PHARMACEUTICAL COMPOUNDS OR DRUGS

Introduction:

Chemical Substances used to prevent and cure diseases by destroying infectious micro-organisms without destroying host tissues and keep us in a state of normal health are called pharmaceutical compounds or drugs.

According to WHO, a drug may be defined as a substance or product that is used or intended to be used for modifying or exploring physiological systems or pathological states for the benefit of the patient.

Characteristics of a Drug:

An ideal drug should possess the requisites as under:

I) When administered to an ailing person, its action should be localized at the site where it is required to act.
II) It should be non-toxic in nature.
III) It should act in a system with safety and efficiency.
IV) It should show minimum side effect.

Classification:

Pharmaceutical drugs can be classified in a number ways . These can be classified on the basis of applications. For example-

1) Antipyretics: These drugs tend to lower the body temperature in high fevers, e. g. aspirin, paracetamol etc.
2) Analgesics: These drugs relieve or decrease pain. These are of two types: a) Narcotics and b) Non- narcotics.

a) Narcotics: These drugs produce depressing action on central nervous system, e. g. Morphine, Codine and Heroin.

b) Non- narcotics: These drugs have antipyretic properties, e. g. Analgin, Aspirin etc.

3) Antibacterial drugs or Antibiotics: These drugs are used against disease producing bacteria called pathogens. For example: Penicillines, Tetracyclines, Chloramphenicol etc.

4) Antiviral drugs: These drugs are used for the treatment of disease caused by viruses. For example, Ampligen, Arbidol etc.

5) Antimalarials: These drugs are used against malarial parasite. For example: Chloroquine, Primaquine etc.

6) Antiseptic Drugs: Used to destroy or inhibit growth of micro-organisms. For example, Phenols, Dettol, Turmeric, Ginger etc.

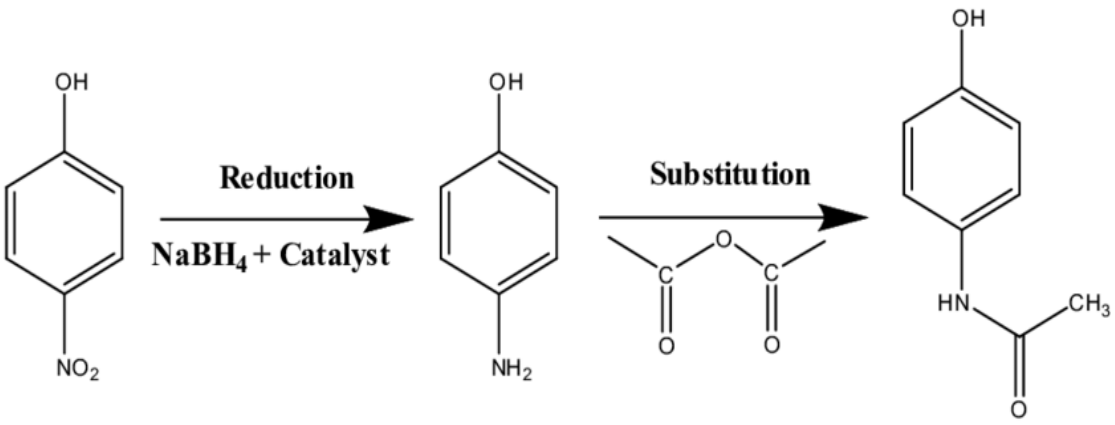
7) Drugs in cancer therapy, antidiabetics, antihistamins, anti-HIV/ AIDS etc.

ANTIPYRETICS:

Drugs used to lower body temperature in feverish condition are called antipyretics. Paracetamol and phenacetin are commonly used antipyretics.

Paracetamol:

Synthesis: It is synthesized from p-amino phenol by reduction followed by acetylation.



Para-nitrophenol **Para-aminophenol** **Paracetamol**

Uses: It has both analgesic and antipyretic activity.

