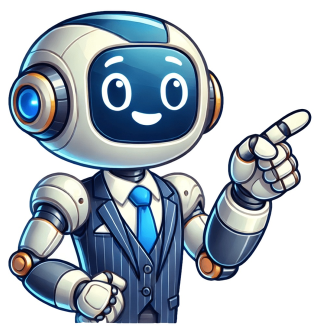
Continue



Antibiotics can be grouped based on their mechanism of action and scope of activity. Beta-lactam antibiotics, derived from natural sources or synthesized chemically, hinder bacterial cell wall synthesis by inhibiting transpeptidation reactions. They bind to penicillin-binding proteins in bacteria, disrupting the formation of peptidoglycan and murein components essential for maintaining cell integrity. These bacteriocidal agents kill bacterial cells by preventing cell wall formation, making them susceptible to external pressures that lead to lysis. Examples of beta-lactam antibiotics include penicillins and cephalosporins produced by Penicillium and Cephalosporium fungi genera. Beta-lactams inhibit the synthesis of cell walls in bacterial cells, particularly those involving peptidoglycan and murein components, and are effective against both Gram-positive and Gram-negative bacteria. Macrolides, such as erythromycin and azithromycin produced by Streptomyces species, specifically inhibit protein synthesis in bacterial cells. Characterized by large lactone rings linked to amino sugars through glycoside bonds, macrolides differ from beta-lactams with their 4-membered beta-lactam ring. Macrolides are primarily bacteriostatic, but some exhibit cidal activity against Gram-positive bacteria. Other examples of macrolides include lincomycin and clindamycin, which also inhibit protein synthesis in bacterial cells by binding to the 50S ribosomal subunit, interfering with peptidyl transferase's role in elongating protein molecules. Chloramphenicol is another antibiotic that targets the 50S ribosomal subunit of bacteria. Quinolones and their derivatives, such as fluoroquinolones, work by inhibiting DNA replication in bacterial cells, targeting key enzymes like DNA gyrase enzyme or topoisomerase IV. They are mainly used to treat urinary tract infections and are bacteriocidal in action. Fluoroquinolones, like quinolones, inhibit DNA replication and are active against Gram-negative bacteria and some Gram-positive bacteria. They can also be used to treat a variety of bacterial infections, including intestinal and lower respiratory tract infections. Tetracyclines block protein synthesis in bacteria by binding to the 30S ribosomal subunit and have a broad spectrum of activity. However, they are bacteriostatic in action. Examples of tetracyclines include doxycycline, tetracycline, and minocycline. Aminoglycosides inhibit protein synthesis or translation in bacteria by binding to the 30S ribosomal subunit. They are naturally synthesized antibiotics that mainly produce streptomycin and gentamicin from fungi like Streptomyces species. Aminoglycosides are bacteriocidal in action and are primarily used to treat infections caused by Gram-negative bacteria, especially those in the family Enterobacteriaceae. Sulphonamides are antimicrobial agents that work by inhibiting the synthesis of folic acid in bacteria, which is necessary for the production of nucleotides and ultimately DNA and RNA. These compounds are structural analogues of Para-Aminobenzoic Acid (PABA), a molecule required by bacteria to synthesize folic acid. By competing with PABA, sulphonamides prevent the conversion of PABA to folic acid, thus disrupting the synthesis of nucleotides and impairing DNA and RNA production in bacterial cells. This mode of action makes sulphonamides effective against pathogenic bacteria, which synthesize their own folic acid, unlike eukaryotic cells that obtain it from their food intake. Examples of sulphonamide antibiotics include Sulphamethoxazole, pyrimethamine, and trimethoprim. These antimicrobial agents are crucial in the treatment of bacterial infections, highlighting the importance of understanding their mechanisms of action and resistance patterns to ensure effective therapy. McDermitt A M (2005). A review of antimicrobial peptides and their therapeutic potential as anti-infective drugs. Current Eye Research, 30(7): 505-515. Various sources discuss antibacterial agents and their functions. Hardman JG, Limbird LE, eds. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York: McGraw-Hill; 2001. Joslyn, L. J. (2000). Sterilization by Heat. In S. S. Block (Ed.), Disinfection, Sterilization, and Preservation (5th ed., pp. 695-728). Kontoyiannis D.P and Lewis R.E (2002). Antifungal drug resistance of pathogenic fungi. Lancet. 