ANTIBIOTICS

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HISTORICAL BACKGROUND

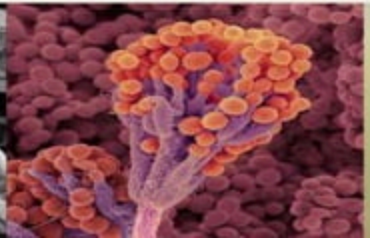
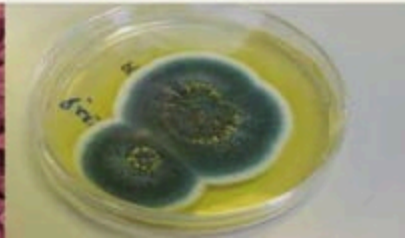
- In 1877 Louis Pasteur discovered inhibition of some microbes by other microbes during research on anthrax.
- 1908 Gelmo synthesized sulfanilamide (1st sulfonamide)
- 1910 –Paul Ehrlich for selective stains of microbes coined the terms a 'magic bullets' , "chemotherapy" or "chemical knife".
- 1913 – Eisenberg studied bactericidal properties of azo dyes with sulfonamide group.
- 1928 – Penicillin was discovered by Alexander Fleming
- 1932 – Ehrlich discovered antimicrobial activity of sulphonamides.
- 1943 – Drug companies started production of penicillins.

- 1948 – Cephalosporins were synthesized by Oxford university
- 1952 – Erythromycin derived from Streptomyces erythreus
- 1956– Vancomycin introduced for penicillin resistant species.
- 1962 – Quinolone antibiotics were first discovered.
- 1980 – Fluoro quinolones were discovered and become clinically useful

  Eg: Ciprofloxacin
- 2000 – Macrolide antibiotics introduced into clinical practice.

HISTORY OF PENCILLINS

- Penicillin was discovered by Alexander Fleming in 1928 ,who noticed that one of his experimental cultures of staphylococcus was contaminated with mold or fungi(yeast).
- This mold caused the bacteria to lyse. Since mold belongs to the family penicillium.Fleming named the compound as penicillin.
- Penicillin is obtained from “Penicillium notatum”.
- Alexander Fleming got nobel prize for explaining ‘Penicillin is a chemical extract obtained from Penicillium notatum which stops the growth of other microbes’.
- Few years later,group of researchers in oxford university discovered Penicillin V,F,G,K,O,X.

- Florey & Chain – introduced the penicillins for chemotherapy.
- Waksman - In 1942 given definition for antibiotics.

ANTIBIOTICS –DEFINITION:

- These are the chemical substanes produced by microorganisms which has the capacity of inhibiting the growth or even destoying other microorganisms (Waksman definition).
- Antibiotics are the chemical substances or drugs produced by living organisms or marine sources which will inhibit the growth of other microorganisms in small concentrations and kill the microorganisms in high concentration.
- Antibiotics are not effective against viral infections.
- Antibiotics also includes synthetic and semisynthetic antimicrobial compounds.

  Eg: Chloramphenicol and sulphonamides.

CLASSIFICATION

Antibiotics are classified into :

1. Based on spectrum of activity.
2. Based on the source of origin.
3. Based on mechanism of action.
4. Based on chemical structure.

- BASED ON SPECTRUM OF ACTIVITY & DEGREE OF SELECTIVITY:

1. Narrow spectrum antibiotics: High degree of selectivity towards single species of microorganism.

Eg: Nystatin ,Bacitracin.

2. Broad Spectrum antibiotics: They inhibit the growth of gram +ve and gram –ve bacteria including different species of microorganisms.

Eg: Tetracyclines and chloramphenicol

- Based on the source from which antibiotics are obtained they are classified as:

1. NATURAL ANTIBIOTICS: They are obtained from the fermentation of microorganisms.

Eg: Bacitracin ,Polymixin-B

2.SEMISYNTHETIC ANTIBIOTICS: They are produced commercially by addition of chemical agent to produce final products.

Eg: Penicillin G or V

3.SYNTHETIC ANTIBIOTICS: Antibiotics which have purely synthetic origin.

Eg: Chloramphenicol

- BASED ON MECHANISM OF ACTION

1. Drugs that interfere with biosynthesis of bacterial cellwall.

   Eg: Cephalosporins,Penicillins,Viomycin,Cycloserin

2. Drugs that interfere with the functioning of cytoplasmic membrane.

   Eg: Nystatin,Amphoterecin-B,Polymixin

3.Drugs that interfere with the protein synthesis of bacteria.

   Eg: Chloramphenicol,Erythromycin,Aminoglycosides,Tetracyclines.

4.Drugs that interfere with the nucleic acid biosynthesis.

   Eg: Actinomycin,Griseofulvin,Rifamycin,Mitomycin

- BASED ON CHEMICAL STRUCTURE:

1. Beta-lactam antibiotics: Drugs that contain β lactam ring in the structure.

   Eg: Pencillins,Cephalosporins,Monobactams, β –lactamase inhibitors.

2. Aminoglycoside antibiotics : Drugs that contain sugar moieties with aminogroups.

   Eg: Streptomycin , Gentamycin,Neomycin,Kanamycin

3. Tetracyclines: Drugs that contain four cyclic compounds.

   Eg: Chlortetracycline and oxytetracycline ,doxycycline

4. Peptide antibiotics: Drugs that contain amino acid groups.

   Eg: Bacitracin,Amphoterecin

5. Macrolides: Drugs that contain macrocyclic ring with lactone groups.

   Eg: Erythromycin, Azithromycin

6. Licomycins: Drugs that contain more than 16 atoms

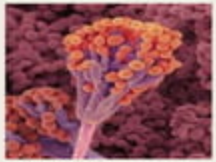
   Eg: Licomycin and clindamycin

7. Antifungal antibiotics: Drugs used to treat fungal infections.

   Eg: Griseofulvin

8. Miscellaneous: Eg: Chloramphenicol

PENICILLINS



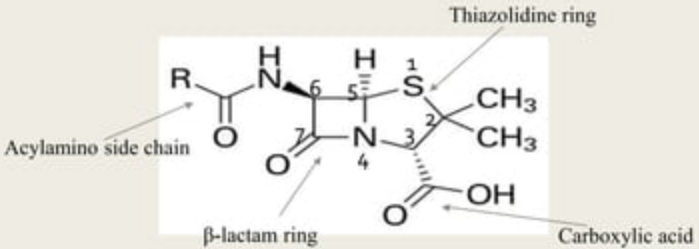
Penicillium notatum

- Penicillin is a secondary metabolite produced by various bacteria.
- Penicillins are β-lactam antibiotics.
- A bacterial infection is caused by millions of tiny bacteria that are trying to survive by multiplying in the host.Antibiotic attacks and kill this bacteria.
- Penicillin is used as an antibiotic.It was obtained from “Penicillium notatum”,now it is extracted from “Penicillium chrysogenum”.
- Before the development of penicillin,many people suffered and died from bacterial infections.
- Alexander fleming discovered Penicillin in 1928.
- Penicillin G is the first antibiotic (penicillin)introduced into chemotherapy.