Mode of action of antipyretics:

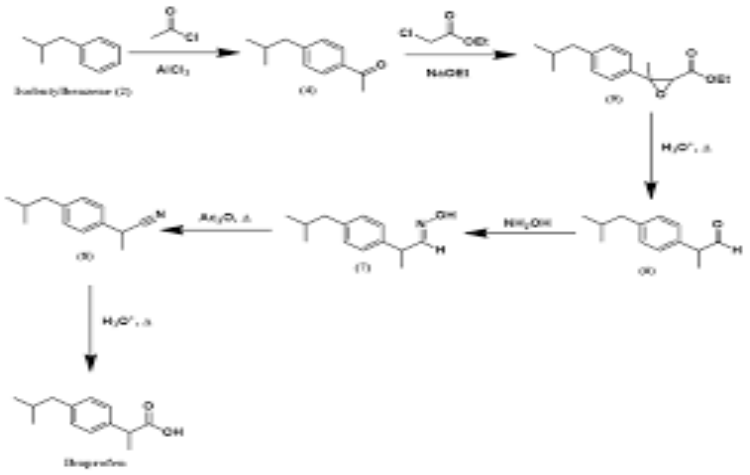
In order to regulate body temperature, there should exist a balance between heat production and heat loss. The central nervous system especially the hypothalamus maintains the balance between the two and act as a thermostat. Antipyretic drugs help to reset the thermostat for normal temperature.

ANALGESICS:

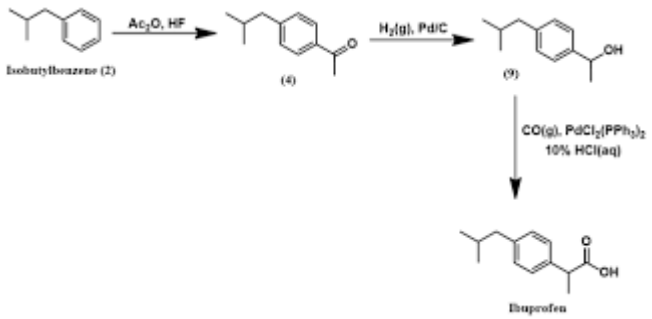
Drugs used to relieve pain in various condition of health without loss of consciousness are called analgesics. Some commonly used analgesics are ibuprofen and aspirin.

Ibuprofen:

Synthesis: Traditionally ibuprofen is prepared from isobutyl benzene in six steps.



Green synthesis:



Uses: Ibuprofen is a nonsteroidal anti – inflammatory drug (NSAID). It works by reducing hormones that causes inflammation and pain in the body. It is used to reduce fever and treat pain or inflammation caused by many conditions such as headache, toothache, backpain etc.

Mode of action of analgesics: Analgesics act by increasing the threshold of pain. The pain is induced by a stimulus, a measure of the threshold of pain. When analgesics are used, the pain is not decreased but only the threshold of pain is increased. Therefore, the patient does not feel pain.

ANTIMALARIALS:

The drugs used for the treatment of the tropical disease of malaria are called antimalarials. The cinchona alkaloid quinine (a quinoline derivative) was the well known natural antimalarial. Quinine has now been replaced by synthetic antimalarials like chloroquine.

Malaria is caused by sporozoan of genus plasmodium. In human beings, it is caused by a few species of plasmodium when an infected female anopheles bites to the man.

There are four distinct species of the malarial parasites. They are Plasmodium vivax, Plasmodium falciparum, Plasmodium malaria and Plasmodium ovale.

