Program	B. Pharmacy
Semester	VI
Subject /Course	Medicinal Chemistry III
Subject/Course ID	BP 601T
Module No.	02
Module Title	Antibiotics
Course coordinator	Noel
Mobile No.	6280907651
Email id	noelchem00@gmail.com

Learning Outcome of module-2

LO	Learning Outcome (LO)	Course Outcome Code
LO1	To Understand the Nomenclature &chemistry of drugs with respect to their biological activity.	BP601.1
LO2	To understand the importance of SAR of drugs.	BP601.4
LO3	To understand the Basic concepts and application of prodrugs design.	BP601.2

Content Table

Topics
Macrolide • Erythromycin Clarithromycin, Azithromycin. **Miscellaneous** • Chloramphenicol*, Clindamycin. **Pro-drugs** • Basic concepts and application of prodrugs design. **Anti-mlarials** • Etiology of malaria. **Quinolines** • SAR, Quinine sulphate, Chloroquine*, Amodiaquine, Primaquine phosphate, Pamaquine*, Quinacrine hydrochloride, Mefloquine. • Biguanides and dihydro triazines • Cycloguanil pamoate, Proguanil. **Miscellaneous** • Pyrimethamine, Artesunete, Artemether, Atovoquone.

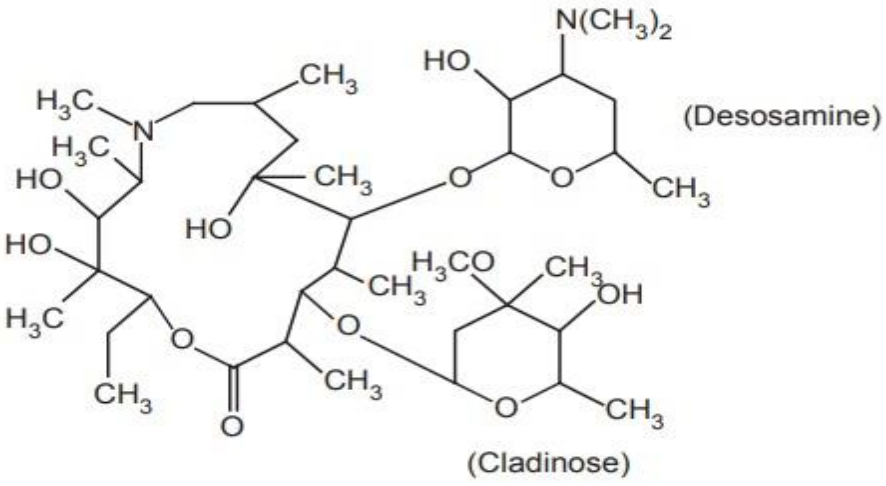
MACROLIDES ANTIBIOTICS

The macrolide antibacterial agents are extremely useful chemotherapeutic agents for the treatment of a variety of infectious disorders and diseases caused by a host of gram-positive bacteria, both *cocci* and *bacilli*; they also exhibit useful effectiveness against gram-negative *cocci*, specially, *neisseria* spp. The macrolides are commonly administered for respiratory, skin, tissue, and genitourinary infections caused by these pathogens.

Chemistry: They are characterized by five common chemical features.

1. A macrocyclic lactone usually has 12–17 atoms, hence the name macrolide.
2. A ketone group.
3. One or two amino sugars glycosidically linked to the nucleus.
4. A neutral sugar linked either to amine sugar or to nucleus.
5. The presence of dimethyl amino moiety on the sugar residue, which explains the basicity of these compounds, and consequently the formation of salts. The antibacterial spectrum of activity of the more potent macrolides resembles that of penicillin. Examples: erythromycin, oleandomycin, clarithromycin, flurithromycin, dirithomycin, azithromycin.

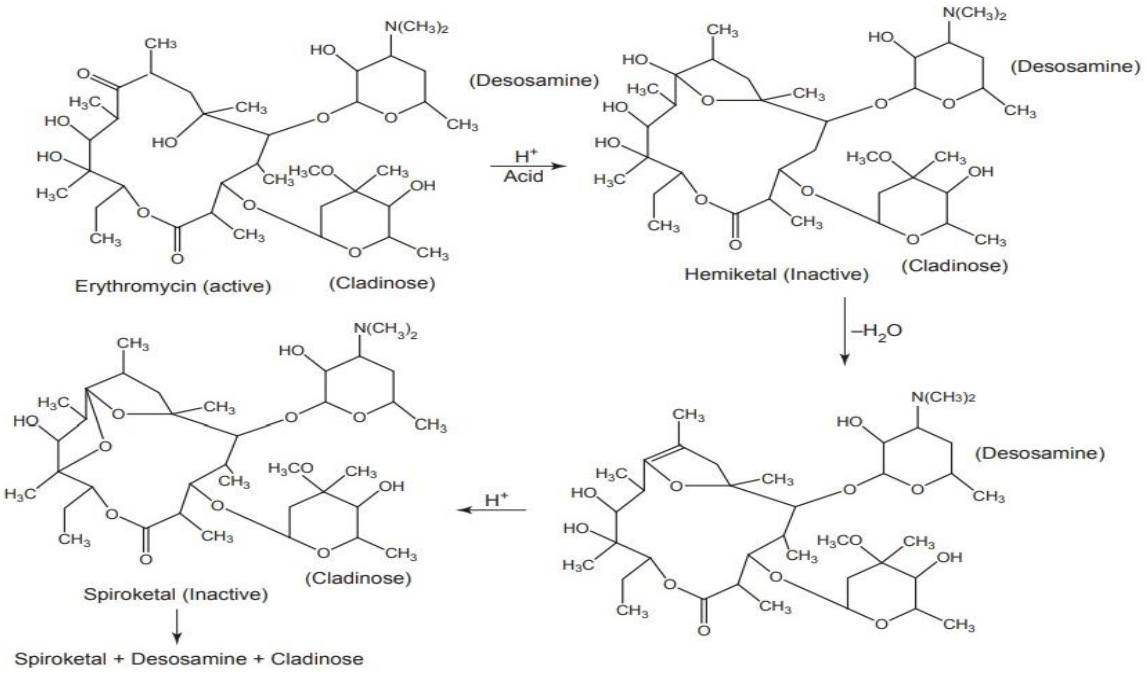
i. Azithromycin



Properties and uses: Azithromycin is a white powder, practically insoluble in water, soluble in anhydrous ethanol and methylene chloride. It is very stable under acidic conditions, is less active against *Streptococci* and *Staphylococci* than erythromycin, and is far more active against respiratory infections due to *H. influenzae* and *Chlamydia trachomatis.*

ACID DEGRADATION OF ERYTHROMYCIN

Erythromycin is unstable in the acid media. The C-6 hydroxyl group reversibly attacks the C-9 ketone giving rise to a hemiketal intermediate. Dehydration prevents regeneration of the parent erythromycin and the C-12 hydroxyl group can subsequently add to produce a spiroketal species. The cladinose group is cleaved from the macrocycle and more harsh conditions lead to the release of desosamine. Useful antibacterial activity last till the dehydration of the hemiketal and the spiroketal is weakly active.



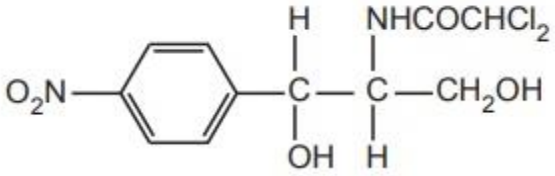
Mode of action:

Macrolide antibiotics are bacteriostatic agents that inhibit protein synthesis by binding irreversibly to a site on the 50S subunits of the bacterial ribosome. Thus, inhibiting the translocation steps of protein synthesis at varying stages of peptide chain elongation (hinder the translocation of elongated peptide chain back from 'A' site to 'P' site). The macrolides inhibit ribosomal peptidyl transferase activity. Some macrolides also inhibit the translocation of the ribosome along with the mRNA template.