Penicillium chrysogenum

Nomenclature of penicillins

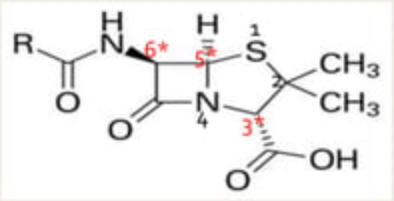
- Penicillins are called as β-lactam antibiotics
- The basic structure of penicillins is:



- According to chemical abstract system numbering starts 'S' atom and assigned as 1 &N is assigned as 4.
- Name of penicillin is 6-Acyl amino -2,2-dimethyl 3-carboxylic acid penam.

Stereochemistry of penicillins

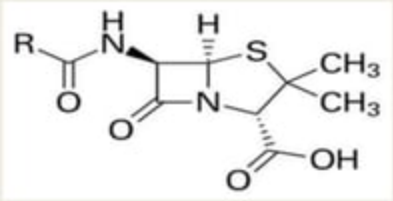
- Penicillin structure contains three chiral carbons at C_3 , C_5 &C_6.



- C_6 -is showing L configuration, C_3 and C_6 chiral centers are trans to each other (facing opposite to each other).
- All synthetic and semi synthetic penicillin have same absolute configuration that of natural. 3S:5S:6R

SAR of penicillins

- At position 1 ,if sulfur atom is oxidized to sulphone or sulphoxide decreases the activity of the compound.
- Methyl groups are necessary for activity at position 2 .
- Replacement of methyl groups decreases the activity.
- At 3rd position, carboxylic group of the thiazolidine ring



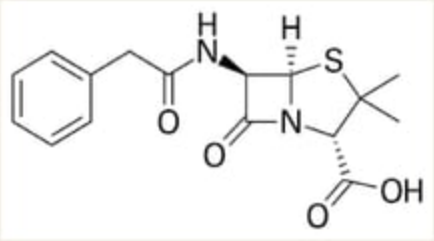
is required for the antibacterial activity.

- Replacement of carboxylic group with ether or alcohol group decreases the activity.
- β-lactam ring is required for the antibiotic activity.
- N atom is must for penicillins.
- No substitution is allowed at 5th position.
- Amide side chain with R group(either alkyl or aryl group) is essential for antibiotic activity.

Penicillin structures and its uses

BENZYL PENICILLIN (Penicillin G)

Structure:



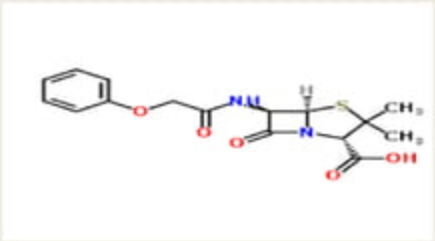
Uses: 1.Narrow spectrum antibiotic

2.Used to treat various bacterial infections caused by streptococci, meningococci, gram+ve bacilli and spirochetes species.

3. strains of Staphylococcus and Nesseiria gonnorhoea species are shows resistant by releasing β – lactamase enzyme.

PHENOXY METHYL PENICILLIN (PENICILLIN V)

Structure:



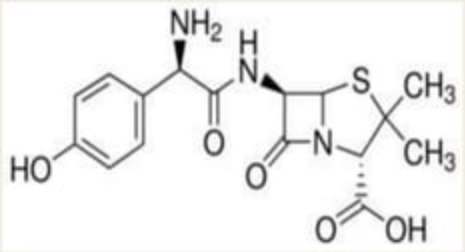
Uses: 1.Penicillin V is effective for the treatment of laryngitis,bronchitis,pneumonia,soft tissue and skin infections caused by susceptible bacteria.

2. To treat reoccurance of rheumatic fever

3.It is effective to treat oral cavity infections.

AMOXYCILLIN

Structure:



Uses: 1.To treat sinusitis and other upper respiratory tract infections

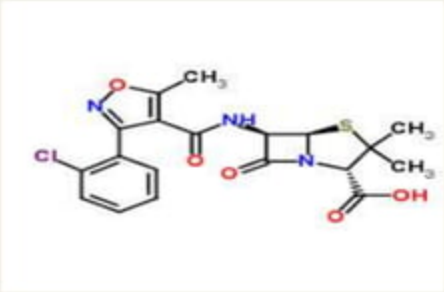
2.To treat urinary tract infections.

3.Prophylaxis treatment of bacterial endocarditis.

4.Amoxycillin is effective to treat bacterial infections of ear,nose,throat and tonsillitis.

CLOXACILLIN

Structure:



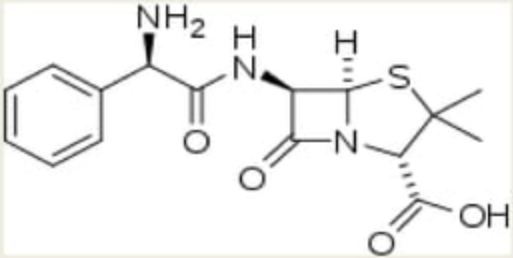
Uses: 1.Cloxacillin is active against gram-ve bacterial infections as well.

2.It is used to treat bacterial infections of bone,heart valve,lungs,skin,blood.

3.To treat staphylococcal infections ,which are resistant to benzyl penicillin.Cloxacillin is less active than Penicillin G.

AMPICILLIN

Structure:



Uses: 1. Ampicillin is used in the therapy of meningitis along with 3rd generation cephalosporins.

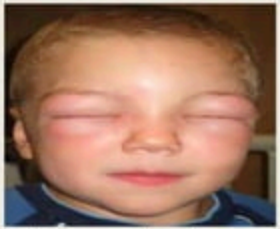
2.Ampicillin + Gentamycin can be given to treat pneumonia,gram- ve infection.

3.To treat hepatic encephalopathy.

4.To treat biliary tract infection.

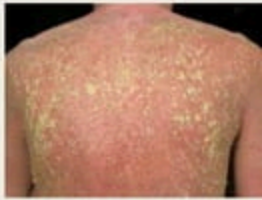
SIDE EFFECTS &TOXICITY

- Allergy
- Hypersensitivity reactions
- Bleeding
- Degenerative changes in the spinal cord
- Convulsions
- Rashes,itching,urticaria &fever
- Wheezing
- Angioneurotic edema
- Serum sickness
- Exfoliative dermatitis
- Anaphylaxis is rare



Angioneurotic edema

Disc degeneration



Exfoliative dermatitis

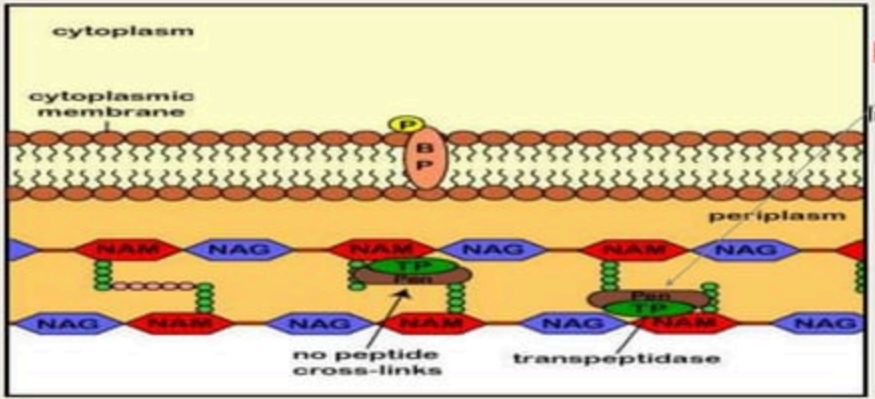
MECHANISM OF ACTION

- Penicillins interferes withthe synthesis of bacterial cellwall.
- Cellwall is composed of peptidoglycan layer,which consists of two amino sugars

