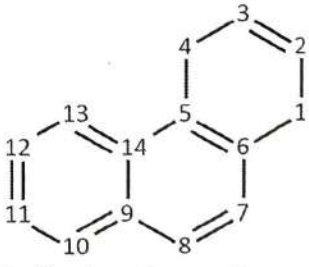

cyclopentane


cyclohexane

Examples of Polynuclear Compounds


naphthalene


anthracene


1,4-dihydrophenanthrene

SYSTEMATIC METHOD OF NOMENCLATURE FOR HETEROCYCLICS

The prefix in the name of monocyclic compound indicates the nature of heteroatoms present, e.g., oxygen-oxa, Sulphur-thia, nitrogen-aza, silicon-sila, phosphorus-phospha.

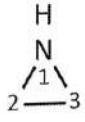
When two or more of the same heteroatoms are present, prefixes di, tri, etc., are used, e.g., dioxa, triaza

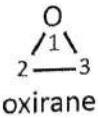
If the heteroatoms are different, their Order of naming will be- O, S, N, P, Si, ...-, e.g., thiaza (S then N)

No. of members in the ring	Rings containing nitrogen		Rings containing no nitrogen	
	Unsaturation	Saturation	Unsaturation	Saturation
3	-irine	-iridine	-iren	-iran
4	-ete	-etidine	-et	-etan
5	-ole	-olidine	-ole	-olan
6	-ine	B	-in	-ane
7	-epine	B	-epin	-epan
8	-ocine	B	-ocin	-ocan
9	-onine	B	-onin	-onan
10	-ecine	B	-ecin	-ecan

B- expressed by prefixing 'perhydro' to the name of the corresponding unsaturated compound

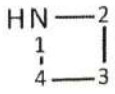
2H-azirene


aziridine


oxirane

thiirane

thiirene

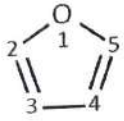

azetidine

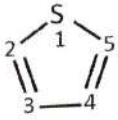
2,3-dihydroazete

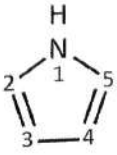
oxetane

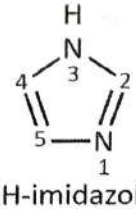
thietane

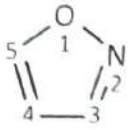
In below figures, the structure is numbered according to nomenclature rules and bold script under the structure indicate the drug which contain the heterocyclic compound as basic skeleton, i.e., the basic ring in Furosemide drug is Furan.



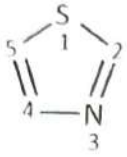

thiophene


1H-pyrrole

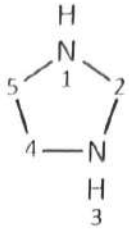

1H-imidazole
Tolazoline



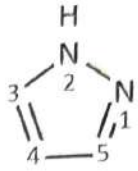
isoxazole
Sulphisoxazole



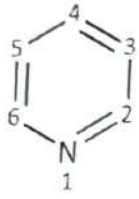
1,3-thiazole
Thiamine



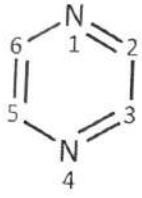
imidazolidine
Mebendazole



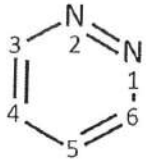
1H-pyrazole
Sulphaphenazole



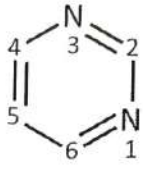
pyridine



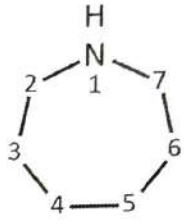
pyrazine
Pyrazinamide



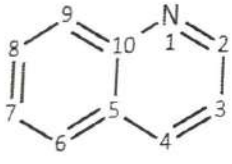
pyridazine



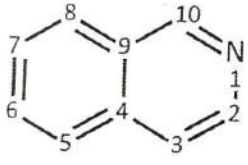
pyrimidine
Trimethoprim



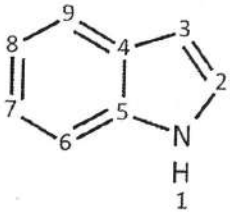
azepane
Carbamazepine



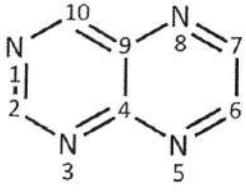
quinoline
Chloroquine



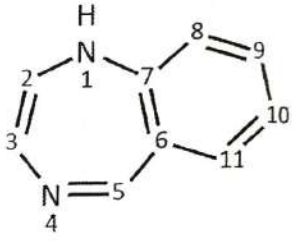
isoquinoline



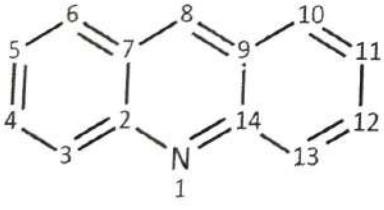
1H-indole
Indomethacin



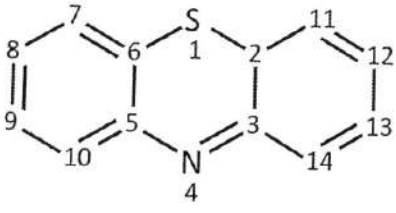
pteridine
Folic acid



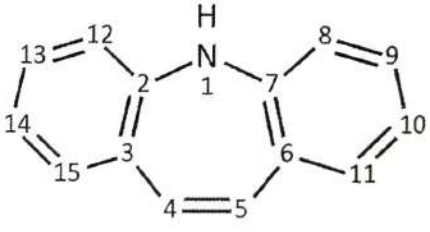
1H-1,4-benzodiazepine
Diazepan



acridine
Mepacrine

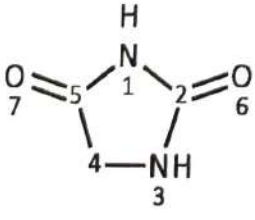


4aH-phenothiazine
Chlorpromazine

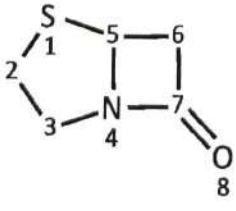


5H-dibenzo[b,f]azepine

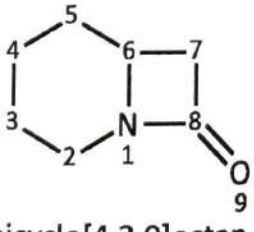
-2-one
illin,
sporin



imidazolidine-2,4-dione
hydantoin
Phenytoin



4-thia-1-azabicyclo[3.2.0]heptan-7-one
Penam
Penicillin



1-azabicyclo[4.2.0]octan-8-one
cepham
Cephalosporin

EXERCISE

Short Answer Type Questions

1. **Give structure and method of numbering for:**
   (a) Pyridine
   (b) Isoindole
   (c) Benzofuran
   (d) Furan
   (e) Thiophene
   (f) Pyrrole
   (g) Quinoline
2. **Write structure of the following groups:**
   (a) Amino
   (b) Nitro
   (c) Methyl
   (d) tert-butyl
   (e) Vinyl
3. What are aromatic hydrocarbons?

Long Answer Type Questions

1. Give the Classification of organic compounds.
2. Explain systematic method of nomenclature for heterocyclics.

5
CHAPTER

Drugs Acting on Central Nervous System

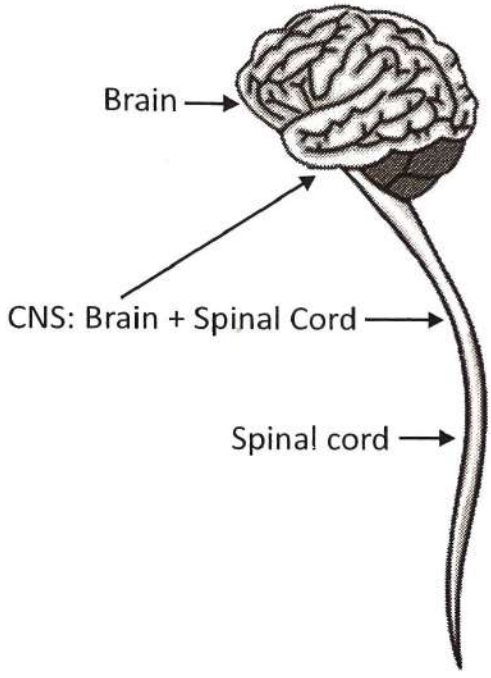


Fig. 5.1: ***Central Nervous System***

ANAESTHETICS

General anesthetics are the agent which produces unconsciousness and losses the all sensation of the body. These drugs are acting on the brain and depress the activity of central nervous system to extent totally loss the sensation of pain and prolong the unconsciousness at the stipulate period of time.

History of General Anesthetics

In 1844, Dr. Horace Will, a dentist had been used N_2O as an anesthetic for tooth extraction. In 1846, Dr. Mortan, a dentist had evaluated ether as an anesthetic and it became trendy as an Ether Day. In 1847, Simpson was used chloroform for obstetrical operation. In 1934, Ralph Waters, firstly introduce intravenous an aesthetic thiopentone sodium in human.

Ideal Properties of General Anesthetics

1. It should be cheap, stable and easily stored
2. It should be non-flammable and non-explosive
3. It should be rapid and pleasant induction
4. It should be non-irritating and not causes nausea and vomiting
5. It should not cause postoperative complication
6. It should be adequate relaxation of skeletal muscle
7. It should not react with rubber tubes and soda glass
8. It should be absence of toxic effect on normal doses

Stages of General Anesthesia

1. **Stage I (Analgesia):** This stage usually loss of pain sensation without loss of memory. It is beneficial for minor surgery.
2. **Stage II (Excitement):** In this stage causes nausea, vomiting, hyperactivity and irregular breathing, further it will start with loss of consciousness.
3. **Stage III (Surgical Anesthesia):** This stage is useful for surgical procedure. This is stage of sleep and paralyzed reflexes. Respiration and blood pressure is normal.
4. **Stage IV (Medullary Paralysis):** In this stage depress the vasomotor and respiratory center further leads to coma and death.

Classification of Anesthesia

1. General Anesthetics
2. Local Anesthetics

1. General Anesthetics

General anesthetics are drugs which produce reversible loss of all sensation and consciousness.

Classification:

A. **Inhalation anesthetics:**

1. **Volatile liquid:**
   (a) Halogenated hydrocarbon, e.g., Halothane
   (b) Ethers, e.g., diethyl ether
2. **Gases:**
   (a) Inorganic gases, e.g., Nitrous oxide
   (b) Hydrocarbons, e.g., Cyclopropane

B. **Intravenous anesthetics:**

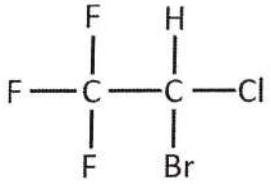
1. Ultrashort acting barbiturate
2. Non-barbiturate, e.g., Ketamine

HALOTHANE

It is utilized for general anesthesia induction and maintenance. It reduces excessive excitation in the brain.

Formula: $C_2HBrClF_3$

Molar Mass: 197.38



IUPAC Name: 2-Bromo-2-chloro-1,1,1-trifluoroethane.

Properties: It is halogenated, colourless, non-flammable liquid, sweet odour compound. It is slightly soluble in water and miscible in ethanol, trichloroethylene.

Storage: It is stored in tightly closed container.

Uses: It is used for induction and maintenance of general anesthesia.

Official Preparation: Fluothane Solution.

Brand Name: Fluothane.

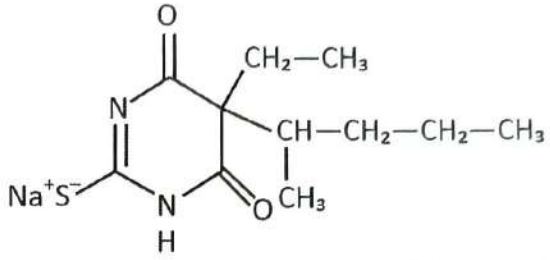
THIOPENTAL SODIUM

Molecular Formula: ($C_{11}H_{17}N_2NaO_2S$)

Molar Mass: 264.3

Chemical Name: 5-Ethyl-5(1-methyl butyl)-2-thiobarbiturate sodium.

Structure:



Properties: It is Yellowish white powder, faintly resembling garlic odour. It is hygroscopic in nature.

Stability and Storage Condition: It is stored in tightly closed container. It is decomposed by atmospheric O_2, it is hygroscopic and protected from light and moisture

Uses:

- It is use as anticonvulsant
- It has poor analgesic and muscle relaxant property
- It induces general anesthesia
- For prevention and treatment of cerebral ischemia

Official Preparation: Thiopentone Sodium injection IP, BP.

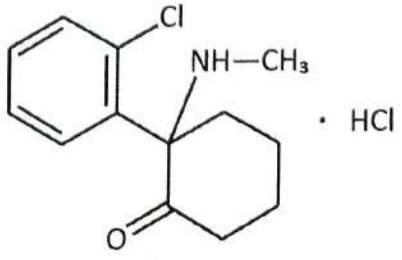
Brand Name: Pentothal sodium, Intraval sodium

KETAMINE HYDROCHLORIDE

Molecular Formula: $C_{13}H_{16}ClNO.\ HCl$

Molar Mass: 274.2

Structure:



IUPAC Name: 2-(2-Chlorophenyl)-2-(methylamino) cyclohexanone hydrochloride.

Properties:

- It is hydrochloride salt of synthetic derivatives of cyclohexanone, nonbarbiturate anesthetic and analgesic.
- It is white crystalline powder.
- It is freely soluble in water and alcohol.

Physical Properties:

- It is a white crystalline powder. It is odourless and tasteless.
- It is freely soluble in water and in methanol, sparingly soluble in Chloroform and practically in soluble in benzene and ether

Stability and Storage Condition: It is store in 20 to 25°C and stored in tightly closed containers, protect from light.

Uses:

- It is most of use in veterinary medicine.
- In humans it can induce and maintain general anesthesia before, during and after surgery.
- It is considered safe as an anesthetic because it is not reduced blood pressure.
- It is also an analgesic in lower dose, it can relieve pain.

Official Preparations:

- Ketamine hydrochloride tablet
- Ketamine hydrochloride nasal spray
- Ketamine hydrochloride injection.

Brand Name: Ketamil, Ketamax, Chlorketam, Keta, Kelavet.

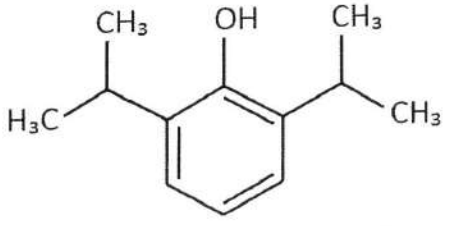
PROPOFOL

Molecular Formula: $C_{12}H_{18}O$

Molar Mass: 178.3

Chemical Name: 2,6 diisopropylphenol

Structure:



Physical Properties: It is colourless or very light clear liquid, it is very slightly soluble in water, miscible with Hexane and alcohol.

Stability and Storage: It is store in tightly close container and protect from light.

Uses:

- It is use as a general anesthesia for surgery or other medical procedure.
- It is also used to sedate a patient who is under critical care and need a mechanical ventilator.

Official Preparations:

- Propofol tablet
- Propofol capsule
- Propofol gel
- Propofol ointment
- Propofol injection

Brand Name: Diprivan, Propoven

SEDATIVES AND HYPNOTICS

Hypnotics: The drug which depress CNS and induce a sleep resembling to natural sleep-in normal dose called as hypnotics.

Sedatives: The drug which produce effect and reduce excitement are called sedatives.

Classifications

1. **Barbiturates:** (Depending up on duration of action)
   A. Long acting barbiturates (6 hours or more), e.g., Barbitone, phenobarbitone
   B. Intermediate acting barbiturate (3 to 6 hours), e.g., Butobarbitone
   C. Short acting barbiturate (less than 3 hours), e.g., Cyclobarbitone
   D. Ultra-short acting barbiturates (1/2 to 1 hours), e.g., Thiopentone sodium, methohexitone sodium.
2. **Non-barbiturates:**
   A. Benzodiazepine, e.g., Diazepam, nitrazepam.
   B. Amides and imides, e.g., Glutethimide, methyprylone.
   C. Acyclic nitrogen containing compound, e.g., Meprobamate, ethinamate
   D. Alcohol and their derivatives, e.g., Ethanol
   E. Aldehydes and derivatives, e.g., Paraldehyde
   F. Miscellaneous: Diphenhydramine, bromides

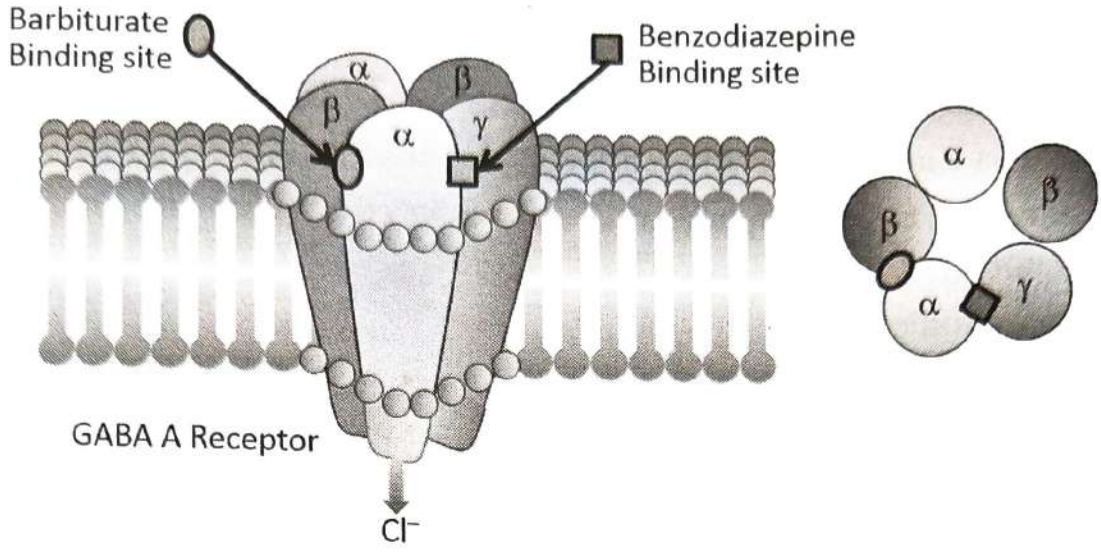


Fig. 5.2: ***Site of action of sedative and hypnotics***

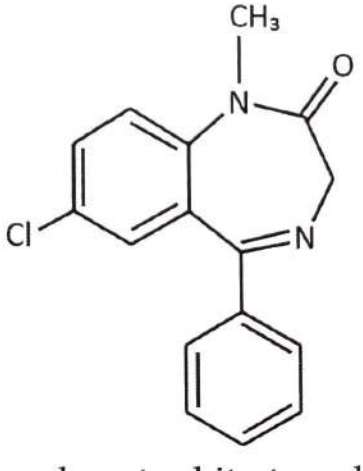
DIAZEPAM

Molecular Formula: $C_{16}H_{13}ClN_2O$

Molar Mass: 284.7

Chemical Name: 7-chloro-1-methyl-5-phenyl-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one

Structure:



Physical Properties: It is white or almost white to pale yellow crystalline powder and odourless, tasteless. It is sparingly soluble in water and soluble in alcohol.

Stability and Storage: It is affected from moisture and light, hence stored in tightly-closed and light resistant container.

Uses:

- It is use to control of anxiety and tension
- It is used to treat epilepsy
- It is treat excitation states

- It is use as premedication for surgical procedures
- It is use as adjunct

Official Preparations:

- Diazepam injection
- Diazepam Capsules
- Diazepam tablet
- Diazepam elixir

Brand Name: Diaclam, Calmpose, Valium.

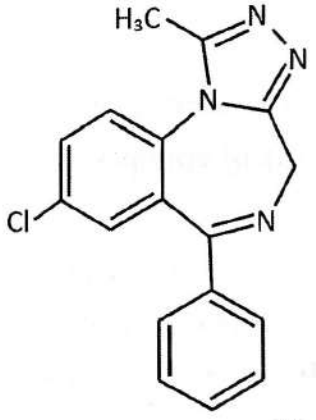
ALPRAZOLAM

Molecular Formula: $C_{17}H_{13}ClN_4$

Molar Mass: 308.8

Chemical Name: 8-chloro-1-methyl-6-phenyl-4*H*- [1,2,4] triazolo[4,3-*a*] [1,4] benzodiazepine

Structure:



Physical properties: It is white to off-white, crystalline powder. It is freely soluble in chloroform, soluble in ethanol, sparingly soluble in ethanol and acetone, slightly soluble in ethyl acetate and insoluble in water.

Stability and storage: It is store in amber colour tightly close container and protect from light

Uses: It is used to treat anxiety disorder and panic disorder.

Official Preparation: Alprazolam Tablet

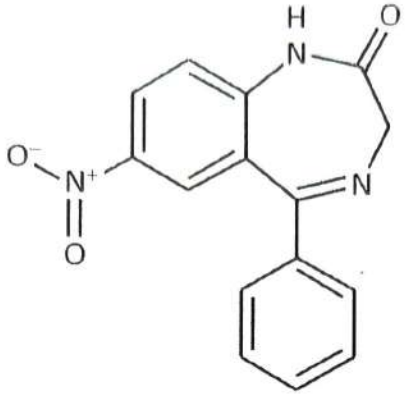
Brand Name: Alap, Abizox, Agcalm

NITRAZEPAM

Molecular Formula: $C_{15}H_{11}N_3O_3$

Molar Mass: 281.3

Structure:



7-nitro-5-phenyl-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one

Physical Properties: It is a yellow, crystalline powder, almost odourless. It is slightly soluble in chloroform and ethanol, practically in soluble in water.

Stability and Storage: It is affected by light and moisture hence it is store in tightly close container

Uses:

- It is a hypnotic and sedative, use in treatment of insomnia
- It is used to treat some forms of epilepsy

Official Preparations:

- Nitrazepam Tablets
- Nitrazepam Capsules

Brand Name: Alodrom, Nitrosun

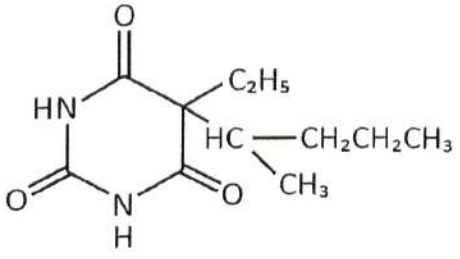
PHENOBARBITAL

Molecular Formula: $C_{12}H_{11}N_3O_3$

Molar Mass: 232.2

Chemical Name: 5-ethyl-5-(pentan-2-yl)-barbituric acid

Structure:



Physical Properties: It is white colour crystalline powder. It is odourless and slightly bitter in test. It is very slightly soluble in water and soluble on solution of alkali hydroxide and carbonates.

Stability and Storage: It is hygroscopic in nature hence stored in tightly closed container

Uses:

- It is used as sedatives in nervous insomnia
- It is anticonvulsant and used to treat grandmal and psychomotor epilepsy
- It is used to treat neonatal jaundice

Official Preparation:

- Phenobarbital tablet
- Phenobarbital capsule
- Phenobarbital elixir
- Phenobarbital sodium injection

Brand Name: Luminal, Garoin, Phenytal

ANTIPSYCHOTICS

The drugs which are used to treat psychiatric disorders are called antipsychotics drug.

1. **Phenothiazine derivatives and related tricyclic compound:**
   (a) **Phenothiazine derivatives,** e.g., chlorpromazine, prochlorperazine
   (b) **Thioxanthenes,** e.g., Chlorprothixene
2. **Butyrophenones,** e.g., Haloperidol, trifluoperidol
3. **Dibenzodiazepines,** e.g., clozapine
4. **Benzamides and salicylamides,** e.g., Sulpiride
5. **Diphenylbutyl piperidine derivatives,** e.g., pimozide
6. **Miscellaneous:** Reserpine

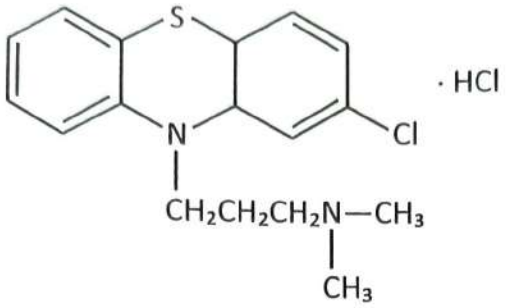
CHLORPROMAZINE HYDROCHLORIDE

Molecular Formula: $C_{17}H_{20}Cl_2N_2S$

Molar Mass: 355.5

Chemical Name: 3-(2-chloro-4a,10a-dihydro-10*H*-phenothiazin-10-yl)-*N*, *N*-Dimethylpropan-1-amine

Structure:



Physical Properties: It is white or creamy-white crystalline powder. It is odourless. It is soluble in ethanol, methanol and water.

Stability and Storage: It is stored in tightly close container.

Uses:

- It is used in psychotic disorder
- It is used to treat Schizophrenia
- It is use to control nausea and vomiting
- It is used to treat anxiety before surgery

Official Preparations:

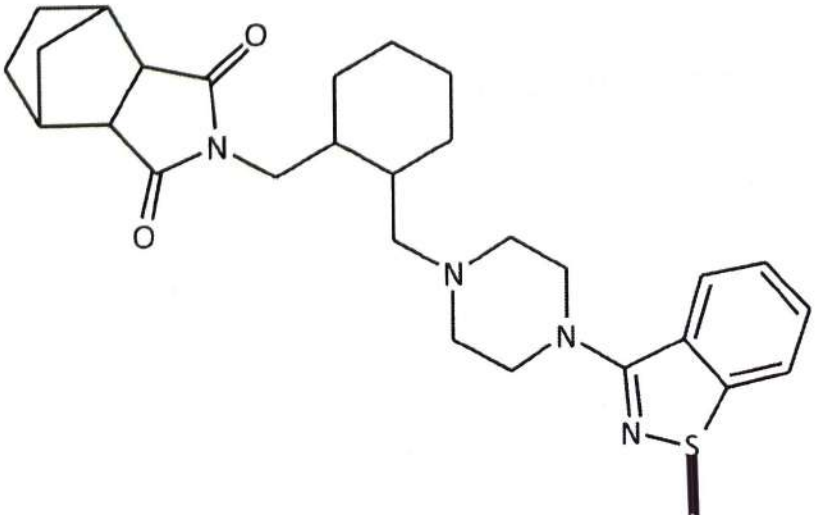
- Chlorpromazine Hydrochloride injection
- Chlorpromazine Hydrochloride Tablet
- Chlorpromazine Injection
- Chlorpromazine Tablet

Brand Name: Clozine Plus, Cain, Chlorectil plus, Chlorpromazine Tab

LURASIDONE

Molecular Formula: $C_{28}H_{36}N_4O_2S$

Molar Mass: 492.68



Chemical Name: 4-[[(1*R*,2*R*)-2-[[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]methyl] cyclohexyl]methyl]-4-azatricyclo[5.2.1.$0^{2,6}$]decane-3,5-dione

Physical Properties: White colour compound, MP more than 250°C

Stability and storage: Store in well closed container

Uses:

- It is used to treat schizophrenia and bipolar disorder
- It is use as antipsychotics

Official Preparation: Lurasidone tablet

Brand Name: Latuda, Luramax

ANTICONVULSANTS OR ANTIEPILEPTICS

Epilepsy: It is defined as paroxysmal (sudden), self-sustaining and self-limiting cerebral dysrhythmia.

It is characterized by an abnormal and excessive neuronal discharge and by disturbance of consciousness. It is proposed that seizures were caused by sudden, occasional, rapid, excessive, local electrical (nervous) discharges which originate in grey matter & spread to other parts of CNS. Epilepsy may or may not be associated with body movements or hyperactivity of ANS.

Convulsive states have been observed in systems where concentration of GABA (Gamma Amino Butyric Acid) in brain is below certain level or the effect of GABA is blocked.

Classifications

- **Hydantoin,** e.g., Phenytoin
- **Barbiturates,** e.g., Phenobarbitone, mephobarbitone
- **Benzodiazepine,** e.g., Diazepam, nitrazepam
- **Carboxylic acid derivative,** e.g., Sodium valproate
- **Succinimides,** e.g., Phensuccimide, ethosuccimide
- **Oxazolidine Dione derivative,** e.g., Paramethadione
- **Sulphonamides,** e.g., Acetazolamide.

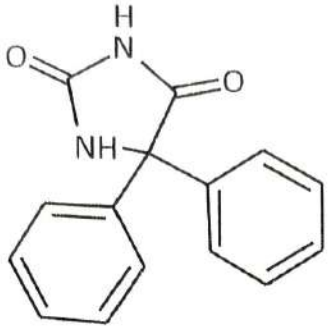
PHENYTOIN

Molecular Formula: $C_{15}H_{12}N_2O_2$

Molar Mass: 252.27

Chemical Name: 5,5-diphenylimidazolidine-2,4-dione

Structure:



Physical Properties: It is white crystalline powder and odourless. It is very slightly soluble in water and slightly hygroscopic in nature.

Stability and Storage: It should be stored in a tightly closed container.

Uses:

- It is used as antiepileptic
- It is use as antiarrhythmic agent
- It is used to treat migraine
- It is used to treat trigeminal neuralgia
- It is use to control status epilepticus

Official Preparations:

- Phenytoin tablets
- Phenytoin capsules
- Phenytoin injections
- Phenytoin oral suspension
- Phenytoin and phenobarbitone tablet

Brand name: Garoin, Eptoin, Fentoin ER, Dilantin.

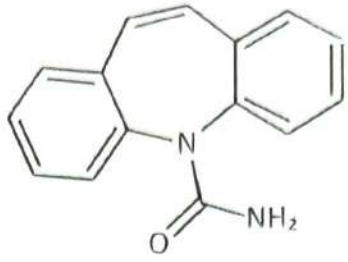
CARBAMAZEPINE

Molecular Formula: $C_{15}H_{12}N_2O$

Molar Mass: 236.27

Chemical Name: benzo[b][1] benzazepine-11-carboxamide

Structure:



Physical Properties:

- It is a white or yellowish-white crystalline powder.
- It is odourless and test less or slightly bitter in test.
- It is freely soluble in dichloromethane, sparingly soluble in ethanol and acetone, practically in soluble in water.

Stability and Storage: It is protected from moisture hence store in well close containers.

Uses:

- It is use as an anticonvulsant in complex partial seizures and clonic-tonic seizures, simple partial seizures.
- It is used to treat seizure and neuropathic pain.
- It is use treat alcohol Withdrawal symptoms.
- It is used to treat insipidus.

Official Preparations:

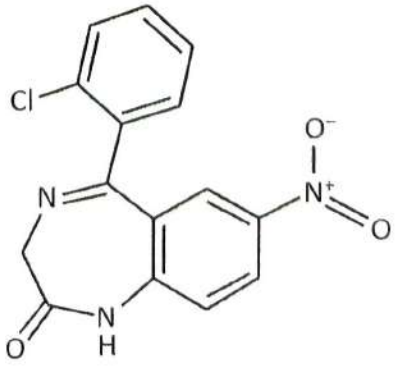
- Carbamazapine Extended-release Tablet
- Carbamazepine Tablets

Brand Name: Carbawell-200, Carbetol, Biotol-200

CLONAZEPAM

Molecular Formula: $C_{15}H_{10}ClN_3O_3$

Molar Mass: 315.7



Chemical Name: 5-(2-chlorophenyl)-7-nitro-1,3-dihydro-1,4-benzodiazepin-2-one

Physical Properties:

- It is slightly yellowish crystalline powder.
- It is practically insoluble in water, slightly soluble in ethanol and methanol.

Stability and Storage: It is affected from light hence, it is store on well close and light resistant.

Uses:

- It is use as anticonvulsant and antiepileptic drug.
- It is use to control seizures
- It is used to treat panic disorder, anxiety

Official Preparations:

- Clonazepam Injection
- Clonazepam Tablet

Brand Name: Klonopin, Klonopinwafer, Clorest-0.25, Clonax-0.25

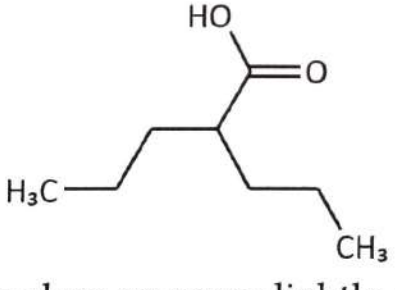
VALPROIC ACID

Molecular Formula: $C_8H_{16}O_2$

Molar Mass: 144.2

Chemical Name: 2-propylpentanoic acid

Structure:



Physical Properties: It is a colourless or very slightly yellow liquid and it is slightly viscous. It is soluble in organic solvent, slightly soluble in water.

Stability and Storage: It is store in well close container because affect from moisture.

Uses:

- It is as broad spectrum anticonvulsant
- It is primarily use as first-line treatment for tonic-clonic seizures, absence seizures and myoclonic seizures
- It is used to treat Mental illness, Bipolar disorder, schizophrenia, Migraines

Official Preparation:

- Valproic Acid Capsules
- Valproic Acid Oral Solution

Brand Name: Valric CR-500, Vallana CR-300, Vepcot-CR

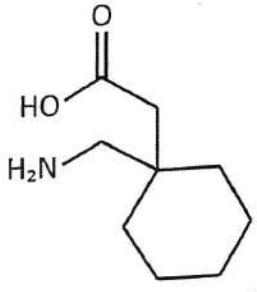
GABAPENTIN

Molecular Formula: $C_9H_{17}NO_2$

Molar Mass: 171.24

Chemical Name: 2-[1-(aminomethyl)cyclohexyl] acetic acid

Structure:



Physical Properties: It is white to off white crystalline powder. It is freely soluble in water and in alkaline and acidic solution

Stability Storage: It is store in well close container

Uses:

- It is used to treat seizures and neuropathic pain
- It is used to treat anxiety and bipolar disorder
- It is used to treat drug dependence

Official Preparations:

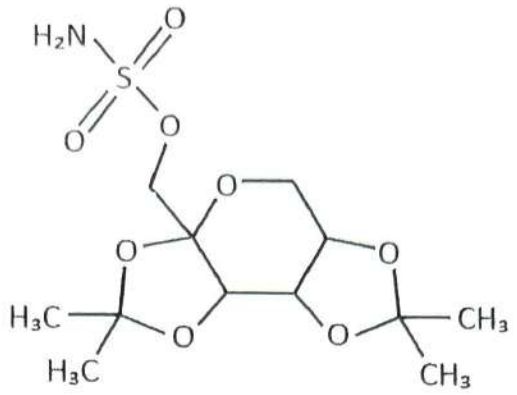
- Gabapentin Tablet USP
- Gabapentin Capsule USP

Brand Name: Gabatop-800, Gabapin-300, Gabatil

TOPIRAMATE

Molecular Formula: $C_{12}H_{21}NO_8S$

Molar Mass: 339.4



IUPAC Name: 4,4,11,11-tetramethyl-3,5,7,10,12-pentaoxatricyclo[7.3.0.0^{2,6}]dodecan-6-yl]methyl sulfamate

Physical Properties: It is white or off-white crystalline powder; it is soluble in most alkaline solution containing sodium hydroxide and sodium phosphate and freely soluble in acetone.

Stability and Storage: It is stored in tightly close and light resistant container, at a temperature not exceeding 30°.

Uses:

- It is used to treat epilepsy
- It is use to treat Anti-convulsant
- It is used to treat in chronic low back pain, bipolar disorder

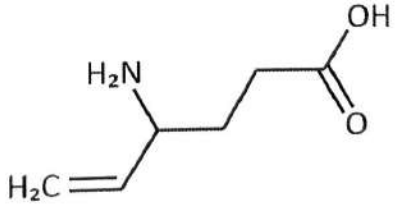
Official Preparation: Topiramate Tablets

Brand Name: Nextop 50, Toper-100, Tormap-25, Topiramate

VIGABATRIN

Molecular Formula: $C_6H_{11}NO_2$

Molar Mass: 129.15



4-aminohex-5-enoic acid

Physical Properties: It is white to off-white powder, it is freely soluble in water and in aqueous solvent, slightly soluble in menthol, very slightly soluble in methanol and ethanol.

Stability and Storage: It is store in tightly close container.

Uses: It is used to treat epilepsy, seizures

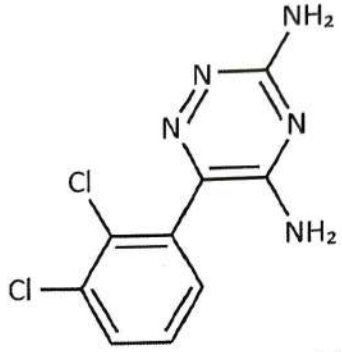
Official Preparation: Vigabatrin tablet

Brand Name: Sabril, Vrgarin.

LAMOTRIGINE

Molecular Formula: $C_9H_7Cl_2N_5$

Molar Mass: 256.09



IUPAC Name: 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine

Physical Properties: It is a white crystalline powder, it is very slightly soluble in water and slightly soluble in 0.1 M

Stability and Storage: Store in well close container

Uses:

- It is use treat Epilepsy, Bipolar disorder, Schizophrenia
- It is used to treat neuropathic pain
- It is used to treat headaches

Official Preparation: Lamotrigine Tablet USP

Brand Name: Lamictal, Lametec-25 DT

ANTI-DEPRESSANT

Depression is characterized by feelings of intense sadness or worry, insomnia, anorexia, loss of enthusiasm, physical changes and mental slowing.

The noradrenergic system appears to be associated with increased drive, whereas the serotonergic system relates more to changes in mood.

Clinical depression is the result of a deficiency in both 5-HT and NE.

Antidepressant drugs are used to restore mentally depressed patients to an improved mental status.

Classification of Antidepressants

I. **Tricyclic Antidepressants (TCAs)**

(a) Norepinephrine and Serotonin Reuptake Inhibitors (NSRIs), e.g., Imipramine, Clomipramine, Trimipramine, Amitriptyline.

(b) Selective Norepinephrine Reuptake Inhibitors (SNRIs), e.g., Desipramine, Nortriptyline, Amoxapine.

II. **Nontricyclic Norepinephrine and Serotonin Reuptake Inhibitors (NSRIs)**, e.g., Venlafaxine, Duloxetine, Milnacipran.

III. **Dopamine, Norepinephrine and Serotonin Reuptake Inhibitors,** e.g., Bupropion.

IV. **Selective Serotonin Reuptake Inhibitors (SSRIs),** e.g., Fluoxetine, Paroxetine, Citalopram, Sertraline, Fluvoxamine.

V. **Monoamine Oxidase (MAO) Inhibitors:**

(a) Nonselective MAO inhibitors, e.g., Iproniazid, Phenelzine, Tranylcypromine

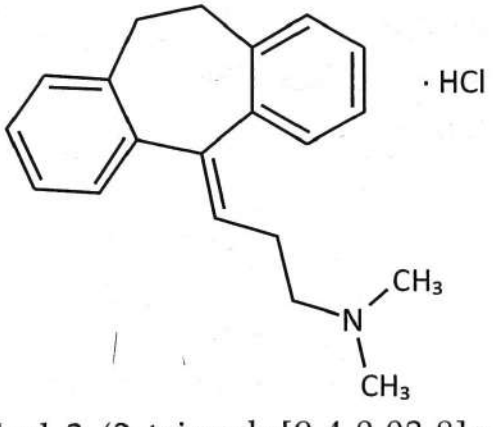
(b) Reversible selective MAO-A inhibitors, e.g., Moclobemide.

AMITRIPTYLINE HYDROCHLORIDE

It is a tricyclic antidepressant primarily used to treat major depressive disorder.

Formula: $C_{20}H_{24}ClN$

Molar Mass: 313.9



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

Properties: Solid, Minute crystals, Freely soluble in water, chloroform, alcohol; insoluble in ether, MP: 196-197°C

Storage: It is stored in well close container, protected from moisture

Uses:

- Amitriptyline is indicated for the treatment of major depressive disorder and neuropathic pain and for the prevention of migraine and chronic tension headache.
- It may help improve mood and feelings of well-being, relieve anxiety and tension, help you sleep better and increase your energy level.

Official Preparation: Amitriptyline Tablet.

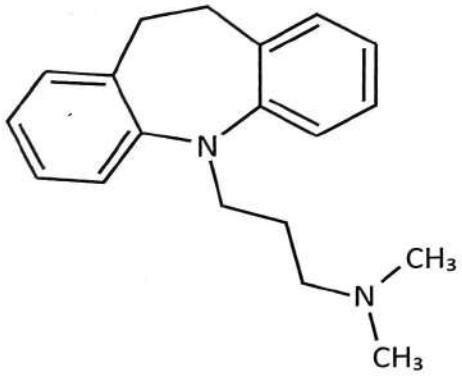
Brand Name: Amitone, Amimax, Amline, Goldep SR.

IMIPRAMINE HYDROCHLORIDE

It is tricyclic antidepressant. It has been used in major depression and panic disorders. It has less sedative effect than some other members of this therapeutic group.

Formula: $C_{19}H_{25}ClN_2$

Molar Mass: 316.9



IUPAC Name: 3-(5,6-dihydrobenzo[b][1] benzazepin-11-yl)-N, N-dimethylpropan-1-amine; hydrochloride.

Properties: Imipramine is a white or slightly yellow, odourless or almost odourless, crystalline powder with a burning taste, 174.0°C

Storage: It is stored in well close container, protected from moisture

Uses:

- It is used to treat depression.
- It is also used with other therapies for the treatment of nighttime bed-wetting (enuresis) in children.
- It is also used to improve your mood, sleep, appetite and energy level and may help restore your interest in daily living

Official Preparation: Imipramine capsule, Imipramine injection, Imipramine tablet

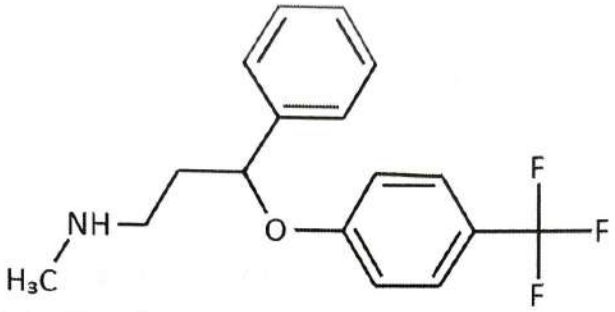
Brand Name: Estidep, Trydep Forte, Elidep -Forte, Antipres, Eldep, Talendep, Depik

FLUOXETINE

It is an antidepressant of the Selective Serotonin Reuptake Inhibitor (SSRI) class.

