12.1 ANTIBIOTICS

- Antibiotics are chemical substances produced by various microorganisms like bacteria, fungi etc. They may either kill or inhibit the growth of bacteria.
- It is the most important type of antibacterial agent for fighting bacterial infections, and antibiotic medications are widely used in the treatment and prevention of such infections.
- Penicillin was the first antibiotic discovered by Alexander Fleming in 1929.

12.1.1 Classification of Antibiotics

➢ **Based on Their Chemical Structure**

CLASS	DRUGS
Sulphonamides and related drugs	Sulfadiazine and others, Sulfones, Dapsone (DDS), Para amino salicylic acid (PAS)
Diaminopyrimidines	Trimethoprim, Pyrimethamine
Quinolones	Nalidixic acid, Norfloxacin, Ciprofloxacin, Prulifloxacin.
Beta-Lactam antibiotics	Penicillins, Cephalosporins, Monobactams, Carbapenems
Tetracyclines	Oxytetracycline, Doxycycline, Minocycline
Nitrobenzene derivative	Chloramphenicol
Aminoglycosides	Streptomycin, Gentamicin, Amikacin, Neomycin
Macrolide antibiotics	Erythromycin, Clarithromycin, Azithromycin,
Lincosamide antibiotics	Lincomycin, Clindamycin
Glycopeptide antibiotics	Vancomycin, Teicoplanin
Oxazolidinone	Linezolid

Polypeptide antibiotics	Polymyxin B, Colistin, Bacitracin, Tyrothricin
Nitrofuran derivatives	Nitrofurantoin, Furazolidone
Nitroimidazoles	Metronidazole, Tinidazole
Nicotinic acid derivatives	Isoniazid, Pyrazinamide, Ethionamide
Polyene antibiotics	Nystatin, Amphotericin B, Hamycin
Azole derivatives	Miconazole, Clotrimazole, Ketoconazole, Fluconazole
Others	Rifampicin, Spectinomycin, Sod. fusidate, Cycloserine, Vancomycin, Ethambutol, Clofazimine, Griseofulvin

12.1.2 BETA-LACTAM ANTIBIOTICS

- β-lactam antibiotics (beta-lactam antibiotics) are the antibiotic agents that contain a beta-lactam ring in their molecular structures.
- Beta-lactam is a cyclic amide with four atoms in its ring system. It is named as such because the nitrogen atom is attached to the beta-carbon atom relative to the carbonyl group in the four-membered ring.

β - LACTUM ANTIBIOTICS

Penicilline
- Penicillin G
- Penicillin V
- Amoxicilline
- Cloxacillin

Cephalosporines
- Cefadroxil
- Cefador
- Cefprozil
- Cefixime
- Cephalexin

Carbapenems
- Erytapenem
- Meropenem
- Imipenem

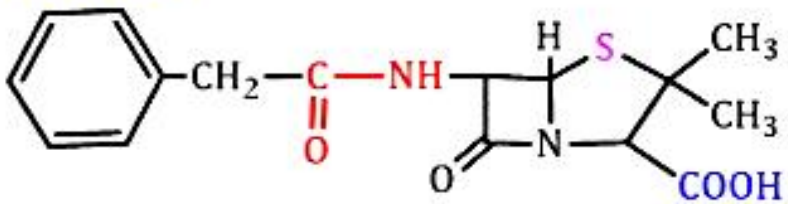
Monobactams
- Aztreonam

❑ PENICILLIN G (BENZYLPENICILLIN)

- It is also known as Benzylpenicillin. It is narrow spectrum, beta-lactam naturally occurring penicillin antibiotic with antibacterial activity.
- It is first generation penicillin's.

❖ **Chemical Formula - $C_{16}H_{18}N_2O_4S$**

❖ **Structure**



❖ IUPAC Nomenclature

- 3,3-dimethyl-7-oxo-6-(2-phenylacetamido)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid

❖ Physiochemical Properties

- It is amorphous white to slightly yellow crystalline powder with a faint odor.
- It is freely soluble in methanol, benzene, chloroform.