Chloramphenicol or chloromycetin

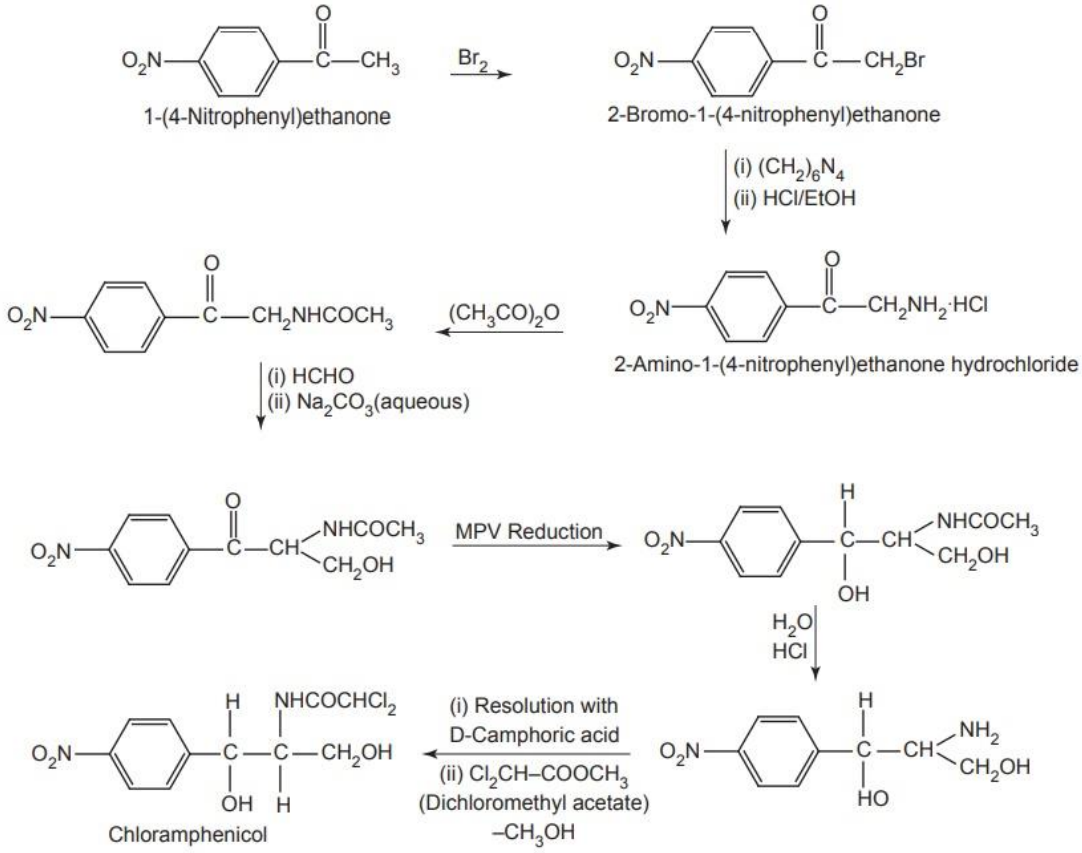
Chloramphenicol has a spectrum of activity resembling that of the tetracyclines except that it exhibits a bit less activity against some gram-positive bacteria. It is isolated from *Salmonella venezuelae* by Ehrlich et al in 1947. It contains chlorine and is obtained from an actinomycete, and thus, named as chloromycetin. It is specifically recommended for the treatment of serious infections caused by *H.*

influnzae, S. typhi (typhoid), *S. pneumoniae, and N. meningitides*. Its ability to penetrate into the CNS presents an alternative therapy for meningitis and exhibits antirickettsial activity.

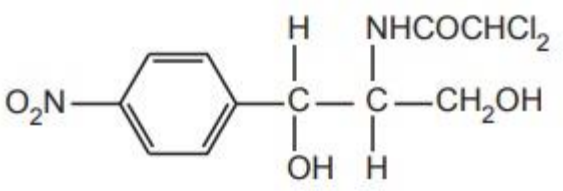


N-(1,3-Dihydroxy-1-(4-nitrophenyl)propan-2-yl)dichloroacetamide

Properties and uses: Chlorampenicol is a white or greyish-white or yellowish-white crystalline powder or fine crystals, slightly soluble in water, soluble in alcohol and propylene glycol. It was the first, and still is the only therapeutically important antibiotic to be produced in competition with microbiological processes. It contains a nitrobenzene moiety and is a derivative of dichloroacetic acid. Since it has two chiral centres, four isomers are possible. The D-(-) threo is the biologically active form. It is used in the treatment of typhoid fever caused by *S. typhi*. The most serious adverse effect of chloramphenicol is bone marrow depression and fatal blood dyscrasias.



SAR of Chloramphenicol



a. Modification of *p*-nitrophenyl group.

b. Modification of dichloroacetamide side chain.

c. Modification of 1, 3-prepanediol.

Modification of *p*-nitrophenyl group: The *p*-nitrophenyl group may be modified through the following ways:

a. Replacement of the nitro group by other substituents leads to a reduction in activity.

b. Shifting of the nitro group from the para position also reduces the antibacterial activity.

c. Replacement of phenyl group by the alicyclic moieties results in less potent compounds.

Modification of dichloroacetamido side chain: Other dihalo derivatives of the side chain are less potent although major activities are retained.

Modification of 1,3-propanediol: If the primary alcoholic group on C-1 atom is modified, it results in a decrease in activity; hence, the alcoholic group seems to be essential for activity

PRO-DRUGS

INTRODUCTION

A pro-drug is a chemically modified inert precursor of the drug that on biotransformation liberates the pharmacologically active parent compound. A pro-drug is also called as pro-agent, bio-reversible derivative, or latentiated drug. The design of pro-drug approach is also called as drug latentiation.

Ideal Properties

The ideal properties of pro-drugs are as follows:

- Drug and the carrier linkage must be cleared in vivo.
- It should not have intrinsic pharmacologic activity.
- It should rapidly transform, chemically or enzymatically, into the active form where desired .The metabolic fragments, apart from the active drug, should be nontoxic.

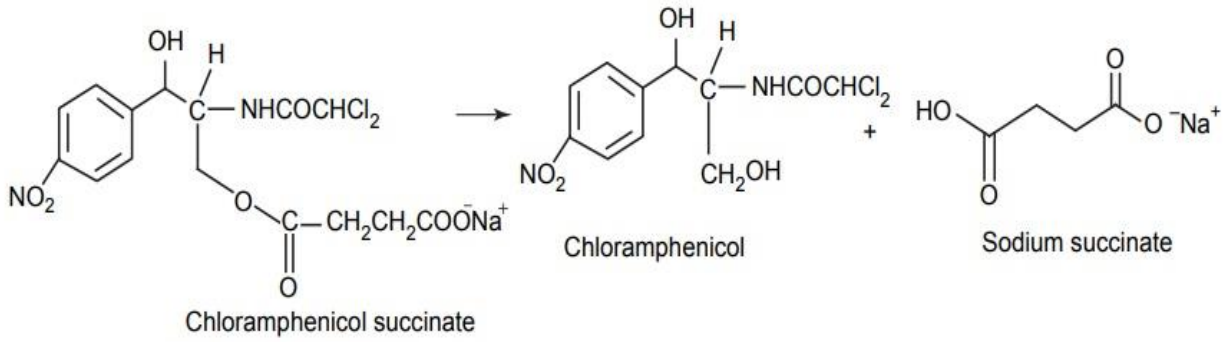
CLASSIFICATION OF PRO-DRUG

Depending on the constitution, lipophilicity, and method of bioactivation, pro-drugs are classified into two categories.

1. Carrier-linked pro-drugs
2. Bio-precursors

Carrier-linked pro-drug or simple pro-drugs: They are generally esters or amides. Carrier-linked prodrugs are the ones where the active drug is covalently linked to an inert carrier or transport moiety. Such pro-drugs modify the lipophilicity due to the attached carrier. The active drug is released by hydrolytic cleavage, either chemically or enzymatically.