Formula: $C_{17}H_{18}F_3NO$

Molar Mass: 309.332



IUPAC Name: N-methyl-3-phenyl-3-[4-(trifluoromethyl) phenoxy] propan-1-amine.

Properties: White or white crystalline solids with a melting point of 158.4 to 158.9°C. Soluble in methanol or ethanol, MP 193-197°C.

Storage: It is stored in well close container, protected from light.

Uses: It is used to treat:

- Major depressive disorder
- Anxiety
- Obsessive–Compulsive Disorder (OCD)
- Bulimia nervosa
- Panic disorder
- Premenstrual dysphoric disorder
- It is also used for obesity and eating disorders.

Official Preparations:

- Fluoxetine Tablet
- Fluoxetine capsule
- Fluoxetine oral suspension

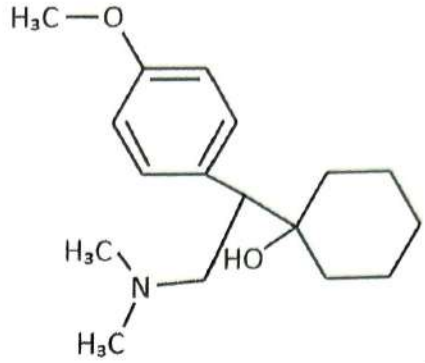
Brand Name: Fludep, Fultop, Exiten Plus, Ateez -F, Oleanz Fort, Oleanz Plus

VENLAFAXINE

It is an antidepressant medication of the Serotonin-Norepinephrine Reuptake Inhibitor (SNRI) class.

Formula: $C1_7H_{27}NO_2$

Molar Mass: 277.408



IUPAC Name: 1-[2-(dimethylamino)-1-(4-methoxyphenyl) ethyl] cyclohexan-1-ol

Properties: White to off-white crystalline solid, melting point 102-104°C

Storage: It is stored in well close container, protected from light

Uses:

- Venlafaxine is used primarily for the treatment of depression, general anxiety disorder, social phobia, panic disorder and vasomotor symptoms.
- Venlafaxine has been used off label for the treatment of diabetic neuropathy and migraine prevention.

Official Preparation:

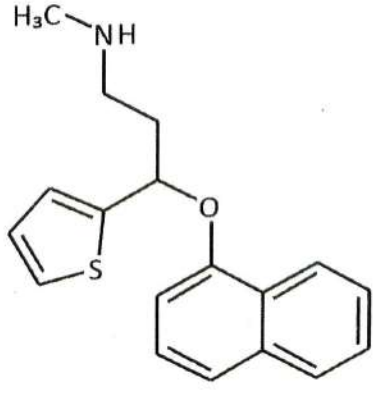
- Venlafaxine Tablet
- Venlafaxine capsule

Brand Name: Venfax - PR, VexorExr, Venset, VenishSR, Dalium, Envelaf, Venlor

DULOXETINE

Formula: $C_{18}H_{19}NOS$

Molar Mass: 297.42



IUPAC Name: (3*S*)-*N*-methyl-3-naphthalen-1-yloxy-3-thiophen-2-ylpropan-1-amine

Properties: White to slightly brownish white solid, slightly soluble in water, 118-122°C

Storage: It is stored in well close container

Uses: It is used to treat:

- Depressive disorder
- Generalized anxiety disorder
- Neuropathic pain
- Chronic musculoskeletal pain
- Fibromyalgia

Official Preparations:

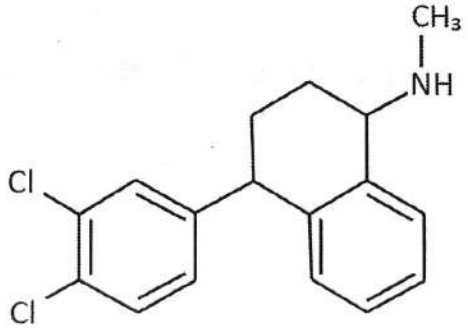
- Duloxetine Tablet
- Duloxetine Capsule

Brand Name: Dumore, Duloxit, Dulojoy, Sympta, Duloxee

SERTRALINE

Formula: $C_{17}H_{17}Cl_2N$

Molar Mass: 306.23



IUPAC Name: (1*S*,4*S*)-4-(3,4-dichlorophenyl)-*N*-methyl-1,2,3,4-tetrahydronaphthalen-1-amine

Properties: White crystalline powder, 245-246°C.

Storage: It is stored in well close container.

Uses: Sertraline is used to treat:

- Depressive disorder
- Obsessive–Compulsive Disorder (OCD)
- Posttraumatic Stress Disorder (PTSD)
- Premenstrual Dysphoric Disorder (PMDD)

- Panic Disorder
- Social Anxiety Disorder

Official Preparations:

- Duloxetine Tablet
- Duloxetine capsule

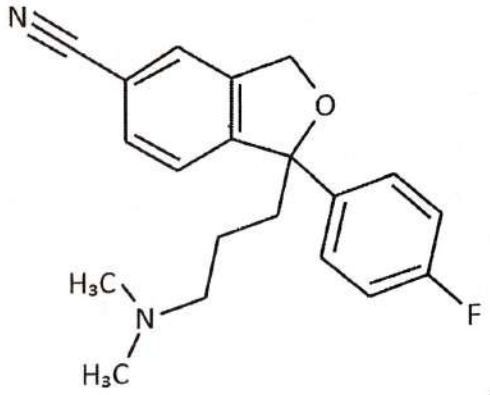
Brand Name: Serlin, Actiser 100, Serenata, Setalin, Inosert, Sertawin, Obzin

CITALOPRAM

Citalopram belongs to a class of antidepressant agents known as selective *serotonin-reuptake inhibitors* (SSRIs) and is widely used to treat the symptoms of depression.

Formula: $C_{20}H_{21}FN_2O$

Molar Mass: 324.399



IUPAC Name:1-[3-(dimethylamino) propyl]-1-(4-fluorophenyl)-3*H*-2-benzofuran-5-carbonitrile

Properties: White or almost white, crystalline powder. 182-188°C

Storage: It is stored in well close container

Uses: Citalopram may be used to treat major depressive disorder, panic disorder, anxiety and dysthymia, premenstrual dysphoric disorder, body dysmorphic disorder and obsessive–compulsive disorder.

Official Preparation: Citalopram tablet

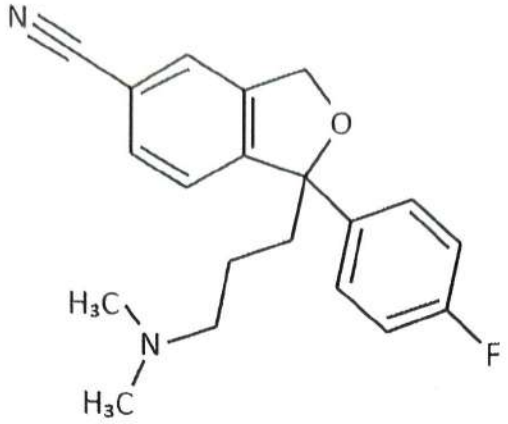
Brand Name: Citalomine, Citara, Citalop, Cipam, Ultidep, C -Pram

ESCITALOPRAM

It is an antidepressant of the Selective Serotonin Reuptake Inhibitor (SSRI) class.

Formula: $C_{20}H_{21}FN_2O$

Molar Mass: 324.399



IUPAC Name:(1*S*)-1-[3-(dimethylamino) propyl]-1-(4-fluorophenyl)-3*H*-2-benzofuran-5-carbonitrile

Storage: It is stored in well close container

Properties: Fine white to slightly yellow powder, freely soluble in methanol, DMSO; soluble in isotonic saline; sparingly soluble in water, ethanol, MP: 147-148°C.

Uses: It is used in treatment of major depressive disorder in adolescents and adults and generalized anxiety disorder in adults, General Anxiety Disorder (GAD), social anxiety disorder (SAD), Obsessive-Compulsive Disorder (OCD) and panic disorder

Official Preparation: Escitalopram tablet.

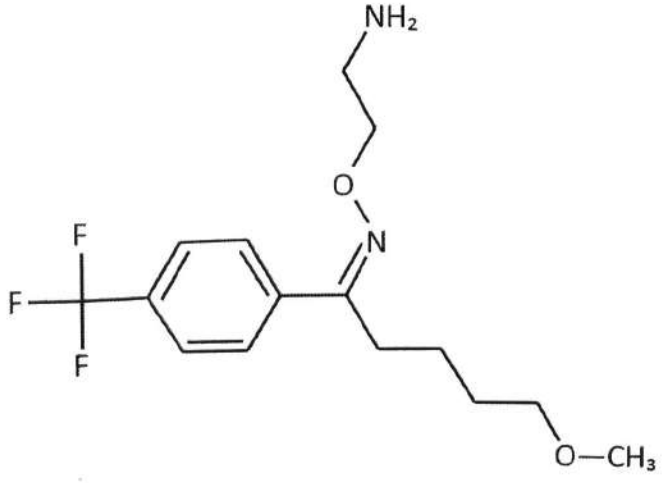
Brand Name: Etizola Plus, Exiety, ETILIVE-ES, Firsito, Escigold

FLUVOXAMINE

A Selective Serotonin Reuptake Inhibitor (SSRI) used as an anti-depressant.

Formula: $C_{15}H_{21}F_3N_2O_2$

Molar Mass: 318.335



IUPAC Name: 2-[(*E*)-[5-methoxy-1-[4-(trifluoromethyl)phenyl] pentylidene] amino] oxyethanamine

Properties: mp 120-121.5°C

Uses: It is used to treat:

- Major depressive disorder and
- Obsessive–Compulsive Disorder (OCD),
- Anxiety disorders such as panic disorder, social anxiety disorder and post-traumatic stress disorder.

Official Preparation: Fluvoxamine tablets

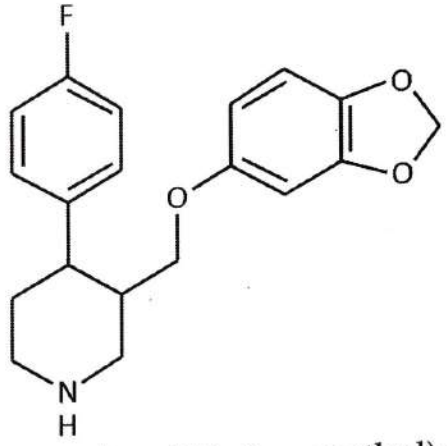
Brand Name: Boxamine, Flumin, Fluoxa, Fluvator, Fluvoxin

PAROXETINE

It is an antidepressant of the Selective Serotonin Reuptake Inhibitor (SSRI) class.

Formula: $C_{19}H_{20}FNO_3$

Molar Mass: 329.371



IUPAC Name: (3*S*,4*R*)-3-(1,3-benzodioxol-5-yloxymethyl)-4-(4-fluorophenyl) piperidine

Properties: Odourless, off-white powder, MP 147-150°C

Uses: It's often used to treat:

- Depression
- Obsessive Compulsive Disorder (OCD)
- Panic attacks
- Anxiety or Post-Traumatic Stress Disorder (PTSD)

Official Preparation: Paroxetine Tablet

Brand Name: Xepar, PARONEX CR, Oxitine PR, Panex, Pari, Raxit

EXERCISE

Short Answer Type Questions

1. **Give two brand names of following drugs:**
   (a) Amitriptyline Hydrochloride
   (b) Imipramine Hydrochloride
   (c) Fluoxetine
   (d) Venlafaxine
   (e) Duloxetine
2. **In what dosage form the following drugs are given:**
   (a) Sertraline
   (b) Citalopram
   (c) Escitalopram
3. **Give uses of following drugs:**
   (a) Amitriptyline Hydrochloride
   (b) Imipramine Hydrochloride
   (c) Fluoxetine
4. **Write structure and give chemical name of following drugs:**
   (a) Amitriptyline Hydrochloride
   (b) Imipramine Hydrochloride
   (c) Fluoxetine
5. **Name the drug present in following brands:**
   (a) Duloxit
   (b) Serlin
   (c) Citalop
   (d) Escigold
   (e) Pari
6. **Define:**
   (a) Hypnotics
   (b) Sedatives
   (c) Antidepressant
   (d) Analgesics
   (e) Antipsychotics

Long Answer Type Questions

1. Classify Antidepressant Agents with examples.
2. Write structure, Give chemical name, properties and uses of Amitriptyline Hydrochloride
3. Write structure, Give chemical name, properties and uses of Imipramine Hydrochloride
4. Write structure, Give chemical name, properties and uses of Fluoxetine
5. Give properties and uses of Duloxetine and Sertraline
6. Give properties and uses of Citalopram and Escitalopram

Multiple Choice Questions (MCQ's)

1. _____ are the agent which produces unconsciousness and losses the all sensation of the body.

(a) General anesthetics (b) Antidepressant
(c) Analgesics (d) All of the above

2. Total stage of anesthesia are:

(a) I (b) II
(c) III (d) IV

3. This drug decomposed by atmospheric O_2

(a) Ketamine (b) Alprazolam
(c) Valproic Acid (d) Thiopental Sodium

4. The drug which depresses CNS and induce a sleep resembling to natural sleep-in normal dose called as:

(a) Hypnotics (b) Sedatives
(c) Antidepressant (d) Analgesics

5. The drug which produce effect and reduce excitement are called as:

(a) Hypnotics (b) Sedatives
(c) Antidepressant (d) Analgesics

6. The drugs which are used to treat psychiatric disorders are called as:

(a) Antipsychotics (b) Sedatives
(c) Antidepressant (d) Analgesics

7. Phenytoin is used in treatment of:

(a) Hypnosis (b) Sedation
(c) Epilepsy (d) All of the above

8. Imipramine Hydrochloride is used in treat:

(a) Hypnosis
(b) Sedation
(c) Epilepsy
(d) Depression

9. Which of the following drug used to treat anxiety?

(a) Venlafaxine
(b) Ketamine
(c) Alprazolam
(d) Valproic Acid

10. The basic structure present in diazepam is:

(a) Pyridine
(b) Benzodiazepine
(c) Furan
(d) Acridine

ANSWERS OF MULTIPLE CHOICE QUESTIONS (MCQ'S)

1. (a)	2. (d)	3. (d)	4. (a)	5. (b)	6. (a)	7. (c)
8. (d)	9. (c)	10. (b)				

CHAPTER 6

Drugs Acting on Autonomic Nervous System

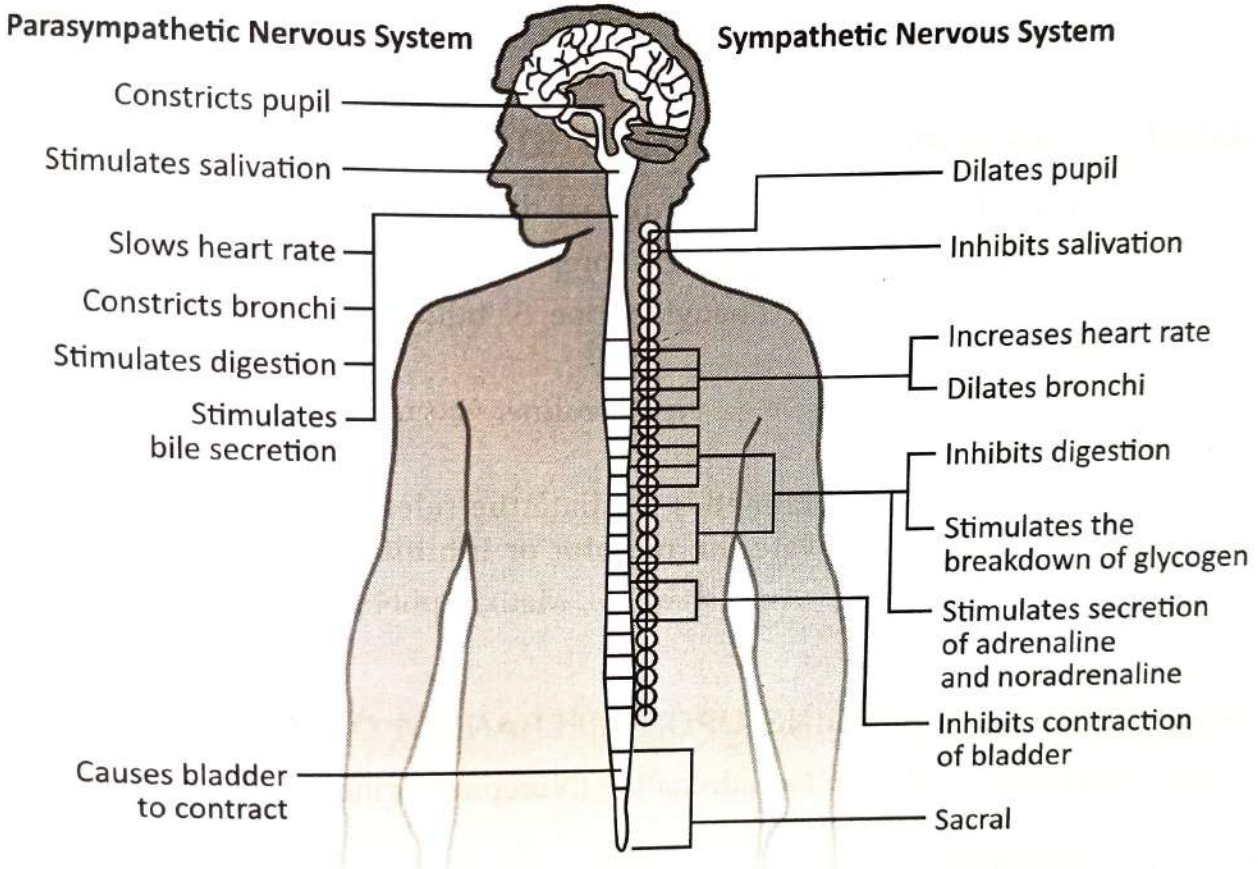


Fig. 6.1: ***Effects on Autonomic Nervous System***

The Autonomic Nervous System (ANS), is a branch of the peripheral neural system that controls the operation of internal organs by supplying smooth muscle and glands. The ANS is a control system that governs body activities such as heart rate, metabolism, breathing rate, pupil response, urine and sexual attraction in a mostly unconscious manner. The fundamental control mechanism for the fight-or-flight response is this system.

Integrated reflexes from the brain to the spine and organs regulate the ANS. Control of breathing, cardiac modulation (the cardiac control centre), vasomotor function (the vasomotor centre) and reflex behaviours like cough, sneezing, swallowing and vomit are all autonomic activities.

The Sympathetic Nervous System and the Parasympathetic Nervous System are two major branches of the ANS. The sympathetic nervous system is frequently referred to as the "fight or flight" system, whereas the parasympathetic nervous system is referred as the "rest and digest" or "feed and breed" system. Both of these systems have "opposite" functions in many circumstances, where one triggers and the other suppresses a physiological response.

The sympathetic nervous system is a "rapid response activating system", while the parasympathetic nervous system is a "more slowly activated relaxing system".

CLASSIFICATION DEPENDING UPON ACTION

1. **Direct Acting Sympathomimetics (Interact directly with adrenergic receptors):**
   (a) Catecholamines, e.g., Epinephrine, Norepinephrine, Isoproterenol.
   (b) Phenylethanolamines, e.g., Phenylephrine, Salbutamol or Albuterol, Terbutaline, Metaproterenol.
   (c) Imidazoline derivatives, e.g., Nephazoline, Oxymetazoline, Xylometazoline, Clonidine.
2. **Indirect Acting Sympathomimetics (Initiate the release of NE from adrenergic nerve terminal which activate the receptor or inhibit its uptake mechanism):**
   (a) Phenylethylamine, e.g., Amphetamine, Methamphetamine

CLASSIFICATION DEPENDING UPON MECHANISM OF ACTION

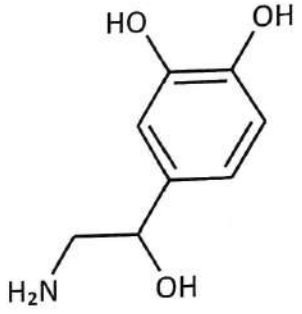
1. **Vasoconstrictors (↑ B. P.):** Noradrenaline (Norepinephrine), Dopamine, Ephedrine etc.
2. **Cardiac stimulants:** Dopamine, Adrenaline, Isoprenaline
3. **CNS stimulants:** Amphetamine
4. **Smooth muscle relaxants:** Adrenaline, Isoprenaline, salbutamol etc.

5. **Drugs used in allergic reactions:** Ephedrine
6. **Local vasoconstrictor/nasal decongestants:** Phenylephrine, pseudoephedrine
7. **Anorectics:** Amphetamine, Phentermine.

DIRECT ACTING SYMPATHOMIMETIC AGENTS

NOR-EPINEPHRINE

Synonym: Noradrenaline (NA)
Mol. Formula: $C_8H_{11}NO_3$
Molar Mass: 169.18
Structure:



IUPAC Name: (R)-4-(2-amino-1-hydroxyethyl) benzene-1,2-diol
Physical Properties:

- It is white crystalline powder or granules; it is odourless and slightly bitter in test.
- It is very slightly soluble in water and in soluble in alcohol.

Stability and Storage: It is oxidized with air hence store in tightly close and light resistant container.
Uses:

- It is used treat heart block
- It is control superficial hemorrhage of nose and throat
- It is use with local anesthetics to prolong local anesthetic effect
- It is use in peripheral vasomotor collapse
- It is use to maintain blood pressure in acute hypotensive statues

Official Preparations:

- Nor-adrenaline injection
- Sterile strong nor-adrenaline solution

Brand Name: Zoloft, Levophed

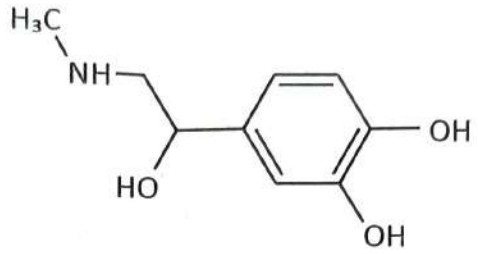
EPINEPHRINE

Synonym: Adrenaline

Mol. Formula: $C_9H_{13}NO_3$

Molar Mass: 183.20

Structure:



IUPAC Name: (R)-4-(1-Hydroxy-2-(methylamino) ethyl) benzene-1,2-diol

Physical Properties: It is white or creamy white microcrystalline powder or granules; it is odourless and slightly bitter in taste. It is insoluble in alcohol and slightly soluble in Water. it is readily soluble in Mineral acids and alkali hydroxides.

Stability and Storage: It is affected from light and air hence store these compounds in tightly close and light-resistant container.

Uses:

- It is use to control superficial hemorrhage of nose and throat.
- It is used to treat heart block.
- It is relieved bronchial spasm in acute asthma condition.
- It is use with local anesthetic for its prolong effect.
- It is used for emergency treatment of severe allergic reactions due to insect bites, medicines, foods or other substances.

Official Preparations:

- Adrenaline eye drop
- Adrenaline Solution
- Adrenaline tartrate injection
- Adrenaline and atropine spray

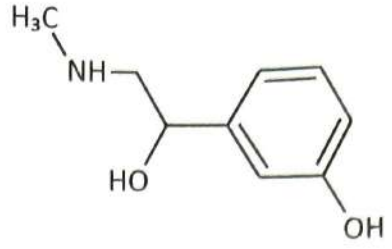
Brand Name: Epipen, Vasocon, Epinealth

PHENYLEPHRINE

Mol. Formula: $C_9H_{13}NO_2$

Molar Mass: 167.20

Structure:



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

Physical Properties: It is white crystalline powder. It is freely soluble in water and in alcohol, practically insoluble in chloroform.

Stability and Storage: It is affected from light hence it is store in light resistant and well-close container.

Uses:

- It is used to relieve nasal discomfort caused by colds and allergies.
- It is used to treat Hemorrhoid are caused by swollen veins in the rectal area.

Official Preparations: Phenylephrine tablet, phenylephrine injection.

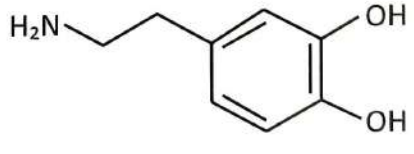
Brand Name: Pancold, Frenin, Sinera

DOPAMINE

Mol. Formula: $C_8H_{11}NO_2$

Molar Mass: 153.18

Structure:



IUPAC Name: 4-(2-Aminoethyl) benzene-1,2-diol

Physical Properties: It is white crystalline powder, freely soluble in water, methanol but practically insoluble in ether.

Stability and Storage: Store in well close container.

Uses: It is commonly use as stimulant drug in the treatment of severe low blood pressure, cardiac arrest.

Official Preparation: Dopamine injection USP

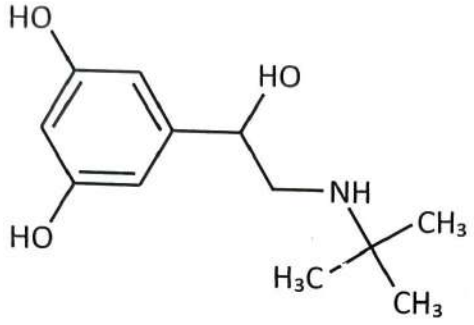
Brand Name: Dopadic, cardidop, Domin

TERBUTALINE

Mol. Formula: $C_{12}H_{19}NO_3$

Molar Mass: 225.28

Structure:



IUPAC Name: (RS)-5-[2-(tert-Butylamino)-1-hydroxyethyl] benzene-1,3-diol

Physical Properties: It is white or grayish white crystalline powder. It is odourless and bitter test. It is freely soluble in water.

Stability and Storage: It is affected from light and air hence store in light resistant and well close container.

Uses:

- It is used to prevent and treat wheezing, shortness of breath.
- It is used to treat chronic bronchitis and emphysema.
- It is used to treat asthma.
- It is used to treat nocturnal enuresis in children.
- It is used to treat nasal congestion, narcolepsy.

Official Preparations:

- Terbutaline tablet
- Terbutaline sulphate syrup.

Brand Name: Brethaire, Brethine, Bricanyl

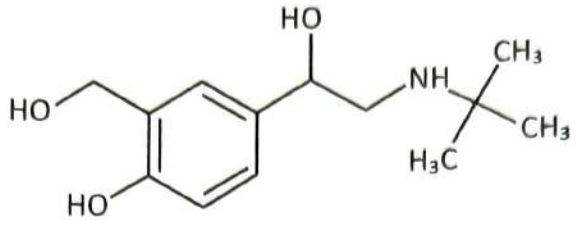
SALBUTAMOL

Synonym: Albuterol

Mol. Formula: $C_{13}H_{23}NO_7S$

Molar Mass: 337.39

Structure:



IUPAC Name: (RS)-4-[2-(tert-Butylamino)-1-hydroxyethyl]-2-(hydroxymethyl)phenol

Physical Properties: It is White crystalline powder. It is tasteless and odourless compound. It is soluble in water.

Stability and Storage: It is affected by light and hence it is stored in well closed and light resistant containers.

Uses:

- It is use to trat bronchial asthma and in chronic bronchitis.
- It is use in chronic obstructive pulmonary disease such as coughing and feeling breathless.
- It is use in emergency such as cardiotoxic shock, heart block and severe bradycardia.
- It is also use in prevention of premature labor.

Official Preparations:

- Salbutamol tablet
- Salbutamol injection
- Salbutamol aerosol inhalation

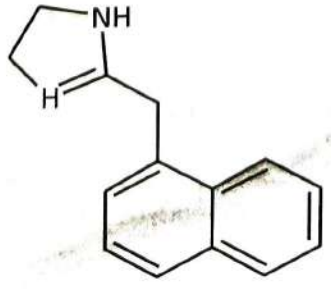
Brand Name: Croysal, Asthalin, Ventrolin, Brethol, foracort

NAPHAZOLINE

Mol. Formula: $C_{14}H_{15}ClN_2$

Molar Mass: 246.73

Structure:



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

Physical Properties: It is white crystalline powder and odourless. It is soluble in ethanol, very slightly soluble in chloroform and sparingly soluble in water. Practically insoluble in ether.

Stability and Storage: It is affected by light hence, it is store in well closed and light-resistant containers.

Uses:

- It is for vasoconstrictive effect as nasal and ophthalmic decongestants.
- It is indicated for use as OTC eyedrops for ocular vasoconstriction or as a nasal preparation for nasal congestion.
- It is use as relieve redness due to minor eye irritations.

Official Preparations:

- Naphazoline nitrate solution.
- Naphazoline nitrate drops.

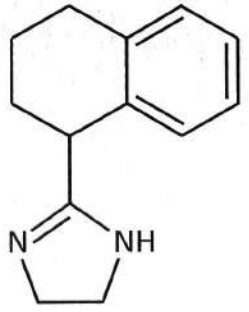
Brand Name: Opticool, Retozol, Visine-A, Naphcon.

TETRAHYDROZOLINE

Mol. Formula: $C_{13}H_{16}N_2$

Molar Mass: 200.28

Structure:



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

Physical Properties: It is a white crystalline powder. It is very soluble in water and ethanol, slightly soluble in chloroform and insoluble in diethyl ether.

Stability and Storage: It is store in well close container.

Uses:

- It is used as an ocular and nasal decongestant.

- It is also found in combination products with other lubricants and anti-irritants nasal spray.

Official Preparation: Tetrahydrozoline solution.

Brand Name: Tyzine, Visine, efemy

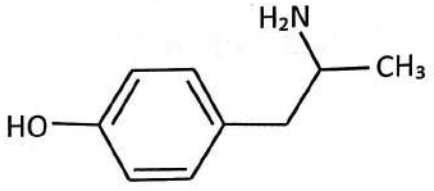
INDIRECT ACTING SYMPATHOMIMETIC AGENTS

HYDROXY AMPHETAMINE

Mol. Formula: $C_9H_{13}NO$

Molar Mass: 151.20

Structure:



IUPAC Name: 4-(2-aminopropyl)phenol

Physical Properties: It is white crystalline powder.

Stability and Storage: It is store in well close container.

Uses:

- It is use as eye drop is the diagnosis of Horner's syndrome
- It is indirect sympathomimetic agent which causes dilation of the eye pupil before diagnostic test.

Official Preparation: Hydroxy Amphetamine eye drops.

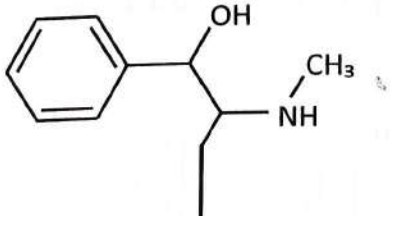
Brand Name: Paremyd, Adderall XR

PSEUDOEPHEDRINE

Mol. Formula: $C_{10}H_{15}NO$

Molar Mass: 201.71

Structure:



IUPAC Name: (S, S)-2-methylamino- 1-phenylpropan-1-ol

Physical Properties: It is hydrochloride salt. It is white crystalline powder which is odourless and bitter taste. It is freely soluble in water.

Stability and Storage: It is affected by light hence it is store in well close and light-resistant containers.

Uses:

- It is use as nasal decongestant
- It is use bronchodilator in bronchial asthma

Official Preparations:

- Pseudoephedrine syrup
- Pseudoephedrine elixir
- Pseudoephedrine and triprolidine tablets

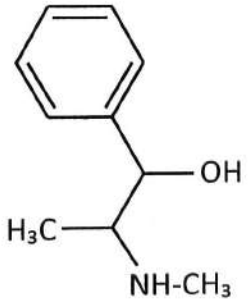
Brand Name: Actifed, Advil, Wel-phed, Solvin-OD

EPHEDRINE

Mol. Formula: $C_{10}H_{15}NO$

Molar Mass: 201.69

Structure:



IUPAC Name: (R, S)-2-(methylamino)-1-phenylpropan-1-ol

Physical Properties:

- It is a white crystalline powder.
- It is odourless or slight aromatic odour and has a bitter taste.
- It is sparingly soluble in water.

Stability and Storage: It is exposure to light hence it is store in well close and light-resistant containers.

Uses:

- It is used to treat Asthma.

- It is used to treat Nasal congestion, Narcolepsy.
- It is use as Nocturnal enuresis in children.

Official Preparations:

- Ephedrine Tablet
- Ephedrine elixir
- Ephedrine nasal drops
- Pediatric belladonna and Ephedrine mixture

Brand Name: Asthamcure, Cofsedyl, Endrine, Ephedrex

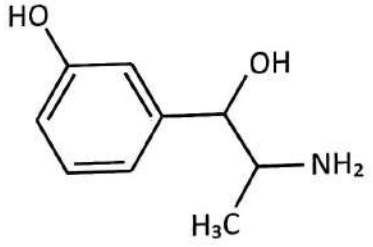
*Ephedrine and pseudoephedrine are diastereomers with little difference in their configuration

METARAMINOL

Mol. Formula: $C_9H_{13}NO_2$

Molar Mass: 167.20

Structure:



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

Physical Properties: It is white crystalline powder.

Stability and Storage: It is store in well-close containers.

Uses:

- It is used to treat severe hypotension brought on by other traumas that induce shock.
- It is used parenterally as a vasopressor in the treatment and prevention of the acute hypotensive state occurring with spinal anesthesia.

Official Preparation: Metaraminol Injection B.P.

Brand Name: Aramine

ADRENERGIC ANTAGONISTS

A. ALPHA ADRENERGIC BLOCKERS

TOLAZOLINE

Mol. Formula: $C_{10}H_{12}N_2$

Molar Mass: 160.22

Structure:

IUPAC Name: 2-Benzyl-4,5-dihydro-1H-imidazole

Physical Properties:

- Its hydrochloride salt which is in white crystalline powder.
- It is odourless and has a bitter taste.
- It is very soluble in water and freely soluble in alcohol.

Stability and Storage: It is affected by light and hence it is stored in tightly closed and light-resistant containers.

Uses:

- It is used to treat peripheral vascular disorders.
- It stimulates gastric secretion.

Official Preparations:

- Tolazoline tablets
- Tolazoline injection

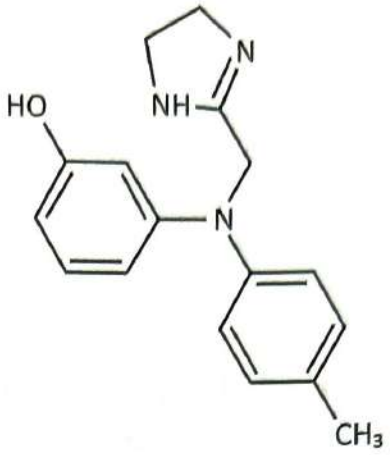
Brand Name: Priscol, Tolazine injection.

PHENTOLAMINE

Mol. Formula: $C_{17}H_{19}N_3O$

Molar Mass: 281.35

Structure:



IUPAC Name: 3-[N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-4-methylanilino] phenol

Physical Properties:

- It is white crystalline powder.
- It is freely soluble in water, ethanol and slightly soluble in chloroform.

Stability and Storage: It is affected from light and moisture hence it is store in tightly close and light-resistant containers.

Uses:

- It is use in combination with papaverine to treat impotence
- It is use for local infiltration to counteract vasoconstriction.
- It is use to prevent or control hypertensive episodes that occur in pheochromocytoma
- It is used to treat hypertensive crisis caused by sympathomimetic amines.
- It is use to prevention of dermal necrosis

Official Preparations:

- Phentolamine injection BP
- Phentolamine Tablet

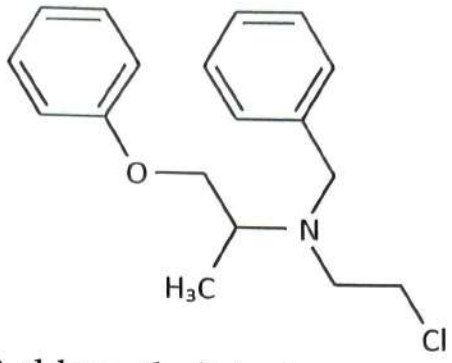
Brand Name: FEBTANOR, Phentolamine-Dibasin

PHENOXYBENZAMINE

Mol. Formula: $C_{18}H_{22}ClNO$

Molar Mass: 303.8

Structure:



IUPAC Name: N-benzyl-N-(2-chloroethyl)-1-phenoxypropan-2-amine

Physical Properties: It is white crystalline powder, odourless compound.

Stability and Storage: It is store in well close containers.

Uses:

- It is use in treatment of Raynaud's phenomenon
- It is use in chronic management of patients whose tumors are not amenable to surgery.
- It is controlling of rise in BP during clonidine withdrawal.
- It is used in PVDs.

Official Preparations: Phenoxybenzamine Capsules BP

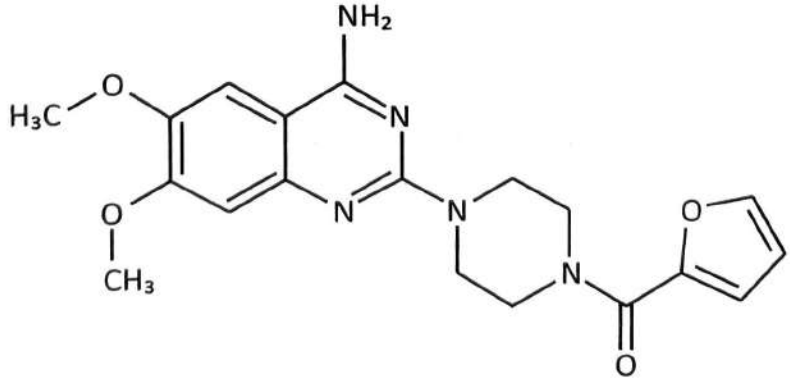
Brand Name: Fenoxene, Cpressin-P, Biophenox

PRAZOSIN

Mol. Formula: $C_{19}H_{22}ClN_5O_4$

Molar Mass: 419.9

Structure:



IUPAC Name: [4-(4-amino-6,7-dimethoxyquinazolin-2-yl) piperazin-1-yl] -(furan-2-yl) methanone.

Physical Properties: It is white colour powder. It is odourless and tasteless, it is soluble in methanol, ethanol and very slightly soluble in water, insoluble in chloroform and acetone.

Stability and Storage: It is protected from light hence. It is store in well-close and light-resistant containers.

Uses:

- Prazosin is used exclusively in the treatment of hypertension.
- Lowering high blood pressure helps prevent strokes, heart attacks and kidney problems.
- It works by relaxing and widening blood vessels so blood can flow easily.

Official Preparation: Prazosin hydrochloride tablet

Brand Name: Prazopress XL, Minipress XL, Prazopill XL

B. BETA ADRENERGIC BLOCKERS

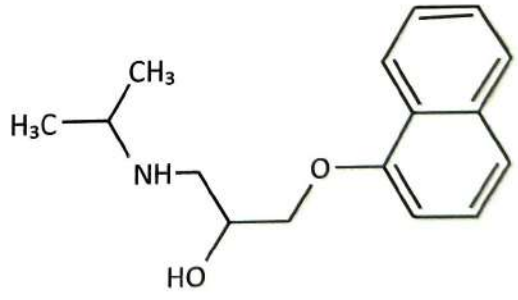
PROPRANOLOL

Mol. Formula: $C_{16}H_{22}ClNO_2$

Molar Mass: 295.80

IUPAC Name: 1-naphthalen-1-yloxy-3-(propan-2-ylamino) propan-2-ol

Structure:



Physical Properties:

- It is white crystalline powder.
- Its hydrochloride salt is odourless and bitter in test.
- It is slightly soluble in water.

Stability and Storage: It is store in well-close and light-resistant containers.

Uses:

- It is use in angina pectoris

- It is used to treat Arterial hypertension.
- It is use in Anxiety symptoms, Cardiac arrhythmia.
- It is used to prevent future heart disease, heart attacks and strokes.

Official Preparations:

- Propranolol tablet
- Propranolol injection

Brand Name: Dideral-40, Inderal, Cipar-LA-20

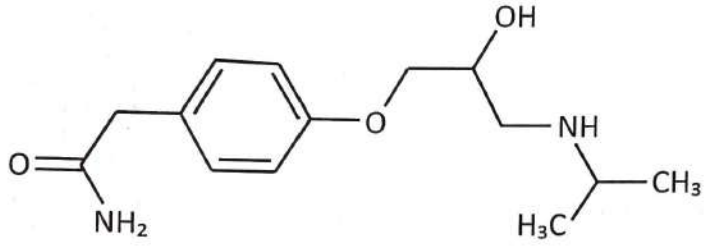
ATENOLOL

Mol. Formula: $C_{14}H_{22}N_2O_3$

Molar Mass: 2636.33

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

Structure:



Physical Properties:

- It is white crystalline powder, odourless and tasteless.
- It is practically in soluble in ether, soluble in ethanol and sparingly soluble in water

Stability and Storage: It is store in well-closed and light-resistant containers on room temperature

Uses:

- It is use in mild to moderate heart failure.
- It is use in combination with antihypertensives
- It is use in angina pectoris, atrial fibrillation.
- It is use in prophylaxis of headaches.
- It can also be used to prevent chest pain caused by angina.

Official Preparation: Atenolol Tablet

Brand Name: Altol, Tenormin, Tenolol, Aten, amlonova, Hipres-50, Azistal.

CARVEDILOL

Mol. Formula: $C_{24}H_{27}ClN_2O_4$

Molar Mass: 442.9

Physical Properties: It is white crystalline powder, odourless, slightly soluble in ethanol and in soluble in water.

Stability and Storage: It is affected by light, hence store in light-resistant and well-close container.

Uses:

- It is used to treat congestive heart failure.
- It is use in hypertension.

Official Preparation: Carvedilol Tablet

Brand Name: Carvil, Carvas, Cardivas.