❖ Pharmaceutical Formulation

- This drug is formulated in the form of tablets, eye drops, eye ointment and injections.

❖ Stability and storage

- Store at room temperature, away from heat, moisture, and direct light. It is stored in a freezer capable of maintaining a temperature of -20°C or -4°F.

❖ Popular Brand Names

- Pfizerpen
- Pentids
- Benzywell

❖ Dose

- Staphylococcal infections: 600,000 – 1,000,000 units intramuscularly, four times a day.
- Pneumonia - 600,000 – 1,000,000 units intramuscularly four times a day.

❖ Medicinal Uses

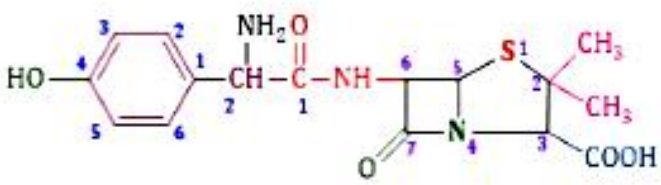
- It is used to treat abscesses, syphilis, and gonorrhea.
- It is used to treat pharyngitis, pneumonia, meningitis, and endocarditis due to staphylococci.
- It is used to treat pneumonia, tetanus, diphtheria, anthrax or otitis media.

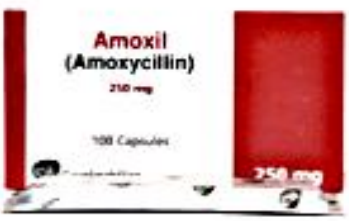
❑ AMOXICILLIN

- Amoxicillin is a beta lactam antibiotic of penicillin group that fight against bacterial infection.

❖ Chemical Formula - $C_{16}H_{19}N_3O_5S$

❖ Structure





❖ **IUPAC Nomenclature**

- 6-{[2-Amino-2-(4-hydroxyphenyl)acetyl]amino}-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid

❖ **Physiochemical Properties**

- It is white crystalline powder.
- It is very soluble in water, sparingly soluble in anhydrous ethanol, very slightly soluble in acetone.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of tablets, eye drops, syrup and injections, capsules, and powder for oral suspension and pediatric oral suspension.

❖ **Stability and storage**

- Amoxicillin sodium is unstable in aqueous solutions stored between 0°C - 20°C.

❖ **Popular Brand Names**

- Amoxil
- Larotid

❖ **Dose**

- The usual dose of amoxicillin is 250mg – 500mg taken 3 times a day.

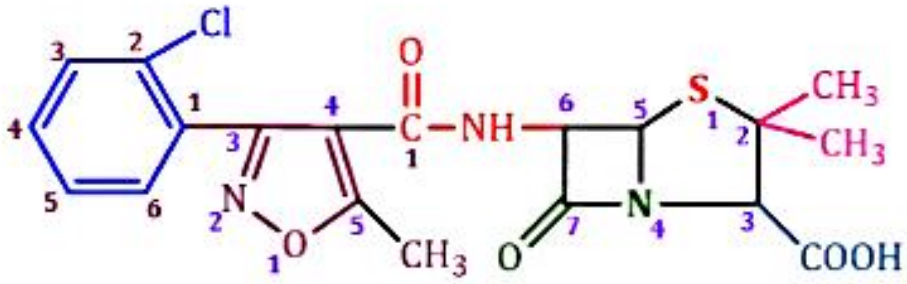
❖ **Medicinal Uses**

- Amoxicillin is used in the treatment of a number of infections, including acute otitis media, streptococcal pharyngitis, pneumonia, skin infections, urinary tract infections, Salmonella infections, Lyme disease, and chlamydia infections.