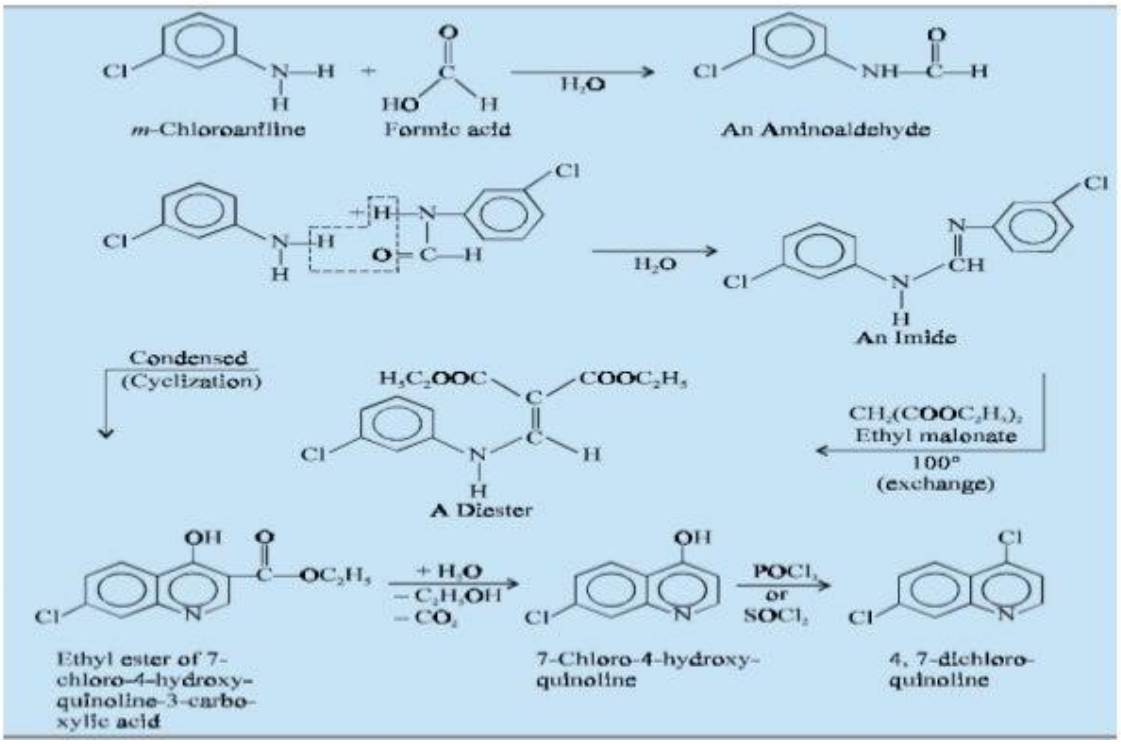
Classification of synthetic antimalarials: The most widely used synthetic antimalarials may be classified into following groups:

- 4-Amino quinoline derivatives.
- 8-Amino quinoline derivatives.
- Acridine derivatives.
- Miscellaneous antimalarials.

Chloroquine:

Chloroquine is 7-chloro –4- (4-diethylamino-1- methyl butyl amino) quinoline. It is a much more effective antimalarial than quinine. Its synthesis from m- chloro aniline (2mole) and formic acid is outlined below:

Chloroquine synthesis



Uses:

1) It acts on erythrocytic cycle of plasmodium vivax malaria. It abolishes acute attack of malaria.

2) It also kills amoeba. It is therefore, effective in intestinal hepatic and cutaneous amoebiosis.

3) In infectious mononucleosis (viral disease)

4) Its hydroxy derivative is recently used to treat COVID-19 patients in combination with other viral drugs.

Disadvantage of chloroquine:

1) It does not completely treat malaria and relapse of malaria occurs after sometimes.

2)It is having several side effects such as general weakness, uneasiness, vomiting etc.

ANTIBIOTICS

An antibiotic may be defined as a chemical compound that gets derived from or produced by a living organism, which can in small concentration, inhibit the live processes or even destroy micro- organisms. The organism which are susceptible to the inhibitory effect of an antibiotic constitute its **spectrum.** Majority of antibiotics are produced from fungi.

Characteristics of an Antibiotic:

An antibiotic satisfied the following conditions:

1) It should be a product of metabolism.
2) If it is a synthetic product, then it should be a structural analogue of a naturally occurring antibiotic.
3) It is able to antagonise the growth and/ or survival of one or more species of micro- organisms.
4) It must be effective at low concentration.