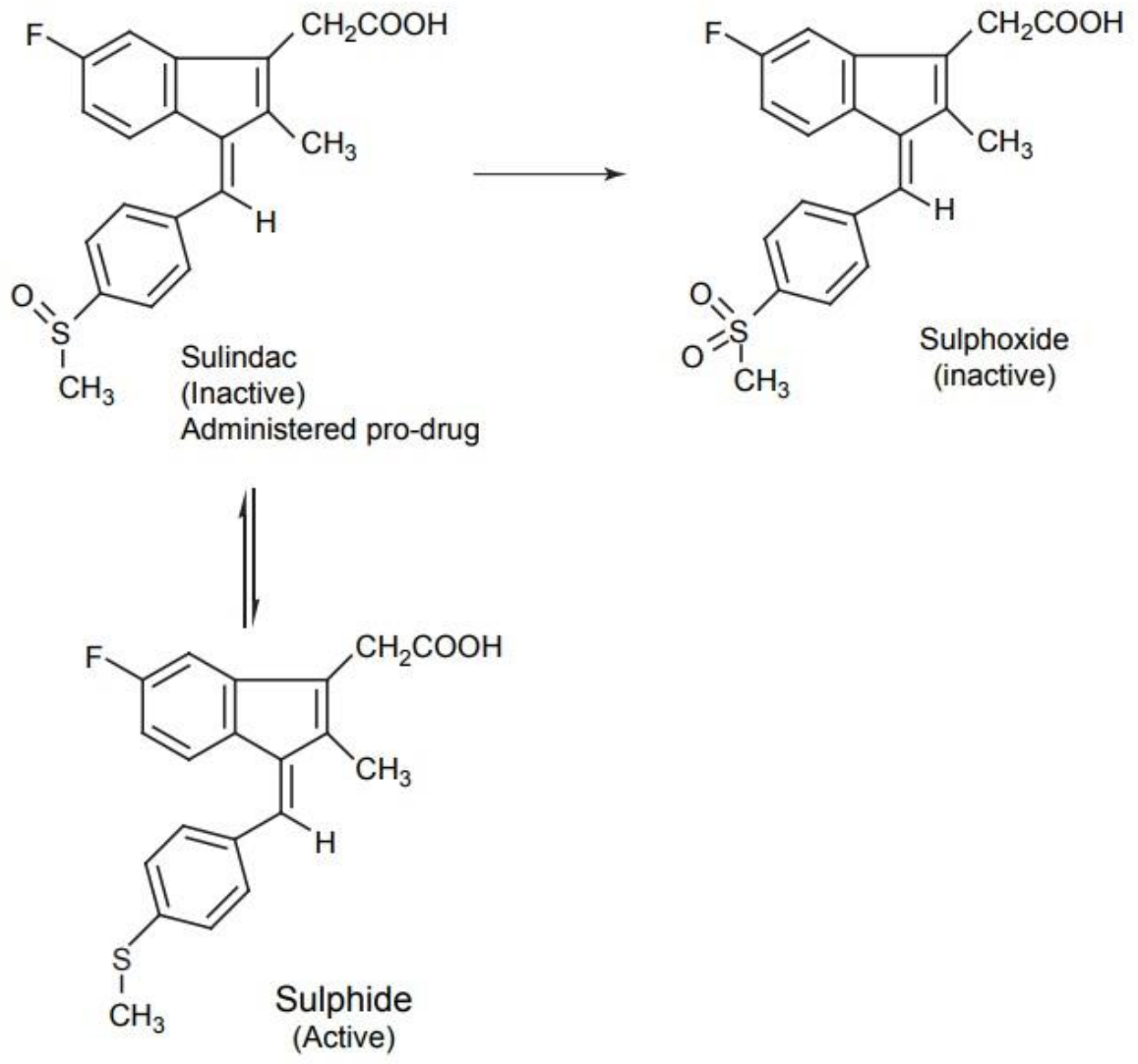
Examples:



Bioprecursors: They are inert molecules obtained by a chemical modification of the active drugs, but do not contain a carrier. For example, nonsterodial anti-inflammatory drug, sulindac, is inactive as sulphoxide and must be reduced metabolically to active sulphide.

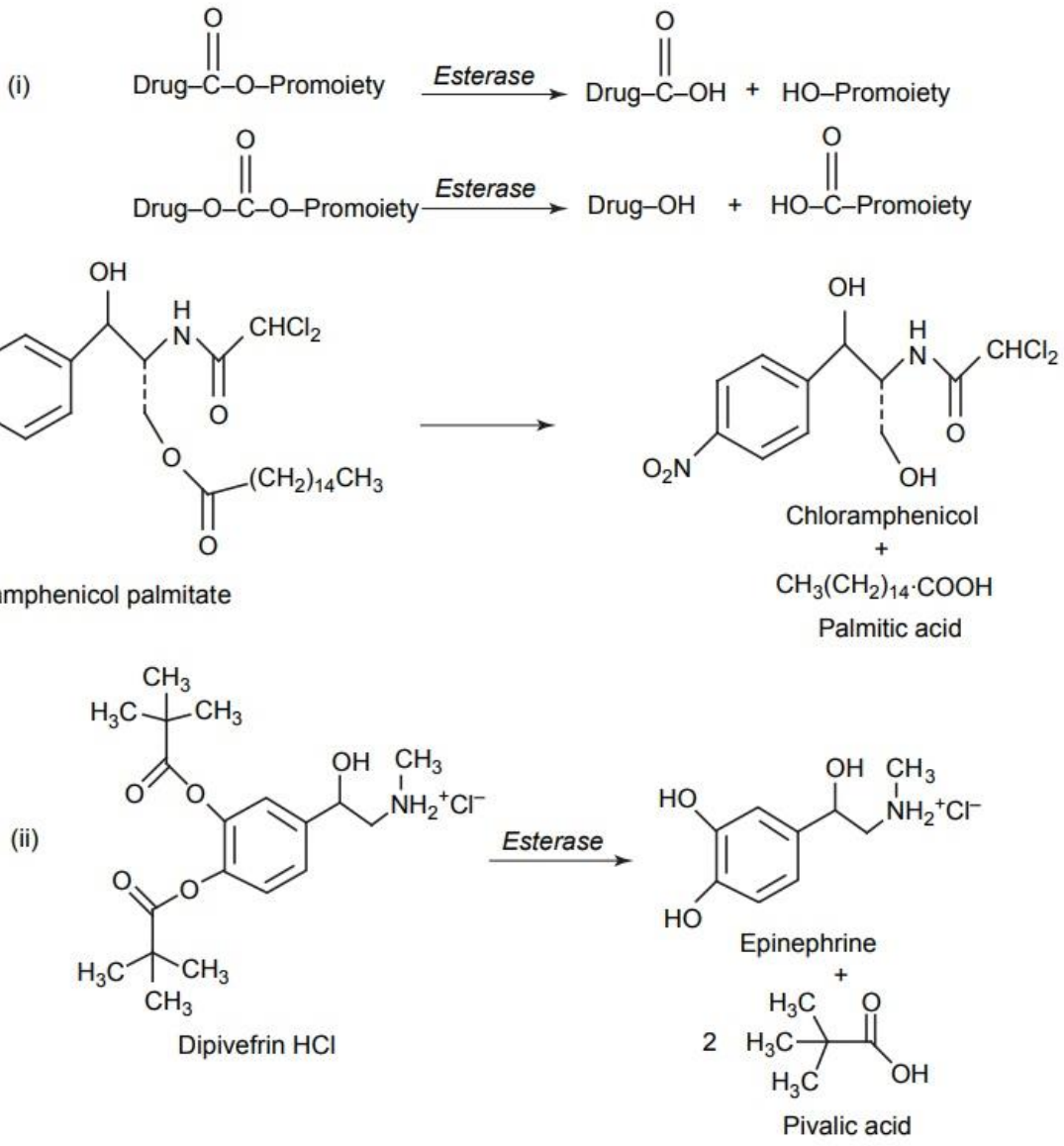
Pro-drugs are also classified according to the functional group. They are

- Carboxylic acids and alcohols
- Amines
- Azo linkages
- Carbonyl compounds

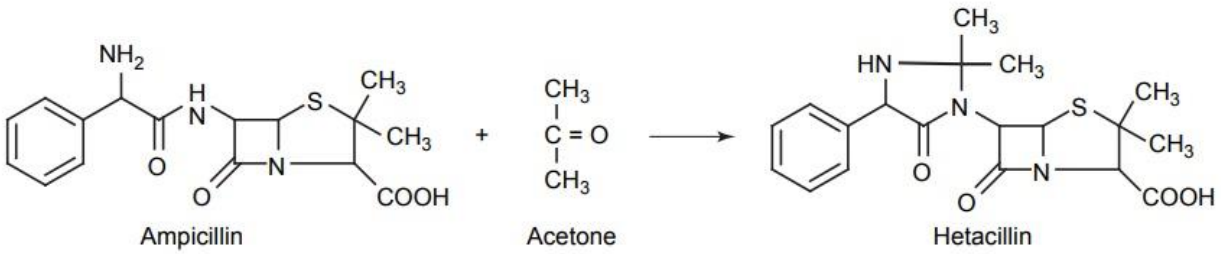


Carboxylic acid and alcohols: Pro-drugs of carboxylic acid and alcohol functionalities can be prepared by conversion to esters. The esters can be easily hydrolyzed by *esterase* enzymes (e.g. lipase, ester hydrolase, cholesterol esterase, acetyl cholinesterase, and carboxy peptidase) present in plasma and other tissues to give active drug.