❑ CLOXACILLIN

❖ **Chemical Formula-** $C_{19}H_{18}ClN_3O_5S$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 6-[[3-(2-chlorophenyl)-5-methyl-1,2-oxazole-4-carbonyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid

❖ **Physiochemical Properties**

- It is a white crystalline powder.
- It is soluble in water, methanol and ethanol. It is slightly hygroscopic.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of syrup, tablet and injections, capsules, powder or oral suspension and pediatric oral suspension.

❖ **Stability and storage**

- Store at room temperature, away from heat, moisture, and direct light. Keep from freezing.

❖ **Popular Brand Names**

- Cloxapen
- Cloxacap
- Wellclox
- Orbenin

❖ **Dose**

- Orally 250 – 500mg every 6 hours (Maximum adult dose 6gm/day).
- I.M. / I.V. 250 – 500mg every 6 hours (Maximum adult dose 6gm/day).

❖ **Medicinal Uses**

- It used to treat impetigo, cellulitis, pneumonia, septic arthritis, and otitis externa.

❑ STREPTOMYCIN

- It is an aminoglycoside antibiotic. It is the first antibiotic active against tuberculi bacilli for treatment of TB in 1952. It works by binding to the bacterial 30s ribosomal subunit.

❖ **Chemical Formula - $C_{21}H_{39}N_7O_{12}$**

❖ **Structure**

❖ IUPAC Nomenclature

- 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

❖ Physiochemical Properties

- It is odourless, white to off-white powder. It is soluble in water.

❖ Pharmaceutical Formulation

- This drug is formulated in the form of tablet and IV/ IM injections.

❖ Stability and storage

- Store at room temperature, away from heat, moisture, and direct light. Keep from freezing.

❖ Popular Brand Names

- Agri-mycin-17
- Plantomycin
- Agrept
- Rimosidin

❖ Dose

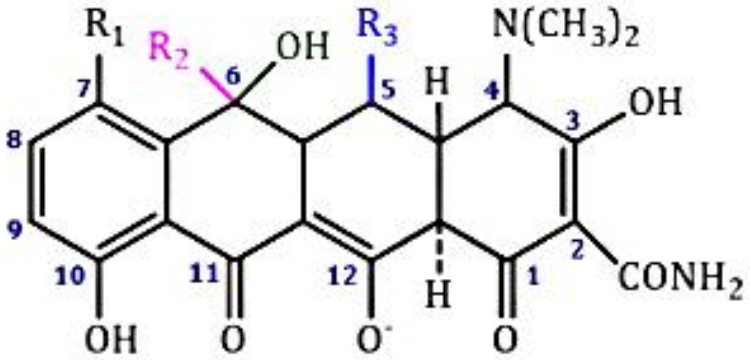
- Adult daily therapeutic dose is 15-25mg/kg body weight/day.

❖ Medicinal Uses

- It used to treat a number of bacterial infections including tuberculosis, Mycobacterium avium complex, endocarditis, brucellosis, Burkholderia infection, plague, tularaemia, and rat bite fever.