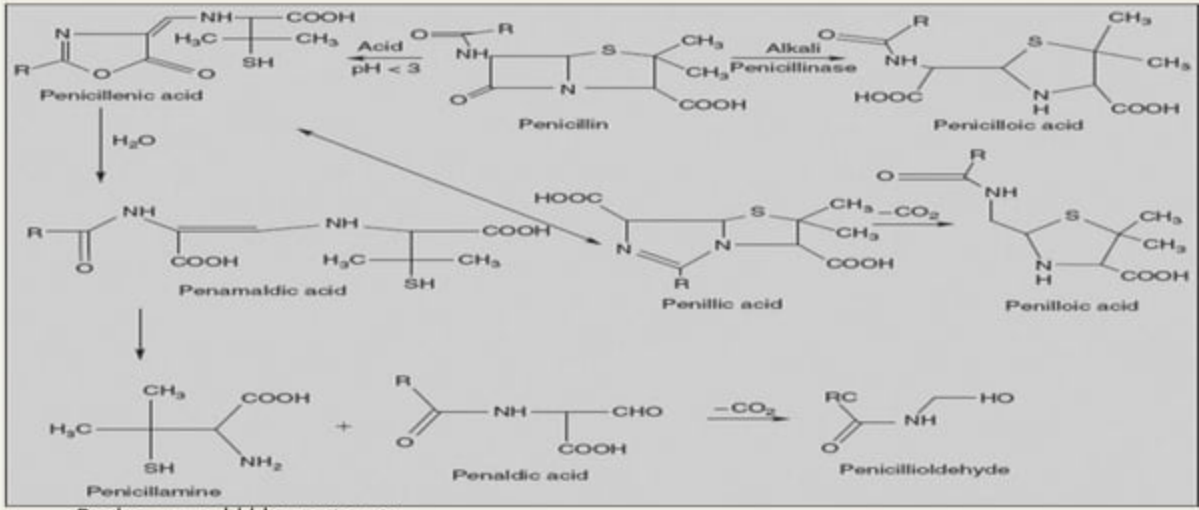
  1.N-Acetyl muramic acid(NAcM)

  2.N-acetylglucosamine(NAcG)
- Peptidoglycan residues are linked together forming long strands &UDP is split off.
- Then the cleavage of terminal-D alanine of the petide occurs by transpeptidase enzyme.This process is called transpeptidation.
- The cross brindging provides necessary strength to bacterial cell wall.

- β- lactam antibiotics inhibit the transpeptidase enzyme so that cross-linking does not takes place.
- This leads to formation of cellwall deficient bacteria and causes shrinkage of the bacterial cell.
- Penicillins shows bactericidal action.



CHEMICAL DEGRADATION OF PENICILLINS

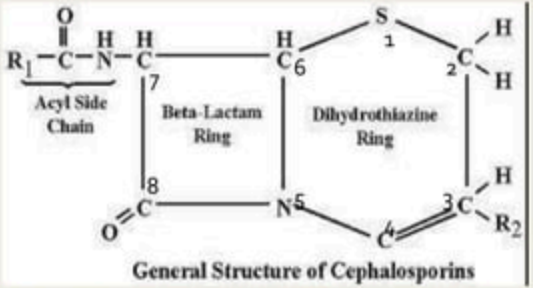


- Degradation of penicillins takes place in alkaline ,acidic conditions,in the presence of enzyme-β-lactamase and in the presence of nucleophiles like H_2O and metal ions.
- Chemical degradation of penicillins gives: Penicilloic acid
  Penicillenic acid
  Penamaldic acid
  Penillic acid
  Penilloic acid
  Penicillamine
  Penaldic acid
  Penicillioldehyde

CEPHALOSPORINS

- Cephalosporin-C was isolated by Guy Newton &Edward Abraham.
- Cephalosporins are β- lactam antibiotics containing β- lactam ring fuse with thiazine heterocyclic group.
- Cephalosporins were isolatedby an Italian scientist 'Giuseppe Brotzu' from cultures of "Cephalosporium acremonium",a fungus .
- He noticed that they are effective against Salmonella typhi (typhoid fever),which had β- lactamases.

SAR of Cephalosporins



General Structure of Cephalosporins

1.β-lactam ring is fused with dihydrothiazine ring is required for the antibiotic activity.The entire ring is called as Cepham.
2.Substitution at 7th position of β-lactam ring alters the spectrum of activity of various cephalosporins.
3.At 3rd position of dihydrothiazine ring ,substitution with various groups shows pharmacokinetic properties of cephalosporins.

Classification of cephalosporins

- Cephalosporins are classified into five generations.

1.First generation cephalosporins:

Cephalexin,Cephradine,Cefadroxil,Cephalothin,cefapirin

2.Second generation cephalosporins:

Cefuroxime,Cefoxitin,Cefaclor

3.Third generation cephalosporins:

Cefixime,Cefpodoxime,Ceftriaxone,Cefoperazone

4.Fourth generation cephalosporins:

Cefepime,Cefpirome,cefquinome

5.Fifth generation cephalosporins:

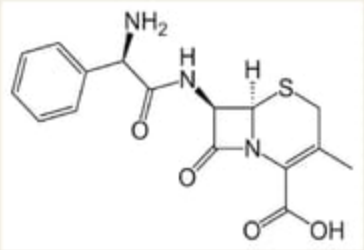
Ceftobiprole,ceftaroline,ceftolozane

- First generation cephalosporins are active against gram+ve bacterial strains,with succeeding generations progressively more active against gram –ve bacterial strains
- Fourth generation cephalosporins are extended spectrum antibiotics.

Structures and its uses

CEPHALEXIN

Structure:



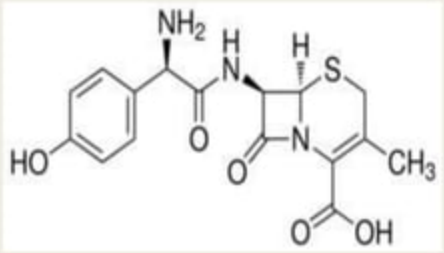
Uses: 1.First generation cephalosporin

2.To treat infections caused by gram+ve bacteria .

3.To treat upper respiratory tract infections,ear,skin,urinary tract and bone infections.

CEFADROXIL

Structure:



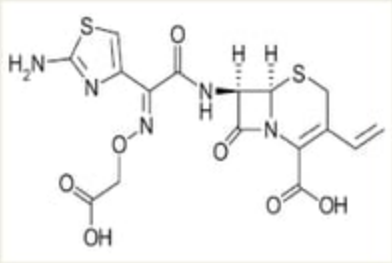
Uses: 1.First generation cephalosporin used to treat bacterial infections

2.To treat infections of throat,skin and urinary tract.