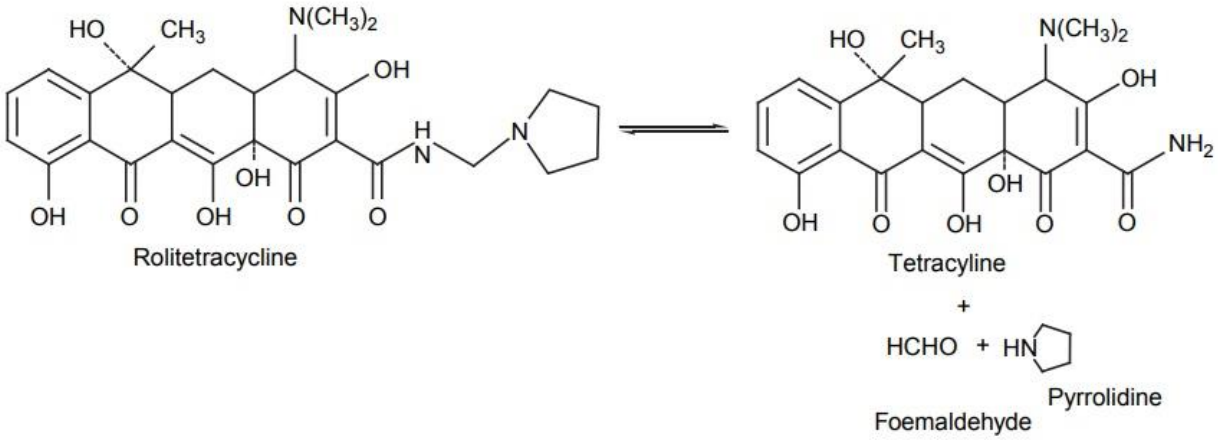
Examples



Amines: Due to the high stablility and lack of *amidase* enzyme necessary for hydrolysis, the conversion of amines to amide as a pro-drug is not been used for most of the drugs. A more common approach adopted is to use Mannich bases as pro-drug form of amines.



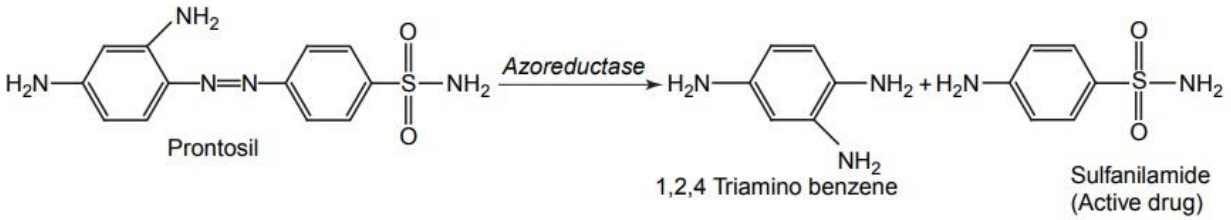
Hetacillin is a pro-drug form of ampicillin in which amide nitrogen and α amino functionalities have been allowed to react with acetone to give a Mannich base (imidazolidine ring system). This leads to decrease in the basicity and increase in the lipophilicity and absorption.



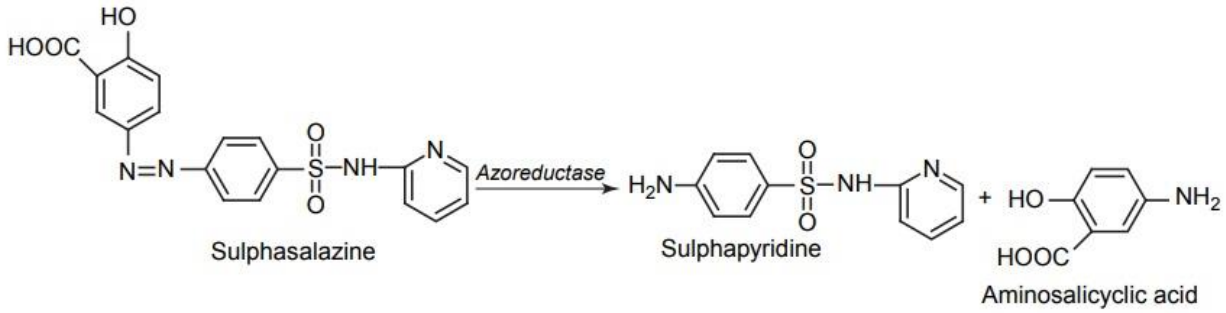
The basic pyrrolidine nitrogen increases water solubility of the parent drug rolitetracycline. The Mannich base hydrolyzes completely and rapidly in aqueous media to give the active tetracycline.

Azo linkage: Pro-drugs of amines are occasionally prepared by incorporating them in to an azo linkage. By the action of *azo reductase* the amino compounds are released in vivo.

- Prontosil drug is inactive in vitro, but it is active in vivo since it is converted to sulphanilamide by *azo reductase* enzymes.

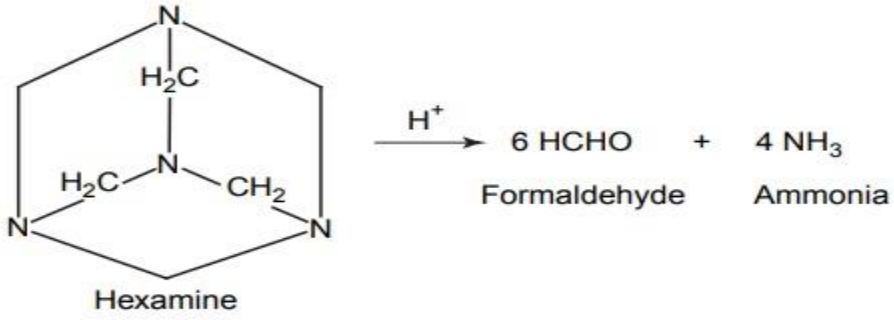


- Sulphasalazine by the action of *azo reductase* releases the amino salicylic acid and sulphapyridine. The generation of anti-inflammatory salicyclic acid prior to absorption prevents the systemic absorption of the agents and enhances the concentration of it in active site.



Carbonyl moiety: Conversion of carbonyl functionalities, such as aldehyde and ketone, to pro-drug have not been found wide clinical use. They are converted into derivatives in which the sp^2 carbonyl carbon is converted as sp^3 hybridized carbon attached to hetero-atoms. These pro-drugs are re-converted to carbonyl compound by hydrolysis.

For example, hexamine releases formaldehyde in the urine (acidic P^H), which acts as an antibacterial agent.



APPLICATIONS OF PRO-DRUG

The aim of pro-drug development is, in most cases, to solve specific pharmaceutic or pharmacological and pharmacokinetic problems. The main objectives of pro-drug are as follows:

- Improvement of taste.
- Improvement of odour.
- Enhancement of bioavailability.
- Improvement of stability and solubility properties.
- Decreased toxicity and adverse reactions.

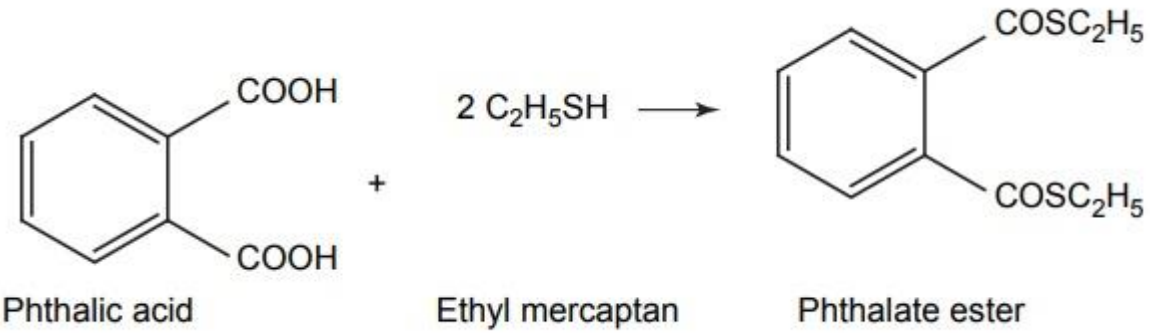
- Increased site specificity.
- Increased duration of pharmacological actions.
- Drug absorption, distribution, metabolism, and excretion affect pharmacokinectis.

