Classification of antibiotics

The antibiotic classified according to spectrum, effectiveness, mode of action and chemical structure

Classification by Spectrum of Activity

Each antibiotic type has a specific mechanism of action, which limits the range of bacterial strains it can target. This range is known as the **antibacterial spectrum** of the antibiotic.

- **Narrow-spectrum antibiotics (selective antibiotics):** These antibiotics are effective against one or a few specific microorganisms. For example, **isoniazid** targets only *Mycobacterium tuberculosis*.
- **Broad-spectrum antibiotics:** These antibiotics act against a wide variety of bacteria, including both Gram-positive and Gram-negative species. Examples include quinolones, macrolides, and carbapenems.

Classification by Chemical Structure

1. Beta-lactam Group

Beta-lactam antibiotics are defined by the presence of a beta-lactam ring in their chemical structure. This group is subdivided into four main categories:

- **Penicillins**
  Derived from 6-aminopenicillanic acid, penicillins include drugs such as benzylpenicillin, methicillin, amoxicillin, and piperacillin. They are active against both Gram-positive and Gram-negative bacteria. However, bacterial resistance mainly through beta-lactamase enzyme production can reduce their effectiveness. To counter this, some penicillins are combined with beta-lactamase inhibitors, e.g., amoxicillin/clavulanic acid and piperacillin/tazobactam.
- **Cephalosporins**
  These antibiotics contain a beta-lactam ring fused with a dihydrothiazine ring.

Altering substituent groups on the ring changes their antibacterial spectrum. Cephalosporins are classified into generations:

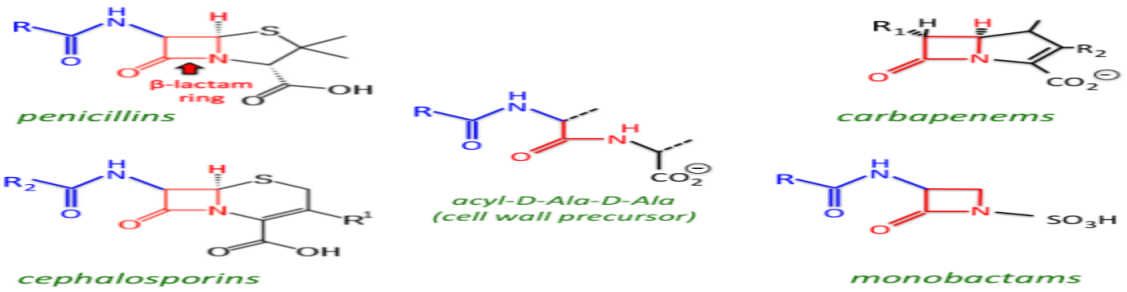
- **First Generation:** Strong activity against Gram-positive bacteria (e.g., cefazolin, cephalexin)
- **Second Generation:** Broader activity against Gram-negative bacteria and some anaerobes (e.g., cefuroxime, cefamandole, cefaclor, cefotetan, cefoxitin)
- **Third Generation:** Enhanced potency against Gram-negative bacteria (e.g., cefotaxime, ceftriaxone, ceftazidime, cefixime)
- **Fourth Generation:** Broad-spectrum activity against both Gram-positive and Gram-negative bacteria, including *Pseudomonas* (e.g., cefepime)
- **Fifth Generation:** Effective against MRSA (*Methicillin-resistant Staphylococcus aureus*) (e.g., ceftaroline)

- **Carbapenems**

  These antibiotics have a strong affinity for penicillin-binding proteins in both Gram-positive and Gram-negative bacteria. Their structure resists degradation by beta-lactamase enzymes, giving them the broadest spectrum of activity among beta-lactams. Examples include meropenem, imipenem-cilastatin, and ertapenem. Carbapenems are considered "last-resort" antibiotics for severe or multidrug-resistant infections.

- **Monobactams**

  Comprising only a beta-lactam ring, monobactams primarily target Gram-negative bacteria. Example: Aztreonam.



2.Aminoglycosides group

Aminoglycosides contain an amino-functional group attached to a sugar moiety, which defines their chemical structure. They are primarily effective against Gram-negative bacteria, with some activity against Gram-positive bacteria (notably gentamicin). Common examples include amikacin, tobramycin, and gentamicin.

3-Macrolide Group: Isolated from Streptomyces. Commonly encountered active substances include erythromycin, clarithromycin, and azithromycin. This group of antibiotics exhibits activity against Gram-positive, Gram-negative, and atypical bacteria.