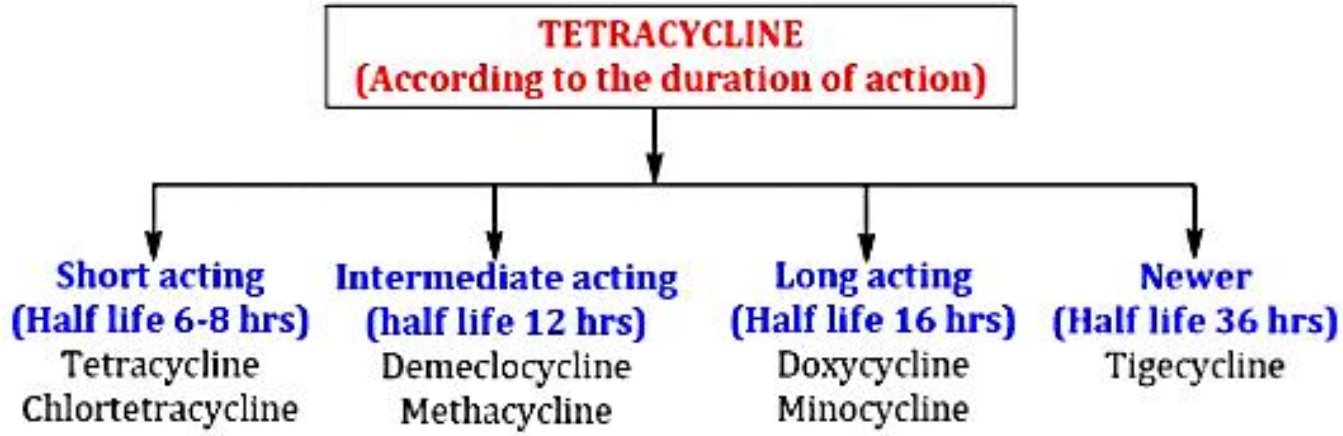
12.2 TETRACYCLINES

- Tetracyclines are broad-spectrum, powerful antibiotics derived from soil Actinomycetes such as Streptomyces fermentation.
- It is derived directly from bacterium known as *Streptomyces coelicolor* and active against gram +ve and gram –ve bacteria.
- Tetracyclines have four linear-annelated six-membered rings in their ring structure. We can call them Octahydrotetracene-2-Carboxamide derivatives.



12.2.1 Classification of Tetracycline

CLASS	DRUG
Naturally occurring Tetracycline	Tetracycline, Chlortetracycline, Oxytetracycline, Bromotetracycline, Demeclocycline.
Semi-synthetic Tetracycline	Doxycycline, Minocycline, Methacycline, Meclocycline, Sancycline.
Pro-Tetracycline	Rolitetracycline.
Glycyl amino	Tigecycline.



12.2.2 Classes of Natural Tetracycline and Semisynthetic Tetracycline

S.NO	DRUG	R_1	R_2	R_3
1	Tetracycline	-H	-CH3	-H
2	Chlortetracycline	-Cl	-CH3	-H
3	Oxytetracycline	-H	-CH3	-OH
4	Bromotetracycline	-Br	-CH3	-H
5	Dexamethyltetracycline	-H	-H	-H
6	Dexamethylchlortetracycline	-Cl	-H	-H
7	Doxycycline	-OH	-H	-CH3
8	Minocycline	-H	-H	-H
9	Methacycline	-OH	=CH2	-
10	Meclocycline	-OH	=CH2	-
11	Sancycline	-H	-H	-H

❑ DOXYCILLINE

- Doxycycline is a broad-spectrum antibiotic of the tetracycline class used in the treatment of infections caused by bacteria and certain parasites.

❖ **Chemical Formula - $C_{22}H_{24}N_2O_8$**

❖ **Structure**

❖ **IUPAC Nomenclature**

- 4-(Dimethylamino)-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrotetracene-2-carboxamide

❖ Physiochemical Properties

- Doxycycline hyclate is a yellow crystalline powder and soluble in water while doxycycline monohydrate is very slightly soluble in water.

❖ Pharmaceutical Formulation

- This drug is formulated in the form of tablet and intravenous injections, capsules, oral suspension.

❖ Stability and storage

- Store at room temperature, away from heat, moisture, and direct light. Keep from freezing.

❖ Popular Brand Names

- DooX
- Doryx
- Vibramycin

❖ Dose

- The usual dose is 100mg to 200mg once or twice a day.

❖ Medicinal Uses

- It is used to treat bacterial pneumonia, acne, chlamydia infections, Lyme disease, cholera, typhus, and syphilis.
- It is also used to prevent malaria in combination with quinine.

❑ MINOCYCLINE

- Minocycline is a tetracycline antibiotic medication used to treat a number of bacterial infections such as pneumonia.