3.Used to treat gram+ve bacterial infections.

CEFIXIME

Structure:



Cefixime capsules

Uses: 1.Cefixime is a third generation cephalosporin.

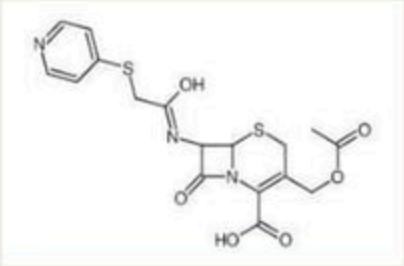
2.It is effective against both gram +ve and gram-ve bacterial infections.

3.Cefixime is resistant towards β-lactamase enzyme.

4.Used to treat typhoid fever and biliary tract infections.

CEFAPIRIN(CEFAPYRIDINE)

Structure:



Uses: 1.Cefapirin is a first generation cephalosporin .

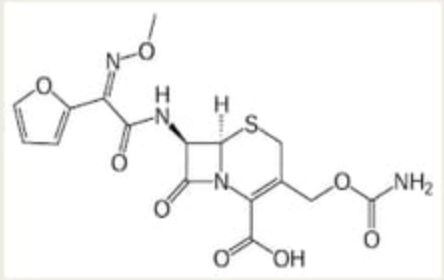
2.Cefapirin is combined with prednisolone to use in cattle for maintainig intramammary glands and its production of milk.

3.Cefapirin acts as a intrauterine preparation in cattle.

4.Cefapirin has been banned for usuage on human beings.

CEFUROXIME(CEFUTROXIME)

Structure:



Uses: 1.Cefuroxime is a second generation cephalosporin used to treat gram-ve bacterial infections.

2.Cefuroxime is the safest antibiotic during pregnancy.

3. Used to treat tonsillitis, laryngitis, bronchitis, throat infections, pneumonia, gonorrhea, urinary tract infection caused by susceptible bacteria

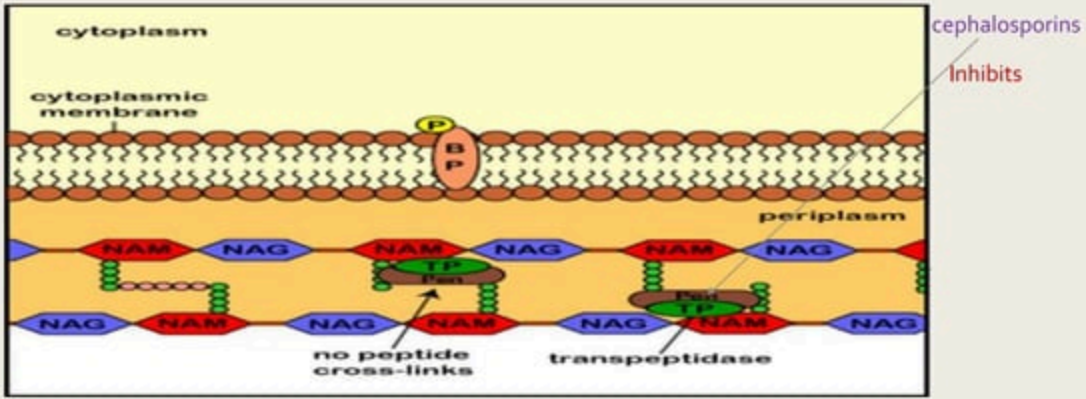
MECHANISM OF ACTION

- Cephalosporins interferes with the synthesis of bacterial cellwall.
- Cellwall is composed of peptidoglycan layer,which consists of two amino sugars

  1.N-Acetyl muramic acid(NAcM)

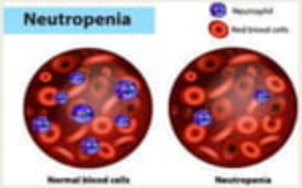
  2.N-acetylglucosamine(NAcG)
- Peptidoglycan residues are linked together forming long strands &UDP is split off.
- Then the cleavage of terminal-D alanine of the petide occurs by transpeptidase enzyme.This process is called transpeptidation.
- The cross bridging provides necessary strength to bacterial cell wall.

- β- lactam antibiotics inhibit the transpeptidase enzyme so that cross-linking does not takes place.
- This leads to formation of cellwall deficient bacteria and causes shrinkage of the bacterial cell.
- Cephalosporins shows bactericidal action.



SIDE EFFECTS AND TOXICITY

- Pain and inflammation at injection site
- Diarrhoea
- Hypersensitivity reactions
- Nephrotoxicity
- Neutropenia and thrombocytopenia
- Bleeding
- Pain on IM injection Eg:Cefalothin
- Nausea and vomiting
- Colitis
- Disulfiram like effects



β- LACTAMASE INHIBITORS

- β- lactamase inhibitors are a class of antibiotic drugs that blocks the activity

of β- lactamase enzyme ,which is responsible for degradation of β- lactam antibiotics.

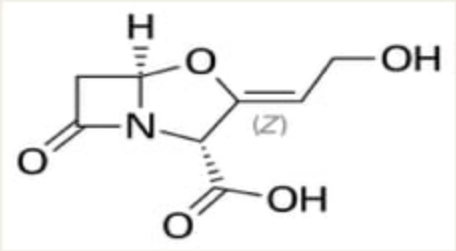
- β- lactamase inhibitors prevents the degradation of β- lactam antibiotics by acting on bacterial microorganisms.

Eg: Clavulanic acid

Thienamycin

CLAVULANIC ACID

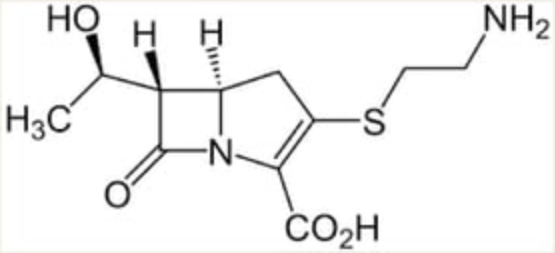
- Structure:



- Uses: 1.Amoxycillin – clavulanic acid is a combination used to treat variety of bacterial infections.
  2. It stops the growth of bacteria.

THIENAMYCIN

- Structure:



- Uses: 1.It is a naturally produced β- lactamase inhibitor.

  2.Thienamycin antibiotic is produced from "streptomyces cattleya" .

  3.Used to treat gram positive and gram negative bacterial infections.

MECHANISM OF ACTION

- All β- lactam antibiotics interfere with the synthesis of bacterial cell wall peptidoglycan.
- After attachment to penicillin binding proteins on bacteria,they inhibit the transpeptidation enzyme that crosslinks the peptide chains attached to the backbone of the peptidoglycan.
- The final bactericidal action is the inactivation and inhibition of autolytic enzymes(β-lactamase)in the cellwall ,leading to lyse of the bacterium.
- Some tolerable microorganisms have defective autolytic enzymes in which lysis does not occur.

MONOLACTAMS

- Monolactams are monocyclic and bacterially produced β- lactam antibiotics.
- The β- lactam ring is not fuse to another ring.
- Monolactams are effective only against aerobic gram negative bacteria.
- Monolactams are also called as monobactams.