Improvement of Taste

One of the reasons for poor patient compliance particularly in case of children is the bitterness, acidity, or causticity of the drug. Two approaches are adopted to overcome the bad taste of drug. The first is reduction of drug solubility in saliva and the other is to lower the affinity of drug towards taste receptors, thus, masking the bitterness.

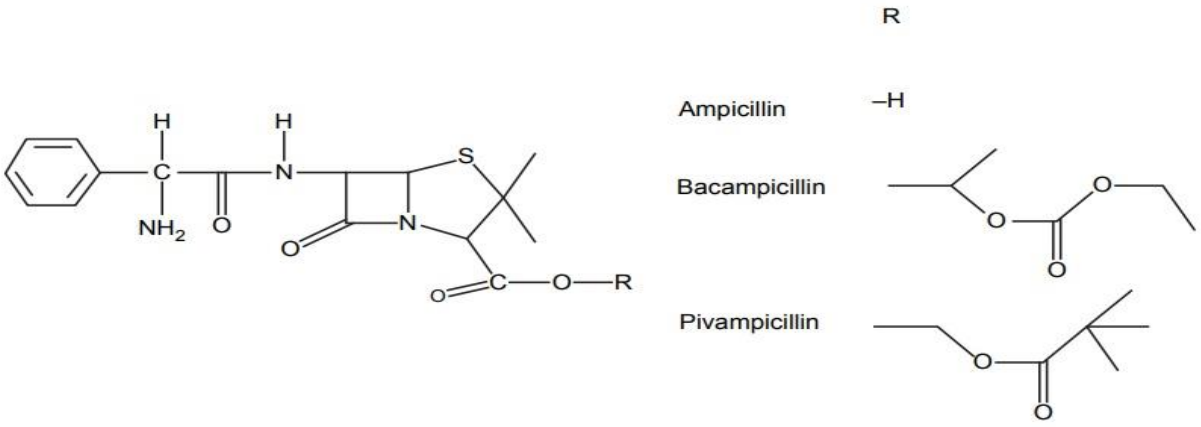
Improvement of Odour

The odour of a compound depends on its vapour pressure; a liquid with high vapour will have a strong odour. For example, ethyl mercaptan is a foul smelling liquid used in the treatment of leprosy. This is converted to phthalate ester, a diethyl dithioisophthalate that has higher boiling point and is odourless.



Enhancement of Bio-Availability (Lipophilicity)

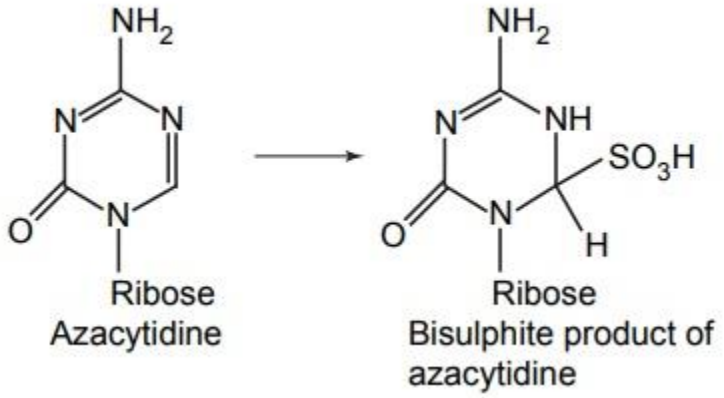
Due to the presence of an amino group in the side chain, Ampicillin possesses low lipophilicity and is only 30%–40% absorbed when taken by oral route.Altering the polarity of this antibiotics,by esterifying the free carboxyl group results in compounds that are completely absorbed, that is, with greater bio-availability than the parent ampicillin.



Improvement of Stability and Solubility

Stability: To improve their stability, prodrug approach is a good technique. Several drugs may decompose in their shelf life or in the gastro intestinal tract (GIT) when used orally.

An antineoplastic drug, Azacytidine, hydrolyse readily in acidic pH, but the bisulphite prodrug of it is more stable

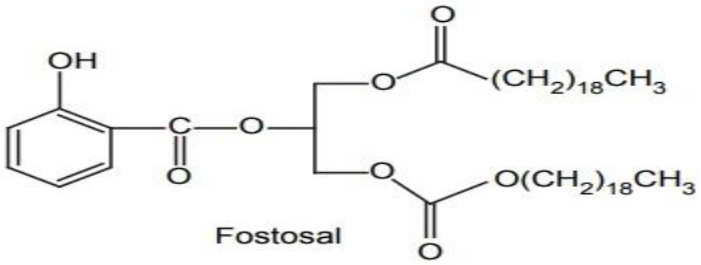


Solubility: Hydrophilic or water-soluble drugs are needed when parenteral or ophthalmic formulation of such agents is desired. Drugs with hydroxyl functional group can be converted to their hydrophilic form through the use of half ester such as hemi-glutarate or hemi-phthalates, the other half of this acid carries sodium, potassium, or amine salts, and renders the moiety more soluble.

Parent drug	Pro-drug with enchanced hydrophilicity
Tocophenols	Sodium succinate ester
Metronidazole	Amino acid esters

Decreased Toxicity and Adverse Reactions

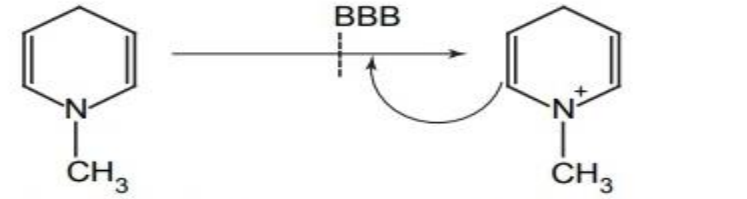
Carboxylic acids and phenols are sometimes too toxic to be employed as such in clinical practice. Ester prodrugs of the acidic nonsteroidal anti-inflammatory drugs are devoid of gastric ulcerogenic activity and is considered as one of the responsible factors for the adverse reaction of these drugs.



Fostosal

Site-Specific Drug Delivery

Many pro-drugs could be so prepared that they will be delivered to a specific site, thus reducing the toxicity to other organs. The dihydropyridine pyridinium redox chemical delivery system is very useful for the brain.



Dihydropyridine
(Lipophilic)

Pyridinum system
(Hydrophilic)

Increased duration of action

The pro-drug di-*p*-toluate ester of *N*-^{t}butyl noradrenaline provides a longer duration of bronchodilator activity than the parent drug. The pro-drug is preferentially distributed into the lung tissues rather than into the plasma or the heart, so that the bronchodilator effect is exerted.

ANTIMALARIALS

INTRODUCTION

Antimalarial agents are drugs used for the treatment or prophylaxis of malaria. Malaria is caused by four species of *Plasmodium*, such as *Plasmodium falciparum, P. malariae, P. ovale*, and *P. vivax*. Three of which produces the mild forms of malaria by destroying red blood cells in peripheral capillaries and thus, causing anaemia. The bouts of fever 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 organs of the body and cause microcirculatory arrest. This disease still affects about 200 million people and causes at least 2 million deaths per year.

LIFE CYCLE OF PLASMODIUM

The different stages of the reproductive cycle (Fig.) of the malarial parasite and the drugs acting at different stages of this cycle are given below:

·Stage-I: No drug is effective in this stage.

·Stage-II: Primaquine and pyrimethamine can block at this stage.

·Stage-III: Primaquine can only prevent because fever occurs at this stage.

·Stage-IV: Chloroquine, amodiaquine, santoquine, proguanil.

·Stage-V: Primaquine only.