For an antibiotic to be useful chemotherapeutically:

1) It must be effective against pathogens.
2) It must not produce any significant toxic side- effects.
3) It must be sufficiently stable.
4) It should be durable for a reasonable long period of time.

Classification of Antibiotics:

The antibiotics may be classified into many ways:

The first classification of antibiotics, divides them into broad- spectrum and narrow- spectrum antibiotics. If an antibiotic is able to antagonise many pathogens, then it is termed as broad- spectrum antibiotic. For example-

Penicillin, Chloramphenicol, Tetracyclines etc. Antibiotics that are specific in their action are designated as narrow- spectrum antibiotics. For example- Bacitracin, Nystatin etc.

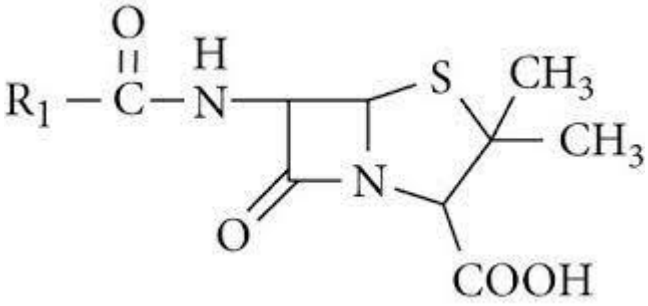
Second type of classification is based upon the type of bacteria (Gram- positive or Gram- negative) that the antibiotic is able to destroy. In Gram- staining method, the bacterial smearis first treated with a solution of crystal violet, and then with iodine solution. The smear is then washed with alcohol and safranin.

The bacteria that retain the colour of crystal violet and appear deep violet, are known as Gram- positive bacteria, while those which loss the violet colour and appears red in colour, are known as Gram- negative bacteria.

Some Gram- positive bacteria are Diphtheria bacillus, Leprosy bacillus, Pneumococcus etc. and some Gram- negative bacteria are Coli and typhoid bacillus, Gonococcus, Plague bacillus etc.

Penicillin:

Penicillin was first discovered in 1928 by Alexander Fleming from a mold Penicillium notatum. In recent years, several penicillin analogs, having beta- lactam thiazolidine structure necessary for penicillin activity have been synthesized. However, they differ from each other in their side chain(R). The basic skeleton of penicillin is as follows:



Some commonly used penicillins are as follows:

