Unit-I

Antibiotics

Presented By,

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Specialization – Pharmaceutical Chemistry

Antibiotic

- Antibiotics are medicines used to treat infections caused by bacteria. They work by either killing bacteria or stopping them from growing and multiplying.
- Antibiotics is a greek word that meaning;- anti- against or bios-life.
- **Some Examples of antibiotics:-**

  Penicillin – one of the first antibiotics discovered.

  Amoxicillin – often used for ear infections or strep throat

  Azithromycin – used for respiratory infections.

  Ciprofloxacin – used for urinary tract infections

Discovery of first Antibiotics

- **The First Antibiotic: Penicillin**
- **Discovered by:** Alexander Fleming
- **Year:** 1928
- **Location:** St. Mary's Hospital, London
- **How It Happened:-**

Fleming was working with *Staphylococcus* bacteria when he noticed that a mold (*Penicillium notatum*) had accidentally contaminated one of his Petri dishes. Remarkably, the bacteria around the mold had been destroyed, while those farther away were unaffected. He realized the mold was releasing a substance that killed bacteria — this substance was **penicillin**.

- **Development into a Usable Drug:-**

Fleming's discovery didn't immediately lead to widespread use. It wasn't until the late 1930s and early 1940s that a team of scientists, including **Howard Florey**, **Ernst Boris Chain**, and **Norman Heatley**, were able to purify and mass-produce penicillin.

History of Antibiotics

- **Empirical phase:-** moulded crude by chines, cinchona bark, chaulmoogra oil by Hindus.
- **Ehlirch phase:-** Dyes, chemotherapy.
- **Modern phase:-** prontosil therapeutics effect by Domagk,

  penicillin discovery by Alexander Fleming.

Classification of antibiotics

Antibiotics are classified based on their chemical structure

1. Beta-Lactam Antibiotics

Mechanism:-Inhibit bacterial cell wall synthesis by binding to penicillin-binding proteins (PBPs).

Examples:-

Penicillins:- Penicillin G, amoxicillin, flucloxacillin.

Cephalosporins:- Cefaclor, cefadroxil, cefalexin.

Carbapenems:- Imipenem, meropenem.

Monobactams:- Aztreonam.

2. Aminoglycoside Antibiotics

Mechanism:- Inhibit bacterial protein synthesis by binding to the 30S ribosomal subunit.

Examples:- Gentamicin, tobramycin, amikacin, streptomycin.

Classification of antibiotics

3. Tetracycline Antibiotics

Mechanism: Inhibit bacterial protein synthesis by binding to the 30S ribosomal subunit, preventing the binding of tRNA.

Examples: Tetracycline, doxycycline, minocycline.

4. Macrolide Antibiotics

Mechanism: Inhibit bacterial protein synthesis by binding to the 50S ribosomal subunit.

Examples: Erythromycin, clarithromycin, azithromycin.

Classification of antibiotics

5. Other Antibiotic Classes

Polypeptide Antibiotics:-

- **Mechanism:** Disrupt bacterial cell membranes or inhibit cell wall synthesis.
- **Examples:** Polymyxin B, bacitracin.

Lincomycins:-

- **Mechanism:** Inhibit bacterial protein synthesis by binding to the 50S ribosomal subunit.
- **Examples:** Lincomycin, clindamycin.

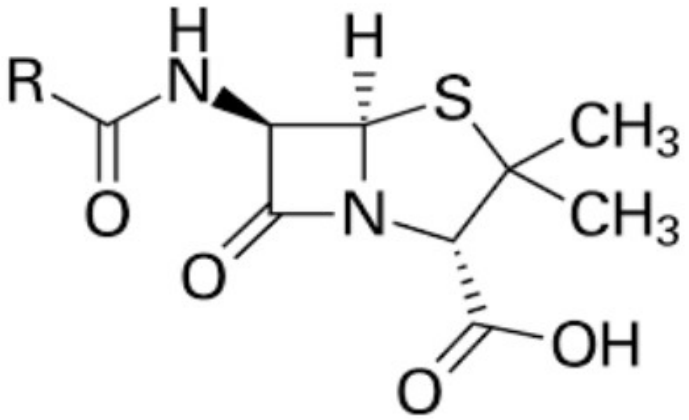
Quinolones:-

- **Mechanism:** Inhibit bacterial DNA replication by targeting DNA gyrase and topoisomerase IV.
- **Examples:** Ciprofloxacin, levofloxacin.