CHLOLINERGIC DRUGS AND RELATED AGENTS

A. DIRECT ACTING AGENTS

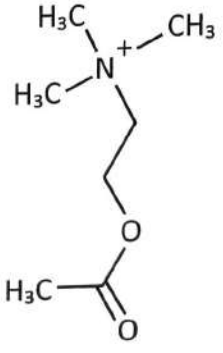
ACETYLCHOLINE

Mol. Formula: $C_7H_{16}ClNO_2$

Molar Mass: 181.66

IUPAC Name: 2-acetyloxyethyl(trimethyl)azanium

Structure:



Physical Properties: It is hygroscopic powder available in admixture with mannitol to dissolved in sterile water fir injection shortly before use.

Uses:

- It is use in cataract surgery.
- It is use in anterior segment surgery where rapid miosis.

Official Preparations:

- Acetylcholine Powder
- Acetylcholine Injection.

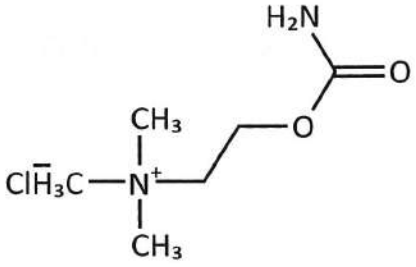
Brand Name: MioganPws, Choline brain food.

CARBACHOL

Mol. Formula: $C_6H_{15}ClN_2O_2$

Molar Mass: 182.65

Structure:



IUPAC Name: 2-carbamoyloxyethyl(trimethyl)azanium; chloride

Stability and Storage: It is stored under dry conditions.

Uses: It is use in ocular surgery

It is use to reduce intraocular pressure.

It is miotic and hence it is used to reduce the intraocular tension of glaucoma.

It is use after cataract surgery to reduce intraocular pressure.

Official Preparations:

- Carbachol Tablet
- Carbachol Injection
- Carbachol Liquid
- Carbachol Solution

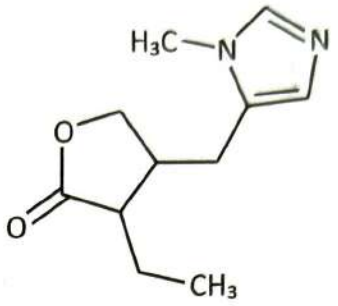
Brand Name: Miostat, Carbastat, Optichol.

PILOCARPINE

Mol. Formula: $C_{11}H_{16}N_2O_2$

Molar Mass: 208.261

Structure:



IUPAC Name: (3*S*,4*R*)-3-ethyl-4-[(3-methylimidazol-4-yl) methyl] oxolan-2-one

Physical Properties: It is hydrochloride salt and white crystalline powder. It is odourless and bitter in test and soluble or very soluble in water.

Stability and Storage: It is hygroscopic in nature and affected by light hence it is store in tightly close and light-resistant containers.

Uses:

- It is use to reduce intraocular pressure.
- It is miotic and hence, it is used to reduce the intraocular tension of glaucoma.
- It is use to counteract anticholinergic side effect.

Official Preparations:

- Pilocarpine hydrochloride tablet USP
- Pilocarpine hydrochloride eye drop
- Physostigmine and pilocarpine eye drop

Brand Name: Pilocarpine hydrochloride Tablet USP-5mg, Pilocar.

B. CHOLINESTERASE INHIBITORS

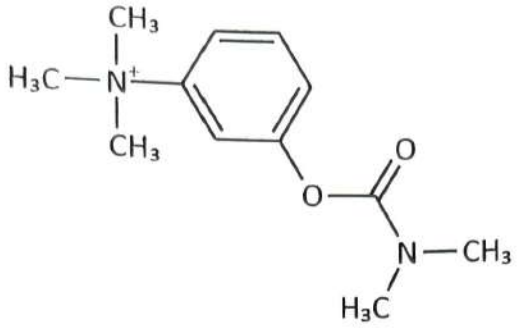
NEOSTIGMINE

Mol. Formula: $C_{12}H_{19}BrN_2O_2$

Molar Mass: 303.20

IUPAC Name: [3-(dimethylcarbamoyloxy)phenyl]-trimethylazanium

Structure:



Physical Properties: It is colourless or white crystalline powder which is odourless and bitter in test, very soluble in water.

Stability and Storage: It is affected by light and air hence, it is store in well-close and light-resistant containers

Uses:

- It is use to improve muscle strength in patients with a certain muscle disease.
- It is used to treat symptoms of myasthenia gravis.
- It is use for treat paralytic ileus
- It is use for postoperative urinary retention
- It is use to promote expulsion of intestinal flatus before radiography of kidney, uterus.

Official Preparations:

- Neostigmine tablet
- Neostigmine injection

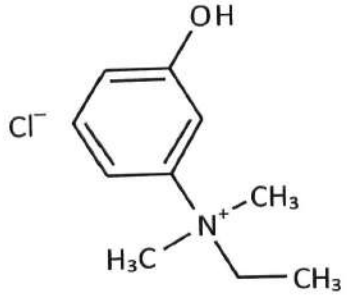
Brand Name: Flagstig, Prostigmine.

EDROPHONIUM CHLORIDE

Mol. Formula: $C_{10}H_{16}ClNO$

Molar Mass: 201.69

Structure:



IUPAC Name: Ethyl-(3-hydroxyphenyl)-dimethylazanium; chloride

Physical Properties: It is bitter in test and soluble in water and alcohol

Stability and Storage: Store at room temperature and control room temperature 15-30°C

Uses:

- It is used to treat respiratory depression, neuromuscular blockade
- It is use in medical test to help diagnose muscle disorder myasthenia gravis.

Official Preparations:

- Edrophonium chloride Liquid
- Edrophonium chloride Injection.

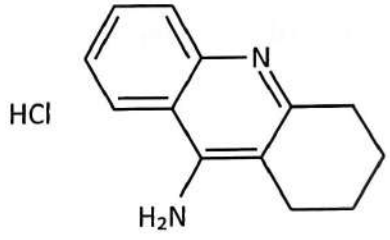
Brand Name: Enlon, Enlon-plus

TACRINE HYDROCHLORIDE

Mol. Formula: $C_{13}H_{15}ClN_2$

Molar Mass: 234.72

Structure:



IUPAC Name: 1,2,3,4-tetrahydroacridin-9-amine; hydrochloride

Physical Properties: It is tacrine hydrochloride is a white solid, it is freely soluble in distilled water, 0.1 N HCL, ethanol and methanol.

Stability and Storage: It is store in well-close container at room temperature.

Uses: It is used to treat the symptoms of mild to moderate Alzheimer disease.

Official Preparations:

- Tacrine hydrochloride capsule
- Tacrine hydrochloride tablet

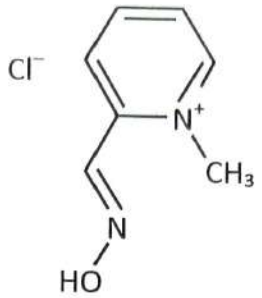
Brand Name: Cognex, THA

PRALIDOXIME CHLORIDE

Mol. Formula: $C_7H_9ClN_2O$

Molar Mass: 172.61

Structure:



IUPAC Name: (*NE*)-*N*-[(1-methylpyridin-1-ium-2-yl) methylidene] hydroxylamine; chloride

Physical Properties: It is white to pale yellow crystalline powder. It is odourless, soluble in water.

Stability and Storage: It is affected by moisture hence store in well-close containers.

Uses: It is a cholinesterase reactivator that reverses muscle weakness or paralysis caused by a poison or certain overdose used as an antidote to treat poisoning by a pesticide.

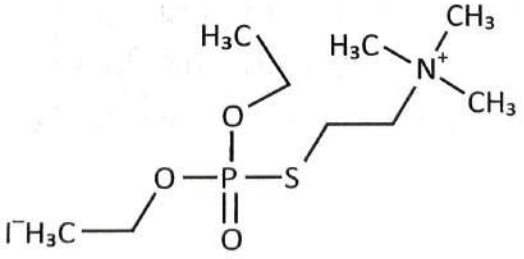
Official Preparation: Pralidoxime Chloride Injection

Brand Name: Neopam, Pam-A

ECHOTHIOPHATE IODIDE

Mol. Formula: $C_9H_{23}NO_3PS^+$

Molar Mass: 256.33



IUPAC Name: 2-diethoxyphosphorylsulfanylethyl(trimethyl)azanium; iodide

Stability and Storage: It is store in refrigeration after reconstitution.

Uses:

- It is use in glaucoma

- It is correct accommodative esotropia
- It is also use in chronic angle-closure glaucoma.

Official Preparations:

- Echothiopate Iodide solution
- Echothiopate Iodide powder for solution

Brand Name: Phospholine Iodide, Echothiophate.

CHOLINERGIC BLOCKING AGENTS

ATROPINE SULPHATE

Mol. Formula: $C_{34}H_{48}N_2O_{10}S$

Molar Mass: 676.8

Structure:

IUPAC Name: [(1*S*,5*R*)-8-methyl-8-azabicyclo [3.2.1] octan-3-yl] 3-hydroxy-2-phenylpropanoate; sulfuric acid

Physical Properties: It is white crystalline powder. It is odourless and has bitter in test .it is sparingly soluble in water.

Stability and Storage: It is affected by light hence store in well-close and light resistant container

Uses:

- It is used to treat parkinsonism
- It is use as C.N.S stimulants
- It is use as antispasmodic
- It is use as mydriatic in ophthalmological practice
- It is used to treat poisoning by organophosphorus compounds

Official Preparations:

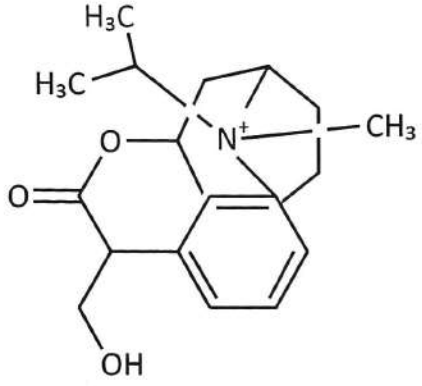
- Atropine eye drop.
- Atropine eye ointment.
- Atropine sulphate tablet
- Atropine sulphate injection

Brand Name: Atrowell, Atrotas, Tropine.

IPRATROPIUM BROMIDE

Mol. Formula: $C_{20}H_{30}BrNO_3$

Molar Mass: 412.4



IUPAC Name: [(1*R*,5*S*)-8-methyl-8-propan-2-yl-8-azoniabicyclo [3.2.1] octan-3-yl] 3-hydroxy-2-phenylpropanoate; bromide

Physical Properties: It is white crystalline powder. Freely soluble in methanol and soluble in water. Slightly soluble in ethanol.

Stability and Storage: It is affected by light and air hence store in well-close and light resistant container.

Uses:

- It is use in treat sialorrhea.
- It is use as bronchodilator for the maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease.
- It is use for symptomatic relief of rhinorrhea associated with the common cold.

Official Preparations:

- Ipratropium Bromide Spray
- Ipratropium Bromide Aerosol
- Ipratropium Bromide solution

and Name: Atrovent, Tiova, Ipravent.

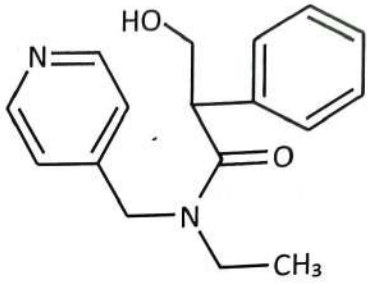
SYNTHETIC CHLOLINERGIC BLOCKING AGENT

TROPICAMIDE

Mol. Formula: $C_{17}H_{20}N_2O$

Molar Mass: 284.35

Structure:



IUPAC Name: *N*-ethyl-3-hydroxy-2-phenyl-*N*-(pyridin-4-ylmethyl) propanamide

Physical Properties: It is white crystalline powder and it is odourless. It is slightly soluble in water and freely soluble in chloroform.

Stability and Storage: It is store in Well-close container.

Uses: To induce mydriasis and cycloplegia for ophthalmoscopy.

Official Preparation: Tropicamide eye drops

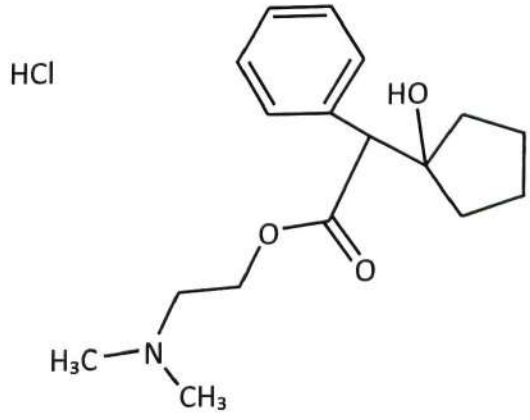
Brand Name: Tropicamate, Tromide, Tropac-P, Eytrop

CYCLOPENTOLATE HYDROCHLORIDE

Mol. Formula: $C_{17}H_{26}ClNO_3$

Molar Mass: 327.8

Structure:



IUPAC Name: 2-(dimethylamino) ethyl 2-(1-hydroxycyclopentyl)-2-phenylacetate; hydrochloride

Physical Properties: It is white crystalline powder. It is odourless and very soluble in water, easily soluble in alcohol.

Stability and Storage: Store in well-close containers.

Uses:

- It is use in management of iridocyclitis.
- It is use in management of keratitis and choroiditis.
- It can treat cycloplegic refraction.

Official Preparations:

- Cyclopentolate Hydrochloride solution
- Cyclopentolate Hydrochloride drops

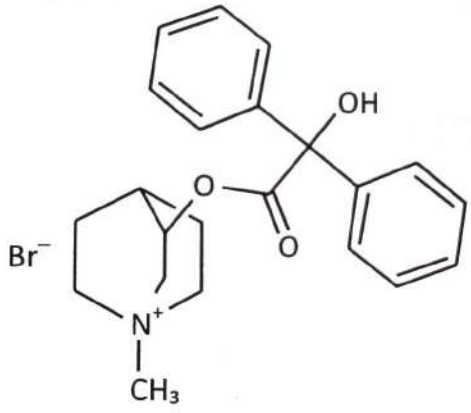
Brand Name: Cyclogyl, Cyclomid Ak-pentolate

CLIDINIUM BROMIDE

Mol. Formula: $C_{22}H_{26}BrNO_3$

Molar Mass: 432.3

Structure:



IUPAC Name:(1-methyl-1-azoniabicyclo [2.2.2] octan-3-yl) 2-hydroxy-2,2-diphenylacetate; bromide

Physical Properties: It is white crystalline powder and slightly soluble in water.

Stability and Storage: It is store in well-close container.

Uses:

- It is use for the treatment of peptic ulcer disease

- It is used in diverticulitis
- It is used to treat irritable bowel syndrome

Official Preparation: Clidinium Capsule

Brand Name: Cibis, Spasril, Arwin, Normaxin.

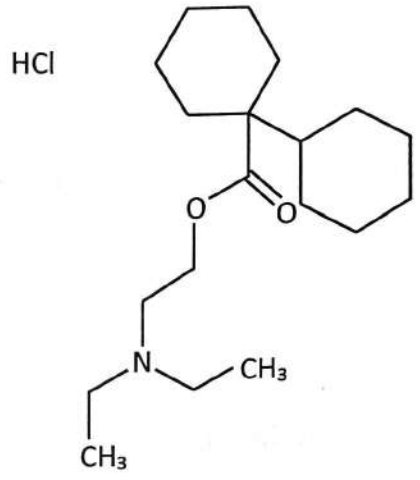
DICYCLOMINE HYDROCHLORIDE

Mol. Formula: $C_{19}H_{36}ClNO_2$

Molar Mass: 345.9

IUPAC Name: 2-(diethylamino) ethyl 1-cyclohexylcyclohexane-1-carboxylate; hydrochloride

Structure:



Physical Properties: It is white crystalline powder and it is odourless. It is freely soluble in ethanol, chloroform and soluble in water, insoluble in ether.

Stability and Storage: It is store in well-close container.

Uses:

- It is use as an anticholinergic for motion sickness.
- It is use in dysmenorrheal.

Official Preparations:

- Dicyclomine Tablet
- Dicyclomine Injection
- Dicyclomine oral solution

Brand Name: Bentyl, Colimex, Colirid.

EXERCISE

Short Answer Type Questions

1. **Give two brand names of following drugs:**
   (a) Phenoxybenzamine
   (b) Prazosin
   (c) Carbachol
   (d) Tropicamide
   (e) Phenylephrine
   (f) Propranolol
2. **In what dosage form the following drugs are given:**
   (a) Salbutamol
   (b) Dopamine
   (c) Atenolol
   (d) Atropine sulphate
   (e) Tropicamide
3. **Give uses of following drugs:**
   (a) Ephedrine
   (b) Naphazoline
   (c) Terbutaline
   (d) Propranolol
   (e) Ipratropium bromide
4. **Write structure and give IUPAC Name of following drugs:**
   (a) Nor-epinephrine
   (b) Dopamine
   (c) Naphazoline
   (d) Propranolol
   (e) Atenolol
   (f) Acetylcholine
   (g) Neostigmine
   (h) Atropine sulphate
5. **Name the drug present in following brands:**
   (a) Dopadic
   (b) Asthalin
   (c) Actifed
   (d) Asthamcure
   (e) Prazopress XL
   (f) Altol

Long Answer Type Questions

1. Classify Drugs Acting on Autonomic Nervous System with examples.
2. **Write structure, give IUPAC name, properties and uses of:**
   (a) Nor-Epinephrine
   (b) Dopamine
   (c) Naphazoline
   (d) Propranolol
   (e) Atenolol
   (f) Acetylcholine
   (g) Neostigmine
   (h) Atropine Sulphate

3. **Give properties and uses of:**
   (a) Carvedilol and Pilocarpine
   (b) Tropicamide and Cyclopentolate HCl
   (c) Tolazoline and Phentolamine
   (d) Terbutaline and Salbutamol

Multiple Choice Questions (MCQ's)

1. **Find out Direct acting Sympathomimetics from following:**
   (a) Terbutaline (b) Salbutamol
   (c) Epinephrine (d) All of the above
2. **Which of the following is Imidazoline derivatives:**
   (a) Naphazoline (b) Salbutamol
   (c) Epinephrine (d) All of the above
3. **Find out Alpha Adrenergic Blockers from following:**
   (a) Tolazoline (b) Phentolamine
   (c) Phenoxybenzamine (d) All of the above
4. **Find out Beta Adrenergic Blockers from following:**
   (a) Propranolol (b) Atenolol
   (c) Carvedilol (d) All of the above
5. **Find out Cholinesterase Inhibitors from following:**
   (a) Neostigmine (b) Edrophonium Chloride
   (c) Tacrine Hydrochloride (d) All of the above
6. **Find out Synthetic cholinergic Blocking Agents from following:**
   (a) Propranolol (b) Tropicamide
   (c) Atenolol (d) Tacrine Hydrochloride
7. **Atenolol is:**
   (a) Alpha Adrenergic Blockers (b) Beta Adrenergic Blockers
   (c) Agents with Mixed Mechanism (d) Direct Acting
8. **The drug used to treat bronchial asthma:**
   (a) Propranolol (b) Atenolol
   (c) Salbutamol (d) Prazosin
9. **The basic ring present in Naphazoline is:**

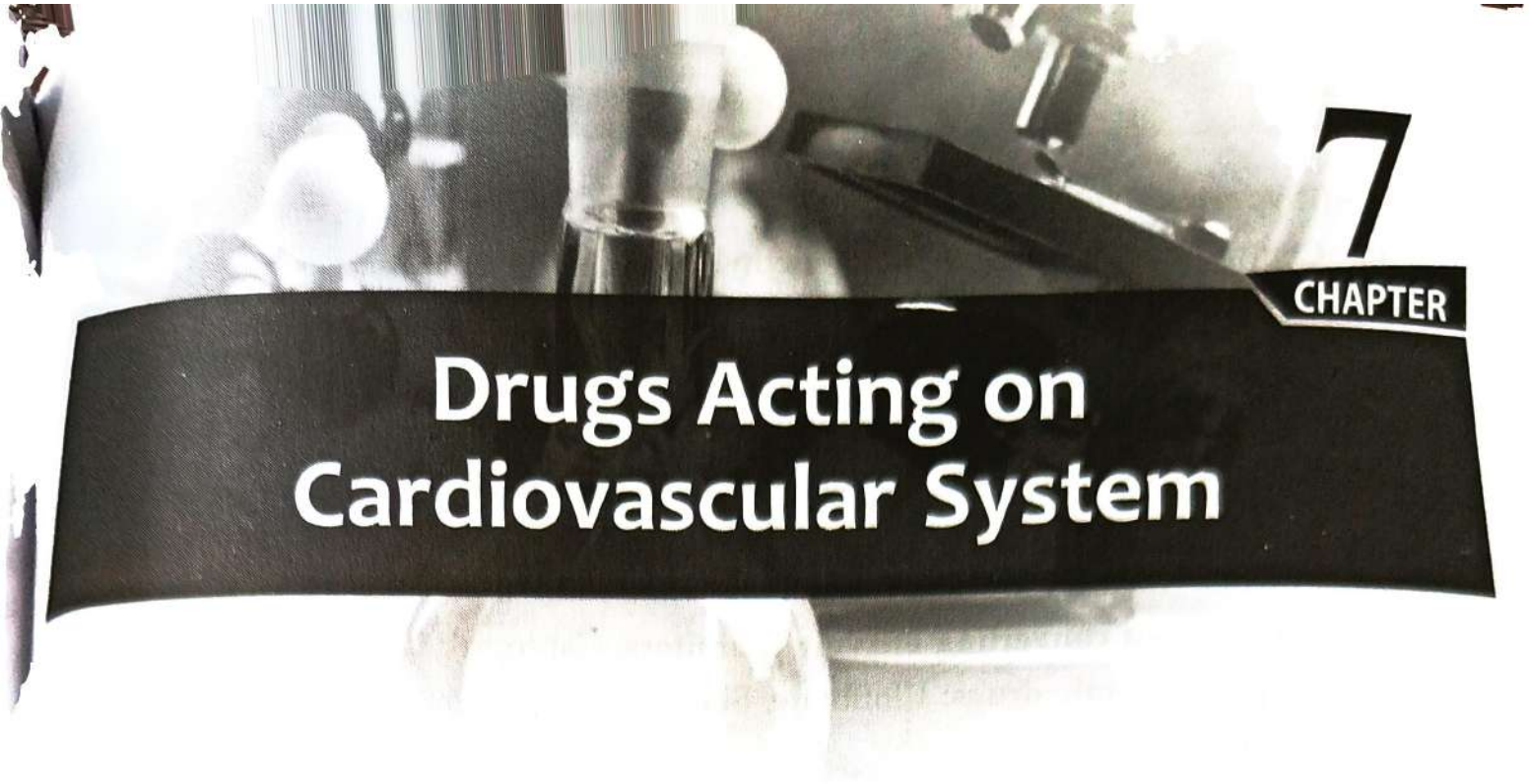
(a) Imidazole
(b) Pyrazole
(c) Pyridine
(d) quinoline

10. The basic ring present in prazosin is:

(a) Quinazoline
(b) Pyrazole
(c) Pyridine
(d) Furan

ANSWERS OF MULTIPLE CHOICE QUESTIONS (MCQ'S)

1. (d)	2. (a)	3. (d)	4. (d)	5. (d)	6. (b)	7. (b)
8. (c)	9. (a)	10. (a)				



CHAPTER 7

Drugs Acting on Cardiovascular System

Cardiovascular agents represent a group of drugs which have direct action on heart or other parts of vascular system so that they modify the total output to the heart or the distribution of blood to certain parts of circulatory system. These drugs are used in the treatment of various cardiac diseases like hypertension, angina pectoris, arrhythmia, CHF, myocardial infarction etc.

CLASSIFICATION

1. **Cardiotonic Drugs:** Cardiac glycosides obtained from Digitalis, strophanthus like Digoxin, Digitoxin, Gitoxin.
2. **Antiarrhythmic Agents:**
   (a) **Membrane stabilizing agent:** Quinidine, Procainamide, Disopyramide, Phenytoin
   (b) **Beta blockers:** Propranolol
   (c) **Drugs that prolong the duration of action potential:** Amiodarone
   (d) **Calcium channel blocker:** Verapamil, Amlodipine, Diltiazem
3. **Antianginal Agents:**
   (a) **Organic nitrates:** Amyl nitrate, Glyceryl trinitrate, Isosorbide dnitrate
   (b) **Calcium channel blocker:** Verapamil
   (c) **Beta blockers:** Propranolol

4. **Antihypertensive drugs:**
   (a) **Centrally acting drugs:** Alpha-methyl Dopa, Clonidine
   (b) **Ganglionic blockers:** Pentolinium, Mecamylamine
   (c) **Adrenergic neuron blockers:** Reserpine, Guanethidine
   (d) **Beta blockers:** Propranolol, Atenolol
   (e) **Alpha blockers:** Prazosin, Tolazoline
   (f) **Direct acting vasodilators:** Hydralazine, Minoxidil
   (g) **Calcium channel blocker:** Verapamil, Diltiazem, Nifedipine
   (h) **Angiotensin converting enzyme inhibitors:** Captopril, Enalapril, Lisinopril
5. **Antihyperlipidemic drugs:** Clofibrate, Simvastatin, Atorvastatin
6. **Anticoagulants:** Heparin
7. **Antiplatelet agents:** Aspirin
8. **Diuretics:** Frusemide, Thiazides

ANTIARRHYTHMIC DRUGS

Antiarrhythmic medicines, commonly known as cardiac dysrhythmia medications, are a class of drugs used to treat irregular heart rhythms such as atrial fibrillation, atrial flutter, ventricular tachycardia and ventricular fibrillation.

Classification of Antiarrhythmic Agents

Class	Known as	Examples
Ia	Fast-channel blockers	Quinidine, Procainamide, Disopyramide
Ib		Lidocaine, Phenytoin, Tocainide
Ic		Encainide, Flecainide
II	Beta-blockers	Carvedilol, Propranolol, Esmolol, Timolol, Metoprolol, Atenolol
III	Potassium Channel Blockers	Amiodarone, Sotalol, Ibutilide
IV	Calcium Channel Blockers	Verapamil, Diltiazem

QUINIDINE SULPHATE

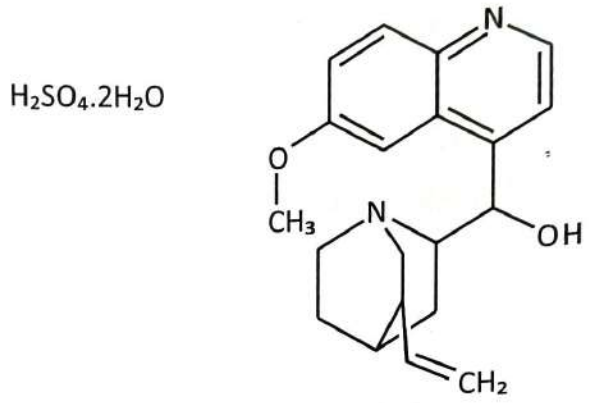
Quinidine is a heart medicine that works as a Class I antiarrhythmic. It's a quinine stereoisomer that comes from the bark of the cinchona tree.

Mol. Formula: $C_{40}H_{50}N_4O_8S$

Molar Mass: 746.9

IUPAC Name: 5-ethenyl-1-azabicyclo [2.2.2] octan-2-yl] -(6-methoxyquinolin-4-yl) methanol; sulfuric acid

Structure:



Physical Properties: Its sulphate salt has white crystals. It is odourless and has bitter in taste. It is sparingly soluble in water, soluble in alcohol.

Stability and Storage: It is affected by light hence it is store in well-close and light-resistant container.

Official Preparation: Quinidine tablets

Brand Name: Mosgard-300, Qinet-300, Quine star

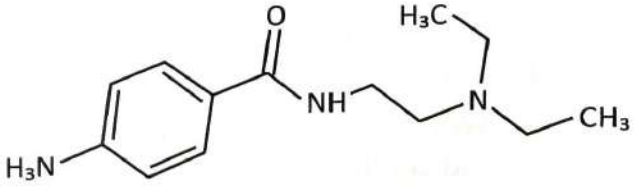
PROCAINAMIDE HYDROCHLORIDE

It is a medication of the antiarrhythmic class used for the treatment of cardiac arrhythmias.

Mol. Formula: $C_{13}H_{22}ClN_3O$

Molar Mass: 271.78

Structure:



IUPAC Name: 4-amino-N-[2-(diethylamino)ethyl] benzamide; hydrochloride

Physical Properties: It is white or yellowish white crystalline powder which is odourless and hygroscopic in nature. It is very soluble in water, freely soluble in alcohol.

Stability and Storage: It is hygroscopic in nature hence store in well closed and light-resistant container.

Use:

- Procainamide is used to help keep the heart beating normally in people with certain heart rhythm disorders of the ventricles
- It is used for treating ventricular arrhythmias: ventricular ectopy and tachycardia and supraventricular arrhythmias: Atrial fibrillation

Official Preparations:

- Procainamide hydrochloride tablet
- Procainamide hydrochloride injection

Brand Name: Pronestyl

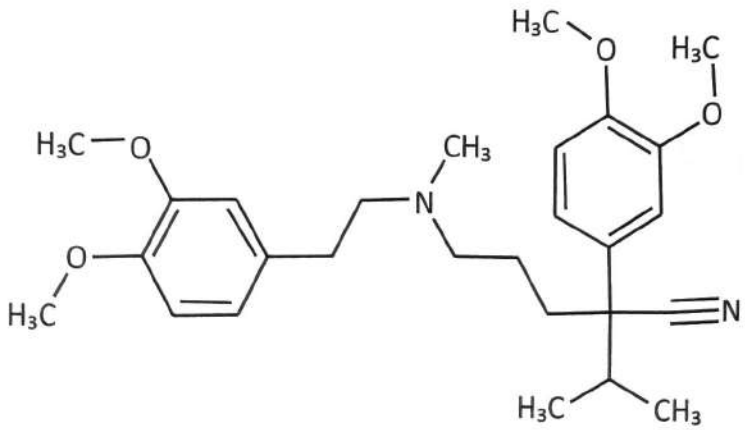
VERAPAMIL

Verapamil is a first-generation calcium channel blocker used for treatment of hypertension, angina pectoris and super ventricular tachyarrhythmias

Mol. Formula: $C_{27}H_{39}ClN_2O_4$

Molar Mass: 491.1

Structure:



UPAC Name: 2-(3,4-dimethoxyphenyl)-5-[2-(3,4-dimethoxyphenyl) ethyl-ethylamino]-2-propan-2-ylpentanenitrile

ysical Properties: Itis almost white crystalline powder, odourless and bitter in test. It oluble in water, chloroform and methanol

Stability and Storage: It is affected by heat, moisture and light hence it is store in well-close and light-resistant container.

Uses:

- It is also used to treat hypertension
- It is used in the treat unstable angina and chronic stable angina.

Official Preparations:

- Verapamil Tablet I.P
- Verapamil Injection I.P

Brand Name: Verelan, covera, calan, calaptin 80.

PHENYTOIN SODIUM

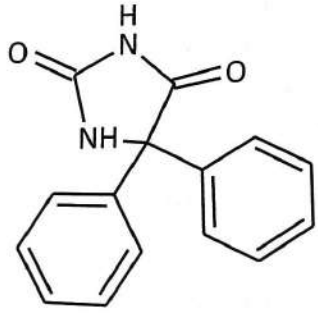
Phenytoin Sodium is a hydantoin derivate and non-sedative antiepileptic drug with anticonvulsant efficacy, as well as an anti-arrhythmic and muscle relaxant.

Mol. Formula: $C_{15}H_{11}N_2NaO_2$

Molar Mass: 252.27

IUPAC Name: Sodium;5,5-diphenylimidazolidin-3-ide-2,4-dione

Structure:



Physical Properties: It is a white crystalline power and odourless. It is very slightly soluble in water but soluble in alkali hydroxide.

Stability and Storage: It is store in well-close container and protect from light.

Uses:

- It is used as antiepileptic
- It is use as antiarrhythmic agent
- It is used to treat myotonia, migraine
- It is used to treat trigeminal neuralgia
- It is use to control status epilepticus

Official Preparations:

- Phenytoin capsules I.P.
- Phenytoin injection I.P.
- Phenytoin tablets I.P.
- Phenytoin oral suspension I.P.

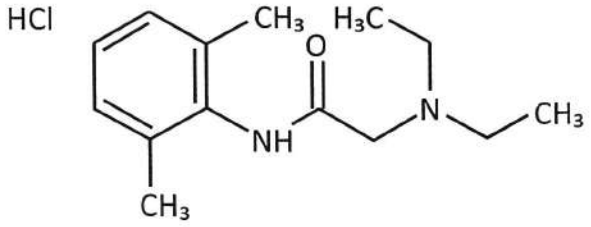
Brand Name: Epitin-100, Dilantin, Epsotoin.

LIDOCAINE HYDROCHLORIDE

Mol. Formula: $C_{14}H_{23}ClN_2O$

Molar Mass: 270.80

Structure:



IUPAC Name: 2-(diethylamino)-N-(2,6-dimethylphenyl) acetamide; hydrochloride

Physical Properties: It is white crystalline powder which is odourless and has slightly bitter taste. It is very soluble in water, freely soluble in alcohol and soluble in chloroform.

Stability and Storage: store in well close containers.

Uses:

- It is mainly used for its local anesthetic activity
- It is use to produce dental analgesia
- It is also used for the prevention and treatment of arrhythmia

Official Preparations:

- Lignocaine injection
- Lignocaine eye drops
- Lignocaine gels

Brand Name: Lignox 2%, Dentonum, Jetlox, Leecaine.

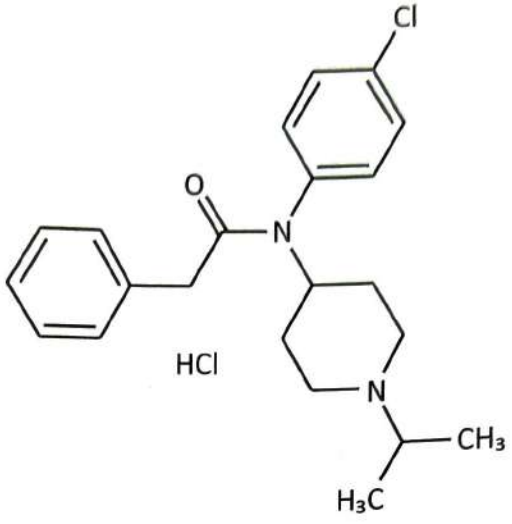
LORCAINIDE HYDROCHLORIDE

It is a Class 1c antiarrhythmic agent that is used to help restore normal heart rhythm and conduction in patients.

Mol. Formula: $C_{22}H_{28}Cl_2N_2O$

Molar Mass: 407.4

Structure:



IUPAC Name: N-(4-chlorophenyl)-2-phenyl-N-(1-propan-2-ylpiperidin-4-yl) acetamide; hydrochloride

Physical Properties: Solid, MP 263.0°C

Uses: It is used to help restore normal heart rhythm with Ventricular Tachycardiac, Wolff-Parkinson-White syndrome.

Stability and Storage: Store in well close containers.

Official Preparation: Lorcainide Hydrochloride tablets.

Brand Name: Aristo Larpin, Lerez, Lotensyl.

AMIODARONE

Amiodarone is an iodine-rich benzofuran derivative with antiarrhythmic and vasodilatory activities, Class III antiarrhythmic agent.

Mol. Formula: $C_{25}H_{30}ClI_2NO_3$

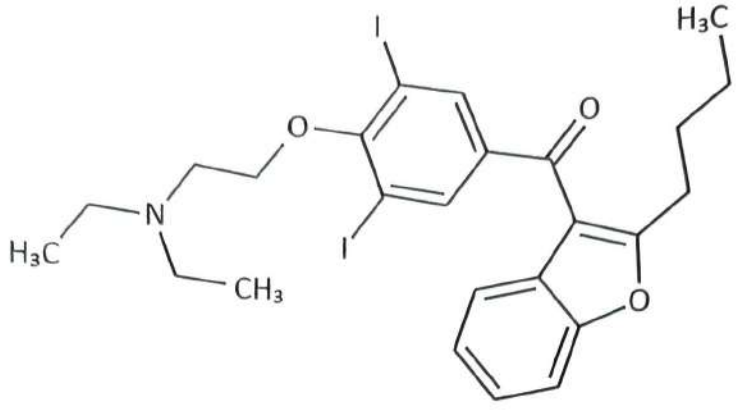
Molar Mass: 681.8

IUPAC Name: (2-butyl-1-benzofuran-3-yl)-[4-[2-(diethylamino) ethoxy]-3,5-diiodophenyl] methanone

Physical Properties: It is a white crystalline powder. It is very slightly soluble in water, freely soluble in dichloromethane soluble in ethanol.

Stability and Storage: It is protected from light and temperature not exceeding 30°C hence it is store in well close and light-resistant containers.

Structure:



Use:

- Amiodarone has been utilized in the treatment of both acute life-threatening arrhythmias and long-term arrhythmia suppression. It's used to treat both supraventricular and ventricular arrhythmias.
- It's utilized to get back into normal cardiac rhythm and keep a steady heartbeat.

Official Preparations:

- Amiodarone Tablet IP.
- Amiodarone Liquid.
- Amiodarone IV infusion IP.
- Amiodarone Solution.
- Amiodarone Injection.

Brand Name: Pacerone, Cordarone, Amiodar-100

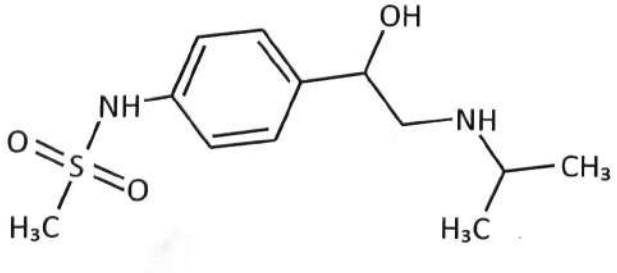
SOTALOL

Sotalol is a nonselective beta-adrenergic blocker used largely in the therapy cardiac arrhythmias.

Mol. Formula: $C_{12}H_{21}ClN_2O_3S$

Molar Mass: 308.83

Structure:



IUPAC Name: *N*-[4-[1-hydroxy-2-(propan-2-ylamino) ethyl] phenyl] methanesulfonamide

Physical Properties: Solid, MP 206.5-207°C.

Stability and Storage: Store in well close containers.

Uses:

- It is used to treat atrial fibrillation.
- It is use life threatening ventricular arrhythmias.

Official Preparations:

- Sotalol tablet
- Sotalol injection

Brand Name: Sotalar-40, Solet, Sotalol-160 mg.

ANTIHYPERTENSIVE AGENT

A type of drug used to treat high blood pressure. Antihypertensive therapy seeks to prevent the complications of high blood pressure, such as stroke and myocardial infarction. There are many different types of antihypertensive agents and they work in different ways to lower blood pressure. Some remove extra fluid and salt from the body. Others slow the heartbeat or relax and broaden the blood vessels. With one medicine, a person may respond better and experience fewer side effects than with another. To lower their blood pressure, some patients require more than one antihypertensive medication.

CLASSIFICATION OF ANTIHYPERTENSIVE AGENT

1. **Sympatholytic agents:**
   - (a) **Centrally acting drugs:** Clonidine, methyldopa
   - (b) **Ganglionic blockers:** Guanethidine
   - (c) **Peripherally acting drugs:**
     - (i) **Alpha adrenergic blockers:** Prazosin, terazosin, doxazocin
     - (ii) **Beta adrenergic blockers:** Propranolol, atenolol, timolol, labetalol
2. **Vasodilators:**
   - (a) **Direct acting:** Hydralazine, sodium nitroprusside
   - (b) **Potassium channel blockers:** Diazoxide, minoxidil
   - (c) **Calcium channel blockers:** Verapamil, diltiazem, nifedipine

3. **Drug acting on renin angiotensin system:**
   (a) ACE- Inhibitors: captopril, enalapril, benazepril
   (b) AT-II Antagonist: losartan, telmisartan
4. **Diuretics:** Chlorothiazide, furosemide, spironolactone

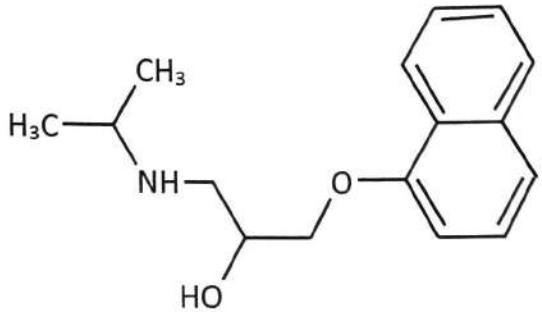
PROPRANOLOL

Mol. Formula: $C_{16}H_{22}ClNO_2$

Molar Mass: 295.80

IUPAC Name: 1-naphthalen-1-yloxy-3-(propan-2-ylamino) propan-2-ol

Structure:



Physical Properties:

- It is white crystalline powder.
- Its hydrochloride salt is odourless and bitter in test.
- It is slightly soluble in water

Stability and Storage: It is affected by light and hence it is stored in well-closed, light-resistant containers

Uses:

- It is use in angina pectoris
- It is used to treat Arterial hypertension
- It is use in Anxiety symptoms, Cardiac arrhythmia.