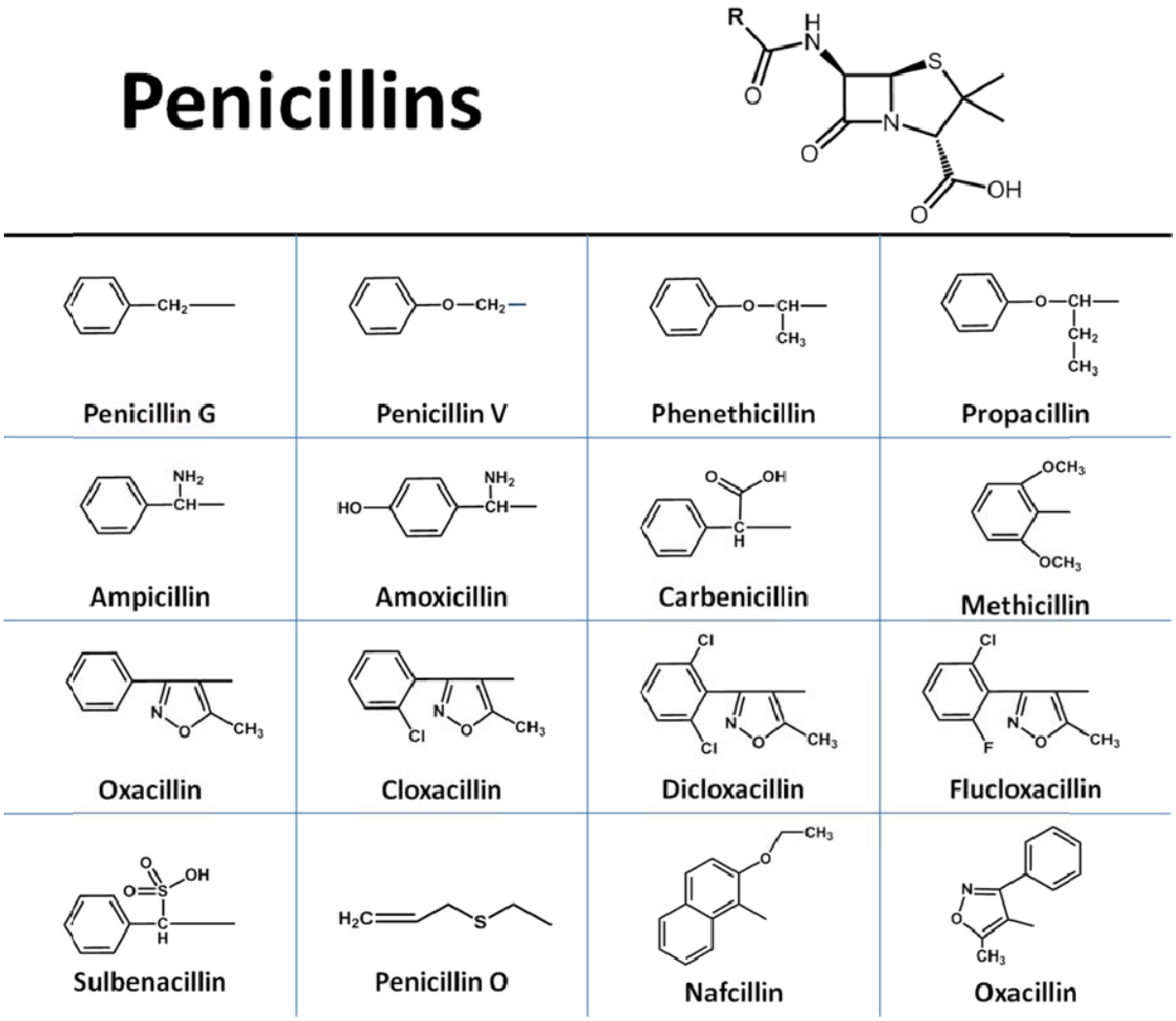


Figure 1. *Chemical structure of penicillin antibiotics with various R groups.*

Uses: Penicillins are used for infections of respiratory system (e.g., pneumonia, acute bronchitis and bronchopneumonia), urinary tract infections due to streptococcus pypgenes, bacterial endocarditis (i.e., inflammation of the inner lining of heart), Meningitis, Gonorrhoea and syphilis.

Ampicillin is a widely used antibiotic as it inhibits the growth of both gram positive and gram-negative bacteria.

Mode of action: Antibacterial action of penicillin is due to inhibition of metabolic functions necessary for the bacterial cell wall. It may be bactericidal or bacteriostatic depending on the age of bacteria. Newly growing bacterial cells are more susceptible to this than a mature cells.