❖ Chemical Formula - $C_{23}H_{27}N_3O_7$

❖ Structure

❖ IUPAC Nomenclature

- 2-(Amino-hydroxy-methylidene)4,7-bis(dimethylamino)-10,11,12a-trihydroxy-4a,5,5a,6- tetrahydro-4H-tetracene-1,3,12-trione

❖ **Physiochemical Properties**

- It is odourless, yellow crystalline solid with slightly bitter taste.
- It is soluble in water.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of tablet intravenous injections, and eye drops, capsules, oral suspension or topical gel.

❖ **Stability and storage**

- Store at room temperature, away from heat, moisture, and direct light. Keep from freezing.

❖ **Popular Brand Names**

- Minocin
- Amzeeq
- Milikind

❖ **Dose**

- The dose orally for adults is 200 mg.

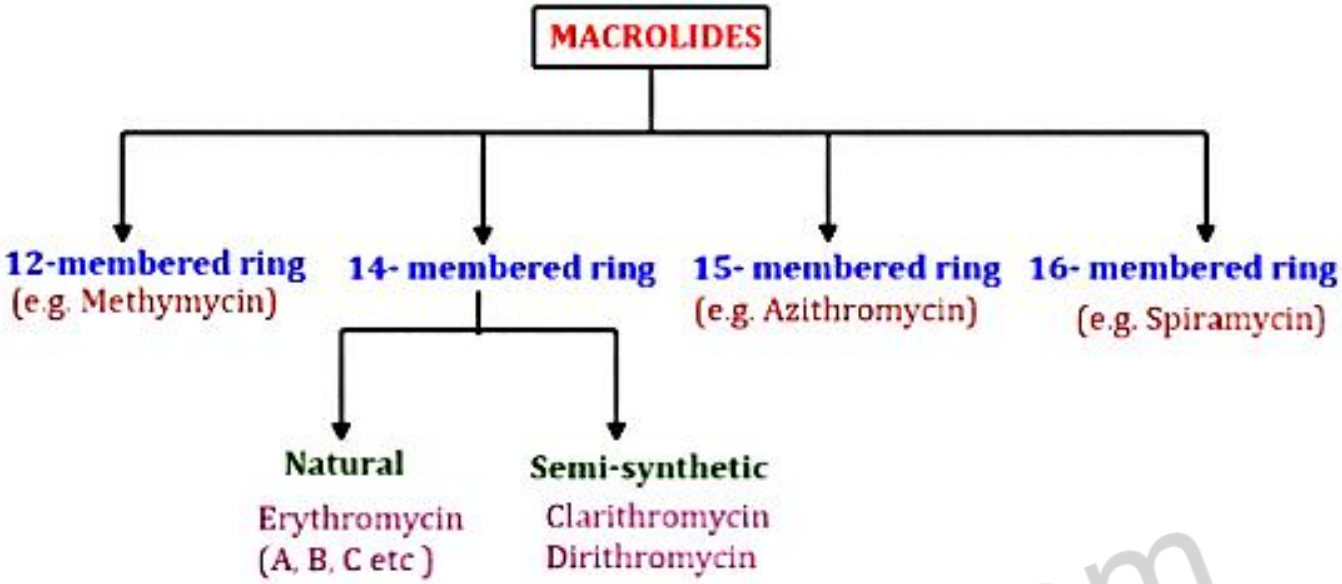
❖ **Medicinal Uses**

- It is used to treat a number of bacterial infections such as pneumonia.
- Minocycline is also used for the treatment of acne and rheumatoid arthritis.

12.3 MACROLIDES

- Macrolides are a class of natural & semi-synthetic products that consist of a large 14 to 16 membered macrolide lactone ring with deoxy sugars like Cladinose and desosamine.
- Macrolides are a class of antibiotics derived from *Saccharopolyspora erythraea* (originally called Streptomyces erythreus), a type of soil-borne bacteria.