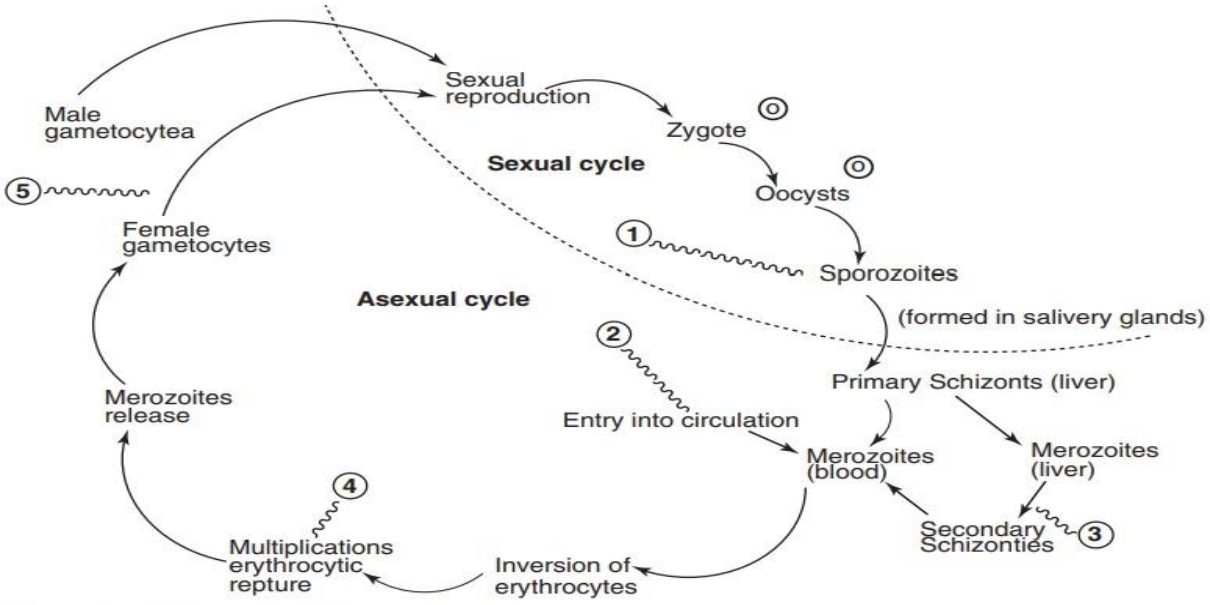


Figure 9.1 Life cycle of plasmodium.

Two important phases of the parasite life cycle are the following:

1. Asexual cycle—occurs in the infected host.
2. Sexual cycle—occurs in the mosquito.

After the insect bite, the parasite forms rapidly. They leave the circulation and localize in the hepatocytes whereby they transform, multiply, and develop into tissue schizonts. The primary asymptomatic tissue stage lasts for 15 days and the tissue schizonts rupture, each releasing thousands of merozites. The released merozites invade more erythrocytes to continue the cycle's synchronous rupture of erythrocytes to continue the cycle. Synchronous rupture of erythrocytes and release of merozytes into the circulation leads to febrile pattern attacks on day 1 and 3; hence, the designation is 'tertian malaria'.

Some erythrocyte parasites differentiate into several forms known as gametophytes. After infecting human blood, female mosquito ingests them. Then the exflagellation of male gametocyte is followed by the male gametogenesis and the fertilization of the female gametocytes in the insect's guts. The resulting zygote, which develops as an oocyte in the gut wall, eventually gives rise to infective sporozoite, which invades the salivary glands of the mosquito. The insect then can infect another human by taking a blood meal.

ETIOLOGY OF MALARIA

There are five major Plasmodium species which cause human disease these are Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae and Plasmodium Knowlesi.

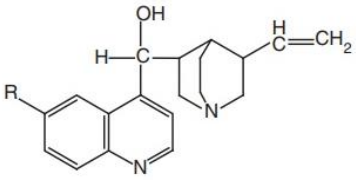
The greater parts of infections are caused by P. falciparum and P. vivax and P. falciparum is liable for the most severe disease. These species are distributed according to the ecological and behavioral parameters which affects the transmission ability of mosquitoes.

- P. falciparum is widespread in the tropic regions of sub-Saharan, Africa, certain areas of Southeast Asia, Oceania and the Amazon basin of South America.
- P. vivax is predominantly found in most of Asia, the Americans, parts of Eastern Europe and North Africa.
- P. ovale is found primarily in tropical western and central Africa and islands in the West Pacific.
- P. malariae has a distribution similar to P. falciparum but a lower prevalence.

- P. knowlesi is found in certain forested areas of southeast Asia.

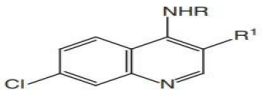
CLASSIFICATION

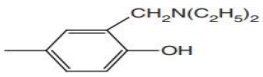
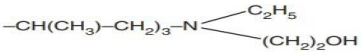
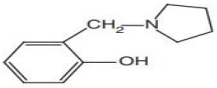
1. CINCHONA ALKALOID



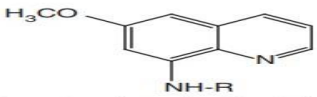
Name	R
Quinine	$-OCH_3$ (–) isomer
Quinidine	$-OCH_3$ (+) isomer (used as antiarrhythmic)
Cinchonine	–H (+) isomer
Cinchonidine	–H (–) isomer

II. 7-Chloro-4-Amino Quinolines



Name	R	R¹
Cholorquine	$-CH(CH_3)(CH_2)_3-N(C_2H_5)_2$	–H
Amodiaquine		–H
Hydroxychloroquine		–H
Sontoquine	$-CH(CH_3)-(CH_2)_3-N(C_2H_5)_2$	$-CH_3$
Amopyroquine		–H

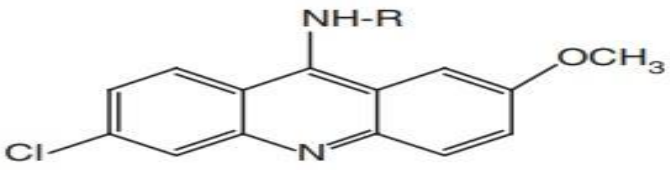
III. 8-Amino Quinolines



6-Methoxy-8-amino quinoline derivatives

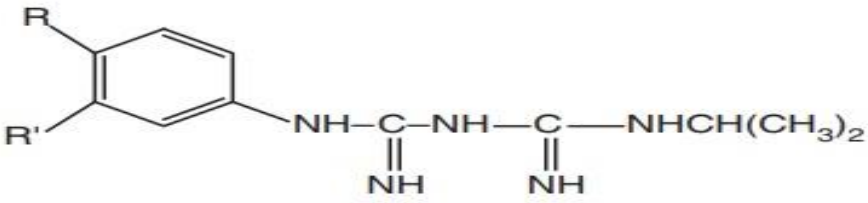
Name	R
Primaquine	$-CH(CH_3)-(CH_2)_3-NH_2$
Pamaquine	$-CH(CH_3)-(CH_2)_3-N(C_2H_5)_2$
Pentaquine phosphate	$-(CH_2)_5-NH-CH(CH_3)_2$
Isopentaquine	$-CH(CH_3)-(CH_2)_3-NH-CH(CH_3)_2$
Quinocide HCl	$-(CH_2)_3-CH(CH_3)-N(C_2H_5)_2$

IV. Acridine derivatives (9-amino acridine derivatives)



Name	R
Quinacrine	$-CH(CH_3)-(CH_2)_3-N(C_2H_5)_2$
Acriquine	$-(CH_2)_4-N(C_2H_5)_2$

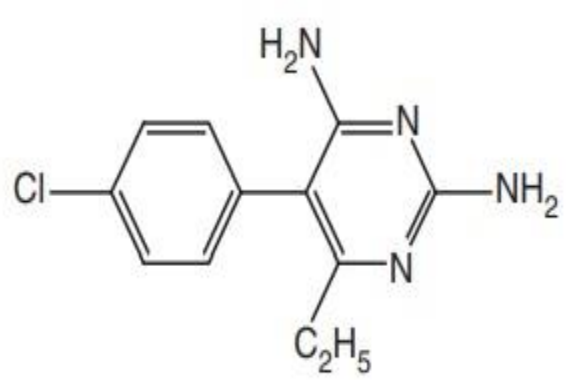
a. Biguanids



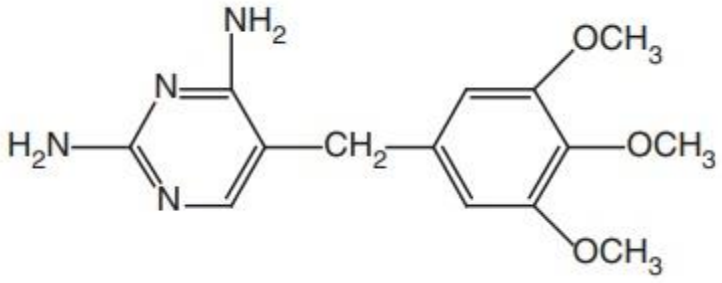
Name	R	R′
Proguanil	–Cl	–H
Chloro proguanil	–Cl	–Cl
Bromoguanil	–Br	–H
Nitroguanil	$-NO_2$	–H

b. Diamino pyrimidines

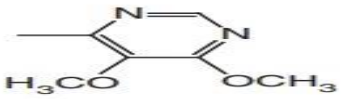
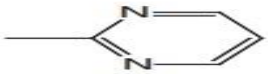
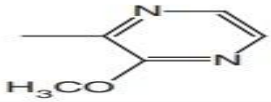
Pyrimethamine (Daraprim)