  Eg: Sulfazecin

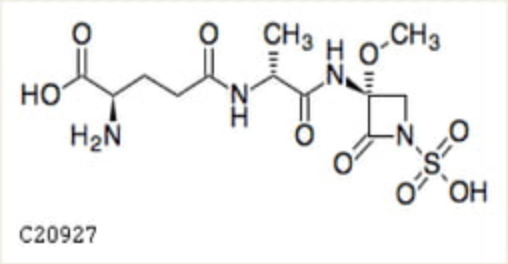
  Aztreonam

  Tigmonam

- Mechanism:Monolactams inhibit bacterial growth by interfering with the transpeptidation reaction of bacterial cell wall synthesis.Monolactams covalently bind to penicillin binding protein (PBP) to prevent growth of the cellwall via peptidoglycan synthesis.

SULFAZECIN

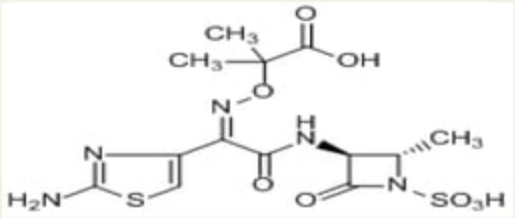
- Structure:



- Uses: It is active against gram negative bacteria and its infections.

AZTREONAM

- Structure:



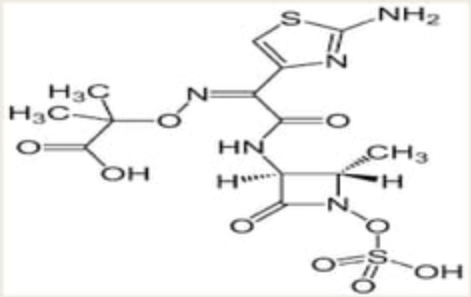
- Uses: 1.To treat sepsis

2.To treat respiratory,urinary,biliary ,gastrointestinal and female genital tract infections.

3.Aztreonam is active against aerobic gram negative bacteria.

TIGMONAM

- Structure:



- Uses: 1. Orally active monobactam

  2.Highly resistant to β- lactamase enzyme.

  3.Tigmonam is active against Enterobacter, E.coli, Klebsiella, Proteus infections.

AMINOGLYCOSIDES

DEFINITION:

- Aminoglycosides are a group of natural and semisynthetic antibiotics having polybasic amino groups linked glycosidically with two or more aminosugars.
- Aminoglycosides are used to treat various bacterial infections caused by gram negative bacteria.
- Aminoglycosides can be combined with penicillins or cephalosporins to show prolonged attack on gram –ve bacterial infections.
- They shows antibiotic action by inhibiting the bacterial protein synthesis.
- The drug will break down in the stomach without showing antibiotic activity through oral route but it shows better activity through parentral route.
- Examples of aminoglycosides are:

  Streptomycin,Amikacin,Neomycin,

  Kanamycin,Gentamycin,Netilmycin
- The above drugs are various aminoglycosides used to treat gram –ve bacterial infections.

STREPTOMYCIN

Structure:

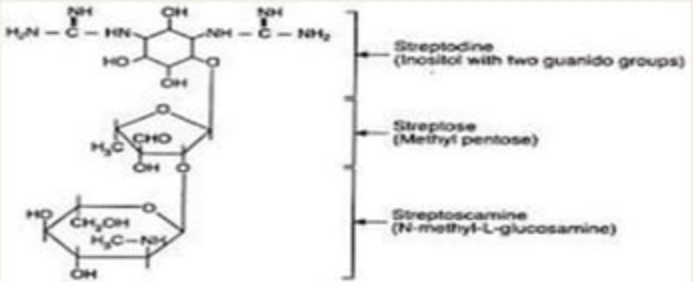


FIG. 45.9. Chemical structure of streptomycin.

Uses: 1. Streptomycin is a first line drug in the treatment of tuberculosis.

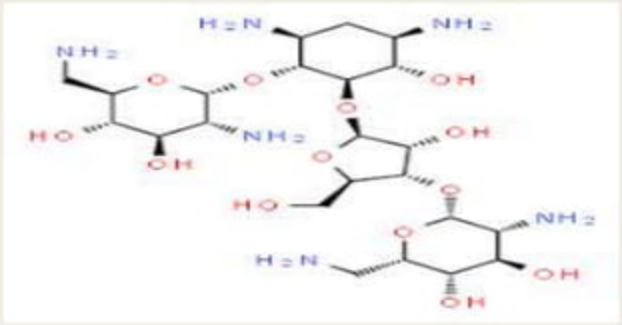
2.To treat plague and brucellosis (disease caused by unpasteurized milk or half cooked meat)

in combination with tetracycline.

3.To treat Enterococcal and streptococcal infections

NEOMYCIN

Structure:

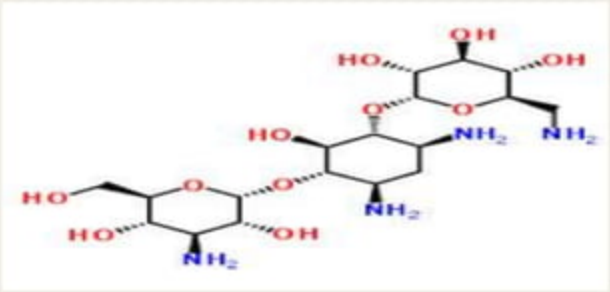


Uses: 1.To treat a variety of skin and mucous membrane infections

2.To treat gram –ve bacilli infections and gram +ve cocci infections.

KANAMYCIN

Structure:



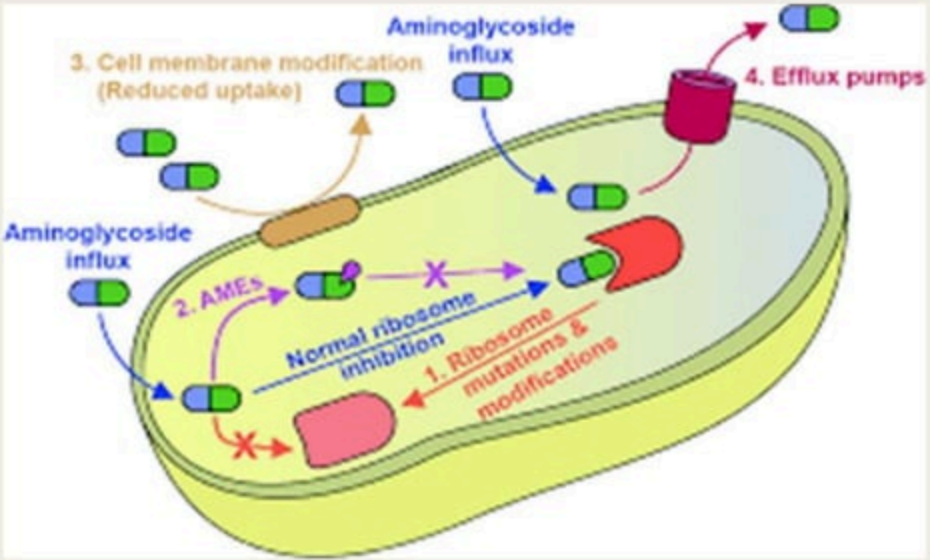
Uses:1.Kanamycin is a narrow spectrum antibiotic.