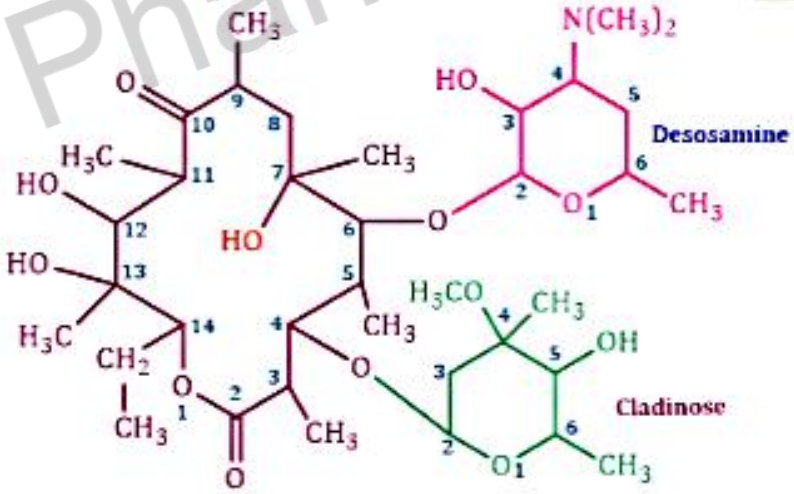
12.3.1 Classification - Classified on the basis of no. of atoms in macro -lactone ring



❑ ERYTHROMYCINE

❖ **Chemical Formula - $C_{37}H_{67}NO_{13}$**

❖ **Structure**



❖ **IUPAC Nomenclature**

- 6-{[4-(Dimethylamino)-3-hydroxy-6-methyloxan-2-yl]oxy}-14-ethyl-7,12,13-trihydroxy-4-{[5-hydroxy-4-methoxy-4,6-dimethyloxan-2-yl]oxy}-3,5,7,9,11,13-hexamethyl-1-oxacyclotetradecane-2,10-dione

❖ **Physiochemical Properties**

- It is white or slightly yellow crystalline powder.
- It is slightly soluble in water, ethanol and dimethyl formamide.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of tablet, injections, capsules, soluble powder, estolate capsule, stearate tablet.

❖ **Stability and storage**

- It is affected by light, moisture and hence it is stored in tightly closed light-resistant container at a temperature below 30 °C.

❖ **Popular Brand Names**

- Althrocin
- Erythrocin

❖ **Dose**

- The usual dosage for adults is 250 mg/6 hours, 333mg/8 hours or 500 mg/12 hours.

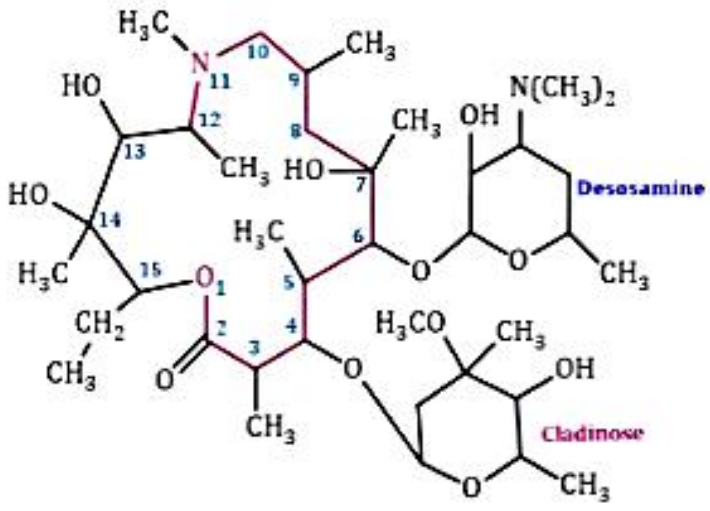
❖ **Medicinal Uses**

- It is a drug of choice to treat pneumonia, urethritis, and pelvic inflammation.
- It is used to treat amoebic dysentery.
- It is used to treat wounds and burn infection.
- It is also used in the treatment of intestinal amoebiasis.