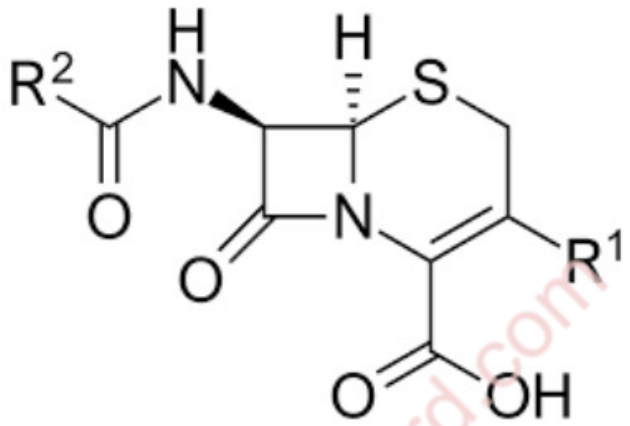
Oxazolidinones:-

- **Mechanism:** Inhibit bacterial protein synthesis by binding to the 23S ribosomal subunit.
- **Examples:** Linezolid.

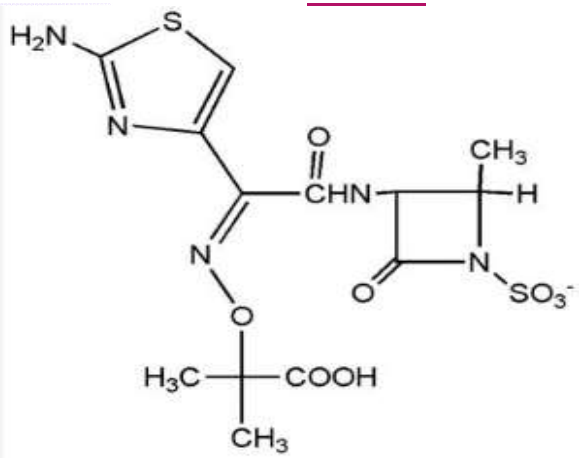
- **Glycopeptides:-**
  - **Mechanism:** Inhibit bacterial cell wall synthesis by binding to the D-alanyl-D-alanine terminus of peptidoglycan precursors.
  - **Examples:** Vancomycin, telavancin.
- **Cyclic Lipopeptides:-**
  - **Mechanism:** Disrupt bacterial cell membranes.
  - **Examples:** Daptomycin.
- **Lipiarmycins:-**
  - **Mechanism:** Inhibit bacterial cell membrane synthesis.
  - **Examples:** Fidaxomicin.