2. To treat serious bacterial infections in body .

3. Used in plants transgenic resistance.

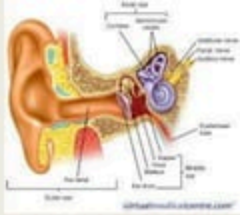
MECHANISM OF ACTION

- Aminoglycosides inhibits protein synthesis by binding to the 30s ribosomal subunits.
- 30s ribosomal subunits interfere with the initiation complex.
- Aminoglycoside -30s ribosomal complex induce misreading of genetic code on mRNA.
- Misreading mutation of the genetic code and the synthesis of nonsense proteins occurs.
- Nonsense proteins are not normal proteins.
- So Nonsense proteins cannot take a part in bacterial cellular activities.
- Nonsense proteins will disturb the permeabitlity of bacterial cell in to the host cell.
- Finally the growth and development of bacterial cell affects and leads to bacterial cell death.


Aminoglycoside
influx
3. Cell membrane modification
(Reduced uptake)
4. Efflux pumps
Aminoglycoside
influx
2. AMEs
Normal ribosome
inhibition
1. Ribosome
mutations &
modifications

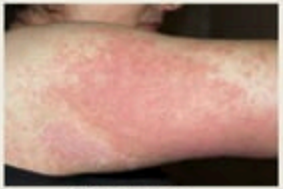
SIDE EFFECTS & TOXICITY

- Nephrotoxicity
- Ototoxicity
- Headache
- Neuromuscular blockade
- Dizziness
- Vertigo
- Fever
- Skin rashes



Ototoxicity

Neuromuscular blockade

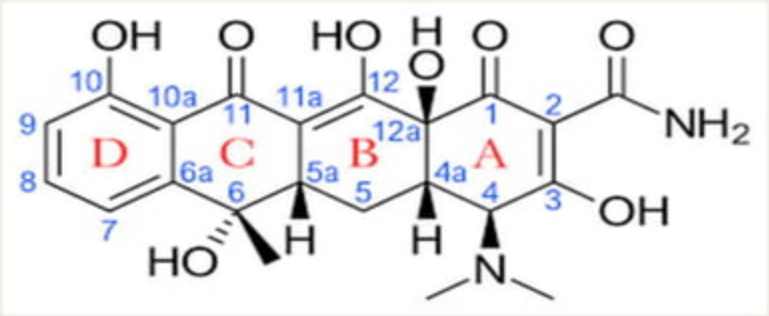


Skin rashes

TETRACYCLINES

- Tetracyclines are octahydro napthacene derivatives which are bacteriostatic and broad spectrum antibiotics that kills various types of infections caused by both gram +ve and gram –ve microorganisms.
- TETRA =four ,CYCLINES = cyclic compounds
- Tetracyclines have been introduced 50 years ago as broad spectrum antibiotics.
- They are biosynthesized from CH_3COOH AND C_3H_7COOH units in the microorganisms.
- They are active against both gram +ve and gram –ve bacteria.
- Tetracyclines are available for oral route and parentral route.

SAR OF TETRACYCLINES



- Tetracyclines containing less than or more than four rings are inactive.

- Conversion of amide group at 2nd position decreases the activity.
- Keto-enol tautomerism between C_2 and C_3 is very important for biological activity.
- Modification of –OH group at 3rd position leads to no activity.
- Dehydration at 5a position leads to no activity.
- Epimerisation at 4th position shows no activity.
- Substitution at 5th position gives hydrophilic nature of the drug.
- Dimethyl aminogroup at 4th position shows good activity.
- $=CH_2$ group at 6th position increases antibacterial activity.
- Elimination of –OH group at 6th position increases lipophilicity Eg:Doxycycline
- Electron donating or electron withdrawing group at 7th position increases antibacterial activity.
- D ring should be always aromatic
- Changes in D ring leads to biological inactivation.
- Addition of any amino group substitution at 9th position leads to new class of antibiotics.
- Tetracycline ring is most important for antibacterial activity.

CLASSIFICATION

According to duration of action:

1. Long acting tetracyclines (12 -16 hrs)

   Doxycline, minocycline, Meclocycline

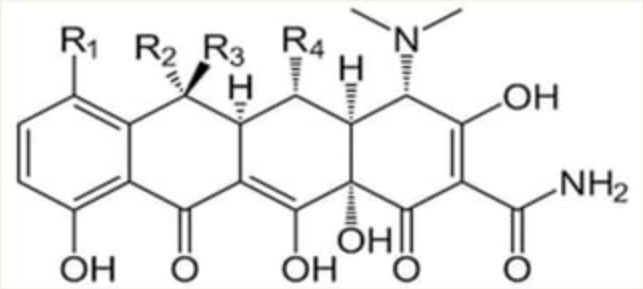
2. Intermediate acting tetracyclines (8 -12 hrs)

   Demeclocycline, methacycline

3. Short acting tetracyclines (6-8 hrs)

   Tetracycline, chlortetracycline, Oxytetracycline

Tetracyclines are obtained from various species of streptomyces bacteria by fermentation technology.

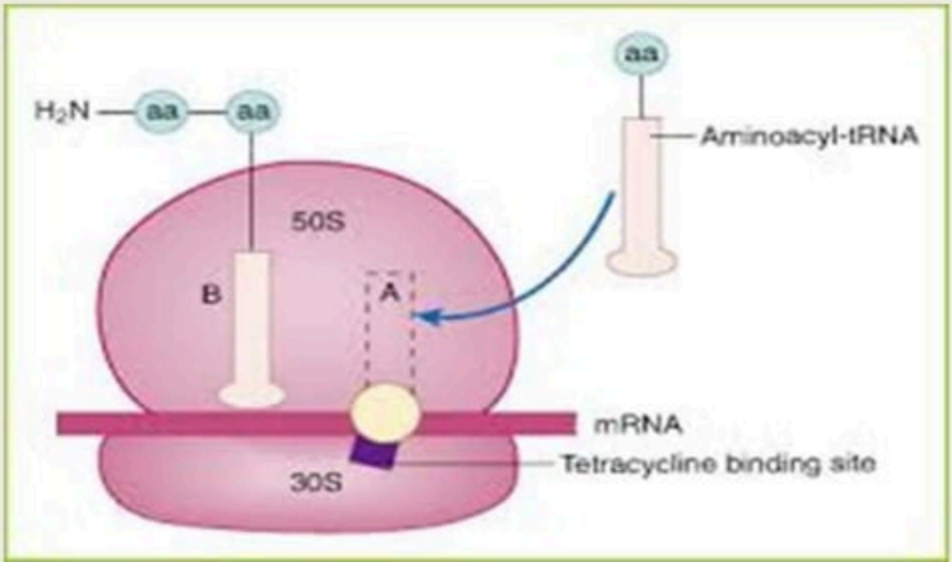


- General structure of tetracyclines

Name of the drug	R1	R2	R3	R4
TETRACYCLINE	H	OH	CH_3	H
CHLORTETRACYCLINE	Cl	OH	CH_3	H
OXYTETRACYCLINE	H	OH	CH_3	OH
MINOCYCLINE	$N(CH_3)_2$	H	H	H
DOXYCYCLINE	H	CH_3	H	OH

MECHANISM OF ACTION

- Tetracyclines inhibit protein syntesis by binding to the bacterial ribosome involved in the translation(protein synthesis) process and shows bacteriostatic activity.
- They bind to the 30s ribosome and inhibit the protein synthesis.
- The 70s bacterial ribosome particle is made of 30s and 50s subunits.
- The 50s subunit combines with the 30s subunit-mRNA complex and binds to t-RNA for building the protein chain.
- t-RNA contains two binding sites . a. P-site (peptidyl site) b. A-site(Acceptor aminoacyl site).
- Tetracyclines reversibly bind to the 30s subunit at the A –site to prevent attachment of the aminoacyl tRNA ,terminating the translation process.