Official Preparations:

- Propranolol Tablet
- Propranolol injection

Brand Name: Dideral-40, Inderal, Cipar-LA-20

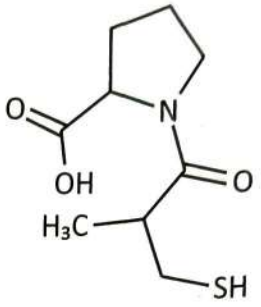
CAPTOPRIL

Mol. Formula: $C_9H_{15}NO_3S$

Molar Mass: 217.28

IUPAC Name: (2*S*)-1-[(2*S*)-2-methyl-3-sulfanylpropanoyl] pyrrolidine-2-carboxylic acid

Structure:



Physical Properties: is a white crystalline powder having a characteristic sulfide-like odour and a melting point between 105 and 108°C. It is freely soluble in water

Stability and Storage: stored in well-closed, light-resistant containers

Official Preparation: Captopril tablets

Brand Name: Aceten, Acezide, Acezide, Aceten, Aceten

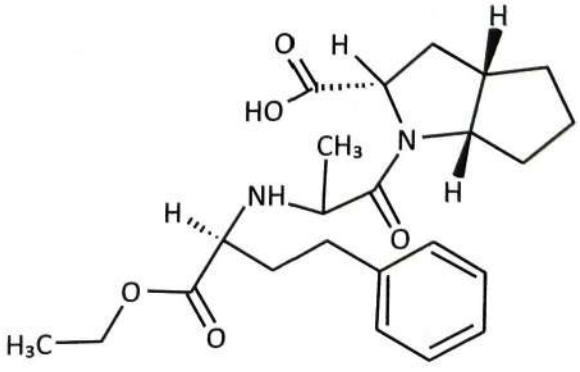
RAMIPRIL

Ramipril is an Angiotensin-Converting Enzyme (ACE) inhibitor used in the therapy of hypertension and heart failure.

Mol. Formula: $C_{23}H_{32}N_2O_5$

Molar Mass: 416.51

Structure:



IUPAC Name: 1-ethoxy-1-oxo-4-phenylbutan-2-yl] amino] propanoyl]-3,3*a*,4,5,6,6*a*-hexahydro-2*H*-cyclopenta[b]pyrrole-2-carboxylic acid

Physical Properties: It is a white, crystalline powder, soluble in polar organic solvents and buffered aqueous solutions.

Stability and Storage: It is affected by light and moisture. Hence it is store in well close container at room temperature.

Uses:

- It is used to treat hypertension.
- It is used to treat heart attacks and kidney problems.
- It is also used to improve survival after a heart attack.
- This is also be used to treat heart failure in patients who have had a recent heart attack.

Official Preparations:

- Ramipril Tablets I.P.
- Ramipril Capsules I.P.

Brand Name: Cardace-5, Ramwell-5, Ramipres-2.5

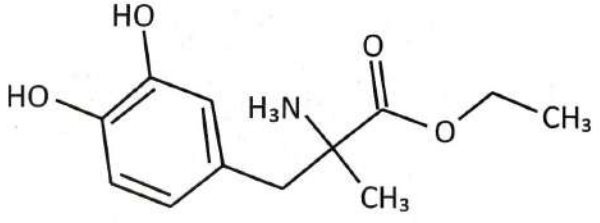
METHYLDOPATE HYDROCHLORIDE

Methyldopate hydrochloride is the hydrochloride salt derivative of methyldopa, a phenylalanine derivate and antihypertensive aromatic amino acid decarboxylase inhibitor.

Mol. Formula: $C_{12}H_{18}ClNO_4$

Molar Mass: 275.73

Structure:



IUPAC Name: ethyl (2*S*)-2-amino-3-(3,4-dihydroxyphenyl)-2-methylpropanoate; hydrochloride

Physical Properties: It is white to yellowish white fine powder; it is odourless and tasteless. is sparingly soluble in water and very soluble in dil. hydrochloric acid.

ability and Storage: It is affected by light and moisture hence store in well-close and ht-resistant container.

Uses:

- It is used control renal hypertension.
- It is used to treat hypertension in pregnancy.
- It is used to control blood pressure in primary hypertension.
- It is used in pheochromocytoma and carcinoid tumor.

Official Preparations:

- Methyldopa tablets IP
- Methyldopa and hydrochlorothiazide tablets IP

Brand Name: Emdopa, Meldopa, Aldomet-250

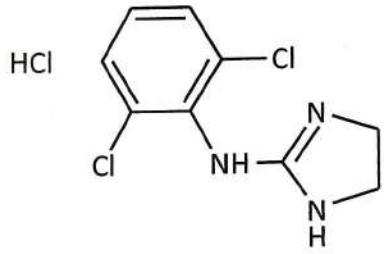
CLONIDINE HYDROCHLORIDE

Clonidine Hydrochloride is the hydrochloride salt form of clonidine, an imidazoline derivate and centrally-acting alpha-adrenergic agonist as well as antagonist with antihypertensive activity

Mol. Formula: $C_9H_{10}Cl_3N_3$

Molar Mass: 266.6

Structure:



IUPAC Name: *N*-(2,6-dichlorophenyl)-4,5-dihydro-1*H*-imidazol-2-amine; hydrochloride

Physical Properties: It is an odourless, bitter, white, crystalline substance soluble in water and alcohol

Stability and Storage: Store in well-close and light-resistant container.

Official Preparations:

- Clonidine Hydrochloride tablets
- Clonidine Hydrochloride injection

Brand Name: Arkamin, Catapres, Clodict

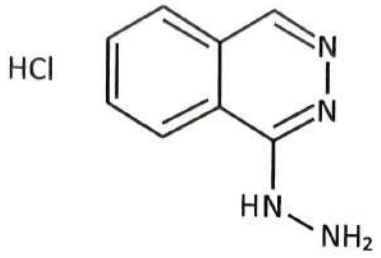
HYDRALAZINE HYDROCHLORIDE

Hydralazine hydrochloride is the hydrochloride salt of hydralazine; a direct-acting vasodilator that is used as an antihypertensive agent.

Mol. Formula: $C_8H_9ClN_4$

Molar Mass: 196.64

Structure:



IUPAC Name: phthalazin-1-ylhydrazine; hydrochloride

Physical Properties: It is white crystalline powder which is odourless. It is soluble in water.

Stability and Storage: It is stable in light, air and heat hence it is store in well close containers.

Uses:

- It is vasodilator, decreases renin release and also causes bradycardia.
- It is used to treat moderate primary hypertension.
- It is used to treat postmenopausal vasomotor instability

Official Preparations:

- Clonidine tablets IP
- Clonidine injection IP
- Clonidine hydrochloride and chlorthalidone tablet.

Brand Name: Arkamin, Clodine, Cdine-0.1

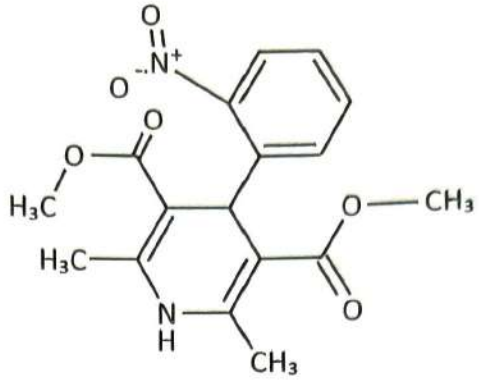
NIFEDIPINE

Nifedipine is a first-generation calcium channel blocker used to treat hypertension and angina pectoris.

Mol. Formula: $C_{17}H_{19}ClN_2O_6$

Molar Mass: 382.8

Structure:



IUPAC Name: dimethyl 2,6-dimethyl-4-(2-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate

Physical Properties: It is yellow crystalline powder compound, practically insoluble in water and slightly soluble in alcohol.

Stability and Storage: It is affected by light hence it is store in well-close container.

Uses:

- It is used to treat atherosclerosis, Raynaud's syndrome.
- It is use in hypertension
- It is also in exercise induced asthma.
- It is use in heart diseases like angina.

Official Preparations:

- Nifedipine Capsules I.P
- Nifedipine Tablet I.P
- Nifedipine prolong release capsules I.P
- Nifedipine prolong release Tablet I.P

Brand Name: Nefedin, Myogard, Adalat-CR, Aminifd-20, Fidonal.

ANTIANGINAL AGENTS

Angina Pectoris

It is ischemic heart disease, i.e., sudden pain. Disease affecting the coronary arteries which supply oxygenated blood from left ventricle to heart tissues. The lumen of artery become restricted and it becomes less efficient in supplying the blood and oxygen to heart called as ischemia. Antianginal drugs that prevent or terminate attack of angina pectoris.

Classification

1. **Nitrates or Nitro-Vasodilators:**
   (a) **Short acting:** Glyceryl trinitrate, amyl nitrite.
   (b) **Long acting:** Isosorbide dinitrate, Erythrityl tetranitrate, pentaerythritol tetranitrate.
2. **Calcium channel blockers:**
   (a) **Phenyl alkylamine:** Verapamil
   (b) **Benzothiazine:** Diltiazem
   (c) **Dihydropyridines:** Nifedipine, nicardipine, nimodipine, felodipine, amlodipine.
   (d) **Diaryl-aminopropyl amine ethers:** Bepridil
   (e) **Benzimidazole:** Mibefradil
3. **Beta adrenergic blockers:**
   (a) **Selective:** Atenolol, metoprolol
   (b) **Non-selective:** Propranolol
4. **Miscellaneous:** Dipyridamole

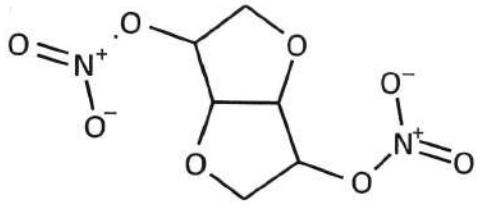
ISOSORBIDE DINITRATE

Isosorbide dinitrate is a Nitrate Vasodilator.

Mol. Formula: $C_6H_8N_2O_8$

Molar Mass: 236.13

Structure:



IUPAC Name: 3-nitrooxy-2,3,3*a*,5,6,6*a*-hexahydrofuro[3,2-b]furan-6-yl] nitrate

Physical Properties: It is a white crystalline powder, odourless compound. It is freely soluble in organic solvent alcohol, acetone, ether, sparingly soluble in water.

Stability and Storage: It is store at room temperature below 25°C.

Uses: It is use to prevent chest pain caused by angina.

Official Preparations:

- Isosorbide Dinitrate Capsule

- Isosorbide Dinitrate Tablet I.P
- Dilute Isosorbide Dinitrate I.P

Brand Name: Isordil, Cardicap-10, Dinitra, Sorbitrate, Bidil.

EXERCISE

Short Answer Type Questions

1. **Give two brand names of following drugs:**
   (a) Quinidine Sulphate (b) Procainamide Hydrochloride,
   (c) Verapamil (d) Lidocaine HCl,
   (e) Lorcainide HCl, (f) Amiodarone
   (g) Clonidine Hydrochloride
2. **In what dosage form the following drugs are given:**
   (a) Phenytoin Sodium (b) Propranolol
   (c) Captopril
3. **Give uses of following drugs:**
   (a) Clonidine Hydrochloride (b) Isosorbide Dinitrate
   (c) Lorcainide HCl
4. **Write structure and give IUPAC Name of following drugs:**
   (a) Phenytoin Sodium (b) Propranolol
   (c) Captopril
5. **Name the drug present in following brands:**
   (a) Mustard (b) Jetlox
   (c) Pronestyl (d) Aceten
   (e) Epsotoin (f) Clodict
   (g) Amiodar

Long Answer Type Questions

1. Classify Anti-Arrhythmic agents with examples.
2. Classify Anti-Hypertensive agents with examples.
3. Classify Antianginal agents with examples.
4. Write structure, give IUPAC Name, properties and uses of Phenytoin Sodium.

5. Write structure, give IUPAC name, properties and uses of Propranolol.
6. Write structure, give IUPAC name, properties and uses of Captopril.
7. Give properties and uses of Hydralazine Hydrochloride and Nifedipine.
8. Give properties and uses of Procainamide Hydrochloride and Verapamil.
9. Give properties and uses of Amiodarone and Sotalol.

Multiple Choice Questions (MCQ's)

1. A group of pharmaceuticals that are used to suppress abnormal rhythms of the heart is known as:

(a) Antihypertensive agents
(b) Antiarrhythmic agents
(c) Antianginal drugs
(d) All of the above

2. Which drug prevent or terminate attack of angina pectoris?

(a) Antihypertensive agents
(b) Antiarrhythmic agents
(c) Antianginal drugs
(d) All of the above

3. Which drug therapy prevent the complications of high blood pressure?

(a) Antihypertensive agents
(b) Antiarrhythmic agents
(c) Antianginal drugs
(d) All of the above

4. Ramipril is:

(a) ACE inhibitor
(b) Beta blocker
(c) Alpha-adrenergic agonist
(d) None of the above

5. Amiodarone is:

(a) ACE inhibitor
(b) Beta blocker
(c) Alpha-adrenergic agonist
(d) Potassium Channel Blockers

6. Propranolol is:

(a) ACE inhibitor
(b) Beta blocker
(c) Alpha-adrenergic agonist
(d) Potassium Channel Blockers

7. Verapamil and Diltiazem are:

(a) Calcium Channel Blockers
(b) Beta blocker
(c) Alpha-adrenergic agonist
(d) Potassium Channel Blockers

8. The basic ring present in phenytoin is:

(a) Imidazolidine Dione
(b) Pyrimidine
(c) Thiophene
(d) Quinoline

9. The basic ring present in clonidine is:

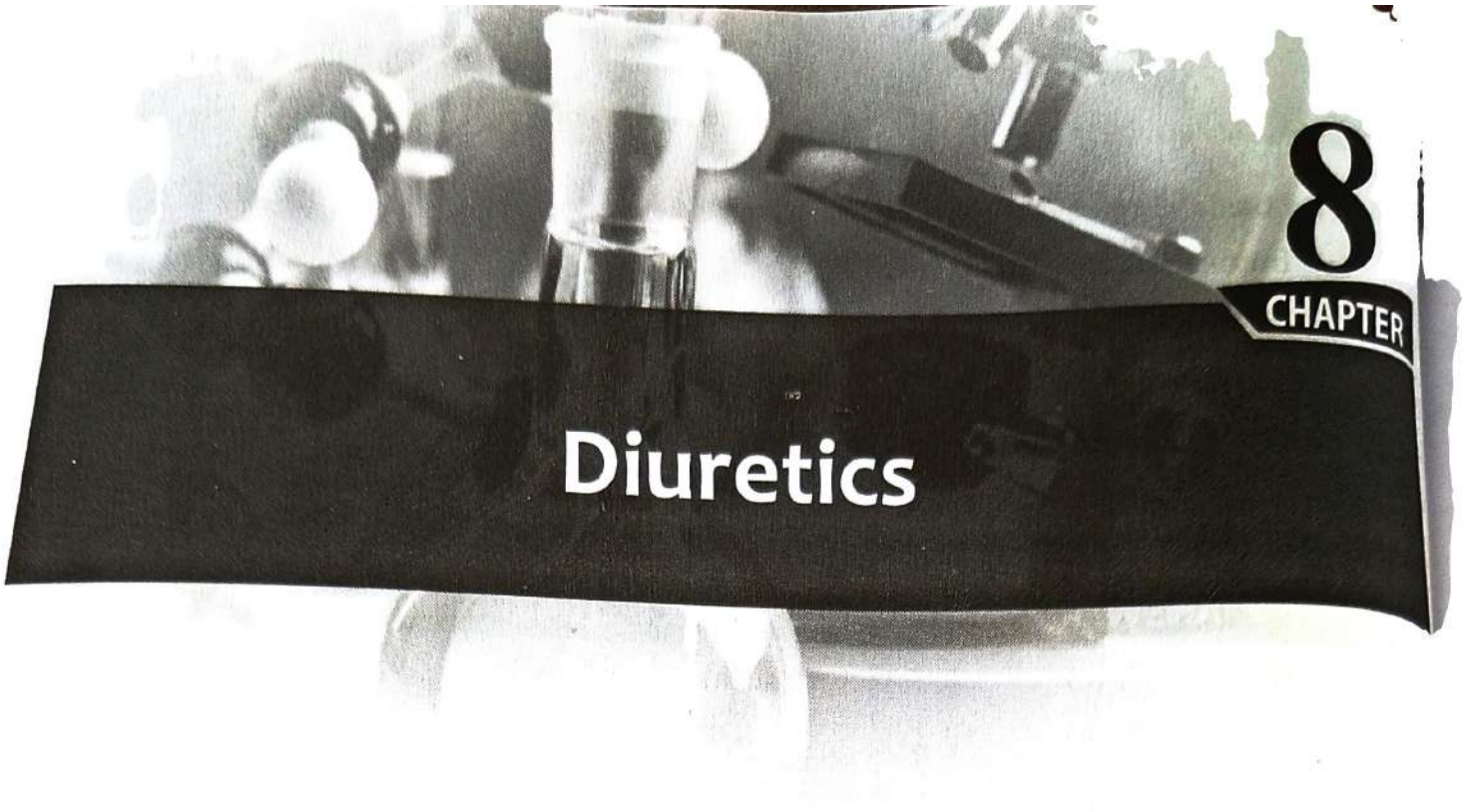
(a) Imidazole
(b) Indole
(c) Isoxazole
(d) Pyridine

10. Which one the following is anti-anginal drug?

(a) Isosorbide dinitrate
(b) Verapamil
(c) Lidocaine HCl
(d) Lorcainide HCl

ANSWERS OF MULTIPLE CHOICE QUESTIONS (MCQ'S)

1. (b)	2. (c)	3. (a)	4. (a)	5. (d)	6. (b)	7. (a)
8. (a)	9. (a)	10. (a)				



CHAPTER 8

Diuretics

INTRODUCTION

Diuretics are medications that accelerate the rate of urine excretion by the kidneys, generally by reducing sodium and its osmotic equivalent quantity of water by tubular reabsorption. They can be used to treat a variety of oedemas, including cardiac oedema (associated to congestive heart failure), nutritional oedema, liver cirrhosis, pregnant oedema, renal oedema and oedema caused by mineralocorticoids. Mild hypertension can be controlled with diuretics alone. They can, however, be used to treat moderate to severe hypertension when combined with antihypertensive drugs. They are also good for lowering intraocular pressure.

CLASSIFICATION

1. **Water and Osmotic agents:**
   (a) **Electrolytes:** Sodium and Potassium salts
   (b) **Non-electrolytes:** Mannitol, Urea
2. **Organic mercurial:** Mersalyl acid
3. **Acidifying agents:** Ammonium chloride, Arginine hydrochloride
4. **Alpha-beta unsaturated ketones:** Ethacrynic acid
5. **Purines and related compound:** Caffeine
6. **Sulphonamides:**
   (a) Carbonic anhydrase inhibitors, e.g., Acetazolamide

(b) Benzothiadiazides, e.g., Chlorothiazide, Hydrochlorothiazide
(c) Sulphamoyl benzoic acid derivatives, e.g., Frusemide

7. **Endocrine antagonists:** Aldosterone antagonists, e.g., Spironolactone
8. **Miscellaneous agents:** Triamterene

Classification

Diuretics can also be classified as:

1. **Weak diuretics:**
   (a) **Osmotic diuretics:** Sodium and Potassium salts
   (b) **Xanthine Derivatives:** Aminophylline
   (c) **Carbonic anhydrase inhibitors,** e.g., Acetazolamide
2. **Moderately efficacious diuretics:**
   (a) **Osmotic diuretics:** Mannitol, Sucrose, Glycerol
   (b) **Benzothiadiazide derivative:** Chlorthalidone, Chloroxozone
3. **Very efficacious diuretics (High celling diuretics),** e.g., Frusemide & Ethacrynic acid.
4. **Potassium sparing diuretics:**
   (a) **Aldosterone antagonists:** Spironolactone
   (b) **Renal epithelial sodium channel inhibitors:** Triamterene, Amiloride

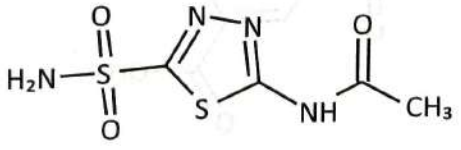
ACETAZOLAMIDE

Acetazolamide is a first-generation Carbonic Anhydrase Inhibitor. The enzyme carbonic anhydrase, allowing the reabsorption of bicarbonate, sodium and chloride.

Formula: $C_4H_6N_4O_3S_2$

Molar Mass: 222.24

Structure:



IUPAC Name: N-(5-sulfamoyl-1,3,4-thiadiazol-2-yl) acetamide

Properties: Acetazolamide appears as white to yellowish-white fine crystalline powder. No odour or taste, slightly soluble in alcohol, MP 260.5°C.

Storage: Store in well closed container, protected from light.

Uses: It is a medication used to treat:

- Glaucoma
- Epilepsy (as adjuvant in absence seizures when primary drugs are not fully effective)
- Altitude sickness
- Periodic paralysis
- Idiopathic intracranial hypertension (raised brain pressure of unclear cause),
- Urine alkalinization
- Heart failure.
- Decreased gastric HCl and pancreatic $NaHCO_3$ secretion.

Official Formulations:

- Acetazolamide Tablets IP.
- Acetazolamide extended-release capsule.
- Acetazolamide powder for solution.

Brand Name: Acetamin, Acetariv, Aceta-SR, Tegrital.

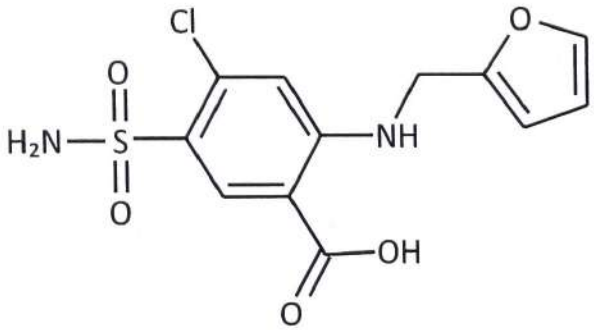
FUROSEMIDE

Furosemide is a loop diuretic that works by blocking the luminal Na-K-Cl cotransporter in the thick ascending limb of the Henle loop, causing more sodium, chloride and potassium to remain in the urine.

Formula: $C_{12}H_{11}ClN_2O_5S$

Molar Mass: 330.74

Structure:



IUPAC Name: 4-chloro-2-(furan-2-ylmethylamino)-5-

Properties: It is a white to slightly

very slightly

Storage: store in well closed container, protected from light and moisture

Use:

- Furosemide is generally used to treat oedema; however, it can also be used to treat hypertension in some circumstances.
- Furosemide is also used to treat cirrhosis of the liver, renal disease, nephrotic syndrome and oedema of the brain or lungs when quick diuresis is required.
- It's also been used to reduce the risk of developing exercise-induced pulmonary bleeding in race horses.

Official **Formulations:**

- Furosemide Tablets IP.
- Furosemide injection.

Brand Name: Laxis, Fruselac DS Spirotic, Lasilactone, Frusemene

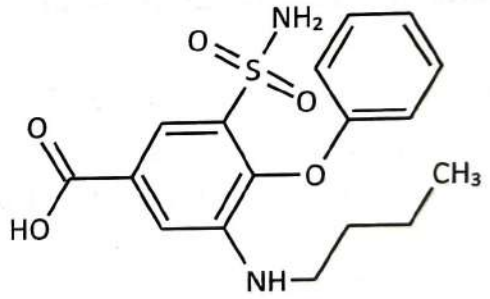
BUMETANIDE

It is a medication used to treat swelling and high blood pressure.

Formula: $C_{17}H_2ON_2O_5S$

Molar Mass: 364.42

Structure:



IUPAC Name: 3-butylamino-4-phenoxy-5-sulfamoyl-benzoic acid

Properties: A white crystalline powder, soluble in acetone and ethanol; slightly soluble in dichloromethane; practically insoluble in water, MP 230-231°C.

Storage: Store in well closed container, protected from light and moisture.

Use: It used to treat swelling and high blood pressure. This includes swelling as a result of heart failure, liver failure or kidney problems. For high blood pressure it is not a preferred treatment. It is taken by mouth or by injection into a vein or muscle.

Official Formulations:

- Bumetanide Injection IP.

- Bumetanide Oral Solution IP.
- Bumetanide Tablets IP.

Brand Name: Bumex and Burinex

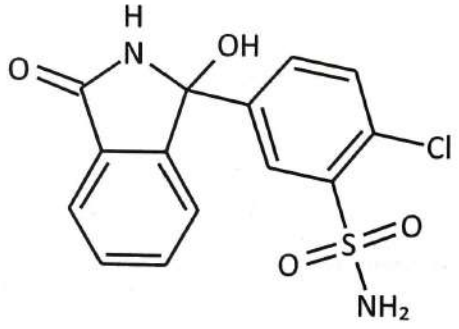
CHLORTHALIDONE

Chlorthalidone is a thiazide-like diuretic.

Formula: $C_{14}H_{11}ClN_2O_4S$

Molar Mass: 338.76

Structure:



IUPAC Name: 2-chloro-5-(1-hydroxy-3-oxo-2H-isoindol-1-yl) benzenesulfonamide.

Properties: white to yellowish-white crystalline powder, MP 218-264°C, Chlorthalidone is practically insoluble in water, in ether and in chloroform; soluble in methanol; slightly soluble in alcohol.

Storage: store in well closed container, protected from light and moisture.

Uses: It is a diuretic drug that is used to treat high blood pressure, swelling caused by heart failure, liver failure or nephrotic syndrome, diabetes insipidus and renal tubular acidosis.

Official Formulations: Chlorthalidone Tablets

Brand Name: Lupiclor, Hythalton, Thalizide

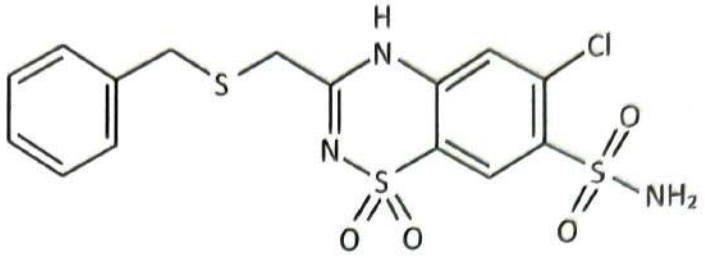
BENZTHIAZIDE

It is a thiazide diuretic used in the treatment of high blood pressure and oedema.

Formula: $C_{15}H_{14}ClN_3O_4S_3$

Molar Mass: 431.92

Structure:



IUPAC Name: 3-(benzylsulfanylmethyl)-6-chloro-1,1-dioxo-4H-1ë6,2,4-benzothiadiazine-7-sulfonamide

Properties: Fine, white, crystalline powder, characteristic odour, bitter taste, practically insoluble in water, soluble in alkaline solution, MP238 to 239°C.

Storage: Store in well closed container, protected from light and moisture.

Uses:

- It is a diuretic medication used to treat hypertension and oedema
- Like other thiazides, benzthiazide promotes water loss from the body (diuretics)

Official Formulations: Benzthiazide Tablets

Brand Name: Aquatag, Dihydrex, Diucen, Edemax, Exna, Foven

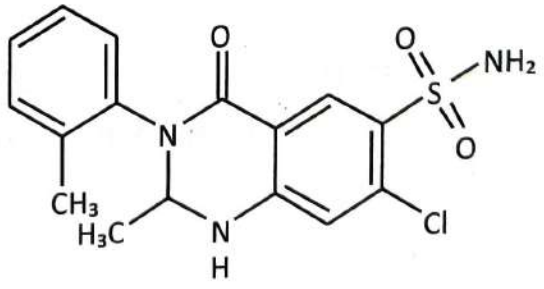
METOLAZONE

It is a quinazoline-sulphonamide that is considered a thiazide-like diuretic.

Formula: $C_{16}H_{16}ClN_3O_3S$

Molar Mass: 365.8

Structure:



IUPAC Name: 7-chloro-2-methyl-3-(2-methylphenyl)-4-oxo-1,2-dihydroquinazoline-[redacted] sulfonamide

Properties: Solid, odourless, tasteless, Insoluble in water and alcohol, light-sensitive. M[redacted] 253-259°C.

Storage: Store in well closed container, protected from light.

Uses:

- Metolazone is in a class of medications called diuretics.
- It is used to reduce the swelling and fluid retention caused by heart failure or kidney disease.
- It also is used alone or with other medications to treat high blood pressure.

Official Formulations: Metolazone Tablets.

Brand Name: Diurem, Metolaz, Metoral, Zytanix.

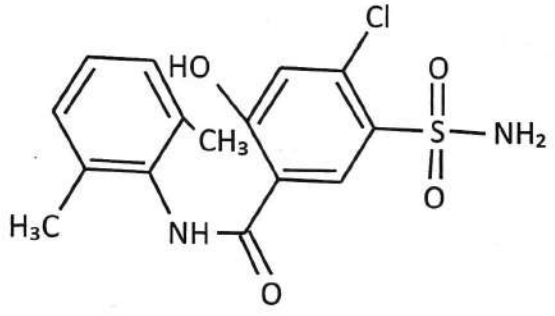
XIPAMIDE

Xipamide is a sulphonamide-based diuretic.

Formula: $C_{15}H_{15}ClN_2O_4S$

Molar Mass: 354.8

Structure:



IUPAC Name: 4-chloro-N-(2,6-dimethylphenyl)-2-hydroxy-5-sulfamoylbenzamide

Storage: Store in well closed container.

Uses: Xipamide is used for:

- Cardiac oedema caused by decompensation of heart failure.
- Renal oedema, chronic renal disease (but not with anuria).
- Hepatic oedema caused by cirrhosis.
- Lymphoedema
- Hypertension in combination with chronic renal disease.

Official Formulations: Xipamide Tablets

Brand Name: Aquaphor, Aquaphoril

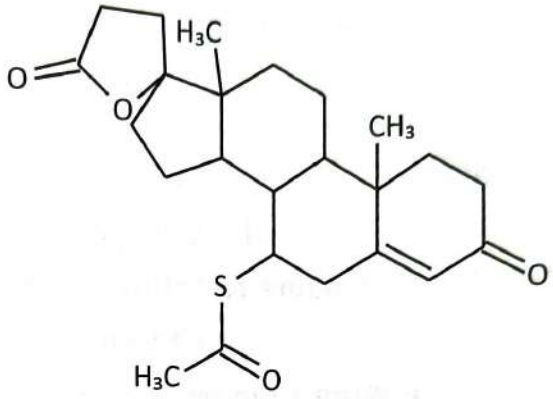
SPIRONOLACTONE

Spironolactone is an aldosterone receptor antagonist and potassium-sparing diuretic.

Formula: $C_{24}H_{32}O_4S$

Molar Mass: 416.58

Structure:



IUPAC Name: 10,13-Dimethyl-3,5'-dioxospiro[2,6,7,8,9,11,12,14,15,16-decahydro-1H-cyclopenta[a]phenanthrene-17,2'-oxolane]-7-yl] ethanethioate

Properties: Light cream-coloured to light tan, crystalline powder; odourless or with a Mild mercaptan-like odour. It exhibits polymorphism, Soluble in most organic solvents, MP 134-135°C.

Storage: Store in well closed container, protected from light.

Uses:

- Spironolactone is used primarily to treat heart failure, oedematous conditions such as nephrotic syndrome or ascites.
- The most common use of spironolactone is in the treatment of heart failure.
- Spironolactone has antiandrogenic activity, so it can be useful in acne, seborrhoea, hirsutism and pattern hair loss in women.

Official Formulations:

- Spironolactone Tablet IP
- Spironolactone capsule
- Spironolactone suspension

Brand Name: Lactone, Aldactone, Lasilactone, Torsid Plus, Spirotic

EXERCISE

Short Answer Type Questions

1. **Give two Brand Names of following drugs:**
   (a) Acetazolamide (b) Frusemide
   (c) Bumetanide (d) Chlorthalidone
2. **In what dosage form the following drugs are given:**
   (a) Benzthiazide (b) Metolazone
   (c) Xipamide
3. **Give uses of following drugs:**
   (a) Bumetanide (b) Chlorthalidone
4. **Write structure and give chemical name of following drugs:**
   (a) Frusemide (b) Chlorthalidone
5. **Name the drug present in following brands:**
   (a) Acetamin (b) Frusemene
   (c) Bumex (d) Thalizide

Long Answer Type Questions

1. Classify Diuretics with examples.
2. Write structure, give chemical name, properties and uses of Frusemide
3. Give properties and uses of Xipamide and Spironolactone
4. Give properties and uses of Benzthiazide and Metolazone

Multiple Choice Questions (MCQ's)

1. **Acetazolamide is classified under:**
   (a) Carbonic Anhydrase Inhibitor (b) osmotic diuretics
   (c) Potassium sparing diuretics (d) High celling diuretics
2. **Frusemide is classified under:**
   (a) Carbonic Anhydrase Inhibitor (b) Osmotic diuretics
   (c) Potassium sparing diuretics (d) High celling diuretics
3. **Spironolactone is classified under:**
   (a) Carbonic Anhydrase Inhibitor (b) Osmotic diuretics
   (c) Potassium sparing diuretics (d) High celling diuretics

4. **Which one of the following is thiazide-like diuretic?**
   (a) Acetazolamide (b) Frusemide
   (c) Spironolactone (d) Chlorthalidone
5. **Find out the sulphonamide derivative from following:**
   (a) Benzthiazide (b) Acetazolamide
   (c) Frusemide (d) Spironolactone
6. **Acetazolamide shows _____ diuretic action.**
   (a) strong (b) weak
   (c) both (d) None of the above
7. **What is the name of basic ring present in acetazolamide?**
   (a) Thiadiazole (b) Pyrrole
   (c) Pyridine (d) Furan
8. **What is the name of basic ring present in Metolazone?**
   (a) Thiadiazole (b) Pyrrole
   (c) Pyridine (d) Quinazoline
9. **What is the name of basic ring present in Chlorthalidone?**
   (a) Isoindole (b) Pyrrole
   (c) Pyridine (d) Quinazoline
10. **What is the name of basic ring present in Benzthiazide?**
   (a) Benzofuran (b) Benzothiadiazine
   (c) Benzopyrrole (d) None of the above

ANSWERS OF MULTIPLE CHOICE QUESTIONS (MCQ'S)

1. (a)	2. (d)	3. (c)	4. (d)	5. (a)	6. (b)	7. (a)
8. (d)	9. (a)	10. (b)				

CHAPTER 9

Hypoglycaemic Agent

DIABETES MELLITUS (DM)

It is hyperglycaemic condition (increased blood glucose level) due to reduced glucose metabolism. Diabetes mellitus is due to either a decrease in circulating level of insulin (insulin deficiency) or a decrease in response of target tissue to insulin (insulin resistance).

Type-1 Diabetes Mellitus

It is called as Insulin Dependent Diabetes Mellitus (IDDM) or juvenile onset diabetes mellitus. There is β cell destruction in pancreatic islets; majority of cases are autoimmune (type 1A), but some are idiopathic (type 1B). In all type 1 cases, circulating insulin level is very low. Approximately 10% of diabetic patients suffers with type-1 DM.

Type-2 Diabetes Mellitus

It is called as Non-Insulin Dependent Diabetes Mellitus (NIDDM) or maturity onset diabetes mellitus. There is no or moderate destruction of β-cells. Insulin in circulation is low, normal or even high. It occurs mostly in past middle-aged people. Over 90% cases are type-2 DM.

- **Type-2 DM is due to:**
  - Abnormality in GLUT-2 glucose transporter of β-cells. So that β-cells respond at higher glucose concentration.
  - Reduced sensitivity of peripheral tissues to insulin (insulin resistance).

CLASSIFICATION OF ANTIDIABETIC AGENTS

Class	Drugs
Insulins	Short-acting insulin (regular insulin)
	Rapid-acting insulins (insulin aspart, insulin glulisine, insulin glulisine)
	Intermediate-acting insulin (insulin isophane)
	Long-acting insulins (insulin degludec, insulin detemir, insulin glargine)
	Combination insulins (insulin aspart protamine-insulin aspart, insulin lispro protamine-insulin lispro, etc.)
Biguanide	Metformin and phenformin
Sulfonylureas	Glimepiride, gliclazide, tolbutamide, chlorpropamide, tolazamide
Meglitinides	Nateglinide, repaglinide
DPP-4 inhibitors	Alogliptin, linagliptin, saxagliptin, sitagliptin
SGLT-2 inhibitors	Dapagliflozin, canagliflozin, empagliflozin
Alpha-glucosidase inhibitors	Acarbose, miglitol, voglibose
Thiazolidinediones	Pioglitazone, Rosiglitazone

INSULIN AND ITS PREPARATIONS

Insulin

Insulin is used parenterally in Type-1 diabetes mellitus. Insulin is a two-chain polypeptide having 21 amino acids in A-chain and 30 amino acids in B-chain. These two chains are connected by disulphide bonds and by connecting peptide (C peptide) of 35 amino acids. Insulin is first synthesized in the β-cells of islets of Langerhans as a single polypeptide

Preproinsulin of 110 amino acids. From preproinsulin, Proinsulin of 86 amino acids is produced. From proinsulin, the connecting peptide or C peptide of 35 amino acids is split off by proteolysis in Golgi apparatus and insulin of 51 amino acids is produced. Both insulin and C peptide are stored in granules within the β-cells and secreted in blood.

Sources of Insulin

Initially, insulin was derived from beef (meat of pig) or pork (meat of cattle) pancreas. Beef insulin differs from human insulin by three amino acids, whereas pork insulin differs from human insulin by only one amino acid.

Insulin derived from these animals was considered to be viable alternatives to human insulin. As early as 1950s, there were limitations to these animal sources of insulin, because 100% of patients developed insulin antibodies. As a result, immunological insulin resistance was reported in these patients.

In 1963, the complete synthesis of human insulin was accomplished. Human insulin could be synthesized via two possible routes: One method involved the synthesis of each chain separately, followed by linkage of the chains to produce the insulin. The other, more favoured route involved the recombinant DNA technology. This involved the insertion of synthesized genes for each of the two chains into *E. coli* and then the use of fermentation method to generate commercial quantities of human insulin.

Insulin Preparations

As the zinc ions have insulin stabilizing effect, all pharmaceutical preparations are either solutions of soluble zinc insulin or suspensions of insoluble zinc insulin.

1. **Conventional Insulin Preparations:** These are beef or pork insulins, which are potentially antigenic. They contain 1% (10,000 ppm) of other proteins (proinsulin, pancreatic peptides, insulin derivatives, etc.) In the developed countries, these have been totally replaced by other insulin preparations.
2. **Highly Purified Pork Insulin:** In the 1970s, improved purification techniques were applied to produce highly purified and practically nonantigenic insulins. Gel filtration reduces proinsulin content to 50-200 ppm, but pancreatic peptides and insulin derivatives remain. It still has significant antigenicity. Further purification by ion-exchange chromatography removes most contaminants and reduces proinsulin to <10 ppm. These are called as highly purified insulins.
3. **Human Insulin:** As stated in sources of insulins, human insulin (Humulin) was prepared by recombinant DNA technology from *E. coli* and approved in 1982.At the concentration of injectable solution, the insulin molecules self-aggregates to form hexamers around zinc ions (stabilized by zinc). These hexamers slow the absorption and reduce postprandial peak of subcutaneously injected insulin. To overcome these pharmacokinetic limitations, insulin analogues are prepared.

Insulin Analogues

1. Short-acting insulin (regular insulin).

2. Rapid-acting insulins (insulin aspart, insulin glulisine, insulin glulisine).
3. Intermediate-acting insulin (insulin isophane).
4. Long-acting insulins (insulin degludec, insulin detemir, insulin glargine).
5. Combination insulins (insulin aspart protamine-insulin aspart, insulin lispro protamine-insulin lispro, etc.).

Storage condition: All insulin preparations must be stored at low temperatures between 2-8°C in a dark place. It should not be allowed to freeze.

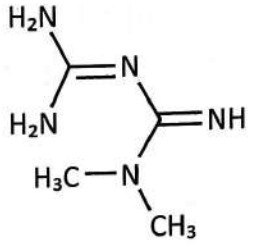
METFORMIN

It is the drug of choice for the treatment of type 2 diabetes

Formula: $C_4H_{11}N_5$

Molar Mass: 129.16

Structure:



IUPAC Name: 3-(diaminomethylidene)-1,1-dimethylguanidine.

Properties: White crystalline powder, odourless, bitter in taste. It is soluble in water; slightly soluble in alcohol, MP 218-220°C.

Storage: Store in well closed container protected from moisture.

Uses:

- It is used in non-insulin dependent diabetes mellitus.
- It is also used in the treatment of polycystic ovary syndrome.

Official Preparations: Metformin tablets IP

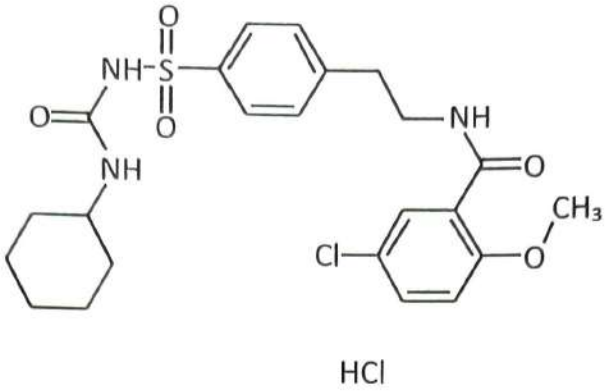
Brand Name: Glycomet, Glyciphage, Mefinda, Obimet, Xmet

GLIBENCLAMIDE

Formula: $C_{23}H_{28}ClN_3O_5S$

Molar Mass: 494.00

Structure:



IUPAC Name: 5-chloro-*N*-[2-[4-(cyclohexylcarbamoylsulfamoyl) phenyl] ethyl]-2-methoxybenzamide; hydrochloride

Properties: White crystalline odourless powder, slightly soluble in water. MP 169 to 170°C.

Storage: Store in well closed container protected from moisture.

Uses: It is used in non-insulin dependent diabetes mellitus.

Official Preparations: Glibenclamide tablet IP.

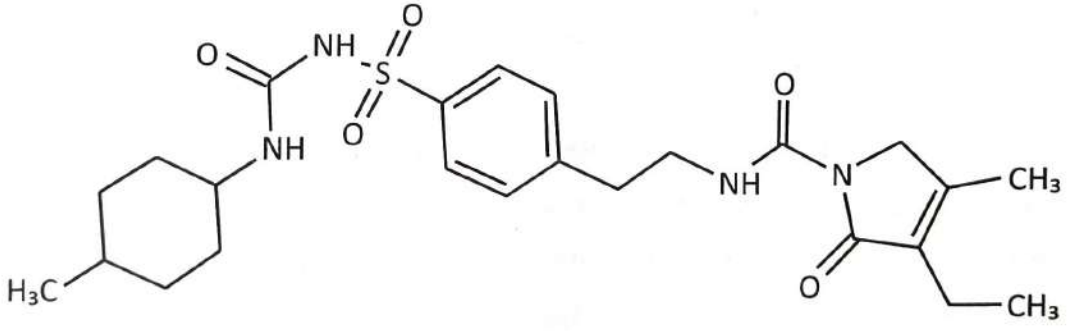
Brand Name: Daonil M, Diabetrol (5+500), Dutrol, Glinil-M, Sugatrol.