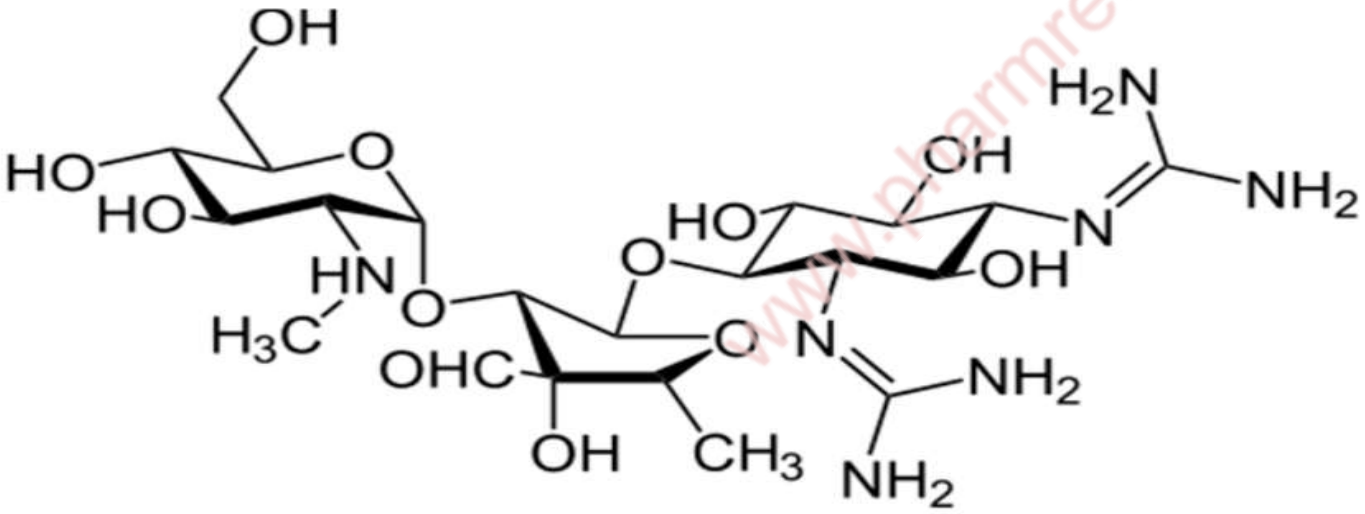
Penicillin



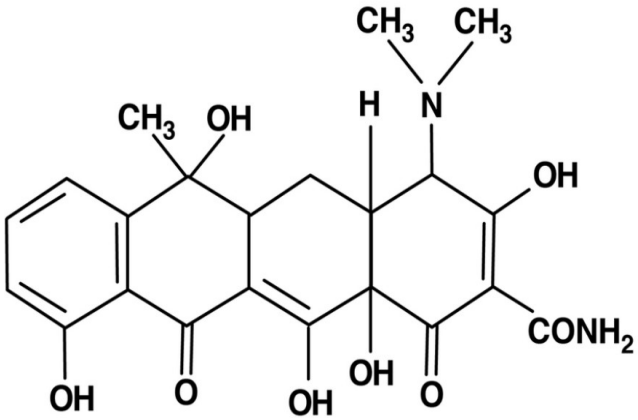
Cephalosporin



Monobactams



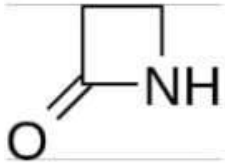
streptomycin



Tetracycline

Beta - Lactam Antibiotics

- **Beta-lactam antibiotics** are a large class of antibiotics that contain a **beta-lactam ring** in their molecular structure.



- They most widely used antibiotics in medicine and are effective primarily against **bacteria with cell walls**, especially Gram-positive bacteria (though some also target Gram-negative).
- This include:- Penicillin, cephalosporin's, monobactams.

1. Penicillin

Penicillins are a group of antibiotics used to treat bacterial infections. They were one of the first antibiotics discovered and are still widely used today.

MOA:- ·

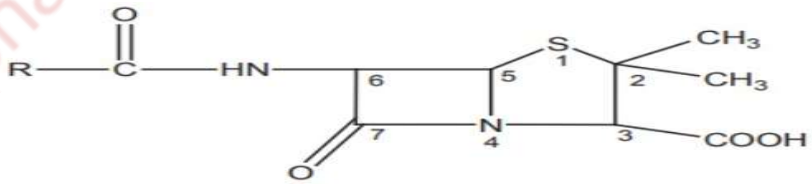
- **Bacterial cell walls** are made of a strong substance called **peptidoglycan**.
- Penicillin **blocks the enzyme** (*transpeptidase*, also known as **penicillin-binding protein or PBP**) that helps link peptidoglycan strands together.
- Without a strong cell wall, the bacteria **can't hold their shape** — they swell up and burst due to osmotic pressure.
- The bacteria **die** as a result.

SAR of Penicillin

Position 1:- Oxidising the sulfur atom of the Thiazolidine ring to a sulfone or sulfoxide enhances acid stability but decreases the activity of the agent.

Position 2:- No substitutes are permitted at this position; any change will result in a lower activity. The methyl groups are required.

Position 3:- Thiazolidine's carboxylic acid is necessary for action. If it is converted to an alcohol or ester, its activity decreases.