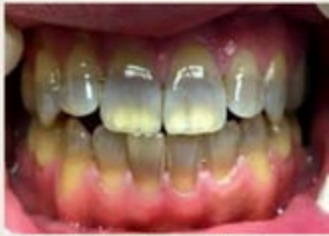

aa
H_2N
aa
aa
Aminoacyl-tRNA
50S
B
A
mRNA
Tetracycline binding site
30S

TETRACYCLINES -USES

- Tetracyclines are broad spectrum antibiotics used to treat various types of infections.
- To treat eye infections.
- Tetracyclines are low cost alternative antibiotics.
- Recently, tetracyclines are used to treat cancer patients.
- To treat respiratory infections,ear,intestine and sinus
- To treat gonorrhea
- Tetracyclines are not used to treat viral infections.

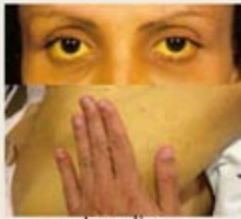
SIDE EFFECTS

- Nausea
- Vomiting
- Diarrhoea
- Teeth staining or teeth colouring
- White patches on skin
- Vaginal itching or discharge
- Trouble in swallowing(Dysphagia)
- Loss of appetite
- jaundice



Teeth staining or colouring

White patches



Jaundice

Dysphagia

Precautions to be taken while using tetracyclines

- Complete the course of prescription
- Pregnant women should avoid tetracyclines
- Take on empty stomach with plenty of water
- Tetracyclines should not taken with milk, antacids and iron.
- Avoid exposure to sun
- Tetracyclines should not be given to Children below 8 years
- Tetracyclines passes through breast milk and affect the bones and teeth in babies.

MACROLIDES

- Macrolides are a group of antibiotics which contains macrocyclic lactone ring (usually containing 14 or 16 atoms) to which deoxysugars are attached.
- Macrolides are obtained from streptomyces species.

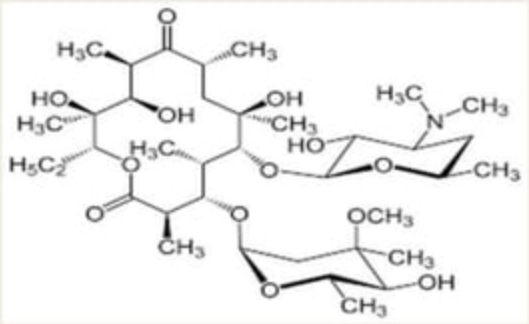
Eg: Erythromycin

Azithromycin

Clarithromycin

ERYTHROMYCIN

- Structure:



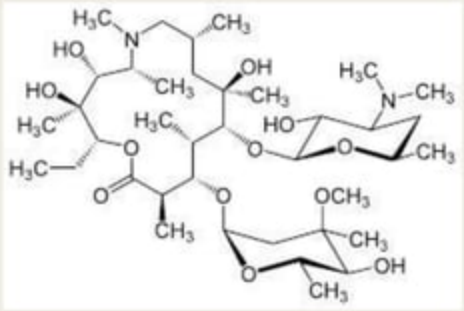
- Uses: 1.Used against gram positive & gram negative bacterial infections

  2.To treat syphilis,diptheria.

  3. To treat Pertussis (whooping cough that can cause severe coughing)

AZITHROMYCIN

- Structure:



- Uses: 1. Azithromycin is active against many respiratory tract pathogens including pneumococci,mycoplasma and chlamydia species.

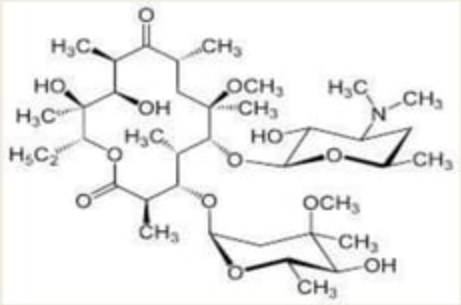
  2.To treat throat infections & non - gonococcal urethritis.

  3.It is expensive drug

  4.Used to prevent bacterial complications in AIDS.

CLARITHROMYCIN

- Structure:

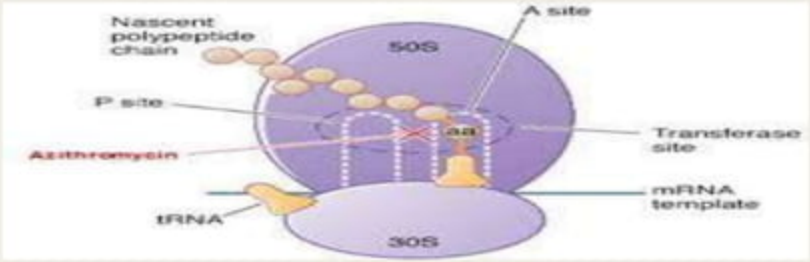


- Uses:1. To treat bacterial infections affecting skin and respiratory tract.

2.Clarithromycin is combined with other drugs to treat stomach ulcers caused by H.pylori

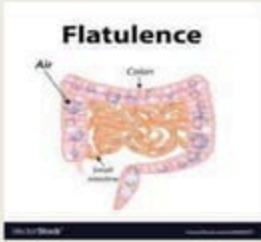
MECHANISM OF ACTION

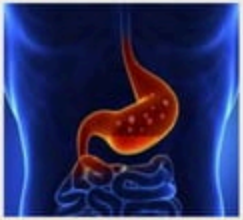
- Macrolides inhibits protein synthesis by binding to the 50s ribosomal subunit.
- Suppression of RNA dependant protein synthesis by inhibition of translocation of mRNA.
- Macrolides are bactericidal at high concentrations against very susceptible microorganisms.



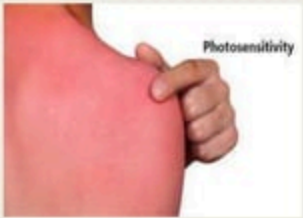
SIDE EFFECTS

- Nausea
- Vomiting
- Abdominal pain
- Chest pain
- Dyspepsia(burning sensation)
- Flatulance
- Vaginitis
- Nephritis
- Dizziness
- Headache
- Photosensitivity
- Rashes and pruritis





Dyspepsia



MISCELLANEOUS ANTIBIOTICS

- The antibiotics which shows bactericidal property but not included under any class of antibiotics like beta-lactam, aminoglycoside and tetracyclines are considered as miscellaneous category of antibiotics.
- This class of drugs shows the antibiotic action by chance.