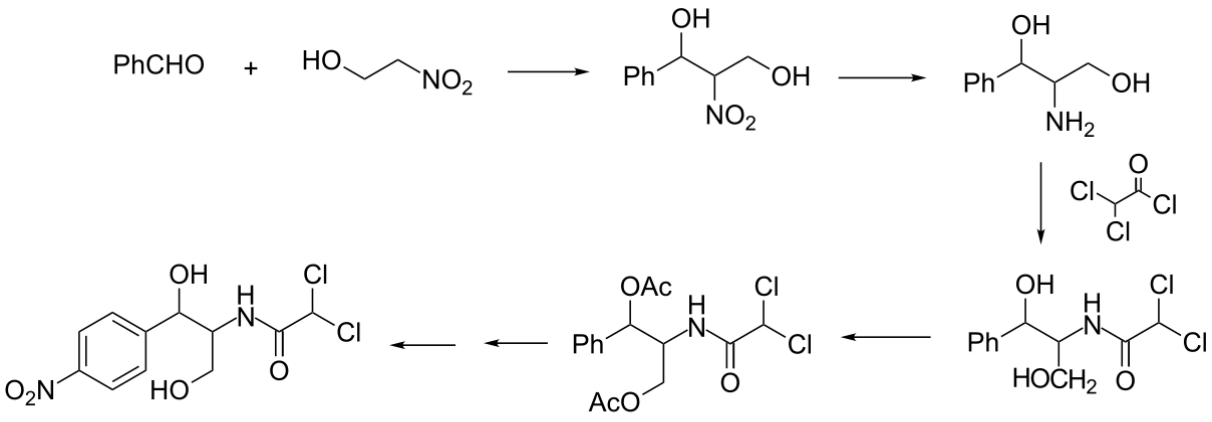
The antibacterial activity of penicillins is due to the presence of beta-lactam ring which opens in the presence of nucleophilic reagents (amine group of enzymes). This reaction of penicillins involves their interference with the synthesis of the bacterial cell walls. This process deactivates enzymes necessary for cell wall formation of bacteria. This causes ultimate death of bacteria due to hindrance in their cell wall formation.

CHLORAMPHENICOL :

Chloramphenicol has been a broad spectrum antibiotic effective against both gram positive and gram-negative bacteria. It was isolated by Ehrlich et al. in 1947 from streptomyces venezuelea (an organism found in soil samples collected from Venezuela). It is the first antibiotic to be produced commercially by a synthetic process.

Synthesis:

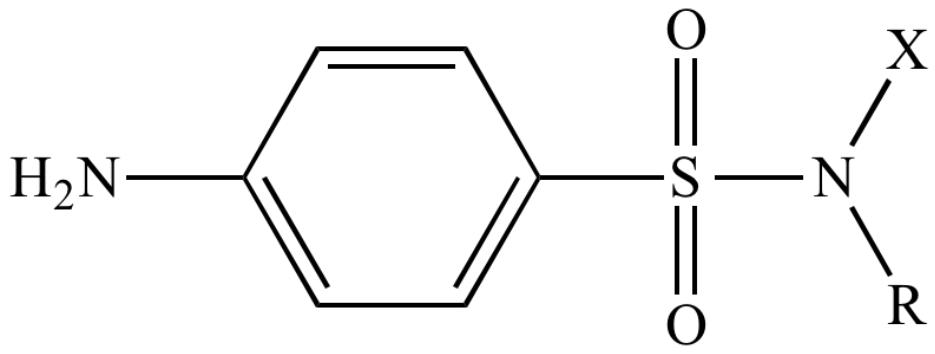
1) From benzaldehyde:



Uses: It is very effective against a number of infections not responding to other drugs. It is particularly effective in typhoid and paratyphoid fever. However, its prolonged use can lead to many toxic reactions. It is used only when other antibiotics fail and that too under strict medical supervision.

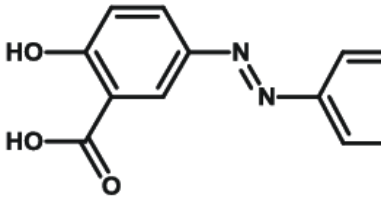
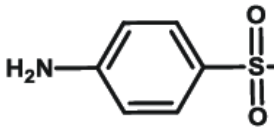
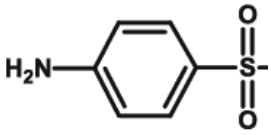
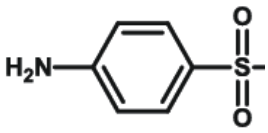
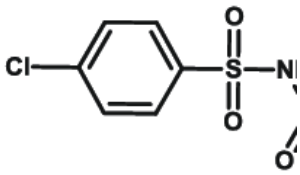
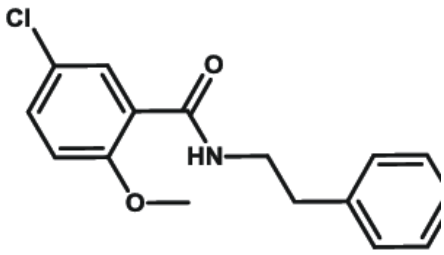
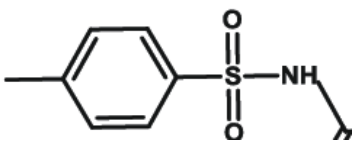
SULPHA DRUGS:

Sulpha drugs are the derivatives of sulphonamides. These compounds were found to be effective against pathogenic organism or bacteria which cause pneumonia, tuberculosis, gonorrhea etc. Some commonly used derivatives of sulphonamides are as follows:

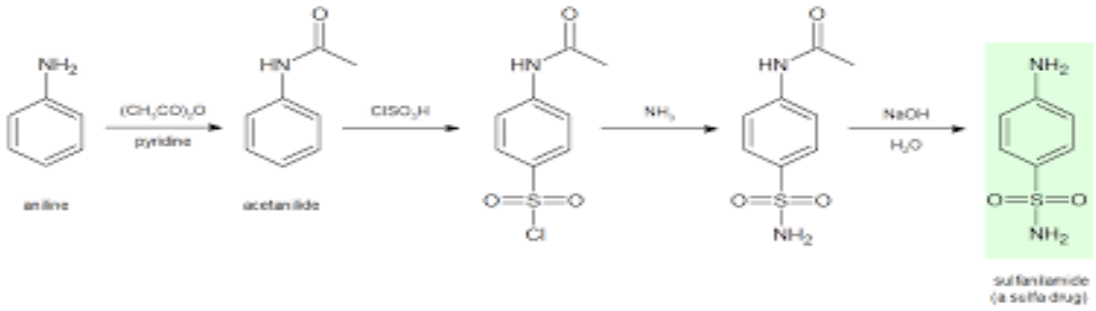


Some Sulpha drugs are:

1) Sulphapyridine: It is useful in the treatment of a certain type of dermatitis.
2) Sulphamethoxazole mixed with trimethoprim is used in wider range of infections, urinary infections and respiratory tract infections.
3) Sulphadoxine is used in the treatment of leprosy.
4) Sulphacetamide is applied locally in infections of the eye.
5) Sulphaguanidine is used in the treatment of bacillary dysentery.
6) Sulphadiazine is used in pneumococcal, meningococcal diseases.
7) Sulphathiazole is used in streptococcal, staphylococcal, pneumococcal and gonococcal infections.

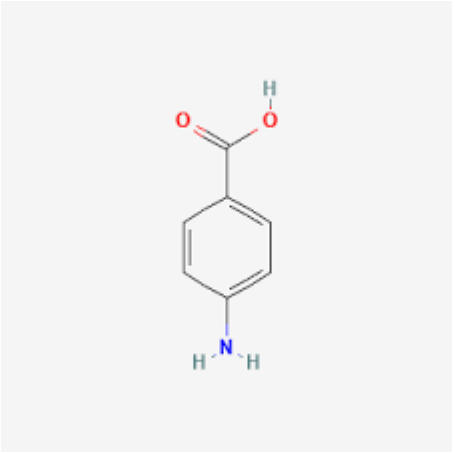
Drug Name	Core Structure	Structure
Sulfasalazine	Sulfonamide	
Sulfathiazole	Sulfonamide	
Sulfapyridine	Sulfonamide	
Sulfamethoxazole	Sulfonamide	
Chlorpropamide	Sulfonylurea	
Glibenclamide	Sulfonylurea	
Tolbutamide	Sulfonylurea	