Trimethoprim



VI. Sulphonamides and Sulphones

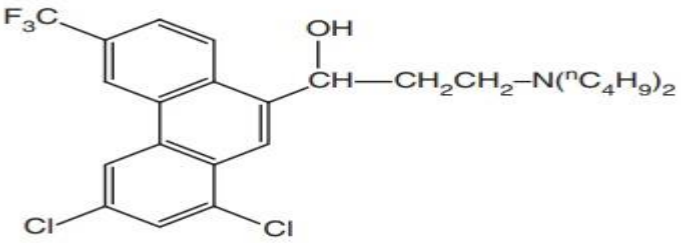
Name	R
Sulphadoxine	
Sulphadiazine	
Sulphamethoxazole	
Sulphalene	

VII. Phenanthrine methanol

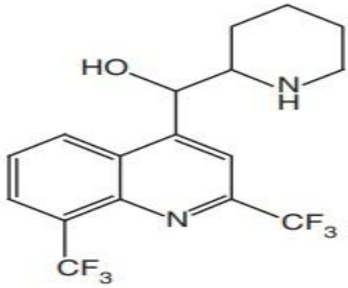
Halofentamine

VIII. Miscellaneous drugs

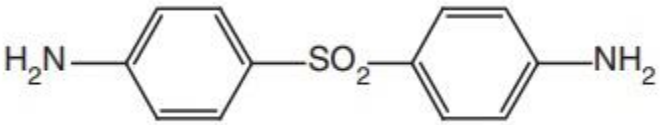
Halofantrine (Hafan)



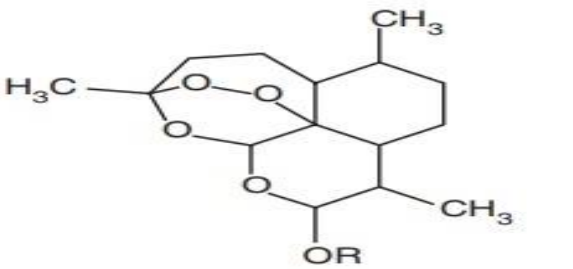
Mefloquine



Dapsone

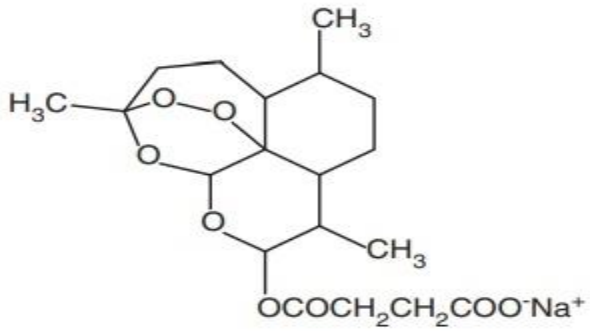


Artemether, Artemotil



R = CH_3 ; Artemether
R = C_2H_5 ; Artether

Artesunate



4-Substituted Quinolines

Mode of Action: Three different mechanisms of actions are suggested for these drugs:

***DNA interaction*:** The mechanism of action for quinine is that the drug gets intercalated into the DNA of the parasite. It is based on the fact that the concentration required for the inhibition of nucleic acid synthesis is significantly higher than that necessary for the inhibition of the plasmodium parasite.

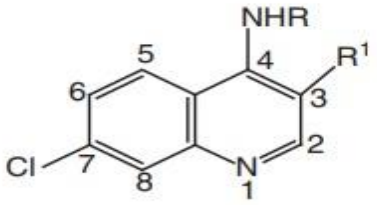
***Ferriprotoporphyrin IX*:** The plasmodium parasite utilizes host haemoglobin as a source of amino acid. On digestion of the haemoglobin, the haem is released as ferriprotoporphyrins IX and it produces haemoly sis of the erythrocyte parasites. Therefore, ferriprotoporphyrin that is released is converted into nontoxic products and they, in turn, to haemozoites by the polymerase enzyme. The steps involved in the conversion to haemozoites are inhibited by the chloroquine.

***Weak base hypothesis*:** The 4-substituted quinolines have weak base and because of this pKa they are thought to accumulate in a location, which is acidic (parasite lysozome pH 4.8–5.2). As the extracellular fluid of the parasite is at pH 7.4, the weak base will move towards a more acidic pH of lysosome. Once the acid–base reaction occurs, elevating the pH in the lysozome, that in turn reduces the parasite's ability to digest haemoglobin, thus reducing the availability of amino acids.

Metabolism of Quinine: It is metabolized in the liver to 2-hydroxy derivative followed by additional hydroxylation on the quinoline ring with the 2,3-dihydroxy derivative, as the major metabolite. This metabolite has low activity and is rapidly excreted in urine.

Properties and uses: Quinine hydrochloride exists as fine, silky needles, often in clusters, colourless, soluble in water and in alcohol. It is used in the treatment of malaria.

STRUCTURE–ACTIVITY RELATIONSHIP



At C-4 position, the dialkylaminoalkyl side chain has 2-5 carbon atoms between the nitrogen atoms, particularly the 4-diethylaminomethyl butyl amino side chain that is optimal for activity, as in chloroquine and quinacrine.

·The substitution of a hydroxyl group on one of the ethyl groups on the tertiary amine (hydroxyl quinoline), reduces toxicity.

·Incorporation of an aromatic ring in the side chain (e.g. amodiaquine) gives a compound with reduced toxicity and activity.

·The tertiary amine in the side chain is important.

·The introduction of an unsaturated bond in the side chain was not detrimental to activity.

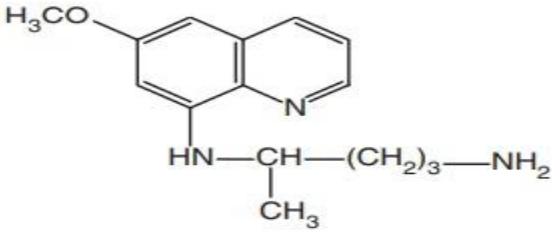
·The 7-chloro group in the quinoline nucleus is optimal, the methyl group in position 3 reduces activity, and an additional methyl group in position 8 abolishes activity.

·The $_{D}$-isomer of chloroquine is less toxic than its $_{L}$-isomer.

8-Amino quinolines

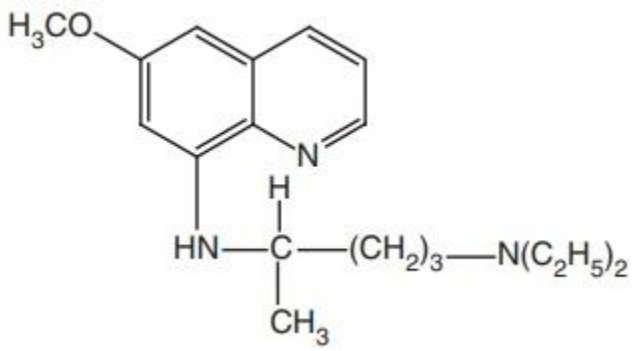
Mode of action: While the mechanism of action of the 8-amino quinolines is unknown, it is known that primaquine can generate reactive oxygen species via an autoxidation of the 8-amino quinoline group with the formation of radical anion. As a result, cell destructive oxidants, such as hydrogen peroxide, super oxide, and hydroxyl radical can be formed.