GLIMEPIRIDE

Formula: $C_{24}H_{34}N_4O_5S$

Molar Mass: 490.62

Structure:



IUPAC Name: 4-ethyl-3-methyl-*N*-[2-[4-[(4-methylcyclohexyl) carbamoyl -sulfamoyl] phenyl] ethyl]-5-oxo-2*H*-pyrrole-1-carboxamide

Properties: White crystalline odourless powder, insoluble in water, MP 207°C.

Storage: Store in well closed container protected from moisture.

Uses: It is used in non-insulin dependent diabetes mellitus.

Official Preparations: Glimepiride tablet IP

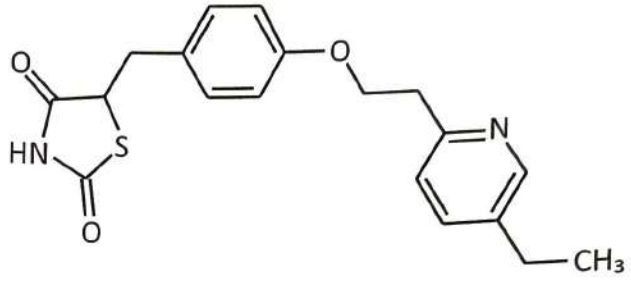
Brand Name: Glimpid, Glimser, Diapride, Prides, Ziglim

PIOGLITAZONE

Formula: $C_{19}H_{20}N_2O_3S$

Molar Mass: 356.44

Structure:



IUPAC Name: (RS)-5-(4-[2-(5-ethylpyridin-2-yl) ethoxy] benzyl) thiazolidine-2,4-dione

Properties: White crystalline odourless powder, insoluble in water, MP 183 to 184°C

Storage: Store in well closed container protected from moisture.

Uses: It is used in non-insulin dependent diabetes mellitus.

Official Preparations: Pioglitazone tablet IP.

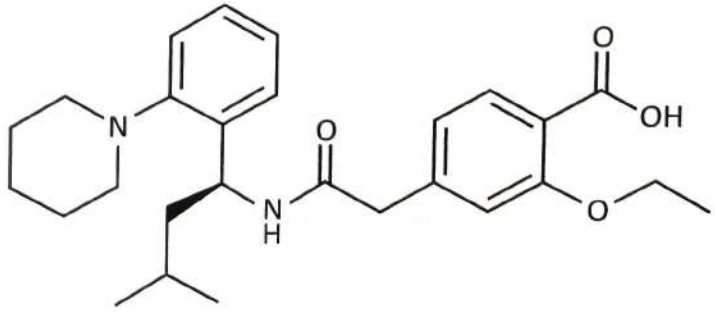
Brand Name: Diavista, Glito, Pio, Piolem, Pioz, Zipio.

REPAGLINIDE

Formula: $C_{27}H_{36}N_2O_4$

Molar Mass: 452.595

Structure:



IUPAC Name: 2-ethoxy-4-[2-(3-methyl-1-[2-(piperidin-1-yl) phenyl] butylamino)-2-oxoethyl] benzoic acid

Properties: Solid, MP 130-131°C.

Storage: Store in well closed container protected from moisture.

Uses: It is used in non-insulin dependent diabetes mellitus.

Official Preparations: Repaglinide tablet IP.

Brand Name: Eurepa, Novonorm, Regan.

GLIFLOZINS

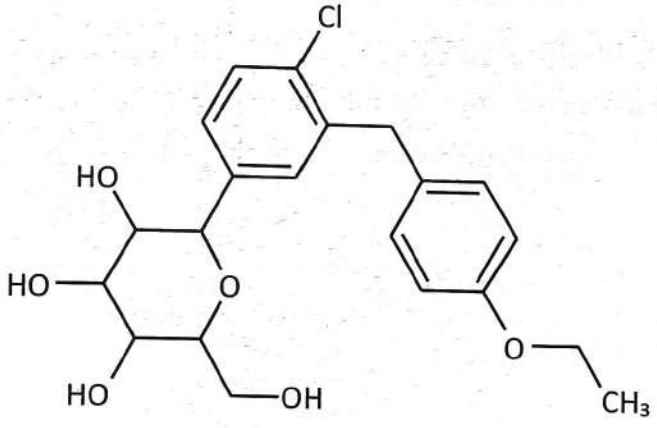
DAPAGLIFLOZIN

Formula: $C_{21}H_{25}ClO_6$

Molar Mass: 408.88

It is a sodium-glucose cotransporter 2 inhibitor indicated for managing diabetes mellitus type 2. When combined with diet and exercise in adults, dapagliflozin helps to improve glycemic control by inhibiting glucose resorption.

Structure:



IUPAC Name: (2*S*,3*R*,4*R*,5*S*,6*R*)-2-[4-chloro-3-[(4-ethoxyphenyl) methyl] phenyl]-6-(hydroxymethyl) oxane-3,4,5-triol

Storage: Store in well closed container protected from moisture.

Official Preparation: Dapagliflozin tablet.

Uses:

- It is used in non-insulin dependent diabetes mellitus.
- It is also used to treat adults with certain kinds of heart failure and chronic kidney disease.

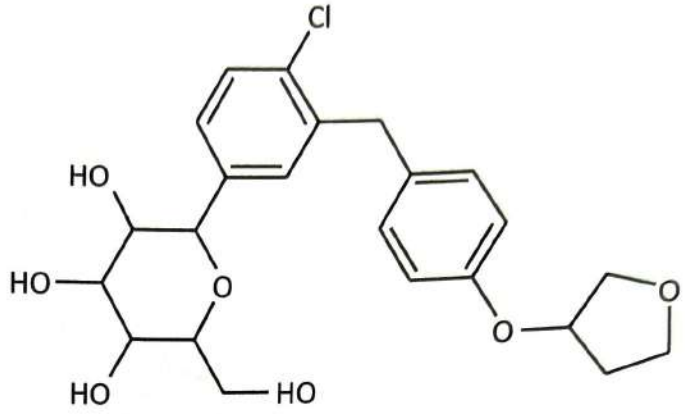
Brand Name: Farxiga, Zanella, Dapalex

EMPAGLIFLOZIN

Formula: $C_{23}H_{27}ClO_7$

Molar mass: 450.91

Structure:



IUPAC Name: 2-[4-Chloro-3-[[4-[(3S)-oxolan-3-yl] oxyphenyl] methyl] phenyl]-6-(hydroxymethyl) oxane-3,4,5-triol

Storage: Store in well closed container protected from moisture.

Official Preparation: Empagliflozin tablet.

Uses: It is used in non-insulin dependent diabetes mellitus.

Brand Name: Jardiance, Gibtulio.

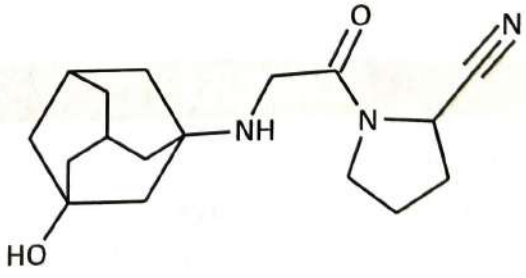
GLIPTINS

VILDAGLIPTIN

Formula: $C_{17}H_{25}N_3O_2$

Molar Mass: 303.406

Structure:



IUPAC Name: 1-[N-(3-Hydroxy-1-adamantyl) glycyl] pyrrolidine-2-carbonitrile

Storage: Store in well closed container protected from moisture.

Uses: It is an oral anti-hyperglycaemic agent (anti-diabetic drug).

Official Preparation: Vildagliptin tablet.

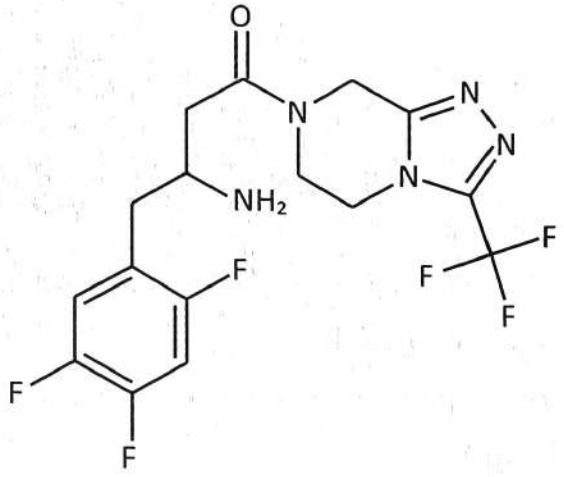
Brand Name: Galvus, Vidaglo, Vildapride.

SITAGLIPTIN

Formula: $C_{16}H_{15}F_6N_5O$

Molar Mass: 407.320

Structure:



IUPAC Name: 3-amino-1-[3-(trifluoromethyl)-6,8-dihydro-5*H*- [1,2,4] triazolo[4,3-a] pyrazin-7-yl]-4-(2,4,5-trifluorophenyl) butan-1-one

Properties: White to off-white crystalline, non-hygroscopic powder. Soluble in water.

Storage: Store in well closed container protected from moisture.

Uses: It is an oral anti-hyperglycaemic agent (anti-diabetic drug).

Official Preparation: Sitagliptin tablet.

Brand Name: Januvia, Glipisit M, Siliptin M.

EXERCISE

Short Answer Type Questions

1. **Give two Brand Names of following drugs:**

   (a) Metformin
   (b) Glibenclamide
   (c) Glimepiride
   (d) Pioglitazone

(e) Repaglinide (f) vildagliptins
(g) Dapagliflozin

2. In what dosage form the following drugs are given:
(a) Metformin (b) Glibenclamide
(c) Glimepiride

3. Give uses of following drugs:
(a) Metformin (b) Glibenclamide
(c) Glimepiride

4. Write structure and give chemical name of following drugs.
(a) Metformin (b) Glibenclamide

5. Name the drug present in following brands:
(a) Galvus (b) Glycomet
(c) Glimpid (d) Piolem
(e) Regan

Long Answer Type Questions

1. Classify Hypoglycaemic Agents with examples.
2. Write structure, give chemical name, properties and uses of Metformin.
3. Write structure, give chemical name, properties and uses of Glibenclamide.
4. Give properties and uses of Repaglinide & vildagliptin.
5. Give properties and uses of Glimepiride & Pioglitazone.

Multiple Choice Questions (MCQ's)

1. Find Rapid-acting insulins from following:
(a) Insulin aspart (b) Insulin glulisine
(c) Insulin glulisine (d) All of the above

2. Insulin isophane is:
(a) Intermediate-acting insulin (b) Rapid-acting insulins
(c) Long-acting insulins (d) None of the above

3. Find Long-acting insulins from following:
(a) Insulin degludec (b) Insulin detemir
(c) Insulin glargine (d) All of the above

4. Metformin is classified under:

(a) Biguanide
(b) Sulfonylureas
(c) Meglitinides
(d) None of the above

5. Find Sulfonylureas drug from following:

(a) Glimepiride
(b) Metformin
(c) Nateglinide
(d) Repaglinide

6. Repaglinide is classified under:

(a) Biguanide
(b) Sulfonylureas
(c) Meglitinides
(d) None of the above

7. Which antidiabetic drug is also used in treatment of polycystic ovary syndrome?

(a) Glimepiride
(b) Metformin
(c) Nateglinide
(d) Repaglinide

8. Insulin Dependent Diabetes Mellitusis also called as:

(a) Type-1 DM
(b) Type-2 DM
(c) Both (a) & (b)
(d) None of the above

9. What is the name of basic ring present in vildagliptine?

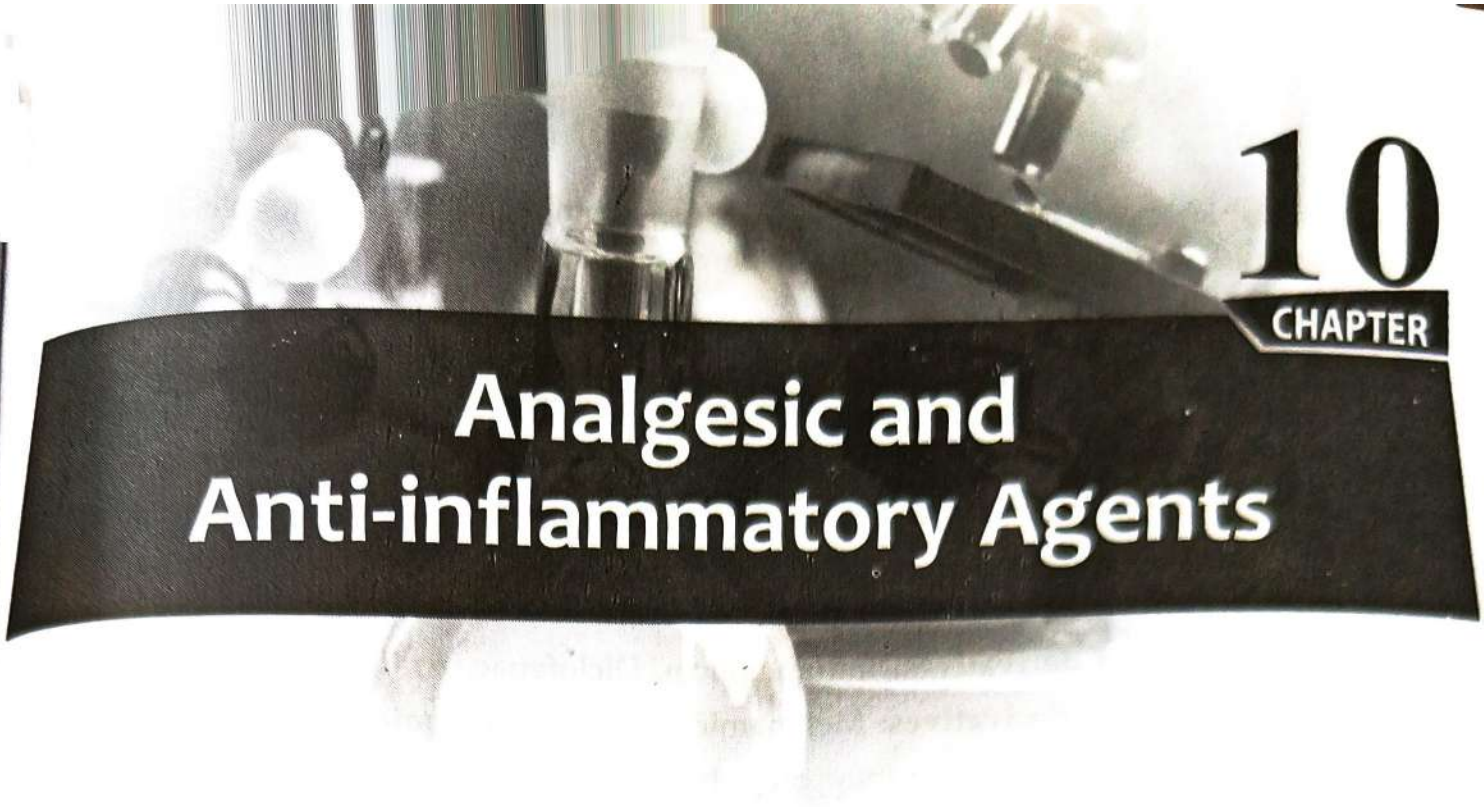
(a) Pyrrolidine
(b) Pyrazine
(c) Pyridine
(d) Pyrimidine

10. Which heterocyclic ring present in the structure of Repaglinide?

(a) Piperidin
(b) Pyrrolidine
(c) Pyrazine
(d) Pyridine

ANSWERS OF MULTIPLE CHOICE QUESTIONS (MCQ'S)

1. (d)	2. (a)	3. (d)	4. (a)	5. (a)	6. (c)	7. (b)
8. (a)	9. (a)	10. (a)				



10

CHAPTER

Analgesic and Anti-inflammatory Agents

Narcotic (Opiate) analgesics are drugs which relieve pain by acting on CNS to elevate pain threshold. Some Non-steroidal Anti-inflammatory Drug (NSAID) agents are analgesic but along with anti-inflammatory action by acting peripheral nervous system. Many drugs are used to relieve analgesia but not analgesic agent such as general anaesthetic, local anaesthetic, antispasmodic agent and some steroidal agent.

The term narcotic, known as opioid which all compounds relate to opium is a natural occurred dark brown resinous material obtain from poppy (*Papaver somniferum*). Opiate alkaloid has two types; Phenanthrene derivatives and Benzoisoquinoline derivatives. Opium has been known from 1500 BC. Serturner, a pharmacist isolated the active principle of opium in 1806 and named it morphine.

It includes morphine, codeine, thebain, many synthetic and semisynthetic derivatives. Opiates analgesics are drugs which relieve pain and depression of CNS associated with drug dependence. A regular used of narcotic drug, it may become habit forming and physical dependence which may leads to withdrawal symptoms.

Anti-inflammatory agents are the chemical compound which used to treat inflammation. Inflammation is a common, defensive response to tissue injury caused by physical trauma, noxious chemicals or microbiological agents.

Antipyretics are the chemical agent which decreases body temperature up to the normal ranges. Analgesics agent is used to prevent from pain. Anti-inflammatory agents which used to prevent from inflammation caused by prostaglandin.

NSAIDs are related with a numeral of side effects. The occurrence of side effects varies according to the drugs; the most common side effects are Gastrointestinal Tract

(GIT) disturbances, such as nausea, diarrhoea, constipation, vomiting, decreased appetite and peptic ulcer.

CLASSIFICATION OF ANTI-INFLAMMATORY AGENT

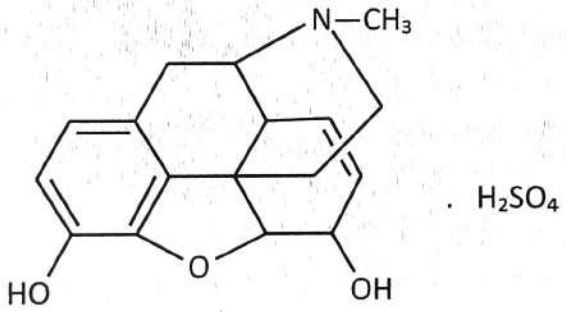
1. **Salicylic acid derivatives:** Sodium Salicylate, Aspirin, Difflunisal.
2. **P-Aminophenol derivatives:** Paracetamol, Phenacetin.
3. **3,5-Pyrazolidinediones derivatives:** Phenylbutazone, Sulfinpyrazone, Methamizole Sodium.
4. **Aryl acetic acid derivatives:** Indomethacin, Diclofenac, Amfenac.
5. **Anthranilic acid derivatives:** Mefenamic acid Meclofenamic acid.
6. **Propionic acid derivatives:** Ibuprofen, Naproxen, Ketoprofen.
7. **Selective COX-II inhibitors:** Celecoxib, Valdecoxib.
8. **Oxicam derivatives:** Piroxicam, Miloxicam.
9. **Miscellaneous agent:** Nimesulide, Analgin, Nabumetone.

MORPHINE SULPHATE

Molecular Formula: $C_{34}H_{40}N_2O_{10}S$

Molecular Weight: 668.8

Structure:



IUPAC Name: 4,5- Epoxy-7,8-didehydro-3,6-diol-17-methyl morphinan sulphate

Properties:

- It is white or colourless silky needle powder.
- It is soluble in water, slightly soluble in ethanol and insoluble in toluene.

Storage: It is store in well closed container, protect from light.

Uses: It is used as potent analgesic, suppression of cough, antianxiety and antidiarrheal.

Official Preparations: Morphine Sulphate Injection (USP) is intended for intravenous administration. Morphine Sulphate extended release tablet, Morphine Sulphate injection (IP), Morphine Sulphate oral solution.

Brand Name: Udidyne, Oramorph

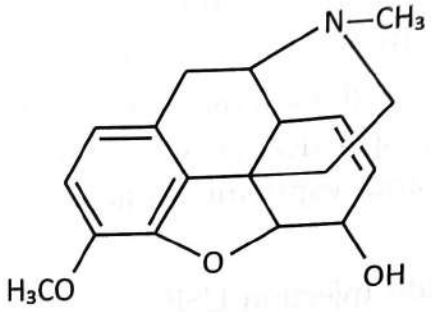
CODEINE

Synonym: N-Methylmorphine

Formula: $C_{18}H_{21}NO_3$

Molar Mass: 299.3

Structure:



IUPAC Name: 4,5- Epoxy-7,8-didehydro-3-methoxy-6-ol-N-methyl morphinan

Properties: It is colourless or white crystalline powder, soluble in boiling water, Sublimes at 154-156°C. Odourless. Bitter taste.

Storage: It stored in well closed container protected from light.

Uses:

- It is used in treatment of mild to moderate pain.
- It is also used in the treatment of cough.

Official Preparations:

- Codeine Phosphate Tablets BP
- Codeine Phosphate Hemihydrate BP

Brand Name: Apidin, Codopyrin, Codopyrin

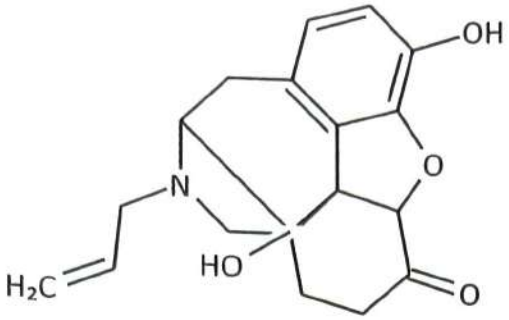
NARCOTIC ANTAGONISTS

NALOXONE

Formula: $C1_9H_{21}NO_4$

Molar Mass: 327.380

Structure:



IUPAC Name: (4R,4aS,7aR,12bS)-4a,9-dihydroxy-3-(prop-2-en-1-yl)-2,3,4,4a,5,6-hexahydro-1H-4,12-methano [1] benzofurano[3,2-e] isoquinolin-7(7aH)-one

Properties: Solid crystalline compound with melting point 200-205°C. Soluble in water, dilute acids, strong alkali; slightly soluble in alcohol.

Use: It is a drug used to counter the effects of opioid overdose, for example heroin or morphine overdose. Naloxone is specifically used to counteract life-threatening depression. of the central nervous system and respiratory system.

Official Preparations:

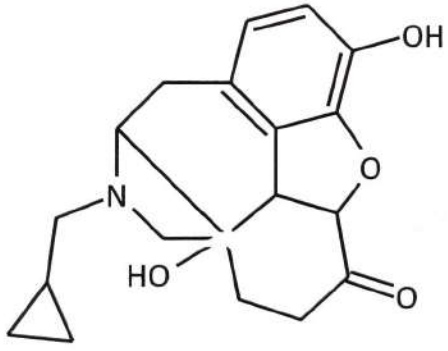
- Naloxone Hydrochloride Injection USP
- Naloxone Hydrochloride Injection IP
- Naloxone Hydrochloride Injection BP

Brand Name: Nalox, Narcotan, Narcotan, Nex 400

NALTREXONE

Formula: $C_{20}H_{23}NO_4$

Molar Mass: 341.407



IUPAC Name: 3-(cyclopropylmethyl)-4a,9-dihydroxy-2,4,5,6,7a,13-hexahydro-1H-4,12-methanobenzofuro[3,2-e] isoquinoline-7-on

Use: It is an opioid receptor antagonist used primarily in the management of alcohol dependence and opioid dependence. It is marketed in generic form as its hydrochloride salt, naltrexone hydrochloride.

Properties: Solid, melting point 168-170°C

Official Preparation: Naltrexone Hydrochloride Tablets USP

Storage: Do not expose the product to temperatures above 25°C

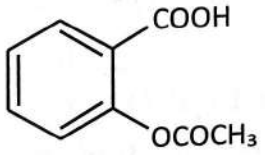
Brand Name: Nalcon, Naltima, Naltrex, Nodict

ASPIRIN

Formula: $C_9H_8O_4$

Molar Mass: 180.16

Structure:



IUPAC Name: *O*-Acetyl salicylic acid

Properties: It is white crystalline colourless powder; it is slightly soluble in water. It is easily hydrolysed by moisture to form acetic acid and salicylic acid, hence kept in air tight container.

Uses:

- It is used as analgesic, antipyretic and anti-inflammatory agent.
- It is also used as antiplatelet agent and in chronic rheumatoid arthritis.

Storage: It stored in well closed container protected from light, kept in cool and dry place

Official Preparations:

- Aspirin tablet BP
- Aspirin tablet BP
- Paediatric dispersible Aspirin tablet BP

Brand Name: Asalite, Ascad, Colsprin, Cotaspirin, CV-Sprin, ispersible, Dispirin, Nusprin, OD Prin.

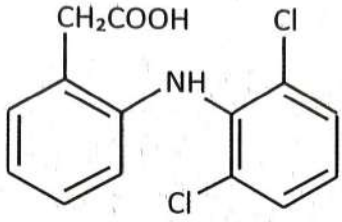
DICLOFENAC

Diclofenac is a commonly used Non-Steroidal Anti-Inflammatory Drug (NSAID) used for the therapy of chronic forms of arthritis and mild-to-moderate acute pain.

Formula: $C_{14}H_{11}Cl_2NO_2$

Molar Mass: 296.15

Structure:



IUPAC Name: {2-[(2,6-dichlorophenyl) amino] phenyl} acetic acid.

Properties: Solid, white Crystals; MP 283-285°C.

Uses: It is used in Ankylosing Spondylitis, Dysmenorrhea, Migraine, Osteoarthritis, Pain

Official Preparations: Diclofenac gel B.P. Diclofenac sodium injection (IP), Diclofenac sodium tablet (IP), Diclofenac sodium gastro-resistant tablet (IP)

Brand Name: Doflex, Fenak, Dicloact, Volini Tab, Diclomax, Diclonac, Dairo.

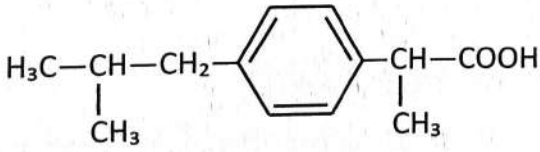
IBUPROFEN

Ibuprofen is a regularly used NSAID which is accessible both by prescription and over-the-counter. Ibuprofen is considered to be amongst the safest NSAIDs and is usually well tolerated

Formula: $C1_3H_{18}O_2$

Molar Mass: 206.285

Structure:



IUPAC Name: 2(*p*-Isobutyl phenyl) propionic acid.

Properties: Colourless, crystalline stable solid, Characteristic odour, MP 75-77.5°C, very soluble in alcohol.

Official Preparations:

- Ibuprofen Tablets BP
- Ibuprofen Tablets IP
- Ibuprofen Orodispersible Tablets BP
- Ibuprofen Oral Suspension BP
- Ibuprofen Tablets USP

Brand Name: Ibucon, Ibugesic, Ibulite, Myofen, Tricofen, Brufen, Sugafen Forte.

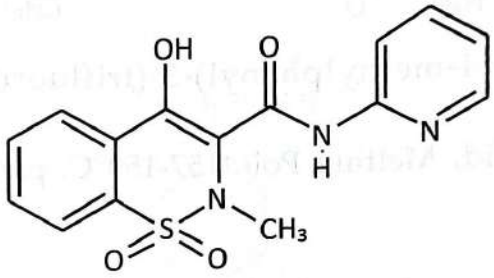
PIROXICAM

Piroxicam is a commonly used Non-Steroidal Anti-inflammatory Drug (NSAID) that is used in therapy of chronic arthritis.

Formula: $C_{15}H_{13}N_3O_4S$

Molar Mass: 331.35

Structure:



IUPAC Name: 4-Hydroxy-2-methyl-*N*-(pyridin-2-yl)-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide

Properties: White crystalline solid, sparingly soluble in water, dilute acid and most organic solvents. It is slightly soluble in alcohol, MP 198-200°C.

Uses: Piroxicam is used to relieve pain, tenderness, swelling and stiffness caused by osteoarthritis.

Official Preparations:

- Piroxicam Capsules USP
- Piroxicam sublingual tablets

Brand Name: Toldin, Dolonex, Dolcam DT, Mobicam DT, Cycladol, Pirox, Dolonex, Dolonex-DT, Pyrodex.

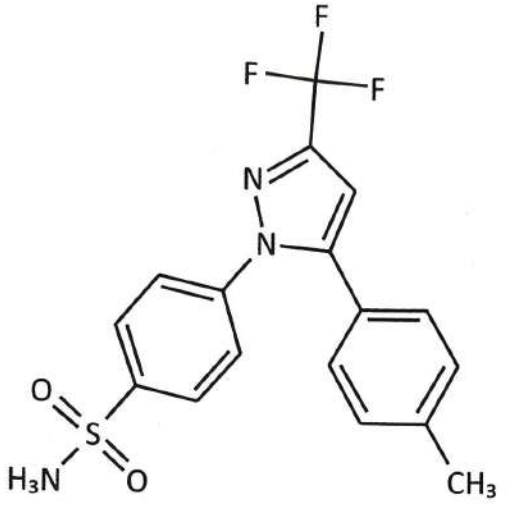
CELECOXIB

Celecoxib is a Non-Steroidal Anti-inflammatory Drug (NSAID) with selectively for inhibition of cycloxgenase-2 (Cox-2), which is widely used in the therapy of arthritis.

Molecular Formula: $C_{17}H_{14}F_3N_3O_2S$

Molecular Weight: 381.4

Structure:



IUPAC Name: 4-[5-(4-methylphenyl)-3-(trifluoromethyl) pyrazol-1-yl] benzenesulfonamide

Properties: Pale yellow solid, Melting Point157-159°C, poorly soluble in water, pKa-11.1.

Uses:

- It is used in the therapy of arthritis.
- It helps to relieve pain, tenderness, swelling and stiffness.

Official Preparations: Celecoxib Capsules.

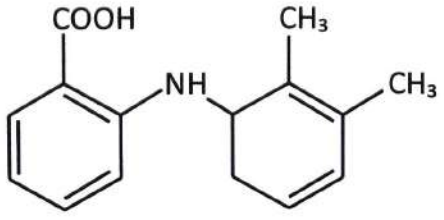
Brand Name: Celedol, Celact MD, Cobix.

MEFENAMIC ACID

Formula: $C_{15}H_{15}NO_2$

Molar Mass: 241.29

Structure:



IUPAC Name: 2-[(2,3-Dimethylcyclohexa-2,4-dien-1-yl) amino] benzoic acid

Properties: It is greyish or white crystalline powder. It is practically insoluble in water and easily absorb in GIT.

Uses: It is primary analgesic property rather than anti-inflammatory. It is used to reprieve mild to moderate pain.

Official Preparations:

- Mefenamic Acid tablets
- Mefenamic Acid Oral suspension

Brand Name: Abdrot-Plus, Dysmen, Dysmen Forte, Flexiwin-MF, Gefplus, Lenagesic, Mefac, Mefacid

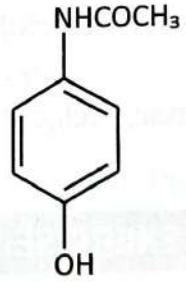
PARACETAMOL

Synonym: Acetaminophen

Formula: $C_8H_9NO_2$

Molar Mass: 151.165

Structure:



IUPAC Name: *N*-(4-hydroxyphenyl) acetamide

Properties: White crystalline powder, odourless with bitter taste, sparingly soluble in water

Storage: It should be stored in tightly closed container, protected from light.

Uses: It is analgesic and antipyretic agent.

Official Preparations:

- Paracetamol tablet BP
- Paracetamol tablet IP
- Paediatric paracetamol elixir BP

Brand Names: Algina, Cipmol, Malidens, Parafast, Paracip, Doliza, Cipflam, Fepanil, Dolo

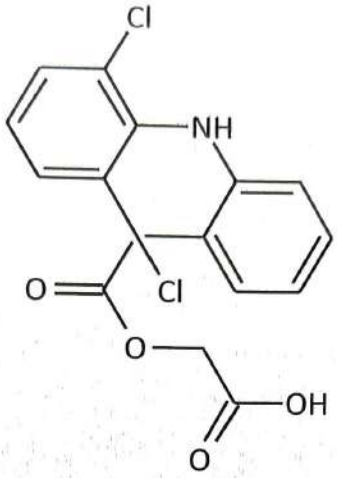
ACECLOFENAC

Aceclofenac is a monocarboxylic acid that is the carboxymethyl ester of diclofenac.

Molecular Formula: $C_{16}H_{13}C_{12}NO_4$

Molecular Weight 354.2

Structure:



IUPAC Name: 2-[2-[2-(2,6-dichloroanilino) phenyl] acetyl] oxyacetic acid

Properties: White colour, Melting Point 149-153, Insoluble in water

Official Preparations: Aceclofenac tablet, Aceclofenac Paracetamol tablet, Aceclofenac sustained release tablet.

Brand Names: Voltanec, Afenak, Eclonac, Aclocta, Achenil, Niplonac, Acenext, Moviz

EXERCISE

Short Answer Type Questions

1. **Give two brand names of following drugs:**
   (a) Aspirin (b) Diclofenac
   (c) Ibuprofen (d) Piroxicam
   (e) Paracetamol
2. **In what dosage form the following drugs are given:**
   (a) Paracetamol (b) Diclofenac
   (c) Aspirin (d) Ibuprofen
3. **Give uses of following drugs:**
   (a) Naltrexone (b) Paracetamol
   (c) Diclofenac (d) Aspirin
   (e) Ibuprofen

4. **Write structure and give chemical name of following drugs:**
   (a) Aspirin
   (b) Ibuprofen
   (c) Paracetamol
5. **Name the drug present in following brands:**
   (a) Nalox
   (b) Naltrex
   (c) Colsprin
   (d) Diclomax
   (e) Ibugesic
   (f) Dolonex

Long Answer Type Questions

1. Classify Nonsteroidal Inflammatory Agents with examples.
2. **Write structure, give chemical name, properties and uses of:**
   (a) Aspirin
   (b) Ibuprofen
   (c) Paracetamol
3. **Give properties and uses of:**
   (a) Morphine and codeine
   (b) Aspirin and Diclofenac
   (c) Ibuprofen and Piroxicam
   (d) Paracetamol and Aceclofenac

Multiple Choice Questions (MCQ's)

1. **Which one is Salicylic acid derivative?**
   (a) Aspirin
   (b) Diclofenac
   (c) Ibuprofen
   (d) Piroxicam
2. **Which one is P-Aminophenol derivative?**
   (a) Ibuprofen
   (b) Piroxicam
   (c) Paracetamol
   (d) Aspirin
3. **Which one is Aryl acetic acid derivative?**
   (a) Aspirin
   (c) Diclofenac
   (d) Ibuprofen
   (d) Piroxicam
4. **Which one is Anthranilic acid derivative?**
   (a) Aspirin
   (b) Diclofenac
   (c) Mefenamic acid
   (d) Piroxicam
5. **Which one is Propionic acid derivative?**
   (a) Aspirin
   (b) Diclofenac

(c) Ibuprofen (d) Piroxicam

6. Which one is Oxicam derivative?

(a) Aspirin (b) Diclofenac

(c) Ibuprofen (d) Piroxicam

7. This drug is also used in treatment of cough:

(a) Aspirin (b) Codeine

(c) Diclofenac (d) Ibuprofen

8. This drug used to counter the effects of opioid overdose:

(a) Diclofenac (b) Ibuprofen

(c) Piroxicam (d) Naloxone

9. This drug used in the management of alcohol dependence:

(a) Naltrexone (b) Ibuprofen

(c) Piroxicam (d) Naloxone

10. _____ is carboxymethyl ester of diclofenac

(a) Aceclofenac (c) Ibuprofen

(d) Piroxicam (d) Naloxone

ANSWERS OF MULTIPLE CHOICE QUESTIONS (MCQ'S)

1. (a) 2. (c) 3. (b) 4. (c) 5. (c) 6. (d) 7. (b)
8. (d) 9. (a) 10. (a)

CHAPTER 11

Anti-Infective Agent

Anti-infectives is a broad phrase that refers to any treatment that can stop an infectious organism from spreading or destroy it completely.

ANTIFUNGAL AGENT

Fungus is a parasite. The human fungi parasitic effect is mycotic illness; the majority involves invasion of skin or the mucous membrane of body orifice. Fungi have different shape and sizes. Some are large while others are minute parasitic and saprophytic cells. They differ from algae by lack of photosynthesis ability and from bacteria by greater size as well possesses of intracellular structure in nuclear membrane and mitochondria. In fungi included both yeasts and moulds.

Antifungal agents are used to treat mycotic infections such as ringworm, athlete's foot, candidiasis and serious systemic infections like cryptococcal meningitis. These agents are either fungicides or fungistatic.

Classifications

1. **Antifungal antibiotics:** Amphotericin B, Nystatin, Natamycin, Griseofulvin
2. **Azole derivatives:**
   (a) **Triazole:** Fluconazole, Itraconazole, Terconazole
   (b) **Imidazole:** Clotrimazole, Econazole, Butoconazole, Miconazole, Ketoconazole

3. **Pyrimidine derivatives:** Flucytosine
4. **Chitin Synthetase inhibitors:** Nikomycin Z
5. **Peptides:** Cispentacin
6. **Miscellaneous:** Tolnaftet, Naftifine

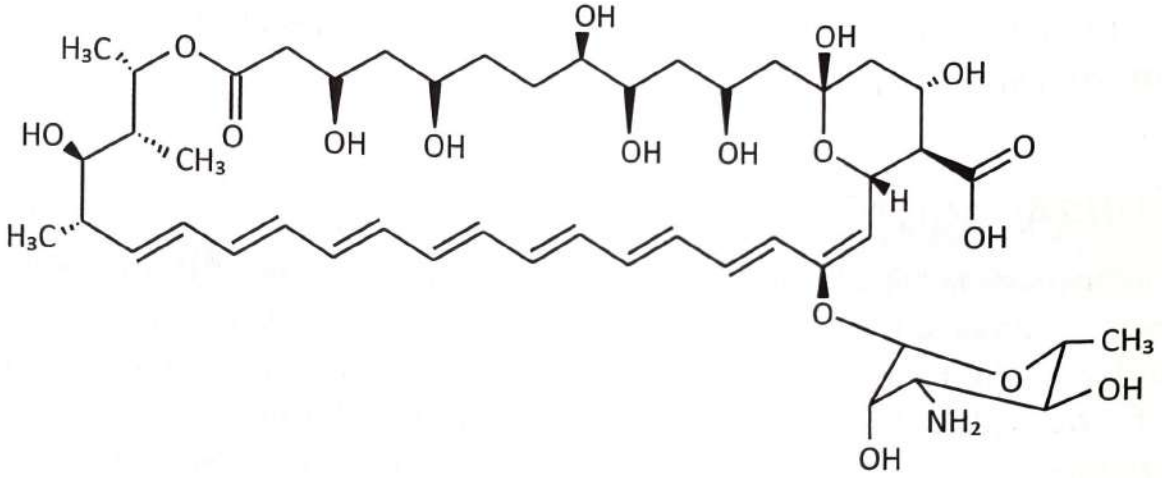
AMPHOTERICIN B

It is polyene antibiotic obtained from *Streptomyces nodosus*. It consists of 7 conjugated double bonds, an internal ester, a free carbonyl group and glycoside side chain with primary amine. The conjugated moiety is usually all *trans*-configuration. D-mycosamine is carbohydrate moiety.

Formula: $C_{47}H_{73}NO_{17}$

Molar Mass: 924.091

Structure:



IUPAC Name: 33- [(3-amino- 3,6-dideoxy- β-D-mannopyranosyl) oxy]- 1,3,5,6,9,11,17,37-octahydroxy- 15,16,18-trimethyl- 13-oxo- 14,39-dioxabicyclo nonatriaconta-19,21,23,25,27,29,31-heptaene- 36-carboxylic acid

Properties:

- It is an amphoteric in nature.
- It is yellow, odourless, tasteless powder insoluble in water.

Storage: Store in tightly closed light resistant container at 2 to 10°C.

Uses:

- It is primarily used as antifungal agent.
- It is drug of choice for invasive candidiasis, aspergillosis and zygomycosis.
- It is effective against life-threatening infection due to *Cryptococcus neoformans*.

Official Preparations:

- Amphotericin B cream
- Amphotericin B lotion
- Amphotericin B ointment
- Amphotericin B injection

Brand Name: Fungitericin, Amfocare, Amphocil, Amfotex, Fungisome, Mycol.

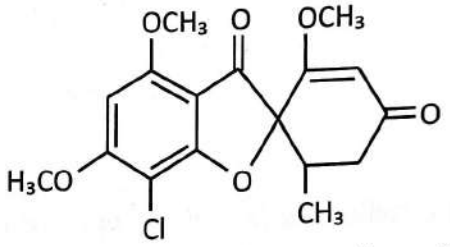
GRISEOFULVIN

It is isolated from Penicilliums Griseofulvin

Formula: $C1_7H_{17}ClO_6$

Molar Mass: 352.76

Structure:



7-chloro-2',4,6-trimethoxy-6'-methyl-3*H*,4'*H*-spiro[1-benzofuran-2,1'-cyclohex[2]ene]-3,4'-dione

Properties:

- It is white or yellowish white microfine powder.
- It is practically insoluble in water.
- It is freely soluble in DMF and tetrachloroethane.
- It is slightly soluble in ethanol and methanol.

Storage: Store in tightly closed container

Uses:

- It is used as fungistatic agent.
- It is effective against Epidermophyton, Microsporum and Trichophyton causes dermatophytid infections.
- It is highly effective in athlete's foot infections.

Official Preparations:

- Griseofulvin tablet.

Brand Name: Dermonorm, Grisomed, Grisoral, Idifulvin, Walavin.