4-Lincosamide Group: This group includes two antibiotics, lincomycin and clindamycin. Clindamycin primarily targets Gram-positive bacteria and anaerobes.

5-Quinolone Group: These are completely synthetic antibiotics. First generation is represented by nalidixic acid, with subsequent generations modified by the addition of fluorine, hence the name fluoroquinolones. Examples include ciprofloxacin, levofloxacin, and moxifloxacin. This group exhibits potent activity against Gram-negative bacteria such as Enterobacteriaceae, Haemophilus spp., and Neisseria spp. Additionally, ciprofloxacin and levofloxacin demonstrate activity against Pseudomonas aeruginosa.

6-Glycopeptide Group (Vancomycin, Teicoplanin): This group consists of semisynthetic antibiotics with activity against Gram-positive bacteria, including various drug-resistant strains. Monitoring drug concentrations in the bloodstream is essential during administration to ensure therapeutic efficacy and minimize nephrotoxicity.

Classification of Antibiotic according to mode of Action:

Inhibition of Bacterial Cell Wall Synthesis

In Gram-negative bacteria:

Beta-lactam antibiotics pass through porin channels located in the outer membrane of the bacterial cell. After entering the periplasmic space, they bind to penicillin-binding proteins (PBPs), which are responsible for cross-linking peptidoglycan strands during

cell wall formation. Inhibiting these enzymes prevents proper cell wall synthesis, leading to bacterial cell death.

In Gram-positive bacteria:

Since Gram-positive bacteria do not have an outer membrane, beta-lactam antibiotics can directly access and bind to PBPs. Glycopeptide antibiotics such as Vancomycin act differently by binding to the D-alanyl-D-alanine (D-Ala-D-Ala) terminus of peptidoglycan precursors, thereby blocking the synthesis and cross-linking of the bacterial cell wall.

Disruption of the Cytoplasmic Membrane

The cytoplasmic membrane acts as a selective barrier that regulates the movement of substances into and out of the bacterial cell. When certain antibiotics interact with this membrane, they disturb its structural integrity and alter its permeability. This disruption causes leakage of essential intracellular ions and molecules, along with the uncontrolled entry of water, ultimately leading to bacterial cell death.

For example, Polymyxin B and Colistin bind to the cell membrane of Gram-negative bacteria, increasing membrane permeability and causing cell lysis.

Inhibition of Protein Synthesis

- **Tetracycline**:
  Binds to the 30S ribosomal subunit and prevents the attachment of tRNA to the mRNA–ribosome complex, thereby blocking the addition of amino acids to the growing peptide chain. It acts as a bacteriostatic agent.
- **Aminoglycosides (e.g., Gentamicin)**:
  Attach to the 30S ribosomal subunit, interfering with protein synthesis by causing misreading of mRNA and inhibiting proper translation. Unlike tetracyclines, they are bactericidal antibiotics.

- **Macrolides (e.g., Azithromycin) and Lincosamides (e.g., Clindamycin)**:
  Bind to the 50S ribosomal subunit and inhibit elongation of the protein chain, thereby stopping protein synthesis. They are generally bacteriostatic.
- **Chloramphenicol:**
  Binds to the 50S ribosomal subunit and inhibits peptidyl transferase activity, preventing peptide bond formation and protein chain elongation. It acts as a bacteriostatic antibiotic.
- **Linezolid**:
  Binds to the 23S rRNA component of the 50S ribosomal subunit, preventing formation of the 70S initiation complex required for protein synthesis. It is primarily bacteriostatic.

Inhibition of Nucleic Acid Synthesis

- **Quinolones (e.g., Ciprofloxacin)**:
  Inhibit bacterial DNA gyrase and topoisomerase IV, enzymes essential for DNA replication and supercoiling. Blocking these enzymes disrupts DNA replication and ultimately leads to bacterial cell death.
- **Rifampicin**:
  Binds to bacterial DNA-dependent RNA polymerase, preventing RNA transcription and thereby inhibiting protein synthesis. It is bactericidal.

Inhibition of Folate Synthesis

- **Sulfonamides (e.g., Sulfamethoxazole)**:
  Structurally resemble para-aminobenzoic acid (PABA) and competitively inhibit its incorporation into folic acid. Since folic acid is required for nucleic acid synthesis, this interference suppresses bacterial growth. They are bacteriostatic agents.
- **Trimethoprim**:
  Inhibits the enzyme dihydrofolate reductase, blocking the conversion of dihydrofolate to tetrahydrofolate, an essential step in folic acid synthesis. It acts as a bacteriostatic antibiotic.