Primaquine (Primaquine Phosphate)



Properties and uses: Primaquine is a crystalline powder, soluble in water, and practically insoluble in alcohol. In vitro and in vivo studies indicate that the stereochemistry at the asymmetric carbon is not important for antimalarial activity. These appears to be less toxicity with the levorotatory isomer, but this is dose–dependent, and may not be of much importance as the doses used to treat exoerythrocytic *P. vivax* malaria. It is extensively used for the radical cure of relapsing *vivax* malaria, but it is not normally employed either for arresting the severe attacks of the disease or for the suppressive therapy. It invariably kills gametocytes of all the species, or inhibits their growth and development in the mosquito. It fails to produce any significant effect on other erythrocytic stages, and hence, it must not be employed alone for the treatment of malaria.

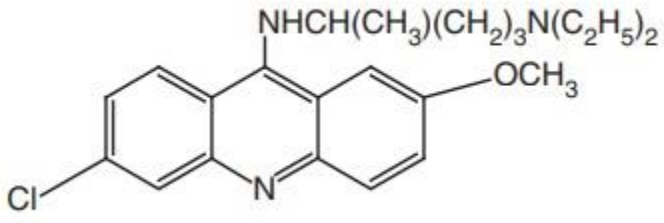
Pamaquine



Properties and uses: It was the first 8-amino quinoline marketed, used as an antimalarial agent.

Acridine Derivatives

Quinacrine



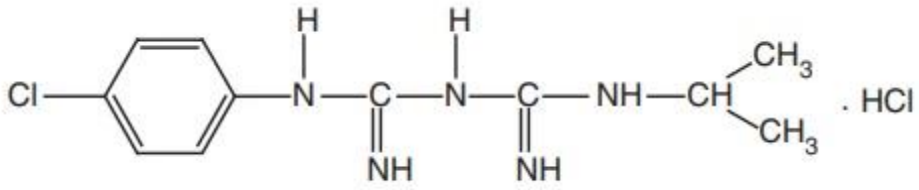
Mode of action: Quinacrine acts at many sites within the cell, including intercalation of DNA strands, succinic dehydrogenase, mitochondrial electron transport, and cholinesterase. It may be tumerogenic and mutagenic and has been used as a sclerosing agent. Because it is an acridine dye, quinacrine can cause yellow discolouration of the skin and urine.

Properties and uses: It acts as a schizontocidal and now it is not used as an antimalarial agent. It is used in the treatment of leishmaniasis and some tape worm infestations.

a. Biguanides

Mode of action: Biguanides inhibit dihydrofolate reductase enzyme and interfere in the folic acid metabolism. This leads to inhibition of the nuclear division in malarial parasites.

Proguanil HCl *(Paludrine)*

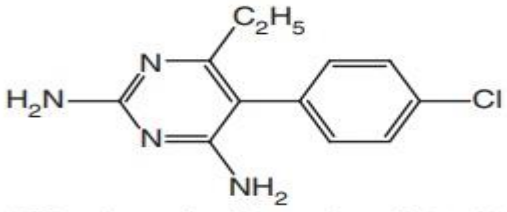


Properties and uses: Proguanil hydrochloride is a white crystalline powder, slightly soluble in water, sparingly soluble in ethanol, and practically insoluble in methylene chloride. It is used mainly for prophylactic treatment of malaria.

b. Diaminopyrimidines

Mode of Action: It inhibits the reduction of folic acid and dihydrofolic acid to the active tetrahydrofolate coenzyme form.

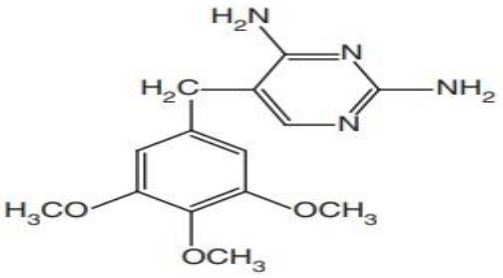
Pyrimethamine *(Daraprim)*



2,4-Diamino-5-(*p*-chlorophenyl)-6-ethyl pyrimidine

Properties and uses: Pyrimethamine exists as a white crystalline powder or colourless crystals, practically insoluble in water, and slightly soluble in alcohol. Pyrimethamine inhibits the reduction of folic acid and dihydrofolic acid to the active tetrahydrofolate coenzyme form. It finds its extensive use as a suppressive prophylactic for the prevention of severe attacks due to *P. falciparum* and *P. vivax*. It is also used in the treatment of taxoplasmosis and as an immuno suppressive agent.

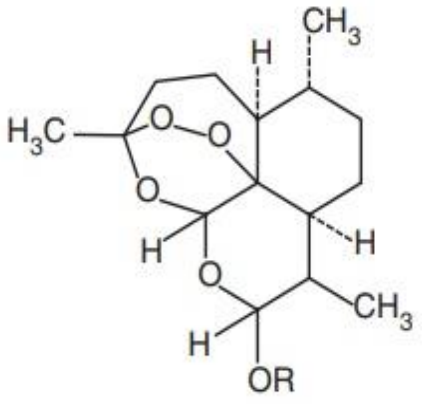
Trimethoprim *(Proloprim)*



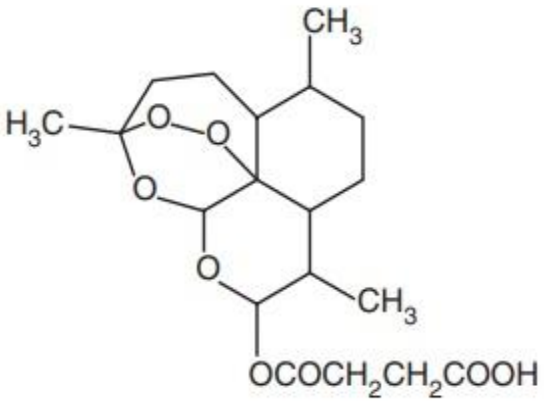
Properties and uses: Trimethoprim exists as a white or yellowish-white powder, very slightly soluble in water, and slightly soluble in ethanol. It is a potent inhibitor of dihydrofolate reductase. It has been employed in conjugation with sulphamethopyrazine in the treatment of chloroquine-resistant malaria. It has also been used in conjugation with sulphonamides in the treatment of bacterial infections. Trimethoprim is an antibacterial, effective against malarial parasite.

Micellaneous

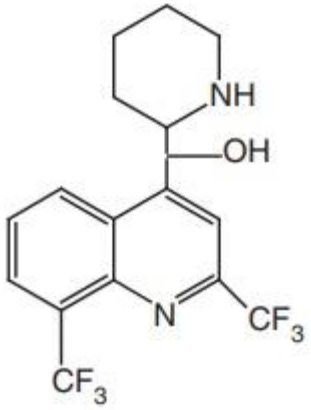
Artemether *(Larither, Paluther)* ***and Artether***



Artesunate *(Asunate, Ultera, Falcigo)*



Mefloquine



Properties and uses: Mefloquine hydrochloride is a white or slightly yellow crystalline powder, very slightly soluble in water, soluble in methanol and in alcohol. It is used as an antimalarial agent.

VERY SHORT ANSWER QUESTIONS (2 marks)

Q1 Features of clindamycin include the?

Q2 Antimicrobials effective against anaerobic bacteria include the except?

Q3 The distinctive features of azilhromycin include the except?

Q4 Erythromycin schizontocide Antimalarial drugs are used as?

Q5 Chloroquine acts as?

Q6 Chloroquine resistant P.falciparum malaria can be cured by Drugs except?

Q7 Dipivefrin is prodrug of?

Q8 what is a prodrug?

SHORT ANSWER QUESTIONS (5 marks)

Q1 What are macrolide antibiotics?

Q2 What are miscellaneous agents?

Q3 Explain etiology of malaria.

Q4 What are Antimalarial agents?

Q5 Explain Biguanides as Antimalarial agents.

Q6 Write a note on Quinolines as Antimalarial agents.

Q7 What are prodrugs?

Q8 What are different types of Prodrugs?

Q9 Write a note on Bioprecursor prodrugs

Q10 What are mutual prodrugs?

LONG ANSWER QUESTIONS (10 marks)

Q1 Explain Azithromycin and Clindamycin in detail.

Q2 Explain macrolide antibiotic in detail giving suitable examples.

Q3 Give Synthesis, uses and mechanism of action of Chloramphenicol.

Q4 what are Antimalarial agents? Classify them. Explain etiology of malaria.

Q5 Explain SAR of Quinolines as Antimalarial agents

Q.6 Give Synthesis of-

a) Chloroquine

b) Pamaquine

Q7 What are prodrugs? Give its types.

Q8 Explain Applications of Prodrugs