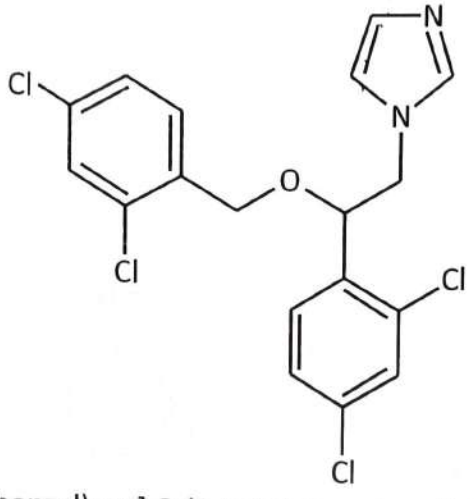
MICONAZOLE

Miconazole is a broad-spectrum azole antifungal agent.

Formula: $C_{18}H_{14}Cl_4N_2O$

Molar Mass: 416.127

Sructure:



1-{2-[(2,4-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl}-1*H*-imidazole

Properties: Crystalline white Solid, the solubilities of miconazole nitrate powder are 0.03% in water, 0.76% in ethanol and up to 4% in acetic acid, MP 170°C.

Storage: Store in tightly closed container, protected from moisture and light.

Uses: It is antifungal agent used in against coccidioidomycosis, cryptococcosis.

Official Preparations:

- Miconazole cream IP
- Miconazole powder
- Miconazole tablets

Brand Name: Mycorid Skin, Candistat, Fungiderm, Micogel, Micoptic, Micozole.

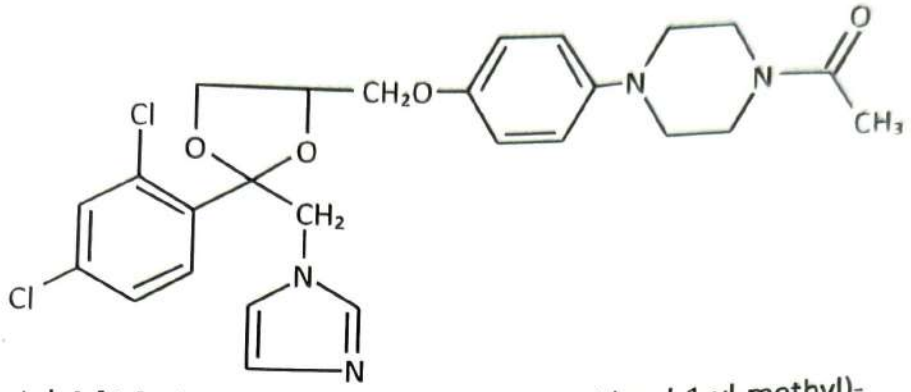
KETOCONAZOLE

t is a racemate consisting of equimolar amounts of (2R, 4S)- and (2S,4R)-ketoconazole vith the chiral centres on the acetal ring.

ormula: $C_{26}H_{28}Cl_2N_4O_4$

olar Mass: 531.43

Structure:



1-Acetyl-4-[4-[2-(2,4-dichlorophenyl)-2-(1-H-imidazol-1-yl-methyl)-1,3-dioxalan-4-yl-methoxy]phenyl]-piperazine

Properties: Colourless crystals or powder, water insoluble, MP148-152°C.

Storage: Store in tightly closed container, protected from moisture.

Uses: It is used for the treatment of the systemic fungal infections- such as tinea, cutaneous candidiasis, pityriasis versicolor, dandruff and seborrheic dermatitis.

Official Preparations:

- Ketoconazole tablets IP
- Ketoconazole lotion
- Ketoconazole shampoo
- Ketoconazole cream

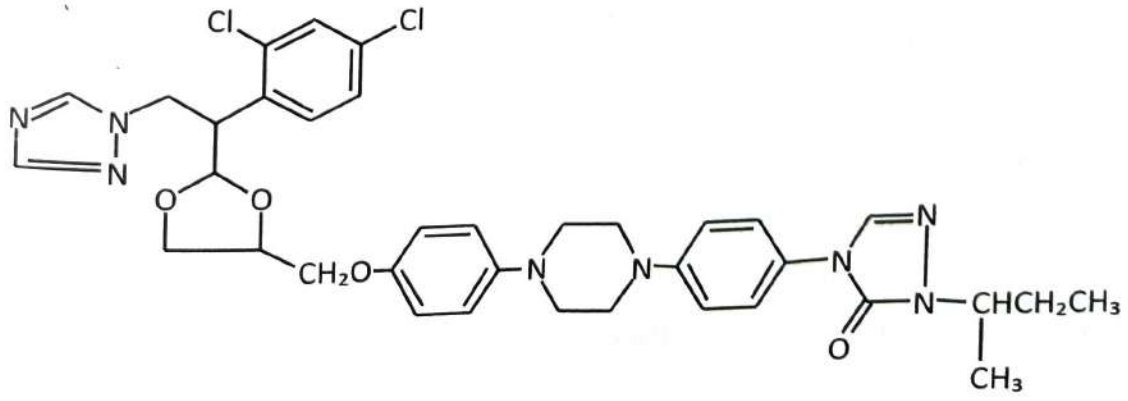
Brand Name: Danrof, Nizral, Funazole, Danclear, Ocona -CT.

ITRACONAZOLE

Molecular Formula: $C_{35}H_{38}Cl_2N_8O_4$

Molecular Weight: 705.6

Structure:



-[4-[4-[2-(2,4-Dichlorophenyl)-2-1H-1,2,4-triazole-1-yl-methyl]-1,3-dioxalan-4-yl]
]phenyl}-2,4-dihydro-2-(1-methylpropyl)-3H-1,2,4-triazole-3-one

Properties: Solid, practically insoluble in water and dilute acidic solutions, MP. 166°C.

Storage: Store in tightly closed container, protected from moisture

Uses: It is used against histoplasmosis, blastomycosis, cryptococcal meningitis & aspergillosis.

Official Preparations:

- Itraconazole capsule BP
- Itraconazole oral suspension BP

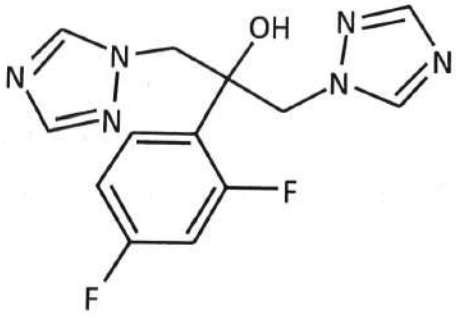
Brand Name: Candiloss, Itracross, Icoz, Itral

FLUCONAZOLE

Formula: $C_{13}H_{12}F_2N_6O$

Molar Mass: 306.277 g·mol⁻1

Structure:



IUPAC Name: 2-(2,4-difluorophenyl)-1,3-bis(1,2,4-triazol-1-yl) propan-2-ol

Properties: Solid, White crystalline powder, Melting Point: 138-140°C.

Storage: Store in tightly closed container, protected from moisture.

Uses: It is used in treatment of fungal infections like-candidiasis, blastomycosis, occidioidomycosis, cryptococcosis, histoplasmosis, dermatophytosis and pityriasis ersicolor.

fficial Preparations:

- Fluconazole tablet IP
- Fluconazole capsule IP
- Fluconazole oral suspension IP

nd Name: Genflu, futiza, fungis, fucon, flutican, aflucoz

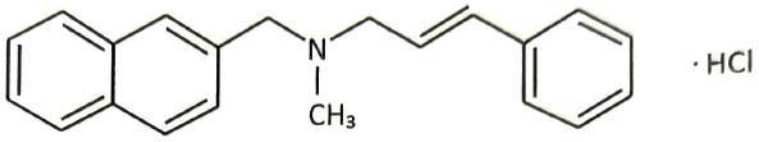
NAFTIFINE HYDROCHLORIDE

Naftifine is a topical broad-spectrum antifungal agent.

Formula: $C_{21}H_{21}N$

Molar Mass: 287.406

Structure:



(2*E*)-*N*-methyl-*N*-(naphthalen-2-ylmethyl)-3-phenylprop-2-en-1-amine-hydrochloride

Properties: White crystalline powder, soluble in ethanol.

Storage: Store in tightly closed container, protected from moisture and light.

Uses: It is antifungal agent.

Official Preparations:

- Naftifine cream
- Naftifine gel

Brand Name: Naftin Gel

URINARY TRACT ANTI-INFECTIVE AGENTS

A Urinary Tract Infection (UTI) is an infection that affects division of the urinary tract. Lower urinary tract infection symptoms include urination pain, excessive urination and the need to urinate notwithstanding of having an unfilled bladder. Flank pain and fever and are common signs of a kidney infection, along with the indications of a lower UTI. Urine may occasionally seem bloody. Symptoms in the elderly and young can be vague or non-specific.

E. coli is the general cause of illness, however other bacteria or fungus can also cause infection.

In a given year, almost 150 million people get a urinary tract infection. Women are more likely to have them than males. They seem to be the most common bacterial infection in women.

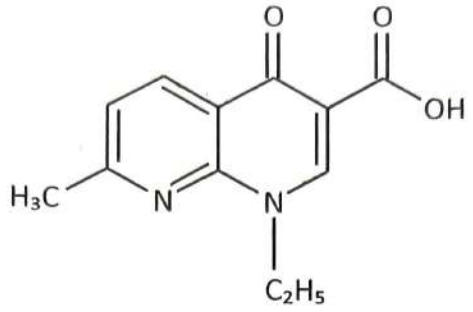
Urinary tract anti-infective agents inhibit growth of many species of bacteria. They are concentrated in the renal tubules so they are used to treat infections of the urinary tract. Examples include nitrofurantoin, nalidixic acid, oxolinic acid, resoxacin, norfloxacin and methenamine. Several other 4-quinolones such as ciprofloxacin, amifloxacin, enoxacin etc.

NALIDIXIC ACID

Formula: $C_{12}H_{12}N_2O_3$

Molar Mass: 232.239

Structure:



1-Ethyl-7-methyl-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid

Properties: It is white or pale-yellow powder, insoluble in water.

Storage: Store in well closed container.

Uses:

- It is effective against gram negative bacteria.
- It is empiric treatment of uncomplicated cystitis.

Official preparation: Nalidixic acid tablet (BP), Nalidixic acid oral suspension, Nalidixic acid syrup.

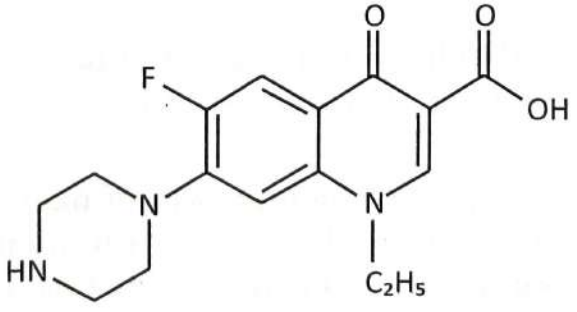
Brand Name: Nal-P, Negadix, Negadix KT, Negamet, Ulix-250.

NORFLOXACIN

Formula: $C_{16}H_{18}FN_3O_3$

Molar Mass: 319.336

Structure:



1-Ethyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid

Properties: It is a white to pale yellow crystalline odourless, bitter powder.

Storage: Store in well closed container protected from light and moisture.

Uses:

- It is active against urinary tract infection.
- It is also used in bacterial diarrhoea.

Official Preparations:

- Norfloxacin eye drop IP.
- Norfloxacin tablets IP.

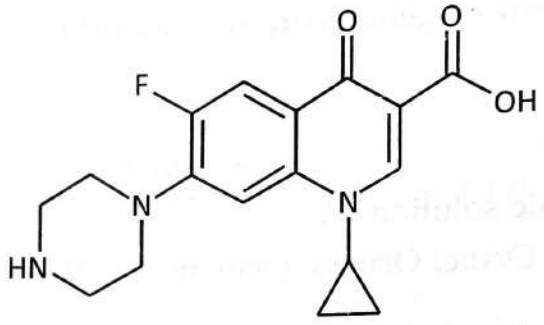
Brand Name: Norbactin, Norbactin Eye, Norbid, Norbid, Norilet, Norspan.

CIPROFLOXACIN

Formula: $C_{17}H_{18}FN_3O_3$

Molar Mass: 331.347

Structure:



1-Cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid

Properties: It is white -pale yellow crystalline powder, insoluble in water and slightly soluble in ethanol.

Storage: Store in well closed container protected from light.

Uses:

- It is effective against gram negative bacteria which cause UTI.
- Ciprofloxacin eye drop is indicated for bacterial corneal ulcers and conjunctivitis.

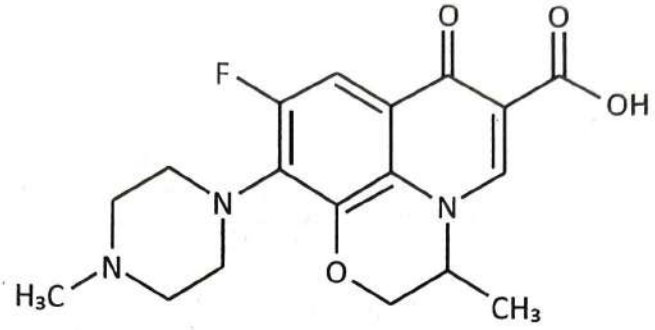
Official Preparations:

- Ciprofloxacin eye drop IP
- Ciprofloxacin tablets IP
- Ciprofloxacin injection IP

Brand Name: Cifran, Ciplo, Ciplox– Od, Ciprind, Ciprobid

OFLOXACIN

Formula: $C_{18}H_{20}FN_3O_4$
Molar Mass: 361.373
Structure:



9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7*H*-[1,4]oxazino [2,3,4-*ij*]quinoline-6-carboxylic acid

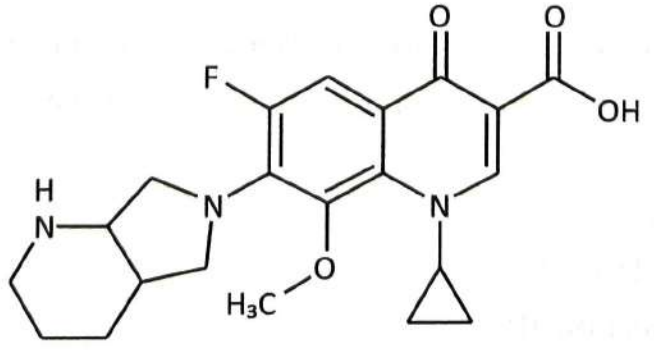
Properties: It is a pale-yellow crystalline compound, it is slightly soluble in water.
Storage: Store in well closed container protected from light and moisture.
Uses: It is used in treatment of genitourinary, respiratory, gastrointestinal, skin and gonorrhoea infections.
Official Preparations:

- Ofloxacin tablets IP.
- Ofloxacin ophthalmic solution IP.
- Ofloxacin oral suspension IP.

Brand Name: Ocin Syrup, Ocinc, Ocucin, Oculone, Odiff, Of - W (200 mg).

MOXIFLOXACIN

Formula: $C_{21}H_{24}FN_3O_4$
Molar Mass: 401.438
Structure:



7-[(4aS,7aS)-1,2,3,4,4a,5,7,7a-octahydropyrrolo[3,4-b]pyridin-6-yl]-1-cyclopropyl-6-fluoro-8-methoxy-4-oxoquinoline-3-carboxylic acid

Properties: It is almost white to yellowish crystalline powder. It is Soluble in water, Methanol, DMSO.

Storage: Store in well closed container protected from light and moisture.

Uses:

- It is effective against sinus and lung infections.
- It is used in treatment of pneumonia.

Official Preparations: Moxifloxacin ophthalmic solution IP.

Brand Name: Mosi (0.5%w/v), Moxflox, Moxibel, Moxicip.

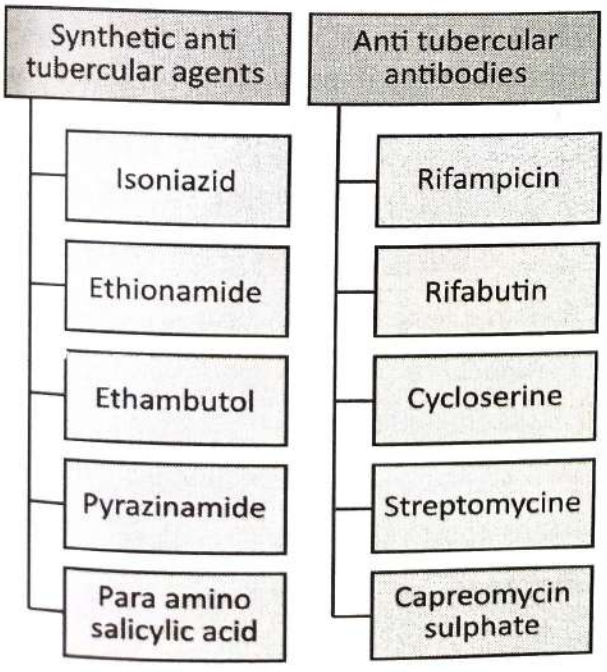
ANTITUBERCULAR AGENTS

These are agents which used to treat Tuberculosis (TB). The tuberculosis is an infectious disease which caused by mycobacterium tubercular bacteria. It is generally affected lungs, but also other part of the body. It involves two forms of TB diseases such as latent and active forms. In latent TB have an infection in body but they don't spread due to immune system. Active TB have an infection multiplies and causes a sick. They are contagious. Common infection sites of tuberculosis are lungs, brain, bone, liver and kidney.

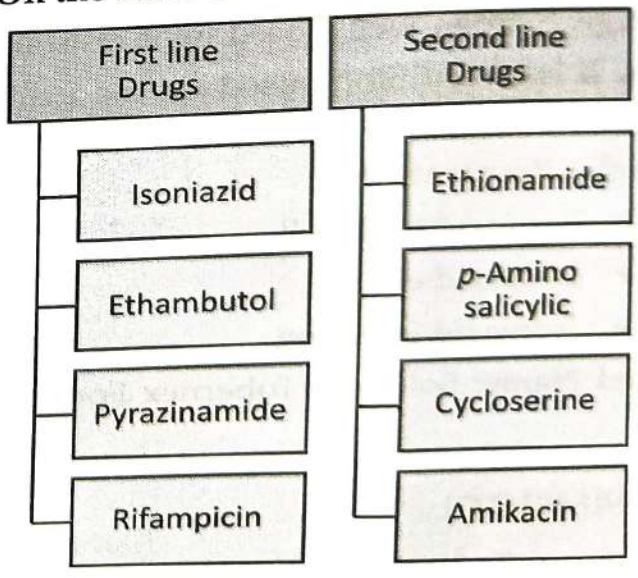
Classification

On the basis of treatment of tuberculosis are divided into two major parts:

1. On the basic of sources:



2. On the basis of treatment of tuberculosis:



On the basis of Chemical structure:

(i) p-amino salicylic acid derivative, e.g., PAS
(ii) Pyridine derivatives, e.g., Isoniazid, Ethionamide
(iii) Pyrazine derivatives, e.g., Pyrazinamide
(iv) Ethylene diamine derivatives, e.g., Ethambutol
(v) Antibiotics, e.g., Cycloserine, Streptomycin, Rifampicin-

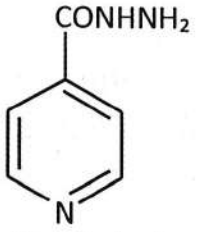
ISONIAZID (INH)

Synonym: Isonicotonic acid hydrate

Formula: $C_6H_7N_3O$

Molar Mass: 137.142

Structure:



Pyridine-4-carbohydrazide

Properties: It is colourless or white crystalline powder, odourless with sweet to bitter taste, soluble in water and sparingly soluble in alcohol.

Storage: Store in well closed light resistant container.

Uses: It is an antibiotic used for the treatment of tuberculosis, it may also be used for atypical types of mycobacteria, such as M. avium, M. kansasii and M. xenop.

Official Preparations:

- Isoniazid tablet IP
- Isoniazid elixir
- Isoniazid injection

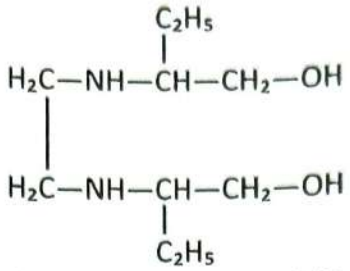
Brand Name: Solonex, Tubernex Forte

ETHAMBUTOL

Formula: $C_{10}H_{24}N_2O_2$

Molar Mass: 204.314

Structure:



2,2'-(Ethane-1,2-diyldiimino)dibutan-1-ol

Properties: It is white crystalline odourless compound, freely soluble in water.

Storage: Store in well closed container.

Uses:

- It is anti-tubercular agent.
- In the primary treatment of pulmonary and extrapulmonary tuberculosis, ethambutol is combined with other antituberculous medications to prevent the establishment of resistance to the other treatments in the regimen.
- It is also included in nontuberculous mycobacterial infection therapy regimens.
- Mycobacterium avium complex and Mycobacterium kansasii may also be treated with it.

Official Preparations: Ethambutol tablet

Brand Name: Den Butol, Dybitol, EBL,Eburiv, Ebutol, Ebuto, Ecox

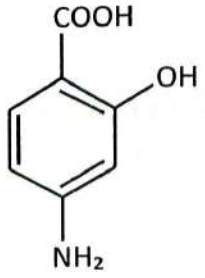
PARA AMINO SALICYLIC ACID (PAS)

Synonym: 4-Aminosalicylic acid

Formula: $C_7H_7NO_3$

Molar Mass: 153.137

Structure:



4-amino-2-hydroxybenzoic acid

Properties:

- White or nearly white bulky powder, also occur as minute crystals. Odourless or has slight acetous door.
- Soluble in dilute nitric acid and dilute sodium hydroxide.

Storage: Darkens on exposure to light and air, Store in well closed light resistant container.

Uses: The treatment of tuberculosis, it has also been used in the treatment of inflammatory bowel disease.

Official Preparations: Amino salicylic acid tablet.

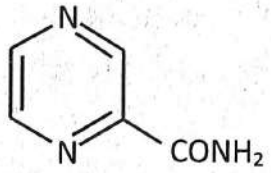
Brand Name: Paser, Isopar.

PYRAZINAMIDE

Formula: $C_5H_5N_3O$

Molar Mass: 123.115

Structure:



pyrazine-2-carboxamide

Properties: It is a white-coloured powder, slightly soluble in water.

Storage: Store in a well-closed container at controlled room temperature.

Uses:

- Pyrazinamide is a first line antituberculosis medication.
- It's an antibiotic that works by preventing bacteria from growing.
- Pyrazinamide is exclusively used in the treatment of Mycobacterium TB in conjunction with other medications such as isoniazid and rifampicin and as Directly Monitored Therapy (DOT).

Official Preparations: Pyrazinamide tablet.

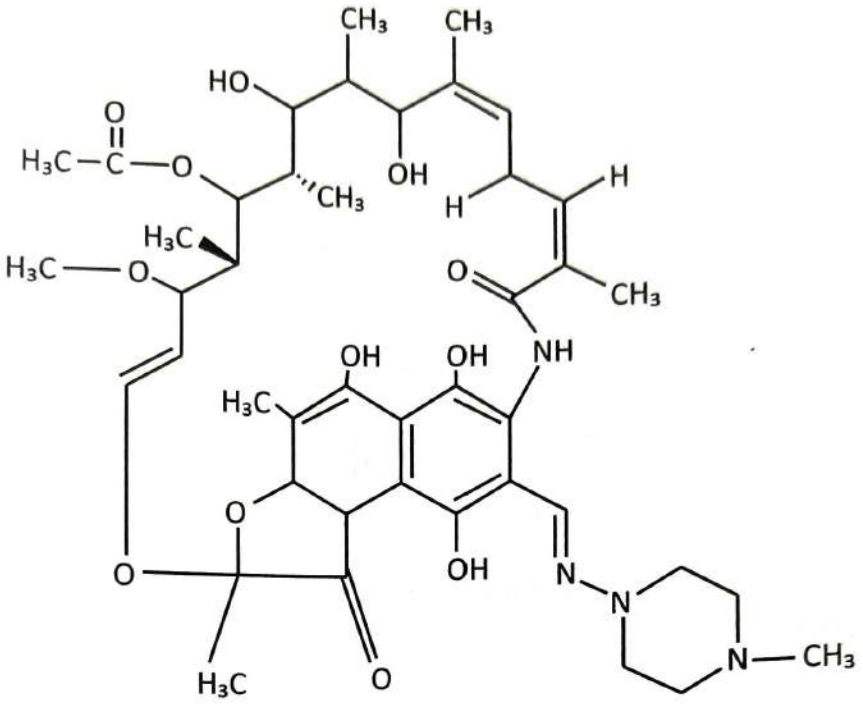
Brand Name: Pyra, Pyrafit, Pyramed, Pyranij, Pyratis, Pyrazid.

RIFAMPICIN

Formula: $C_{43}H_{58}N_4O_{12}$

Molar Mass: 822.953

Structure:



Properties: It is violet-red crystalline powder, soluble in chloroform bur slightly soluble in water.

Use: It is used to treat several types of bacterial infections, including tuberculosis (TB), Mycobacterium avium complex, leprosy and Legionnaires' disease.

Official Preparations: Rifampicin capsule.

Brand Name: R –Cin, Rifacept, Rifacilin, Rifamycin, Rimactane.

BEDAQUILINE

Bedaquiline is a diarylquinoline antibiotic that works by inhibiting mycobacterial ATP synthase.

Molecular Formula: $C_{32}H_{31}BrN_2O_2$

Molecular Weight: 555.5

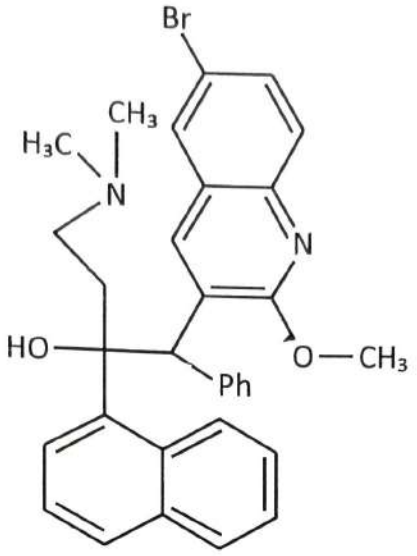
IUPAC Name: (1*R*,2*S*)-1-(6-bromo-2-methoxyquinolin-3-yl)-4-(dimethylamino)-2-naphthalen-1-yl-1-phenylbutan-2-ol

Properties: White to almost white powder; practically insoluble in aqueous media, Melting Point 118°C,

Storage: Store in well closed light and moisture resistant container

Use: [illegible] used to treat active tuberculosis

Structure:



Official Preparations: Bedaquiline tablet

Brand Name: Sirturo

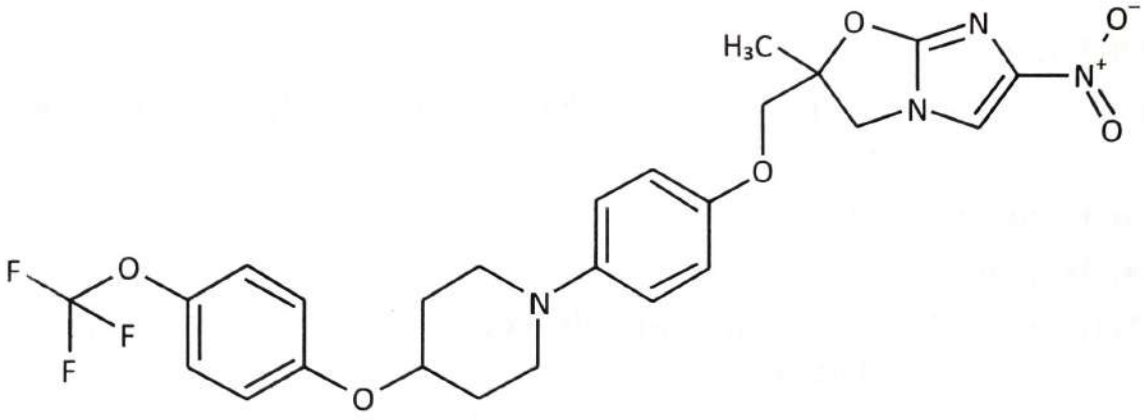
DELAMANID

Delamanid is a member of piperidines. Delamanid is a nitro-dihydro-imidazooxazole derivative, with antimycobacterial activity.

Molecular Formula: $C_{25}H_{25}F_3N_4O_6$

Molecular Weight: 534.5

Structure:



IUPAC: (2*R*)-2-methyl-6-nitro-2-[[4-[4-[4-(trifluoromethoxy) phenoxy] piperidin-1-yl] phenoxy] methyl]-3*H*-imidazo[2,1-b] [1,3] oxazole

Properties: Solid compound with MP 189°C.

Storage: Store in well closed light and moisture resistant container.

Uses: It is a tuberculosis treatment medicine. It is used to treat active multidrug-resistant tuberculosis in combination with other antituberculosis drugs. It is taken orally.

Official Preparations: Delamanid tablet.

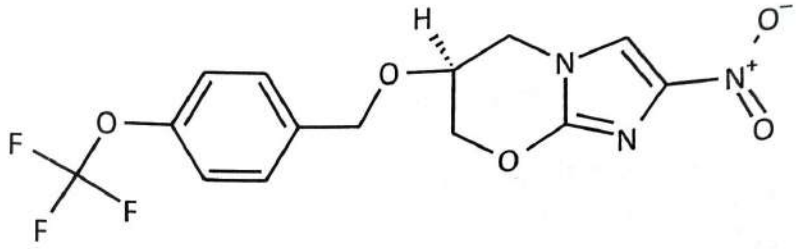
Brand Name: Delamanid, Deltyba.

PRETOMANID

Molecular Formula: $C_{14}H_{12}F_3N_3O_5$

Molecular Weight: 359.26

Structure:



IUPAC: (6*S*)-2-nitro-6-[[4-(trifluoromethoxy) phenyl] methoxy]-6,7-dihydro-5*H*-imidazo[2,1-b] [1,3] oxazine

Uses: Pretomanid is a nitroimidazole-based antibiotic used for the treatment of multi-drug-resistant pulmonary tuberculosis. It is active against replicating and non-replicating *Mycobacterium tuberculosis*.

Official Preparations: Pretomanid tablet.

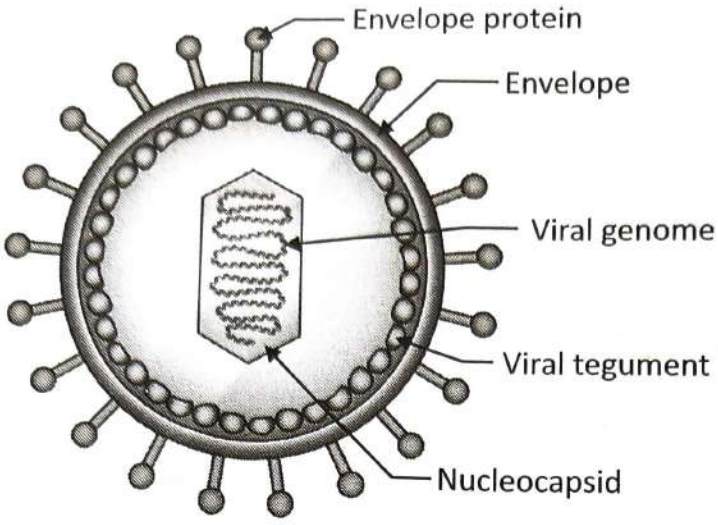
Brand Name: MD Pride, Mdpride, ProtokoxFC, Protomid, Protomid.

ANTIVIRAL AGENTS

Antiviral agents are substances which used in the management and prophylaxis of diseases caused by viruses. Virus is a small infectious agent with a simple constitution that reproduces only in the living cells of animals, plants and microorganisms. The name virus is from Latin word meaning "slimy liquid" or "poison". A virus has constituted that lack of protein synthesizing system and metabolic enzyme machinery.

Virus Characteristics

A virus consists of one or more nucleic acid (either DNA or RNA) surrounded by a protein coat known as a capsid. The capsid is made up by capsomers, which are smaller protein components. A nucleocapsid is a combination of a capsid and a genome. Viruses can also include other elements, the most common of which is an envelope, which is a membranous covering those envelopes the nucleocapsid. The envelope is obtained from the diseased



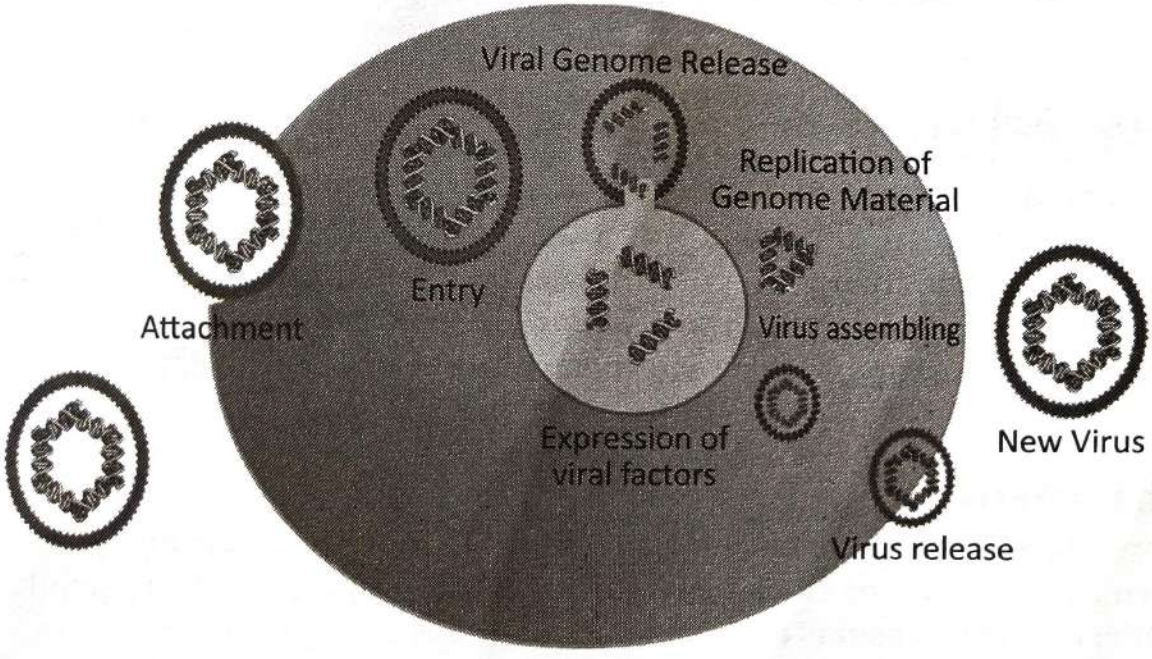
Simple Structure of Virus

host cell's nuclear or plasma membrane and then altered by means of viral proteins known as *peplomers*. few viruses have viral enzymes encoded within their genomes that are important for host cell infection. A virion is a complete virus that comprises all of the components needed to infect a host cell.

Virus Replication Cycle

The replication cycle of viruses can vary from virus to virus, there is a general pattern that can be described, consisting of five steps:

1. **Attachment:** The virion attaches to the correct host cell.



Replication Cycle of Virus

2. **Penetration or Viral Entry:** The virus or viral nucleic acid gains entrance into the cell.
3. **Synthesis:** The viral proteins and nucleic acid copies are manufactured by the cells' machinery.
4. **Assembly:** Viruses are produced from the viral components.
5. **Release:** Newly formed virions are released from the cell.

Classification of Viruses

Virus are classified as per the type of nucleic acid present in them as follows:

Virus	Diseases
DNA Virus	
Herpes virus	Chicken pox, Glandulan fever, Shingles
Adenovirus	Sore throat, Conjunctivitis
Pox virus	Small pox
Papilloma virus	Warts
Parvo virus	Canine distemper
RNA Virus	
Retrovirus	AIDS, T-cell leukemia
Arena virus	Meningitis, Lassa fever
Reo virus	Diarrhoea
Filo virus	Ebola, Marburg
Orthomyxovirus	Influenza
Paramn virus	Measles, Mumps, Rabies
Picor virus	Poliomyelitis
Bunya virus	Encephalitis, haemorrhagic fever

Classification of Antiviral Agents

1. **Anti-Retrovirus:**
   (a) Nucleoside Reverse Transcriptase Inhibitors (NRTIs), e.g., Zidovudine (AZT), Didanosine, Zalcitabine, Stavudine, Lamivuldine, Abacavir.

(b) Nonnuleaside Reverse Transcriptase Inhibitors (NNRTIs), e.g., Nevirapine, Efavirenz, Delavirdine.

(c) Protease inibitors, e.g., Ritonavir, Indinavir, Nelfinavir, Saquinavir.

(d) Inhibitor of HIV fusion with host cells: e.g., Enfurvitide.

(e) Integrase inhibitor, e.g., Ratelgravir.

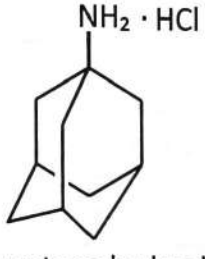
2. **Anti-Herpes virus,** e.g., Idoxuridine, Acyclovir, Foscarnet, Trifluridine, Cidoclovir.
3. **Anti-Influenza virus,** e.g., Amantadine, Rimantadine, Oseltamiv, Zanamivir.
4. **Anti-hepatitis virus/non-selective antiviral drugs:** Lamivuldine, Tenofovir, Ribavirin, Intreferon α.

AMANTADINE HYDROCHLORIDE

Formula: $C_{10}H_{17}N$

Molar Mass: 151.253

Structure:



1-Amino adamantane hydrochloride

Properties: It is white, odourless, crystalline powder with bitter taste. Freely soluble in water.

Storage: Store in tightly closed container.

Uses:

- It is effective in the prophylaxis and therapy of infection caused by influenza A virus.
- It is also used to treat Parkinson's disease related dyskinesia and drug-induced Parkinsonism syndromes.

Official Preparations:

- Amantadine tablets
- Amantadine capsule

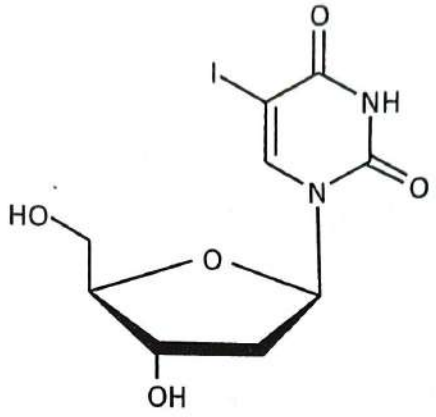
Brand Name: Amantral, Amantrel, Comantrel, Neaman.

IDOXURIDINE

Formula: $C_9H_{11}IN_2O_5$

Molar Mass: 354.100

Structure:



5-Iodo-2'-deoxyuridine

Properties: It is a white, crystalline powder which is slightly *soluble* in water.

Storage: Store in tightly closed container protected from light.

Uses:

- It is treated infection caused by herpes simplex virus (HSV).
- It is used to treat ophthalmic infection.

Official Preparations:

- Idoxuridine eye drops IP.
- Idoxuridine ophthalmic solution.

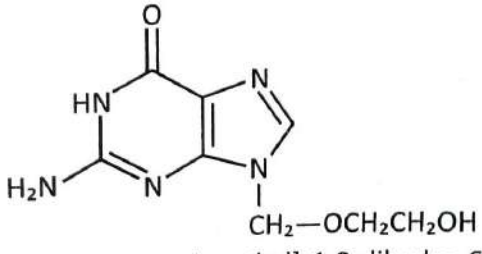
Brand Name: IdurinEye, Ifex -M, Ridinox, Toxil, Toxil Ointment, Xurin Eye.

ACYCLOVIR

Formula: $C_8H_{11}N_5O_3$

Molar Mass: 225.208

Structure:



2-Amino-9-[(2-hydroxyethoxy)methyl]-1,9-dihydro-6*H*-purin-6-one

Properties: It is white crystalline powder, slightly soluble in water, DMSO, mineral acids and alkali and very slightly soluble in ethanol.

Storage: Store in tightly closed container protected from light and moisture.

Uses: It is antiviral agent against herpes simplex viruses, chickenpox and shingles.

Official Preparations:

- Acyclovir intravenous infusion IP.
- Acyclovir oral suspension IP.
- Acyclovir tablets IP.
- Acyclovir eye ointment IP.

Brand Name: Acivir, Cyclovir Ointment (3%), Ocuvir.

FOSCARNET

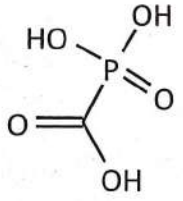
Foscarnet is an antiviral medication which is primarily used to treat viral infections involving the Herpesviridae family. It is classified as a pyrophosphate analogue DNA polymerase inhibitor.

Synonym: Phosphonoformic acid

Formula: CH_3O_5P

Molar Mass: 126.004

Structure:



Properties: White Solid powder, completely soluble in water, MP 88.06°C.

Storage: Store in tightly closed container protected from light and moisture.

Uses: Foscarnet is second line drug for treatment of retinitis in AIDS patients.

Official Preparations: Foscarnet intravenous infusion BP.

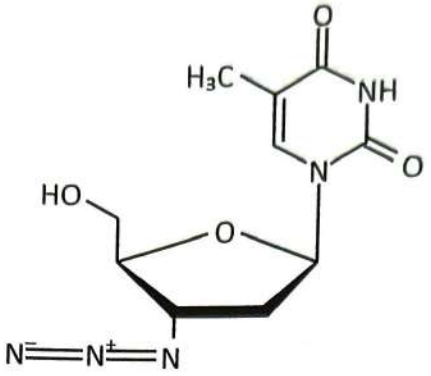
Brand Name: Foscarnet, Foscavir.

ZIDOVUDINE (AZT)

Formula: $C_{10}H_{13}N_5O_4$

Molar Mass: 267.245

Structure:



1-[(2*R*,5*S*)-4-azido-5-(hydroxymethyl)tetrahydrofuran-2-yl]-5-methylpyrimidine-2,4(1*H*,3*H*)-dione

Properties: It is a white or brownish powder, sparingly soluble in water and ethanol.