❑ **AZITHROMYCIN**

❖ **Chemical Formula - $C_{38}H_{72}N_2O_{12}$**

❖ **Structure**



❖ **IUPAC Nomenclature**

- 11-[4-(dimethylamino)-3-hydroxy-6-methyloxan-2-yl]oxy-2-ethyl-3,4,10-trihydroxy-13-[5-hydroxy-4-methoxy-4,6-dimethyloxan-2-yl]oxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-azacyclopentadecan-15-one

❖ **Physiochemical Properties**

- Azithromycin is a white powder, practically insoluble in water, soluble in anhydrous ethanol and methylene chloride

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of film-coated tablet, capsule, oral suspension, intravenous injection, granules for suspension in sachet, and ophthalmic solution.

❖ **Stability and storage**

- Store at room temperature, away from heat, moisture, and direct light. Keep from freezing.

❖ **Popular Brand Names**

- Zithromax
- Azithrocin
- Sumamed

❖ **Dose**

- The usual dose is 500mg/vial.

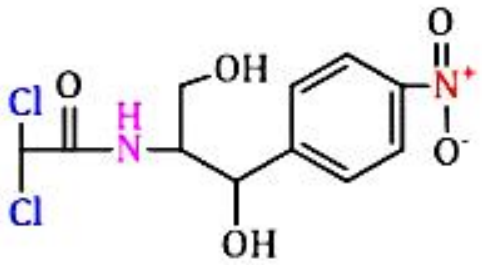
❖ **Medicinal Uses**

- It is used in bacterial infection, middle ear infections, strep throat, pneumonia, traveler's diarrhoea, and certain other intestinal infections and malaria.

❑ **CHLORAMPHENICOL**

❖ **Chemical Formula - $C_{11}H_{12}Cl_2N_2O_5$**

❖ **Structure**



❖ **IUPAC Nomenclature**

- 2,2-dichloro-N-[1,3-dihydroxy-1-(4-nitrophenyl)propan-2-yl]acetamide

❖ Physiochemical Properties

- Chloramphenicol is a white or greyish-white or yellowish-white crystalline powder or fine crystals, slightly soluble in water, soluble in alcohol and propylene glycol.

❖ Pharmaceutical Formulation

- This drug is formulated in the form capsule, eye drop, eye ointment, palmitate suspension and injection.

❖ Stability and storage

- It is stored in tightly closed containers protected from light.

❖ Popular Brand Names

- Chloromycetin
- Chlorostrep
- Biophenicol

❖ Dose

- The usual adult dose is 500 mg every 6 hours.

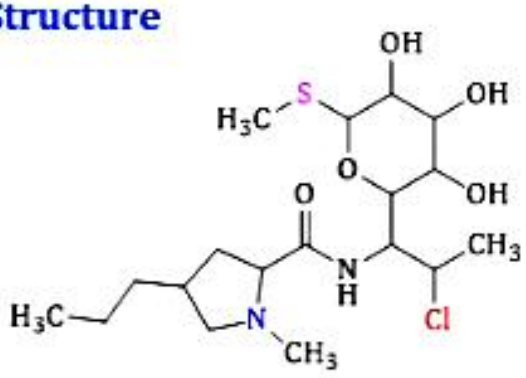
❖ Medicinal Uses

- It is used to treat typhoid and paratyphoid fever, Meningitis, Urinary tract infection, Rickettsial infection, Infection of eye and ear, superficial infection of the skin, and Septicaemia (brain abscess).

❑ CLINDAMYCINE

❖ Chemical Formula - $C_{18}H_{33}ClN_2O_5S$

❖ Structure



❖ IUPAC Nomenclature

- N-[2-chloro-1-[3,4,5-trihydroxy-6-methylsulfanyloxan-2-yl]propyl]-1-methyl-4-propylpyrrolidine-2-carboxamide