Position 4:- Nitrogen is required.

Position 5:- No substitutes are permitted.

Position 6:-Substitutions on the amide's side chain are permitted.

Position-7:- Carbonyl on the Beta-lactam ring is required because it improves acid stability.

2. Cephalosporin

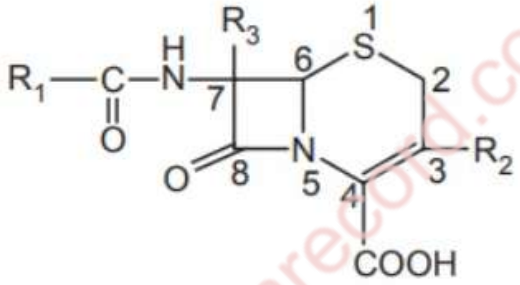
- Cephalosporins are a **large class of β-lactam antibiotics** derived from the fungus *Acremonium* (formerly *Cephalosporium*).
- Structurally related to penicillins, they are widely used to treat **bacterial infections.**

MOA:-

Cephalosporin's, a class of beta-lactam antibiotics, disrupt bacterial cell wall synthesis by binding to penicillin-binding proteins (PBPs), which are essential for peptidoglycan cross-linking, leading to bacterial cell death.

SAR Of Cephalosporin

Structure of Cephalosporin



1. 7-Acylamino substitution:-

a) The addition of amino group and a hydrogen to α and α_1 position produces basic compound, which is protonated under acidic conditions of stomach. The ammonium ion improves the stability of β-lactum of cephalosporins and make active orally.

b) When the new acyl groups are derived from carboxylic acids, it shows good spectrum of antibacterial action for gram-positive bacteria

c) Substitutions on the aromatic ring phenyl that increase lipophilicity provide higher gram-positive activity and generally lower gram-negative activity.

SAR Of Cephalosporin

2. Modification in the C-3 substitution:-

a) The pharmacokinetic and pharmacodynamics depends on C-3 substituents.

b) Modification at C-3 position has been made to reduce the degradation of cephalosporins.

3. Other modifications

a) Methoxy group at C-7, shows higher resistance to hydrolysis by β-lactamase.

b) Oxidation of ring spectrum to sulphoxide or sulphone greatly diminishes or destroys the antibacterial activity.

c) The carboxyl group position-4 has been converted into ester prodrugs to increase bioavailability of cephalosporins, and these can be given orally as well.

3. Beta- Lactamase Inhibitors

- **"Beta-Lactamase Inhibitors"**, which refers to a class of compounds used in combination with β-lactam antibiotics (like penicillins and cephalosporins) to overcome bacterial resistance.

- Some Beta-Lactamase Inhibitors are:-
    a) Clavulanic acid
    b) Sulbactam
    c) Tazobactam

Beta- Lactamase Inhibitors

MOA:-

- Inhibitor binds to β-lactamase enzyme.
- Prevents the enzyme from hydrolyzing the antibiotic's β-lactam ring.
- Protects the antibiotic from degradation.
- Restores or enhances antibiotic activity.

Clavulanic acid

Commonly used in **combination therapies** (e.g., **Amoxicillin + Clavulanic Acid = Augmentin**)

Sulbactam

Ampicillin + Sulbactam (brand name: Unasyn)

Tazobactam

Piperacillin + Tazobactam
Brand name: Zosyn (in the U.S.), Tazocin (in some other countries)

4. Monobactams

- Monobactams are a subclass of β-lactam antibiotics.
- Monobactams are characterized by a monocyclic (single-ring) β-lactam structure, unlike penicillins or cephalosporins which have fused rings.

MOA:-

Like other β-lactam antibiotics, monobactams inhibit bacterial cell wall synthesis by binding to penicillin-binding proteins (PBPs), also known as transpeptidases, which are essential for the final step of peptidoglycan synthesis.

Examples:-

Aztreonam:- The only commercially available monobactam antibiotic.

Nocardicin A:- A naturally occurring monocyclic β-lactam antibiotic produced by the actinomycete Nocardia uniformis.

Thank You

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