Storage: Store in tightly closed container protected from light and moisture, store at 15°C.

Uses: It is active in treatment of AIDS.

Official Preparations:

- Zidovudine capsule IP
- Zidovudine injection IP
- Zidovudine tablets IP

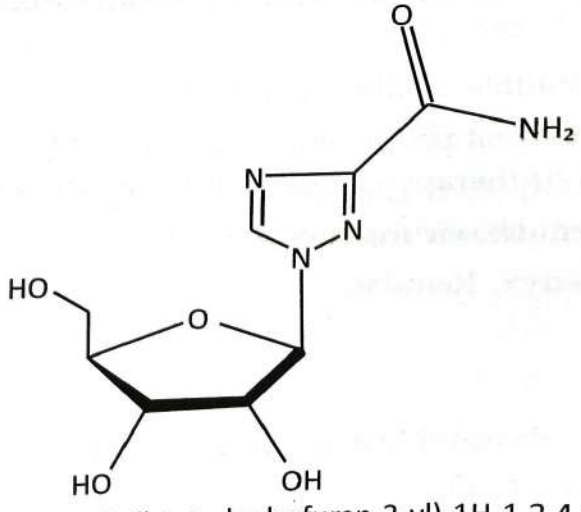
Brand Name: Retrovir, Zydowin, Ziddivir, RAZIV 100 Tablet.

RIBAVIRIN

Formula: $C_8H_{12}N_4O_5$

Molar Mass: 244.207

Structure:



-5-(hydroxymethyl)-tetrahydrofuran-2-yl)-1H-1,2,4-triazole-3-carboxamide

Properties: It is white crystalline powder, freely soluble in water, slightly soluble in ethanol and methylene chloride.

Storage: Store in tightly closed container protected from light.

Uses: It is used in treatment of influenza type-A and B, hepatitis, genital herpes.

Official Preparations:

- Ribavirin inhalation solution IP.
- Ribavirin capsule.

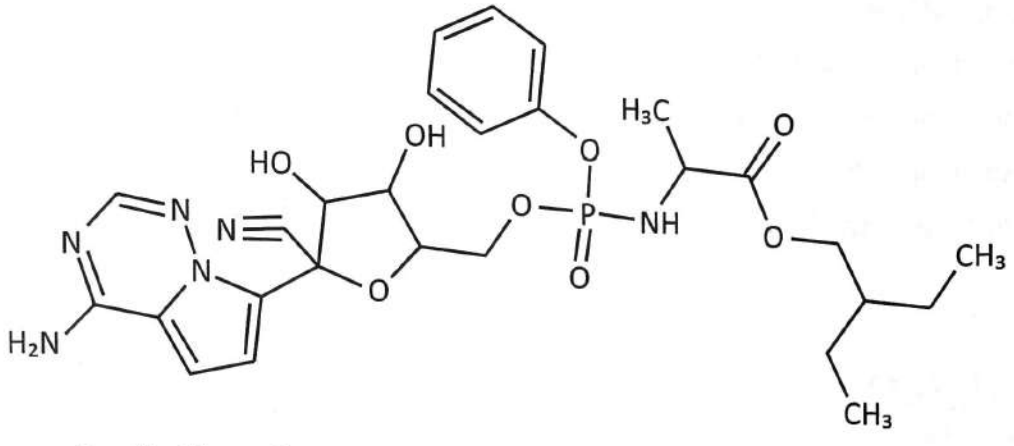
Brand Name: Rebetol, Ribavin, Virazide.

REMDESIVIR

It is a prodrug of an Adenosine Triphosphate (ATP).

Molecular Formula: $C_{27}H_{35}N_6O_8P$

Molecular Weight: 602.6



IUPAC Name: 2-ethylbutyl (2S)-2-[[[(2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4] triazin-7-yl)-5-cyano-3,4-dihydroxyoxolan-2-yl]methoxy-phenoxyphosphoryl] amino]propanoate

Properties: Very slightly soluble, melting point 133°C.

Uses: Remdesivir is used to treat people with coronavirus disease 2019 (COVID-19) who are in a hospital. Remdesivir therapy is given intravenously for 5 to 10 days.

Official Preparations: Remdesivir injection.

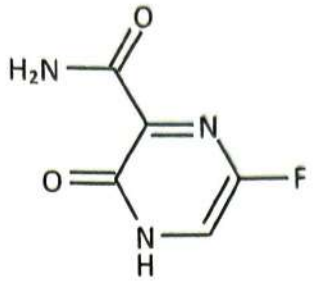
Brand Name: Veklury, Redyx, Remdac.

FAVIPIRAVIR

avipiravir is a pyrazine carboxamide derivative with activity against RNA viruses.

Molecular Formula: $C_5H_4FN_3O_2$

Molecular Weight: 157.10



IUPAC: 5-fluoro-2-oxo-1H-pyrazine-3-carboxamide.

Properties: Slightly soluble in water, pKa 5.1, Melting Point 187°C to 193°C.

Uses: It is used in treatment of novel influenza and SARS-CoV-2.

Official Preparation: Favipiravir tablets.

Brand Name: FluGuard, BDFAVI, covihalt.

ANTIMALARIAL AGENT

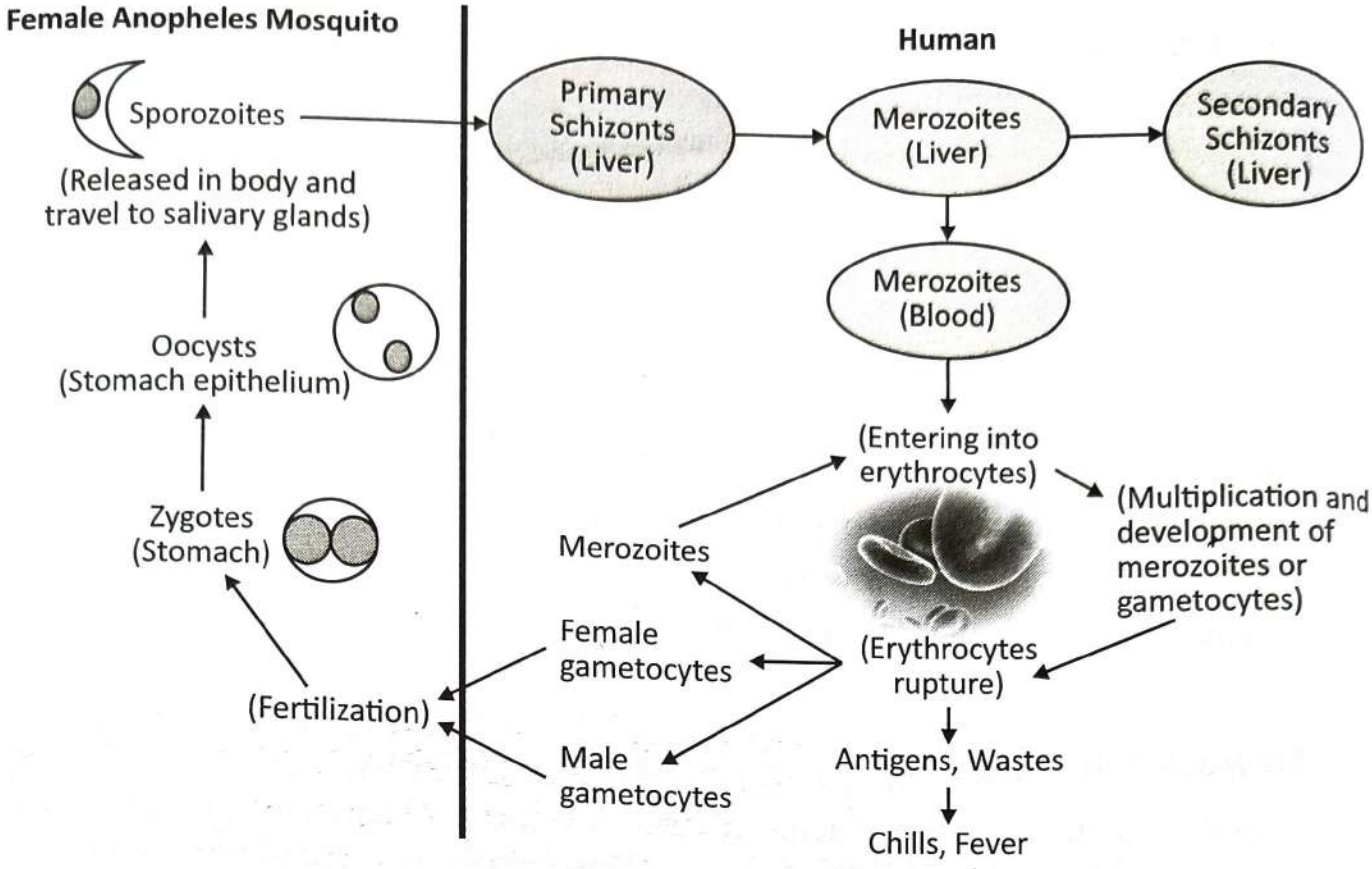
These are the agents which used against malarial infections. Malaria, one of widespread disease is caused by *Plasmodium* parasite and is transmitted to human by the anopheles mosquito. It infects several hundred million people each year. The causative agent is a group of parasitical protozoa of the *Plasmodium* genus transmitted by the female anopheles mosquito. Its original treatment was quinine that became the prototypical molecule for the first generation of synthetic antimalarial drugs.

The four species of *Plasmodium* are mainly causing malaria, such as *Plasmodium falciparum, P. malariae, P. ovale*and*P. vivax*. The chills and fever symptoms are seen in correspond to the reproductive cycle of the parasite. However, the most dangerous is the *P. falciparum*. In this case, the infected red blood cells become sticky and form lumps in the capillaries of the deep organ of the body and cause microcirculatory arrest.

Etiology of Malaria

Malaria is mainly caused by female anophele mosquito, thus, the etiology of malaria is depending upon the life cycle of malarial parasite which divide in two parts:

1. Female Anopheles Mosquito
2. Human



Life Cycle of Malaria

Classification of Antimalarial Agent

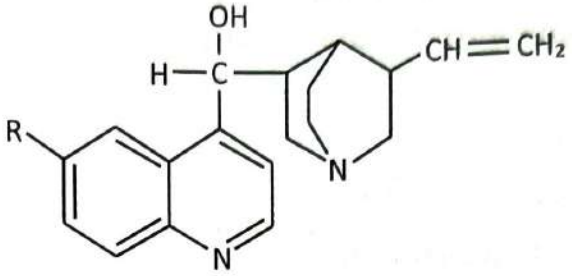
Class	Example
Chinchona alkaloids	Quinine, Quinidine, Cinchonine, Cinchonidine
7-Chloro-4-Amino Quinoline	Chloroquin, Hydroxychloroquin, Amodiaquin
8-Amino quinoline	Primaquin, Pamaquin
Acridine derivatives	Acriquin, Quinacrine
2,4-Diamino pyrimidine	Pyrimethamine, Trimethoprim
Biguanide derivatives	Proguanil, Chloro proguanil
4-Quinoline methanol	Mefloquin
Sesquiterpene Lactone	Artesunete, Artemether
Phenanthrine methanol	Lumefantrin, Halofantrine
Hydroxyl napthoquinone	Atovaquone, Buparvaquone

QUININE SULPHATE

Formula: $C_{20}H_{24}N_2O_2$

Molar Mass: 324.424

Structure:



IUPAC Name: (R)-(6-Methoxyquinolin-4-yl) [(1S,2S,4S,5R)-5-vinylquinuclidin-2-yl] methanol.

Properties: It is Bulky, white, amorphous powder or crystalline alkaloid, crystals darkens on exposure to air, It is odourless, Very bitter taste, Soluble in ether, chloroform, carbon disulphide, glycerol, alkali and acids.

Storage: Store in well closed container protected from light.

Uses: It is used in the treatment of malaria and leg cramps.

Official Preparations:

- Quinine Sulphate tablets IP
- Quinine bisulphate tablets IP

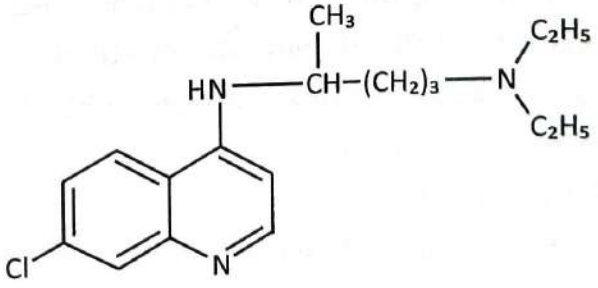
Brand Names: Qinarsol–300, Queenolar, Cinkona, Quinlex.

CHLOROQUINE

Formula: $C_{18}H_{26}ClN_3$

Molar Mass: 319.872

Structure:



IUPAC Name: (RS)-N′-(7-chloroquinolin-4-yl)-N, N-diethyl-pentane-1,4-diamine.

Properties: It is white to slightly yellow, crystalline powder, very slightly soluble in water, soluble in dil. acids, chloroform and ether.

Storage: Store in well closed container protected from light.

Uses: It is used for the treatment of malaria, hepatic amoebiasis, lupus erythematosus, light-sensitive skin eruptions and rheumatoid arthritis.

Official Preparations:

- Chloroquine syrup IP
- Chloroquine sulphate tablets IP
- Chloroquine sulphate injection IP

Brand Names: Chlorotek Drops, Laquin, Clokit, Malaquin, Cloquin.

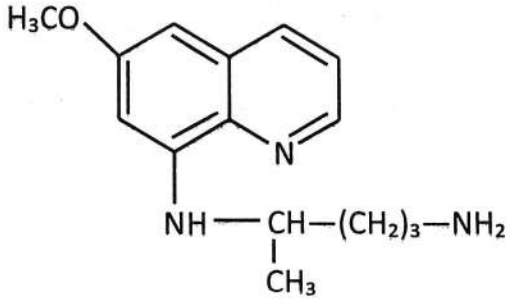
PRIMAQUINE

Primaquine is an N-substituted diamine that is pentane-1,4-diamine substituted by a 6-methoxyquinolin-8-yl group at the N (4) position. It is a drug used in the treatment of malaria and Pneumocystis pneumonia. It has a role as an antimalarial. It is an aminoquinoline, a N-substituted diamine and an aromatic ether.

Formula: $C_{15}H_{21}N_3O$

Molar Mass: 259.347

Structure:



IUPAC Name: (RS)-N-(6-methoxyquinolin-8-yl) pentane-1,4-diamine.

Properties: Yellow crystals from 80% ethanol. MP 182-185°C.

Storage: Store in well closed container protected from light.

Uses: It is used in the treatment of malaria.

Official Preparation: Primaquine tablets.

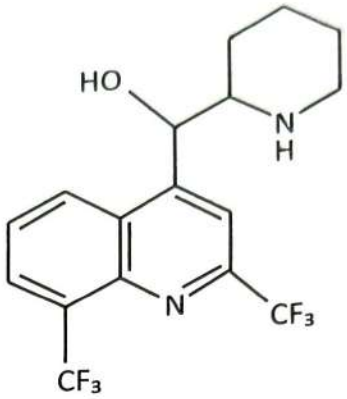
Brand Names: Malirid D.S., Primacip, Pimaquin, PMQ.

MEFLOQUIN

Formula: $C_{17}H_{16}F_6N_2O$

Molar Mass: 378.318

Structure:



IUPAC Name: [(R*, S*)-2,8-Bis(trifluoromethyl)quinolin-4-yl] -(2-piperidyl) methanol.

Properties: White or slightly yellow crystalline powder; odourless; MP 259-260°C (decomposes). Exhibits polymorphism. Freely soluble in methanol; soluble in ethanol, ethyl acetate; very slightly soluble in water.

Storage: Store in well closed container protected from light.

Uses: Mefloquine is used to both prevent and treat certain forms of malaria.

Official Preparation: Mefloquine tablets IP.

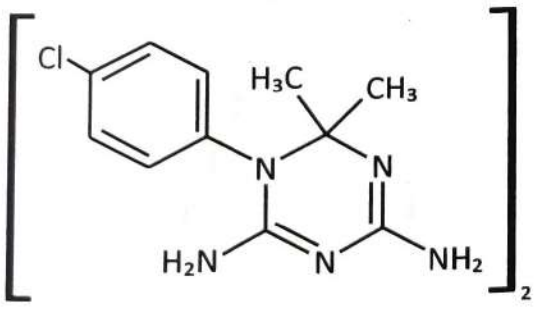
Brand Names: Mafloma, Malacure-MF, Mefax, Meflar, Mefloc, Meflotas.

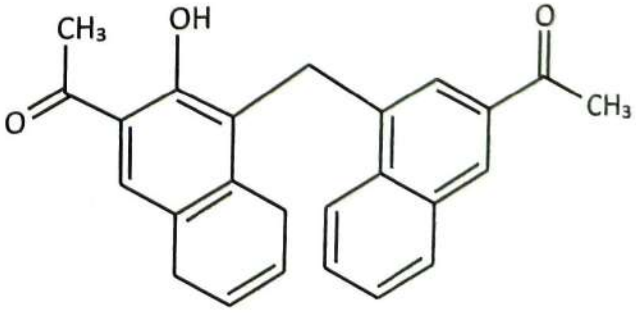
CYCLOGUANIL PAMOATE

Molecular Formula: $C_{23}H_{16}O_6.2C_{11}H_{14}ClN_5$

Molecular Weight: 891.8018

Structure:





IUPAC Name: 1-(4-chlorophenyl)-6,6-dimethyl-1,3,5-triazine-2,4-diamine.

Properties: Cycloguanil is a dihydrofolate reductase inhibitor and is a metabolite of the antimalarial drug proguanil. The parent drug proguanil was suggested to contribute to the antimalarial activity, MP 146.0°C.

Storage: Store in well closed container protected from light.

Uses: It is used in the treatment of malaria.

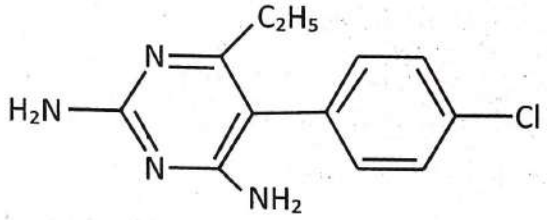
Brand Names: Proguanil, Atovaquone.

PYRIMETHAMINE

Formula: $C_{12}H_{13}ClN_4$

Molar Mass: 248.71

Structure:



5-(4-chlorophenyl)-6-ethylpyrimidine-2,4-diamine

Properties: Pyrimethamine is an odourless white crystalline powder. Tasteless.

Storage: Store in well closed container protected from light.

Uses: For the treatment of toxoplasmosis and acute malaria.

Official Preparation: Pyrimethamine tablets IP.

Brand Names: Fansidar, Fanlar, *Daraprim*

ARTEMISININ

Artemisinin is extracted from the plant Artemisia annua. The key antimalarial centre of the compound is an endoperoxide 1,2,4-trioxane ring.

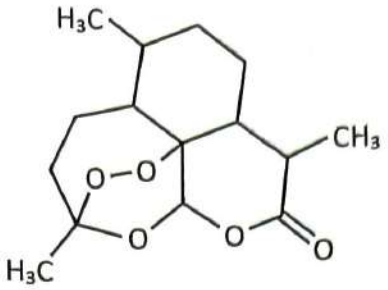
Formula: $C_{15}H_{22}O_5$

Molar Mass: 282.336

IUPAC Name (1*R*,4*S*,5*R*,8*S*,9*R*,12*S*,13*R*)-1,5,9-trimethyl-11,14,15,16- etraoxatetracyclo [10.3.1.$0^{4,13}$.$0^{8,13}$] hexadecan-10-one

Properties: Melting point 152 to 157°C.

Structure:



Uses:

- It is used as an antimalarial for the treatment of multi-drug resistant strains of falciparum malaria
- It is also used for parasitic worm (helminth) infections

Official Preparation: Artemisinin tablet.

Brand Names: Coartem, arte-fast, artequick, tesquin care.

SULPHONAMIDE

The sulphonamide is employed as derivatives of para aminobenzene sulphonamide (Sulphanilamide). The sulphonamide drugs were the first effective chemotherapeutic agent to be used systemically for the prevention and bacterial infection in human.

These antimicrobial compounds contain sulphonamido group (SO_2NH_2), which is also present in other compounds such as antidiabetic agent (Tolbutamide), diuretics (Chlorthiazide, Furosemide and Acetazolamide) and anticonvulsant (Sulthiame).

Sulphonamides are selectively drugs used to treat urinary tract infection, bacterial respiratory infections and gastrointestinal infections. Sulphonamides are effective in vitro against many microorganisms included *Streptococcus pyogens, Streptococcus pneumonia, Haemophilus influenza*and *Chlamydia trachomatis*. Now days, sulphonamide use in combination (Sulfamethoxazole + Trimethoprim) to treat infection by *Pneumocystis carinii* in AIDs patients.

Classification

Classification of sulphonamide depending on duration of action:

1. **Ultra-long-acting sulphonamide:** Sulphasalazine, Sulphalene, Sulphacetamide.
2. **Long-acting sulphonamide:** Sulphamethoxdiazine, Sulphadiamethoxin.
3. **Intermediate acting sulphonamide:** Sulphosomizole, Sulphamethoxazole.
4. **Short acting sulphonamide:** Sulphamethizole, Sulphisoxazole.

Classification of sulphonamide depending upon their therapeutic uses:

1. **Sulphonamides are used for systemic infections:**
   (a) Those used in urinary tract infections, e.g., Sulphamethoxazole, Sulphacetamide.
   (b) Those used in respiratory tract infections, e.g., Cotrimoxazole, Sulphadiazine.
   (c) Those used in meningeal infections, e.g., Sulphadiazine.

B. **Sulphonamides are used for local infections:**
   (a) Those used for intestinal infections, e.g., Sulphaguanidine, Phthalylsulphathiazole, Succinyl sulphathiazole
   (b) Those used for ophthalmic infections, e.g., Sulphacetamide.
   (c) Those used in burn therapy, e.g., Mefenide, Silver sulphadiazine

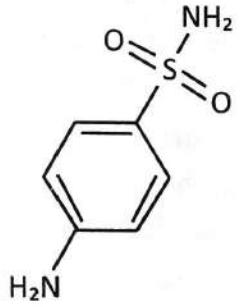
SULPHANILAMIDE

Sulfanilamide (also spelled sulphanilamide) is a sulfonamide antibacterial drug.

Formula: $C_6H_8N_2O_2S$

Molar Mass: 172.20

Structure:



IUPAC Name: 4-aminobenzenesulfonamide

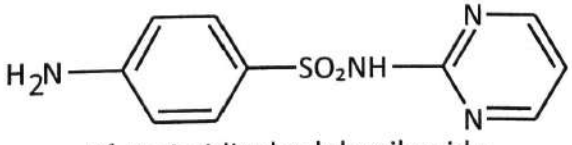
Properties: Sulfanilamide is a white powder. pH of 0.5% aqueous solution: 5.8-6.1, soluble in ethanol, MP 165.5°C.

SULPHADIAZINE

Formula: $C_{10}H_{10}N_4O_2S$

Molar Mass: 250.28

Structure:



N¹-Pyrimidinyl sulphanilamide

Properties: It is a white or yellowish white or pinkish white crystalline powder, insoluble in water, slightly soluble in acetone.

Storage: Store in well closed container.

Uses:

- It is used in treatment of rheumatic fever.
- It is used to treat urinary tract infections and burns.

Official Preparations:

- Sulphadiazine tablet.
- Sulphadiazine sodium injection.

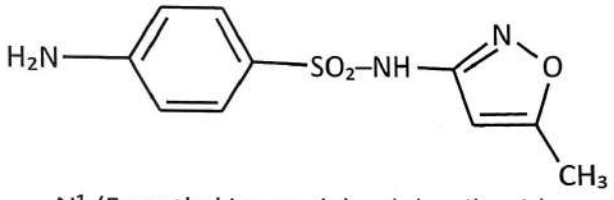
Brand Name: Triglobe, trizin, unitrimzad G.

SULFAMETHOXAZOLE

Formula: $C_{10}H_{11}N_3O_3S$

Molar Mass: 253.28

Structure:



N^1-(5-methyl isoxazole)-sulphonilamide

Properties: It is a white, odourless, crystalline powder and bitter in taste.

Storage: Store in well closed container.

Uses: It is employed for lower urinary tract and systemic infections caused by *E. coli* and *P. mirabilis*. In combination with trimethoprim, it is used in AIDS infections.

Official Preparations: Sulfamethoxazole tablet.

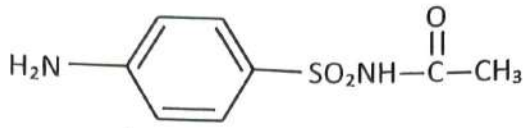
Brand Name: Azo Gantanol, Septra.

SULPHACETAMIDE

Formula: $C_8H_{10}N_2O_3S$

Molar Mass: 214.24 $g \cdot mol^{-1}$

Structure:



N^1-Acetylsulphanilamide

Properties: It is a white crystalline powder and bitter in taste.

Storage: Store in well closed container protected from light and moisture.

Uses: It is mainly used locally for ophthalmologic infections.

Official Preparations:

- Sulphacetamide eye drops IP.
- Sulphacetamide eye ointment.

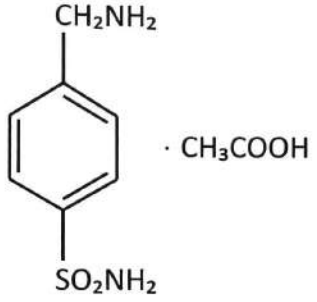
Brand Name: (Eye Drops) Opthocid, paristin, scarmide, suncetamide.

MAFENIDE ACETATE

Formula: $C_7H_{10}N_2O_2S$

Molar Mass: 186.23

Structure:



p-Aminomethyl-benzenesulfonamide acetate

Properties: It is a white crystalline powder, freely soluble in water.

Storage: Store in well closed container protected from light and moisture

Uses: It is effective against *Clostridium welchii* on topical application.

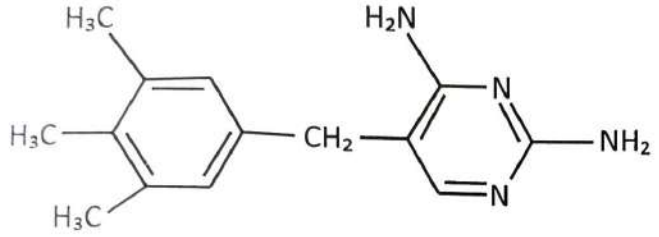
Official Preparations:

- Mafenide acetate cream
- Mafenide acetate creampowder for solution

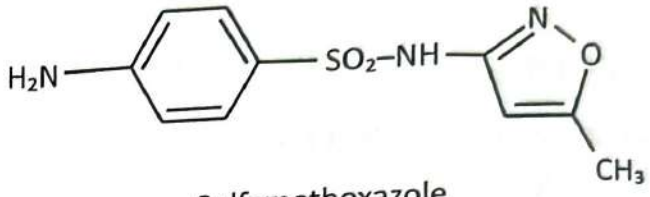
Brand Name: Sulfamylon.

COTRIMOXAZOLE

Cotrimoxazole is combination of Trimethoprim and Sulfamethoxazole which gives synergistic action on bacteria (5:1 ratio). These drugs sequentially block the synthesis of DNA in bacteria. Sulfamethoxazole inhibits the incorporation of PABA in to folic acid by which dihydropteroate synthtase as a coenzyme and trimethoprim is acompetative inhibitors of dihydrofolate reductase which responsible for the generation of tetrahydrofolic acid from dihydrofolic acid.

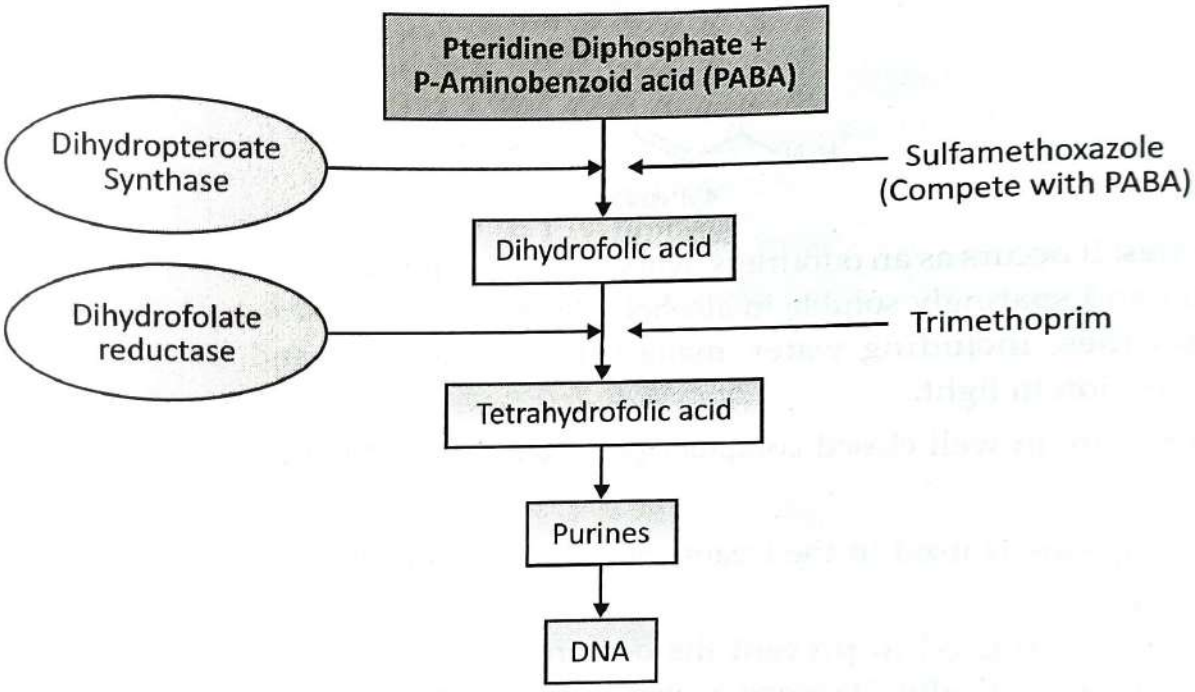


Trimethoprim



Sulfamethoxazole

Mechanisms of Action:



Uses:

- Cotrimoxazole has widely used in the treatment of uncomplicated, acute and chronic lower urinary tract infections.
- Cotrimoxazole is the drug of choice for infections caused by *Shigella* and *Pneumocystis carinni*which latter causes infections in AIDS patients.

- It is also effective for typhoid fever and in management of infection caused by S. *typhi, nocardia* and *brucellosis*.
- A parenteral preparation is useful against infection of pneumocytis carinii pneumonia.

Official Preparations:

- Cotrimoxazole tablets
- Cotrimoxazole injection

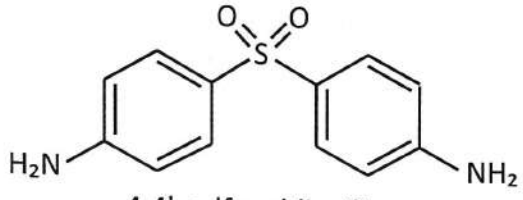
Brand Name: Alcorim-F, bactrim P, Cipilin DS, Colizol, monatrim, septran P.

DAPSONE

Formula: $C_{12}H_{12}N_2O_2S$

Molar Mass: 248.30

Structure:



4,4'-sulfonyldianiline

Properties: It occurs as an odourless, white crystalline powder that is very slightly soluble in water and sparingly soluble in alcohol. The pure compound is light stable, but traces of impurities, including water, make it photosensitivity and thus, susceptible to discolouration in light.

Storage: Store in well closed container protected from light and moisture.

Uses:

- Dapsone is used in the treatment of both lepromatous and tuberculoid types of leprosy.
- It is also used to prevent the occurrence of multiciliary leprosy when given prophylactically. Dapsone is also a drug of choice for dermatitis herpentiformis and is sometimes used with pyrimethamine for treatment of malaria and with trimethoprim for Pneumocystis pneumonia.
- Additionally, it has been used for acne, dermatitis herpetiformis and various other skin conditions.

Official Preparation: Dapsone tablets.

Brand Name: Acnesone (Gel), Dapsone (tab).

EXERCISE

Short Answer Type Questions

1. Give two Brand Names of following drugs:
   (a) Itraconazole, Fluconazole, Naftifine Hydrochloride
   (b) Ciprofloxacin, Ofloxacin
   (c) Remdesivir, Favipiravir
   (d) Primaquine Phosphate, Mefloquine
   (e) Mafenide Acetate, Cotrimoxazole
2. In what dosage form the following drugs are given:
   (a) Amphotericin B
   (b) Ciprofloxacin
   (c) Griseofulvin
   (d) Idoxuridine
   (e) Fluconazole
3. Give uses of following drugs:
   (a) Griseofulvin
   (b) Methotrexate
   (c) Dactinomycin
   (d) Sulphacetamide
   (e) Idoxuridine
4. Write structure and give chemical name of following drugs:
   (a) Ketoconazole
   (b) Fluconazole
   (c) Ofloxacin
   (d) INH
   (e) Pretomanid
   (f) Acyclovir
   (g) Chloroquine Phosphate
   (h) Mefloquine
   (i) Sulfacetamide
   (j) Dapsone
5. Name the drug present in following brands:
   (a) Retrovir
   (b) Mefloc
   (c) Malaquin
   (d) Rimactane

Long Answer Type Questions

1. Explain Life cycle of Malarial parasite
2. Classify:
   (a) Antifungal Agents with examples.
   (b) Anti-Tubercular Agent with examples.
   (c) Antiviral Agent with examples.
   (d) Anti-malarial with examples.
   (e) Sulphonamides with examples.

3. **Write structure, give chemical name, properties and uses of:**
   (a) Ketoconazole
   (b) Fluconazole
   (c) Ofloxacin
   (d) INH
   (e) Pretomanid
   (f) Acyclovir
   (g) Chloroquine Phosphate
   (h) Mefloquine
   (i) Sulfacetamide
   (j) Dapsone
4. **Give properties and uses of:**
   (a) Griseofulvin and Miconazole
   (b) Norfloxacin and Ciprofloxacin
   (c) Foscarnet and Zidovudine
   (d) Quinine Sulphate and Chloroquine Phosphate
   (e) Sulfadiazine and Sulfamethoxazole

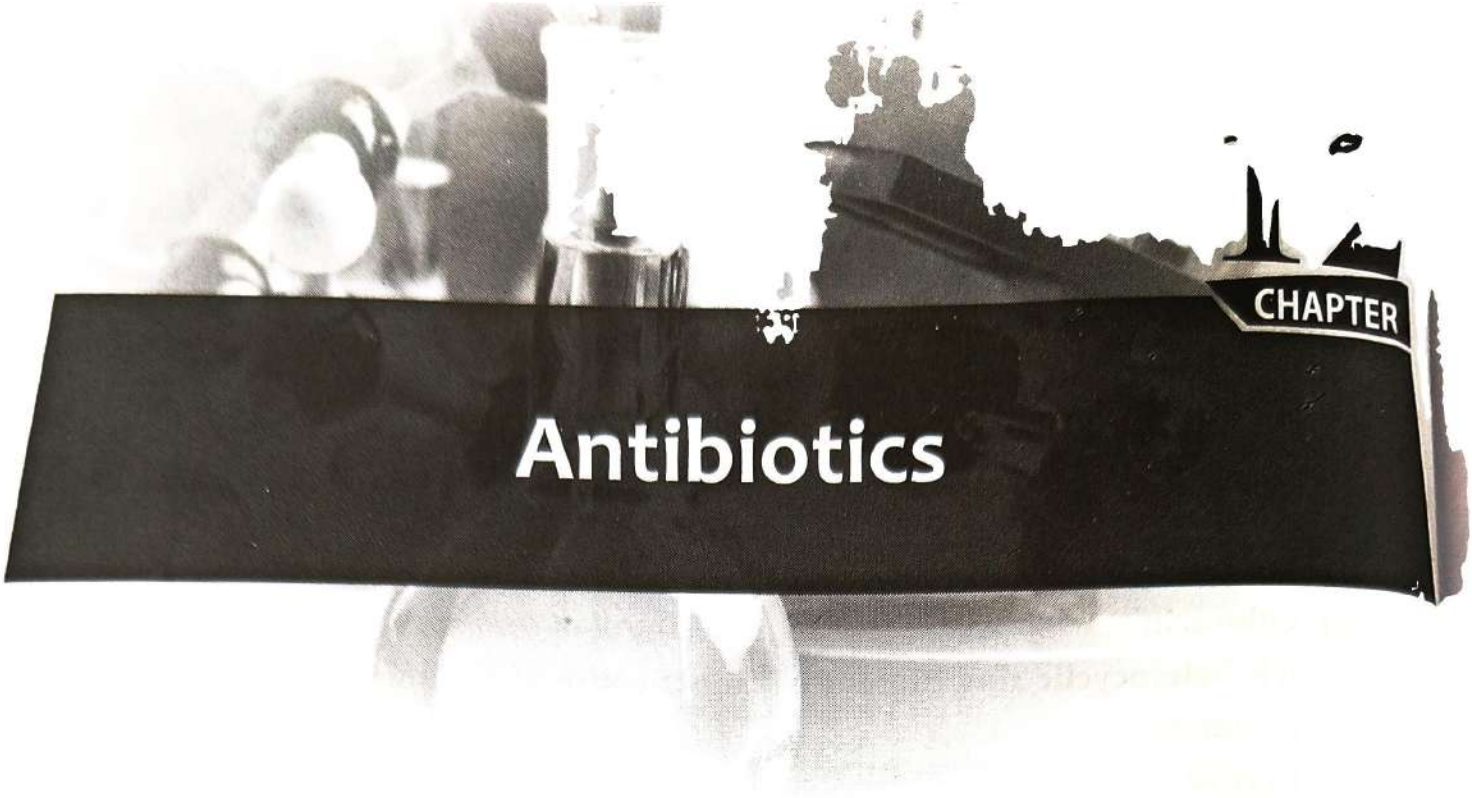
Multiple Choice Questions (MCQ's)

1. **This is the example of antifungal antibiotic:**
   (a) Amphotericin B
   (b) Fluconazole
   (c) Naftifine
   (d) Clotrimazole
2. **_____ obtained from Streptomyces nodosus:**
   (a) Amphotericin B
   (b) Fluconazole
   (c) Naftifine
   (d) Clotrimazole
3. **_____ is isolated from Penicillum griseofulvum.**
   (a) Amphotericin B
   (b) Fluconazole
   (c) Griseofulvin
   (d) Clotrimazole
4. **Drug used in urinary tract infection:**
   (a) Miconazole
   (b) Norfloxacin
   (c) Ketoconazole
   (d) Itraconazole
5. **Isoniazid is:**
   (a) p-amino salicylic acid derivative
   (b) Pyridine derivatives
   (c) Pyrazine derivatives
   (d) Ethylene diamine derivatives
6. **_____ is Chinchona alkaloids:**
   (a) Primaquine
   (c) Pamaquine
   (d) Quinine
   (d) Mefloquine

7. **Cotrimoxazole is the mixture of:**
   (a) Sulfamethoxazole and Trimethoprim (b) Sulphacetamide and Trimethoprim
   (c) Sulphadiazine and Trimethoprim (d) Dapsone and Trimethoprim
8. **INH is synonym for:**
   (a) Ethambutol (b) Pyrazinamide
   (c) Isoniazid (d) Delamanid
9. **Which one is anti-TB Antibiotics?**
   (a) Streptomycin (b) Ciprofloxacin
   (c) Ofloxacin (d) All of the above
10. **Which heterocyclic ring present in the structure of pyrimethamine:**
   (a) Pyrimidine (b) Pyridine
   (c) Pyrrole (d) Furan

ANSWERS OF MULTIPLE CHOICE QUESTIONS (MCQ'S)

1. (a)	2. (a)	3. (c)	4. (b)	5. (b)	6. (c)	7. (a)
8. (c)	9. (a)	10. (a)				



CHAPTER

Antibiotics

INTRODUCTION

The word antibiotic comes from the Greek word antibiosis, which means "against life". Antibiotics are chemical compounds derived from a variety of microorganisms (bacteria, fungi and actinomycetes) that inhibit the growth of other microorganisms and may finally kill them. Physical, chemical and pharmacological properties, antibacterial spectrum and mode of action are all possible grounds of differentiation among antibiotics. They have made it possible to cure diseases caused by bacteria, such as pneumonia, tuberculosis and meningitis and they save the lives of millions of people around the world.

CLASSIFICATIONS

A. On the basis of spectrum of antimicrobial activity

1. Narrow spectrum antibiotics, e.g., Benzyl penicillin, Bacitracin
2. Broad spectrum antibiotics, e.g., Chloramphenicol, Streptomycin

B. On the basis of chemical structure:

1. **β-Lactam antibiotics,** e.g., Benzyl Penicillin, Phenoxymethyl penicillin, Cephaloridine, cephalothin.
2. **Non-β-Lactam antibiotics:**
   (a) Tetracyclines, e.g., Chlortetracycline, oxytetracycline.
   (b) Aminoglycoside antibiotics, e.g., Streptomycin, neomycin, gentamicin.
   (c) Macrolide antibiotics, e.g., Erythromycin.

(d) Ansamycins, e.g., Rifamycin
(e) Polyene macrolide antibiotics, e.g., Nystatin, Hamycin
(f) Anthracycline antibiotics, e.g., Actinomycin, daunorubicin
(g) Peptide antibiotics, e.g., Bacitracin.
(h) Steroidal antibiotics, e.g., Fusidic acid
(i) Nucleoside antibiotics, e.g., Puromycin
(g) Non-classifiable antibiotics, e.g., Chloramphenicol

C. Based on **mechanism of action:**

1. **Cell wall synthesis inhibitor:**
   (a) Penicillin
   (b) Cephalosporins
   (c) Cycloserine
   (d) Bacitracin
   (e) Vancomycin
   (f) Clotrimazole
   (g) Monobactum
2. **Cell membrane synthesis inhibitor:**
   (a) Amphoterecin B
   (b) Polymyxin
   (c) Nystatin
   (d) Meconazole
3. **Protein synthesis inhibitor:**
   (a) Binding with 50s RNA unit, e.g., Chloramphenicol, Tetracyclines, Clindamycin, Macrolides
   (b) Binding with 30s RNA unit, e.g., Tetracyclines, Aminoglycosides, Spectinomycin
   (c) Inhibiting elongation factor, e.g., Fusidic acid
4. **Nucleic acid synthesis inhibitor:** RNA synthesis inhibitor, e.g., Rifamycin, Rifampicin.