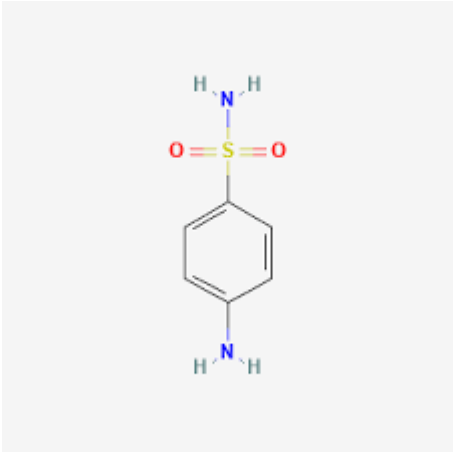
General synthesis of sulpha drugs:



Mode of action of Sulpha drugs:

Para- amino benzoic acid (PABA) is an essential nutrient for those bacteria which are sensitive to sulpha drugs. Para- amino benzoic acid is needed for the enzyme within these bacteria for the synthesis of folic acid. Sulpha drugs inhibit the growth of those micro- organism which need p-amino benzoic acid for the synthesis of folic acid. The bacterial enzymes are unable to distinguish between the molecule of PABA and that of sulphonamide due to close structural similarity of the two. Thus, sulphonamides inhibit the activity of bacterial enzyme which is unable to synthesise folic acid essential for living bacteria resulting in the death of bacteria.





MEDICINAL USES / VALUES OF CURCUMIN (TURMERIC):

Polyphenolic compound 3-6% collectively known as curcuminoids which is a mixture of curcumin, dimethoxy curcumin and bis- dimethoxy curcumin. Curcuminoids are major components responsible for various biological actions.

Curcumin (Turmeric) have many scientifically proven health benefits as follows:

1) Curcumin has the potential to prevent heart disease, Alzheimer's and cancer.
2) It is a potent anti- inflammatory and antioxidant.
3) It helps to improve symptoms of depression and arthrities.
4) Curcumin is fat soluble, therefore it may be taken with fatty meal.
5) It lowers the risk of brain diseases.
6) It help to delay aging and chronic diseases.

MEDICINAL USES / VALUES OF AZADIRACHTIN (NEEM)

Azadirachtin (Dihydro azadirachtin) is extracted from the fruit of neem trees. It is used as a commercial insect growth regulator. The neem tree also yields extracts from its bark, leaves and wood that has the following medicinal uses/ values:

1) Neem leave is used for leprosy, eye disorders, bloody nose, intestinal worms, loss of apetite, heart diseases, fever, diabetes and liver problems.
2) Neem bark is used for treating malaria, stomach and intestinal ulcers, skin diseases pain and fever.
3) The neem flower is used for reducing bile and treating intestinal worms.
4) The neem fruit is used for reducing bile, intestinal worms, urinary tract disorder, leprosy and wounds.
5) The neem twigs are used for cough, intestinal worms and diabetes.

MEDICINAL USES / VALUES OF VITAMIN C (ASCORBIC ACID)

Vitamin C is an essential vitamin and can not be produced by the body. It is soluble in water and in many fruits and vegetables like oranges, lemons, strawberries, broccoli, cabbage etc. The recommended daily intake for vitamin C is 75 mg for women and 90 mg for men. The following are the medicinal values of vitamin C.

1) It acts as antioxidant that may reduce the risk of chronic diseases.
2) It helps to maintain blood pressure of the body.
3) It lowers heart disease risk.
4) It can reduce blood uric levels.
5) It helps to prevent iron deficiencies.
6) Its deficiency causes **Scurvy** which is characterized by sore, spongy gums, loosening of teeth etc.

MEDICINAL USES / VALUES OF ANTACID (RANITIDINE)

Ranitidine belongs to histamine- H_2- receptor antagonist that inhibits stomach acid production. It has following medicinal uses/ values:

1) Ranitidine is used to treat ulcers of the stomach and intestine.
2) This is also used to treat certain throat (esophagus) and gastro-esophagus reflux disease.
3) It relieves symptoms such as cough, stomach pain, heart burn and difficulty in swallowing.