Eg: Chloramphenicol

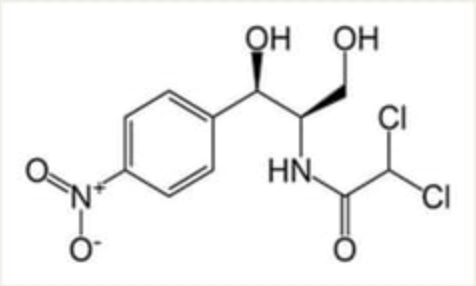
Vancomycin

Novobiocin

Clindamycin

CHLORAMPHENICOL

Structure:



Uses: 1.To treat typhoid fever,meningitis,rocky mountain spotted fever.

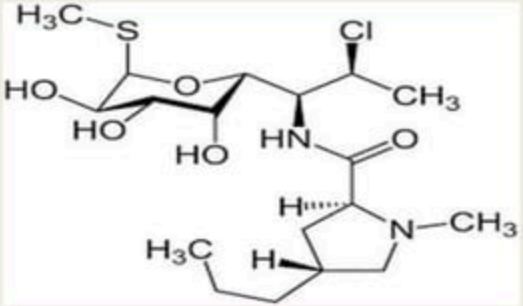
2.To treat Enteric fever

3.Chloramphenicol is alternative drug in place of cephalosporins.

4.To treat anaerobic infections and intraocular infections.

CLINDAMYCIN

- Structure:



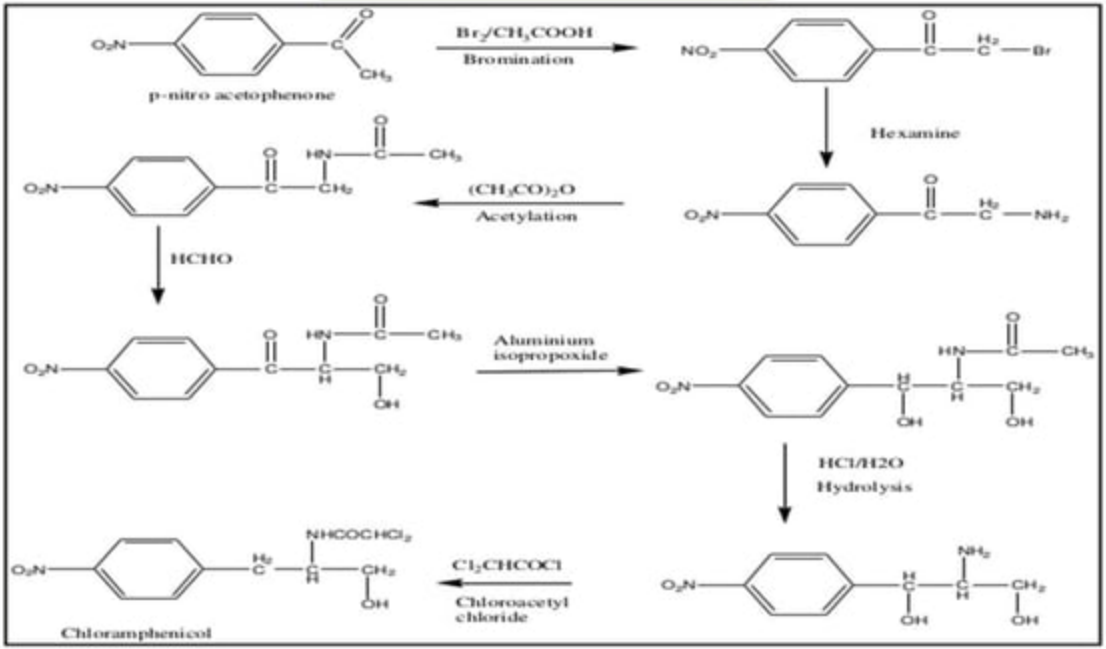
- Uses: 1.Clindamycin is a semisynthetic derivative of lincomycin

  2.It is rarely used today and reserved for patients allergic to penicillins.

Mechanism of action

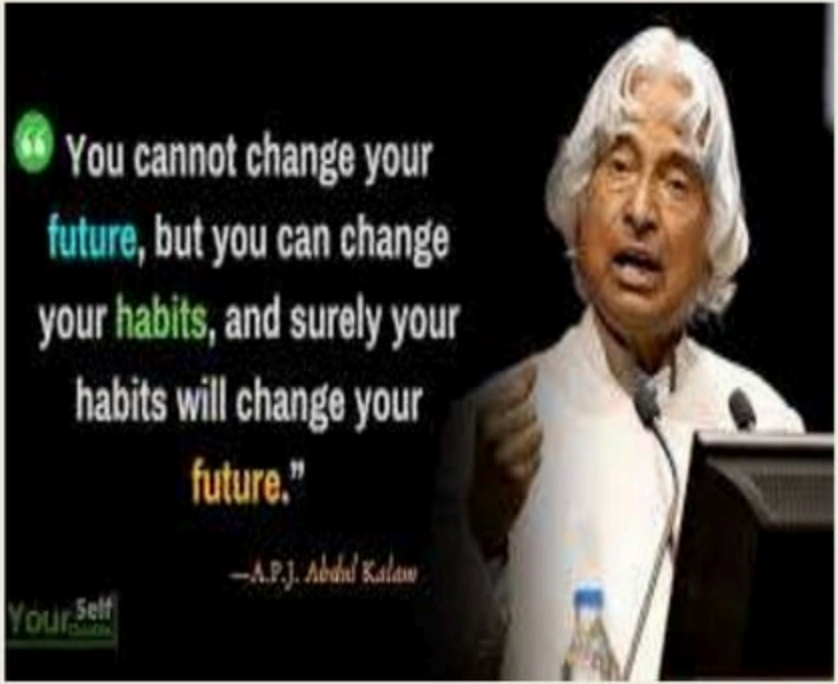
- Chloramphenicol is a bacteriostatic drug by inhibiting protein synthesis.It prevents protein chain elongation by inhibiting the peptidyl transferase activity of the bacterial ribosome .It specifically binds to the 50s ribosomal subunit and prevents the peptide bond formation.
- Clindamycin inhibits protein synthesis by binding with the 50s ribosomal subunit of the bacteria.Topical clindamycin reduces free fatty acid concentrations on the skin and suppresses the growth of bacteria,found in sebaceous glands and follicles.

Synthesis of Chloramphenicol



REFERENCES

- Wilson and Gisvold's textbook of organic ,medicinal and pharmaceutical chemistry
- A textbook of medicinal chemistry by V.Alagarswamy
- Medicinal chemistry by Ashutosh kar
- Principles of organic medicinal chemistry by Rama rao Nadendla
- Foye's principles of medicinal chemistry
- Textbook of medicinal chemistry by Valentine .Ilango
- Medicinal chemistry by Graham Patrick
- www.nlm.nih.gov.pubmed
- Pharmafactz.com – online library for medicinal chemistry
- United states national library of medicine – A research centre


You cannot change your future, but you can change your habits, and surely your habits will change your future."
—A.P.J. Abdul Kalam
YourSelf


THANK YOU
THANK YOU!
THANK YOU


GET WELL SOON
WITHOUT ANTIBIOTICS