CLASSES OF PENICILLINS

Natural Penicillins:

- Penicillin G (Benzylpenicillin)
- Penicillin V (Phenoxymethylpenicillin)

Aminopenicillins:

- Ampicillin
- Amoxicillin

Penicillinase-resistant Penicillins (Anti staphylococcal Penicillins):

- Methicillin (prototype)
- Cloxacillin
- Oxacillin

Extended Spectrum Penicillins (Antipseudomonal Penicillins):

- Carbenicillin
- Piperacillin

Beta-lactamase Inhibitors:

- Clavulanic acid

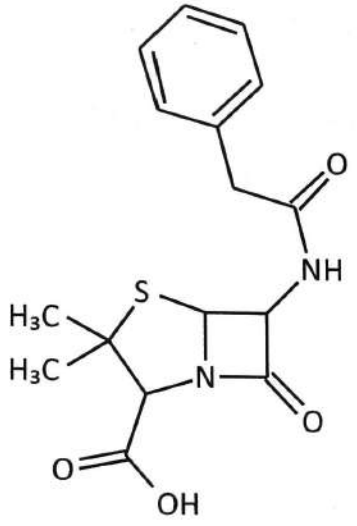
PENICILLIN G

Benzylpenicillin (Penicillin G) is narrow spectrum antibiotic used to treat infections caused by susceptible bacteria. As it has β-Lactam ring, it is classified under β-Lactam antibiotic.

Molecular Formula: $C_{16}H_{18}N_2O_4S$

Molecular Weight: 334.4

Structure:



IUPAC Name: (2*S*,5*R*,6*R*)-3,3-dimethyl-7-oxo-6-[(2-phenylacetyl) amino]-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid

Properties:

- White, finely crystalline powder with faint characteristic odour, Melting Point 214-217°C.

- Hygroscopic, Dextrorotatory.
- Very Slightly soluble in water.
- Degraded rapidly in strong acidic and basic media.
- Inactivated by enzyme penicillinase and gastric juice.
- Structural modifications are possible.

Storage: Store in well closed container protected from light and moisture.

Uses: Penicillin G is licensed for use to treat septicaemia, empyema, pneumonia, pericarditis, endocarditis and meningitis caused by streptococci.

It is used to treat:

- Respiratory tract infection
- Urinary tract infection
- Gonorrhoea
- Syphilis
- Meningitis
- Enteric infection
- Septicaemia.
- Abscesses

Official Preparation: Benzylpenicillin IP

Brand Name: Benzyl penicillin, Penticillin

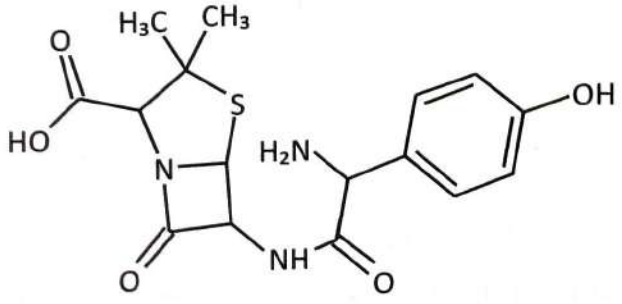
AMOXICILLIN

As it has β-Lactam ring, it is classified under β-Lactam antibiotic.

Formula: $C_{16}H_{19}N_3O_5S$

Molar Mass: 365.40

Structure:



IUPAC Name: (2S,5R,6R)-6-[[(2R)-2-amino-2-(4-hydroxyphenyl) acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid

Properties: Solid crystalline bitter tasting powder, Melting Point 194°C, Soluble in water

Storage: Store in well closed container protected from light and moisture

Uses:

- Amoxicillin is an antibiotic used to treat a number of bacterial infections.
- These include middle ear infection, strep throat, pneumonia, skin infections and urinary tract infections among others.

Official Preparations:

- Amoxicillin capsule IP
- Amoxicillin Injection IP
- Amoxicillin oral suspension IP

Brand Name: Amoxil, amoxipen, amoxybid, amyn, glamoxin

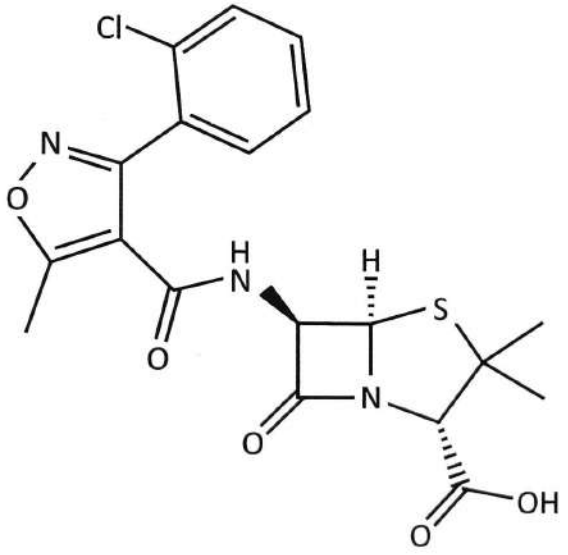
CLOXACILLIN

As it has β-Lactam ring, it is classified under β-Lactam antibiotic.

Formula: $C_{19}H_{18}ClN_3O_5S$

Molar Mass: 435.88

Structure:



IUPAC Name: 5 methyl 3(2 chlorophenyl)4 isoxazoyl penicillin.

Properties: White crystallinje hygroscopic powder, freely soluble in water, MP170°C.

Storage: store in well closed container protected from light and moisture.

Uses: Cloxacillin is an antibiotic useful for the treatment of a number of bacterial infections. This includes impetigo, cellulitis, pneumonia, septic arthritis and otitis externa. It is used by mouth and by injection.

Official Preparations:

- Cloxacillin capsule IP
- Cloxacillin Injection IP
- Cloxacillin syrup IP

Brand Name: Klox, Duoclox, zeeclox, Baxin

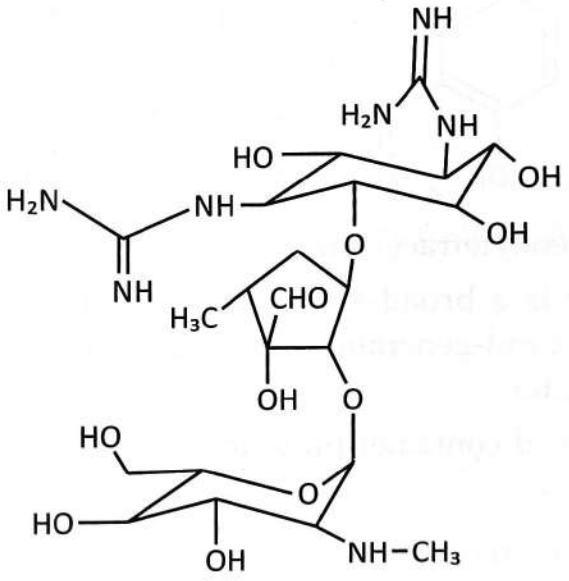
STREPTOMYCIN

It is classified under Aminoglycoside antibiotics.

Formula: $C_{21}H_{39}N_7O_{12}$

Molar Mass: 581.580

Structure:



IUPAC Name: 5-(2,4-diguanidino- 3,5,6-trihydroxy-cyclohexoxy)- 4-[4,5-dihydroxy-6-(hydroxymethyl)-3-methylamino-tetrahydropyran-2-yl] oxy-3-hydroxy-2- methyl – tetrahydrofuran -3-carbaldehyde

Properties: It is white, odourless, hydroscopic powder. It is heat sensitive but stable toward light and air. It is water soluble and slightly soluble in alcohol and insoluble in organic solvents.

Storage: Store in well closed container protected from light and moisture.

Uses: It is used as antitubercular drug. It is also used in combination with other drugs to treat tularaemia and plague.

Official Preparations:

- Streptomycin tablets IP.
- Streptomycin Injection IP.

Brand Name: Ambostryn, streptomac.

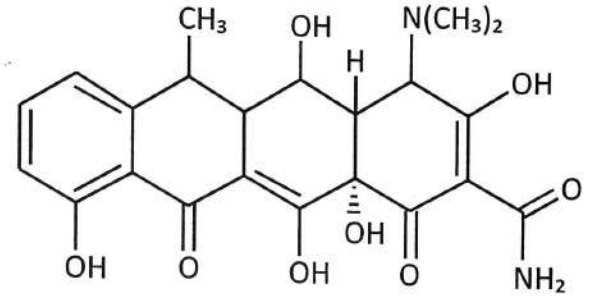
DOXYCYCLINE

It is classified under tetracycline antibiotics.

Formula: $C_{22}H_{24}N_2O_8$

Molar Mass: 444.440

Structure:



IUPAC Name: 5-oxy-6-deoxytetracycline

Properties: Doxycycline is a broad-spectrum antibiotic synthetically derived from oxytetracycline. It is a second-generation tetracycline. It is yellow crystalline powder, very slightly soluble in water

Storage: Store in well closed container protected from light and moisture.

Uses:

- It is used as antibacterial agent.
- It is used to treat infections such as chest infections, skin infections, rosacea, dental infections and sexually transmitted infections.

Official Preparations:

- Doxycycline dispersible tablets IP.
- Doxycycline capsule IP.

Brand Name: Biodox, ceedox, doxt, Doxy-1, DX-24, Geeox, Martidox.

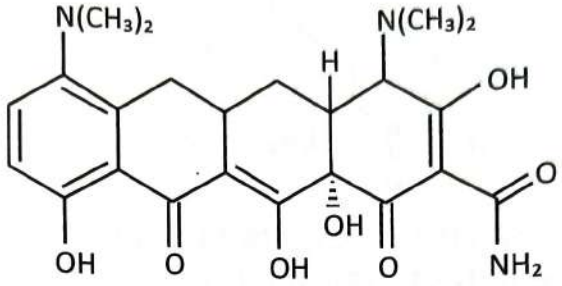
MINOCYCLINE

It is classified under tetracycline antibiotics.

Formula: $C_{23}H_{27}N_3O_7$

Molar Mass: 457.483

Structure:



IUPAC Name: 7-Dimethylamino-6-demethyl-6-deoxytetracycline

Properties: It is yellow crystalline powder with slightly bitter in taste, soluble in water

Storage: store in well closed container protected from light and moisture

Uses:

- It is used as antibacterial agent
- Minocycline is prescribed to treat bacterial infections such as pneumonia and other respiratory tract infections, as well as infections of the skin, eye, lymphatic, intestinal, vaginal and urinary systems, as well as infections transferred by ticks, lice, mites and infected animals.

Official Preparations:

- Minocycline tablets IP
- Minocycline capsule IP

Brand Name: Cycnomycin, divaine, minolox, minostar, minoz, nimolin.

ERYTHROMYCIN

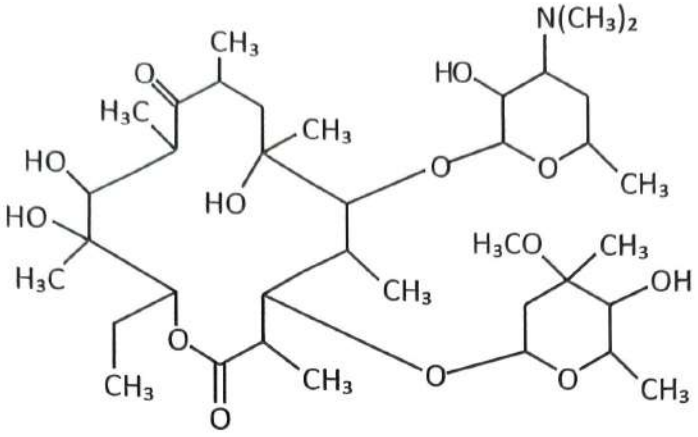
It is classified under Macrolide antibiotics.

Formula: $C_{37}H_{67}NO_{13}$

Molar Mass: 733.937

McGuire isolated erythromycin from *Streptomyces erythreus* in 1952.

Structure:



IUPAC Name: [(3R,4S,5S,6R,7R,11R,12R,13S,14R)-4-[(2,6-dideoxy-3-methyl-α-L-ribo-hexopyranosyl)-oxy]-14-ethyl-7,12,13-trihydroxy-3-5,7,9,11,13-hexamethyl-6-[(3,4,6-trideoxy-3-(dimethylamino)-β-D-xylo-hexapyranosyl)oxy]oxacyclotetradecan-2,10-dione]

Properties:

- It is white or slightly yellow, odourless, crystalline powder.
- It is bitter in taste.
- It is hygroscopic in nature.
- It is soluble in water, alcohol, chloroform and ether.
- It is unstable in pH 4 or lower.

Storage: Store in well closed container protected from light and moisture.

Uses:

- It is drug of choice in pneumonia by Legionella pneumophila.
- It is also useful in penicillin allergic pregnant woman with syphilis.
- It is useful in Chlamydia, Campylobacter, Streptococcal and Staphylococcal infections.
- It is used in the therapy of pertussis.

Official Preparations:

- Erythromycin stearate tablets IP
- Erythromycin ointment

Brand Name: Acnederm (Ointment), acnicin (Ointment), eltocin, erase, eroma

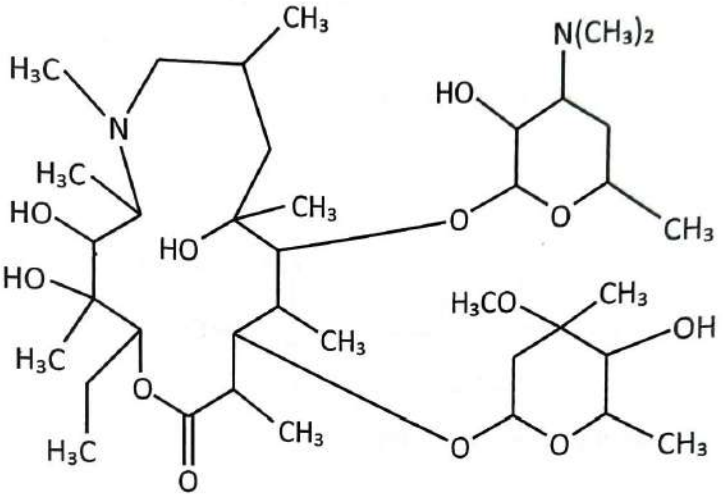
AZITHROMYCIN

It is classified under Macrolide antibiotics.

Formula: $C_{38}H_{72}N_2O_{12}$

Molar Mass: 748.996

It is produced by the Beckmann rearrangement of erythromycin 9-oxime give ring expansion to a 15-membered intermediate which furthered gone through reduction and N-methylation. It is very stable to acidic conditions. It does not undergo metabolism. Elimination half-life is 68 hours.



IUPAC Name: [2R-(2R,3S,4R,5R,8R.10R,11R,12S,13S,14R)-3-(2,6-dideoxy-3-C-methyl-3-O-methyl-α-L-ribo-hexopyranosyloxy)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-11-{(3,4,6-trideoxy-3-dimethylamino)-β-D-xylo-hexapyranosyl}-oxy]-1-oxa-6-azacyclopentadecan-15-one

Properties:

- It is white powder
- It is practically insoluble in water
- It is soluble in anhydrous ethanol and methylene chloride
- It is very stable in acidic condition

Storage: store in well closed container protected from moisture

Uses:

- It is more effective against Haemophilus influenzae and Chlamydia trachomatis respiratory infections.
- It's commonly used to treat chest infections like pneumonia, nose and throat infections like sinusitis, skin infections, Lyme disease and some sexually transmitted illnesses.

Official Preparations:

- Azithromycin tablets IP
- Azithromycin capsule IP
- Azithromycin oral suspension IP

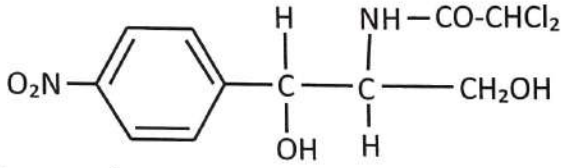
Brand Name: Acithroc, AG, AHZ, Aicin, Althro, Amithro, Atm, azax, azee, azi

CHLORAMPHENICOL

It was isolated from *Streptomyces venezuelae* by Ehrlich in 1947. However only natural isomer that is D- (-)-threo is biological active. It contains chlorine and is obtained from an *actinomycets* and thus, named as chloromycetin.

Formula: $C_{11}H_{12}Cl_2N_2O_5$

Molar Mass: 323.13



N-(1,3-Dihydroxy-1-(4-nitrophenyl)propan-2-yl)dichloroacetamide

Properties:

- It is a fine, white to greyish-white or yellowish-white, needle shaped crystal.
- It is bitter in taste
- It is slightly soluble in water, soluble in alcohol and propylene glycol.
- It has a melting point of 150.5 to 151.5°C. It sublimes in high vacuum and is sensitive to light.

Storage: Store in well closed container protected from moisture

Uses:

- It was used in the treatment of typhoid.
- It may be used as a second-line agent in the treatment of tetracycline-resistant cholera.
- It is also useful in the treatment of brain abscesses.
- It is also applied locally for treatment of ear, eye and skin infection.
- It is used in treatment of Rickettsia, Chlamydia and mycoplasma.

Official Preparations:

- Chloramphenicol ear drops IP

- Chloramphenicol capsule IP.
- Chloramphenicol eye ointment IP.

Brand Name: Chloromycetin. Paraxin, starphenicol, vitacetin, reclor.

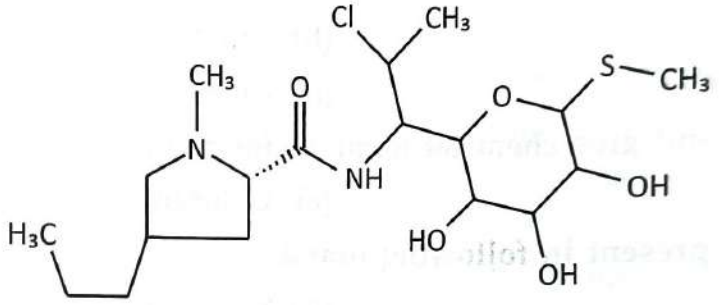
CLINDAMYCIN

It is a sulphur-containing semisynthetic derivative of lincomycin, a natural antibiotic produced by the Streptomyces.

Formula: $C_{18}H_{33}ClN_2O_5S$

Molar Mass: 424.98

Structue:



7(S)-Chloro-7-deoxylincomycin

Properties: Yellow, amorphous solid, Characteristic taste; odourless or has faint mercaptan-like odour; freely soluble in water, MP 141-143°C.

Storage: Store in well closed container protected from moisture

Uses:

- For the treatment of acne.
- Effective against Gram-positive cocci.
- Given with chloroquine or quinine, clindamycin is effective and well tolerated in treating Plasmodium falciparum malaria.
- Clindamycin may be useful in skin and soft tissue infections caused by Methicillin-Resistant Staphylococcus Aureus (MRSA).

Official Preparations:

- Clindamycin injection IP
- Clindamycin capsule IP
- Clindamycin Gel

Brand Name: Acneris (Gel), Acnesol (Gel), biolinx (Capsule), braclin (Injection), D'Acne (Capsule), dalcinex (Capsule)

EXERCISE

Short Answer Type Questions

1. **Give two Brand Names of following drugs:**
   (a) Penicillin G (b) Amoxicillin
   (c) Cloxacillin (d) Streptomycin
   (e) Chloramphenicol (f) Clindamycin
2. **In what dosage form the following drugs are given:**
   (a) Penicillin G (b) Amoxicillin
   (c) Cloxacillin
3. **Give uses of following drugs:**
   (a) Penicillin G (b) Amoxicillin
   (c) Chloramphenicol (d) Clindamycin
4. **Write structure and give chemical name of following drugs:**
   (a) Amoxicillin (c) Chloramphenicol
5. **Name the drug present in following brands:**
   (a) Klox (b) Streptomac
   (c) Martidox (d) Minoz
   (e) Acneris
6. **Name one drug used for treatment of throat infection.**

Long Answer Type Questions

1. Classify antibiotics with examples.
2. Write a note on β-Lactam antibiotics with example.
3. Write structure, Give chemical name, properties and uses of Amoxicillin
4. Write structure, Give chemical name, properties and uses of Chloramphenicol
5. Give properties and uses of Erythromycin and Azithromycin
6. Give properties and uses of Cloxacillin and Streptomycin

Multiple Choice Questions (MCQ's)

1. **_____ is the example of β-Lactam antibiotics:**
   (a) Doxycycline (b) Minocycline
   (c) Penicillin G (d) Clindamycin

2. **Based on their mechanism of action _____ inhibits cell wall synthesis.**
   (a) Doxycycline (b) Minocycline
   (c) Penicillin G (d) Clindamycin
3. **_____ is broad spectrum antibiotics.**
   (a) Chloramphenicol (b) Streptomycin
   (c) Both (a) & (b) (d) None of the above
4. **Chemically Streptomycin is classified under:**
   (a) Tetracyclines (b) Macrolides
   (c) β-Lactam antibiotics (d) Aminoglycoside antibiotics
5. **Which one of the following is macrolide antibiotic?**
   (a) Doxycycline (b) Minocycline
   (c) Erythromycin (d) Clindamycin
6. **_____ was isolated from *Streptomyces venezuelae*.**
   (a) Chloramphenicol (b) Clindamycin
   (c) Doxycycline (d) Minocycline
7. **Chloromycetin is synonym for:**
   (a) Chloramphenicol (b) Clindamycin
   (c) Doxycycline (d) Minocycline
8. **_____ is useful against acne:**
   (a) Chloramphenicol (b) Clindamycin
   (c) Doxycycline (d) Minocycline
9. **_____ is used as antitubercular drug:**
   (a) Doxycycline (b) Minocycline
   (c) Penicillin G (d) Streptomycin
10. **Chloramphenicol is _____ antibiotic:**
   (a) Tetracyclines (b) Macrolides
   (c) β-Lactam antibiotics (d) non-classified

ANSWERS OF MULTIPLE CHOICE QUESTIONS (MCQ'S)

1. (c)	2. (c)	3. (c)	4. (d)	5. (c)	6. (a)	7. (a)
8. (b)	9. (d)	10. (d)				

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CHAPTER

Anti-Neoplastic Agents

Cancer is a disease in which some of the body's cells grow out of control and spread to other places. In the millions of cells that make up the human body, cancer can start almost anywhere. Cell division is the method by which human cells expand and proliferate to form new cells as needed by the body. As cells age or become harmed, they die and are replaced by new cells.

TYPES OF CANCER

1. **Carcinoma** develops in the skin or the tissues that surround or border internal organs.

   Some of the subtypes include adenocarcinoma, basal cell carcinoma, squamous cell carcinoma and transitional cell carcinoma.

2. **Sarcoma** is a type of cancer that begins in the body's connective or supporting tissues, such as bone, fat, muscle, cartilage and blood vessels.
3. **Leukaemia:** This is a malignancy that affects the white blood cells. It starts in the bone marrow and other blood-producing organs.
4. **Lymphoma and myeloma** are cancers that begin in the immune system.
5. **Central nervous system malignancies** are malignancies of the brain and spinal cord.

CLASSIFICATION OF ANTINEOPLASTIC AGENTS

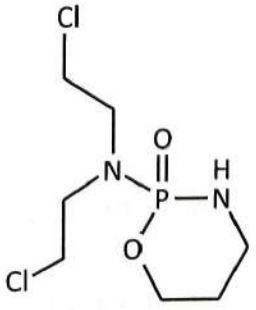
1. Cytotoxic drugs (directly act on cells):
   - (a) **Alkylating agents:**
     - (i) Ethyleneimine
     - (ii) Nitrogen mustards
     - (iii) Nitrosoureas
     - (iv) Alkyl sulfonate
     - (v) Triazine
   - (b) **Antimetabolites:**
     - (i) Purine antagonist
     - (ii) Folate antagonist
     - (iii) Pyrimidine antagonist
   - (c) **Plant derivatives:**
     - (i) Taxanes
     - (ii) Vinca alkaloids
     - (iii) Epipodophyllotoxin
   - (d) **Antibiotics**
2. **Hormones:**
   - (a) Estrogen
   - (b) Progestins
   - (c) Glucocorticoids
   - (d) Antiandrogens
3. **Miscellaneous:** Hydroxyurea, Cisplatin and Monoclonal antibodies

CYCLOPHOSPHAMIDE

Formula: $C_7H_{15}Cl_2N_2O_2P$

Molar Mass: 261.08

Structure:



IUPAC Name: (RS)-N, N-bis(2-chloroethyl)-1,3,2-oxazaphosphinan-2-amine 2-oxide

P[illegible]hamide is a fine white crystalline powder. Odourless with a slightly

Storage: store in well closed container protected from moisture.

Uses:

- Cyclophosphamide is an alkylating agent used in the treatment of several forms of cancer including leukaemia, lymphomas and breast cancer.
- Cyclophosphamide medication has been connected to rare incidences of acute liver injury and has been linked to small temporary blood enzyme increases.
- Furthermore, cyclophosphamide can produce acute sinusoidal obstruction syndrome when given in high dosages as part of myeloablative therapy.

Official Preparations:

- Cyclophosphamide tablet IP.
- Cyclophosphamide injection IP.

Brand Name:

- Injection: cydoxan, Cycloxan, oncophos, oncoxan.
- Tablet: endoxan-Asta, ledoxan.

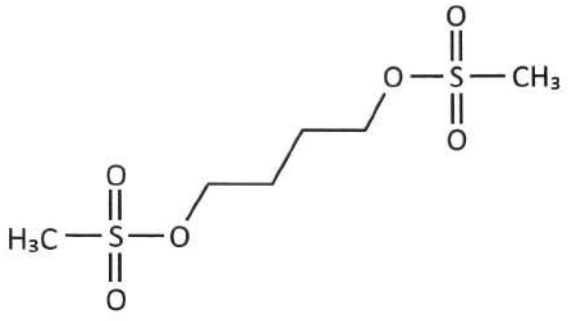
BUSULFAN

Busulfan is a methane sulfonate ester that is butane-1,4-diol.

Formula: $C_6H_{14}O_6S_2$

Molar Mass: 246.29

Structure:



IUPAC Name: Butane-1,4-diyl dimethane sulfonate or 4-methylsulfonyloxybutyl methane sulfonate

Properties: White needles shaped Crystalline powder, slightly soluble in water but soluble in acetone, MP: 114-118°C.

Storage: Store in well closed container protected from light and moisture.

Uses:

(i) It is an alkylating antineoplastic agent.

(ii) It is choice of treatment for chronic myeloid leukaemia.

(iii) It is also used as an insect sterilant.

(iv) It has a role as an insect sterilant, an antineoplastic agent, a teratogenic agent, a carcinogenic agent and an alkylating agent.

Official Preparation: Busulfan tablet.

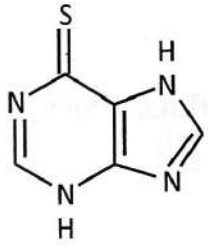
Brand Name: Mylefan, myelosam.

MERCAPTOPURINE

Synonym: 6-mercaptopurine, 6-MP

Formula: $C_5H_4N_4S$

Molar Mass: 152.18



IUPAC Name: 3,7-dihydropurine-6-thione.

Properties: Yellow crystalline powder, odourless, Insoluble in water, Soluble in boiling water, MP 313°C.

Storage: store in well closed container protected from light and moisture.

Uses: It is effective both as an anticancer and an immunosuppressive agent and is used to treat leukaemia and autoimmune diseases as a corticosteroid-sparing agent.

Official Preparation: Mercaptopurine tablet.

Brand Name: Purinetone, empurine, merapcto, puri-nethol.

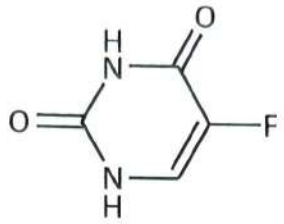
FLUOROURACIL

It is a pyrimidine analogue that is used to treat cancer.

Formula: $C_4H_3FN_2O_2$

Molar Mass: 130.078

Structure:



IUPAC Name: 5-Fluoro-1H,3H-pyrimidine-2,4-dione

Properties: Fluorouracil is a white to nearly white crystalline powder; practically odourless. MP 280-282°C.

Storage: store in well closed container protected from light and moisture.

Uses: It is used to treat multiple solid tumours including colon, rectal, breast, gastric, pancreatic, ovarian, bladder and liver cancer.

Official Preparations:

- Fluorouracil injection IP
- Fluorouracil Capsule

Brand Name:

- Injection: fivocil, tevafluoro, flutas, flucil
- Capsule: flucono, Chemoflura

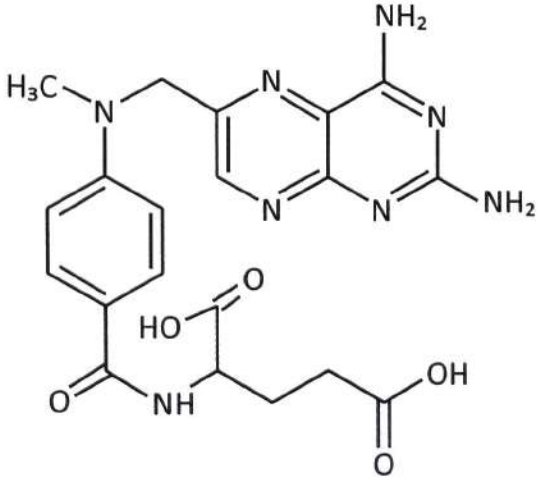
METHOTREXATE

Methotrexate is an antineoplastic and immunosuppressive agent.

Formula: $C_{20}H_{22}N_8O_5$

Molar Mass: 454.447

Structure:



IUPAC Name: (2S)-2-[[4-[(2,4-diaminopteridin-6-yl) methyl-methylamino] benzoyl] amino] pentanedioic acid

Properties: Methotrexate is an odourless yellow to orange-brown crystalline powder. Melting point: 185-204°C. Practically insoluble in water and in alcohol.

Storage: store in well closed container protected from light and moisture

Uses: It is widely used in the therapy of leukaemia, lymphoma, solid tumours, psoriasis and rheumatoid arthritis.

Official Preparations:

- Methotrexate injection IP
- Methotrexate tablets IP

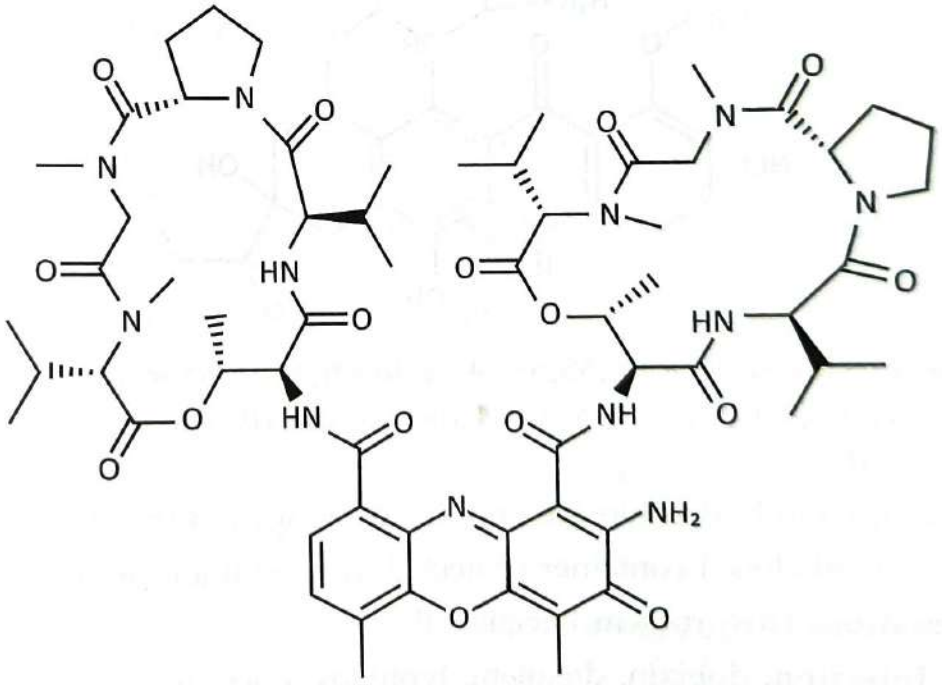
Brand Name: Folitrax, zexate, alltrex, carditrex, folitrax, imutrex

DACTINOMYCIN

Formula: $C_{62}H_{86}N_{12}O_{16}$

Molar Mass: 1255.438

Dactinomycin is an antineoplastic antibiotic that is given intravenously to treat solid tumours in children and choriocarcinoma in adult women.



IUPAC Name: 2-amino-4,6-dimethyl-3-oxo-1-*N*,9-*N*-bis[(3*R*,6*S*,7*R*,10*S*,16*S*)-7,11,14-trimethyl-2,5,9,12,15-pentaoxo-3,10-di(propan-2-yl)-8-oxa-1,4,11,14-tetraazabicyclo[14.3.0]nonadecan-6-yl]phenoxazine-1,9-dicarboxamide

Properties: Dactinomycin appears as bright red rhomboid prisms or red powder.241.5-243°C.

Storage: store in well closed container protected from light and moisture.

Uses: Dactinomycin is used to treat different types of cancers, this includes Wilms tumour, testicular cancer, etc.

Official Preparation: Dactinomycin injection IP.

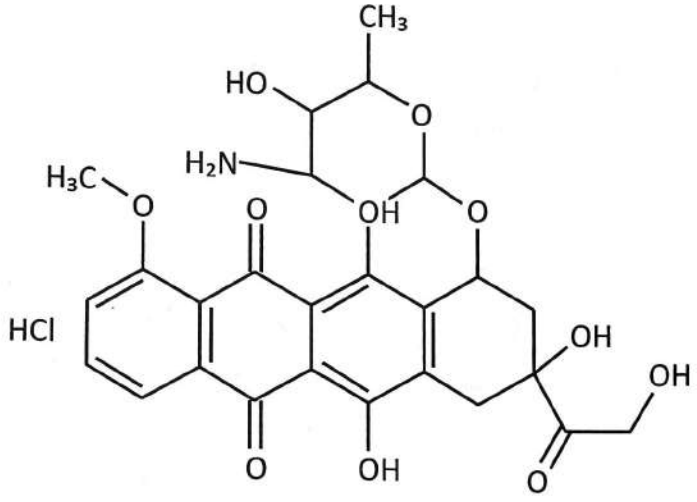
Brand Name: Injection: Cosmogen, dacmozen, dactino, dactinoget.

DOXORUBICIN HYDROCHLORIDE

Formula: $C_{27}H_{29}NO_{11}$

Molar Mass: 543.525

Doxorubicin Hydrochloride is the hydrochloride salt of doxorubicin, an anthracycline antibiotic with antineoplastic activity. Doxorubicin, isolated from the bacterium Streptomyces peucetius var. caesius



IUPAC Name: (7*S*,9*S*)-7-[(2*R*,4*S*,5*S*,6*S*)-4-amino-5-hydroxy-6-methyloxan-2-yl]oxy-6,9,11-trihydroxy-9-(2-hydroxyacetyl)-4-methoxy-8,10-dihydro-7*H*-tetracene-5,12-dione;hydrochloride

Properties: Adriamycin hydrochloride appears as orange-red thin needles.

Storage: store in well closed container protected from light and moisture.

Official Preparation: Doxorubicin injection IP.

Brand Name: Injection: dobixin, doxolem, lyphidox, oncodox, zodox.

VINBLASTINE SULPHATE

Formula: $C_{46}H_{58}N_4O_9$

Molar Mass: 810.989

IUPAC Name: Methyl(1*R*,9*R*,10*S*,11*R*,12*R*,19*R*)-11-acetyloxy-12-ethyl-4-[(13*S*,15*R*,17*S*)-17-ethyl-17-hydroxy-13-methoxycarbonyl-1,11-diazatetracyclo[13.3.1.$0^{4,12}$.$0^{5,10}$] nonadeca-4(12),5,7,9-tetraen-13-yl]-10-hydroxy-5-methoxy-8-methyl-8,16-diazapentacyclo [10.6.1.$0^{1,9}$.$0^{2,7}$.$0^{16,19}$]nonadeca-2,4,6,13-tetraene-10-carboxylate;sulfuric acid

Properties: White to slightly yellow crystalline powder.

Storage: Store in well closed container protected from light and moisture.

Uses: It is used in the treatment of Breast Cancer, Choriocarcinoma, Testicular Cancer.

Official Preparation: Vinblastine injection.

Brand Name: Velban.

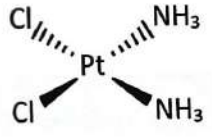
CISPLATIN

Formula: [Pt $(NH_3)_2Cl_2$]

Molar Mass: 300.05

Synonym: Azane; dichloroplatinum

Structure:



IUPAC Name: cis-diamminedichloroplatinum (II).

Properties: White lyophilised powder, slightly soluble in water, MP 207°C.

Storage: Store in well closed container protected from light and moisture.

Uses: Cisplatin is a chemotherapy drug used to treat testicular, ovarian, bladder, head and neck, lung and cervical cancer.

Official Preparation: Cisplatin injection IP.

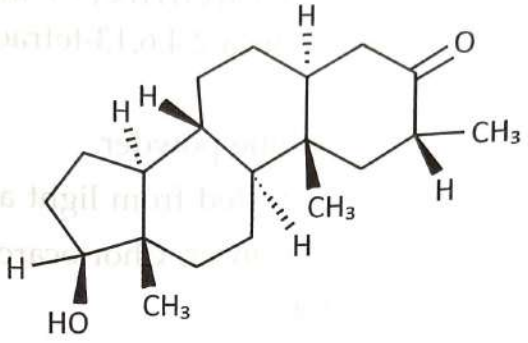
Brand Name: Injection: Ciplat, kemoplat, paltikem, cisteen, duplat, oncoplatin-AQ, platin.

DROMOSTANOLONE PROPIONATE

Formula: $C_{23}H_{36}O_3$

Molar Mass: 360.538

Drostanolone propionate, or dromostanolone propionate, is an Androgen and Anabolic Steroid (AAS).



IUPAC Name: (2R,5S,8R,9S,10S,13S,14S,17S)-17-hydroxy-2,10,13-trimethyl-1,2,4,5,6,7,8,9, 11,12,14,15,16,17-tetradecahydrocyclopenta[a]phenanthren-3-one

Properties: White to creamy white, crystalline powder; odourless or has faint odour; practically insoluble in water; soluble in chloroform, ether and methanol, Melting Point 151°C.

Uses: It which was used to treat breast cancer in women, Muscle Building.

Official Preparation: Dromostanolone injection (for IM use).

Brand Name: Drolban, Masteril and Masteron.

EXERCISE

Short Answer Type Questions

1. **Give two Brand Names of following drugs:**
   (a) Cyclophosphamide (b) Busulfan
   (c) Mercaptopurine (d) Doxorubicin Hydrochloride
2. **In what dosage form the following drugs are given:**
   (a) Cyclophosphamide (b) Fluorouracil
3. **Give uses of following drugs:**
   (a) Methotrexate (b) Dactinomycin
4. **Write structure and give chemical name of following drugs.**
   (a) Cyclophosphamide (b) Fluorouracil

(c) Cisplatin

5. **Name the drug present in following brands:**
   (a) Merapcto
   (b) Cycloxan
   (c) Chemoflura
6. **Name one drug used for treatment of liver cancer.**

Long Answer Type Questions

1. Classify Antineoplastic agent drugs with examples.
2. Write structure, Give chemical name, properties and uses of Cyclophosphamide
3. Write structure, Give chemical name, properties and uses of Fluorouracil
4. Write structure, Give chemical name, properties and uses of Cisplatin
5. Give properties and uses of Mercaptopurine and Methotrexate
6. Give properties and uses of Dromostanolone Propionate and Vinblastine Sulphate

Multiple Choice Questions (MCQ's)

1. **_____ is a condition in which some cells in the body grow out of control and spread to other parts of the body.**
   (a) Diabetes
   (b) Angina pectoris
   (c) Cancer
   (d) All of the above
2. **_____ is butane-1,4-diol derivative drug.**
   (a) Dactinomycin
   (b) Busulfan
   (c) Doxorubicin Hydrochloride
   (d) Vinblastine Sulphate
3. **_____ is a pyrimidine analogue used as an antineoplastic agent.**
   (a) Cyclophosphamide
   (b) Busulfan
   (c) Mercaptopurine
   (d) Fluorouracil
4. **The antineoplastic agent isolated form Streptomyces peucetius var. caesius is:**
   (a) Methotrexate
   (b) Dactinomycin
   (c) Doxorubicin Hydrochloride
   (d) Vinblastine Sulphate
5. **Dichloroplatinum is synonym for:**
   (a) Doxorubicin Hydrochloride
   (b) Vinblastine Sulphate
   (c) Cisplatin
   (d) Dromostanolone
6. **Which one of the following is not antineoplastic agent?**

(a) Busulfan
(b) Primaquine
(c) Fluorouracil
(d) Methotrexate

7. Which antineoplastic agent is also used for Muscle Building?

(a) Doxorubicin Hydrochloride
(b) Vinblastine Sulphate
(c) Cisplatin
(d) Dromostanolone Propionate

8. Which type of cancer affects white blood cells?

(a) Leukaemia
(b) Sarcoma
(c) Carcinoma
(d) All of the above.

9. Cyclophosphamide is given in which form?

(a) Tablet
(b) Injection
(c) Both (a) & (b)
(d) None of the above

10. What is the name of heterocyclic ring present in Methotrexate?

(a) Pteridin
(b) Pyrimidine
(c) Pyrizinamide
(d) Benzpyrrole

ANSWERS OF MULTIPLE CHOICE QUESTIONS (MCQ'S)

1. (c) 2. (b) 3. (d) 4. (c) 5. (c) 6. (b) 7. (d)
8. (a) 9. (c) 10. (a)

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