359:1135–1144. To combat infectious diseases, antibacterial agents were discovered. These agents can be classified into five major groups based on their type of action, source, spectrum of activity, chemical structure, and function. Bacteria are simple one-celled organisms that cause diseases when they get into the body and begin to reproduce. To cure these infections, researchers developed antibacterial agents. Antibacterials Classification Antibacterials can be classified into five groups: type of action, source, spectrum of activity, chemical structure, and function. cefamycins, benzylpenicillin, and gentamicin are classic examples of natural antibiotics/antibacterials. These substances often exhibit higher toxicity levels compared to synthetic antibacterials. Ampicillin and amikacin belong to the semi-synthetic category, which aims to minimize toxicity while increasing effectiveness. Synthetic antibiotics, like moxifloxacin and norfloxacin, are designed to be even more potent with reduced toxicity. This approach allows these compounds to target specific bacteria before they become widespread. Another way to classify antibiotics is based on their target specificity, dividing them into narrow-spectrum and broad-spectrum agents. Narrow-spectrum antibacterials primarily target a limited range of microorganisms, such as Gram-positive or Gram-negative bacteria only. In contrast, broad-spectrum antibacterials affect a wide range of pathogenic bacteria, including both Gram-positive and Gram-negative organisms. The narrow-spectrum antibacterials are generally considered ideal due to their lower ability to cause superinfections, as they target specific bacteria rather than healthy microorganisms in the body. Furthermore, these antibiotics tend to elicit less resistance from bacteria since they only address a particular type of bacteria. Both categories have a vast array of antibacterial agents, with examples listed in Table 2. Examples of broad-spectrum antibacterials include Ampicillin and its derivative Amoxicillin. Conversely, narrow-spectrum antibacterials comprise penicillin G and its derivatives, such as Penicillin V and Procaine Penicillin. Cephalosporins and other classes of antibiotics differ in their spectrum of activity and structure. Cephalosporins can be divided into three generations: first and second generation have a narrower spectrum, while third, fourth, and fifth generations have a broader spectrum. This group also includes vancomycin, clindamycin, isoniazid, rifampin, ethambutol, pyrazinamide, bacitracin, polymixins, sulfonamides, glycopeptide, and nitroimidazoles. Carbepenems like imipenems show a broad pattern of activity, while macrolides such as erythromycin, roxithromycin, clarithromycin, azithromycin, and dirithromycin are considered broad-spectrum antibacterials. Tetracycline, chlortetracycline, oxytetracycline, demeclocycline, lymecycline, meclocycline, methacycline, minocycline, and tigecycline also fall under this category. In contrast, chloramphenicol has a broad spectrum of activity. Other antibiotics such as ticarcillin, rifamycins, and carbepenems exhibit broad coverage. The classification of antibacterials is based on their chemical structure, which can be divided into several groups: beta-lactams, beta-lactam/beta-lactamase inhibitor combinations, aminoglycosides, macrolides, quinolones, and fluoroquinolones. Beta-lactams are the most popular class of drugs, characterized by a four-membered lactam ring with varying side chains. Beta-lactam modifications have led to the development of new antibiotics such as clavulanate, latamoxef, loracarbef, and oxacephems and carbacephems. These modified agents show improved antimicrobial activity against various pathogens. Aminoglycoside antibiotics, such as netilmicin and kanamycin, have varying levels of effectiveness due to differences in their structural units. The number and location of amino groups on hexoses and the site of attachment of other rings to deoxystreptamine significantly impact their ability to inhibit protein synthesis. For example, kanamycin B is more effective than A or C. Macrolide antibiotics, such as erythromycin and roxithromycin, have a macrocyclic lactone ring with attached deoxy sugars. Studies have shown that modifying the macrolactone ring at specific sites can improve in vitro activity against mycobacterium tuberculosis. Quinolones, derived from quinine, are synthetic antibacterial agents with a basic skeleton and variations at positions 1-8 affecting their therapeutic behavior. Adding fluorine at position 6 creates flouroquinolones, which have improved anti-Gram-positive activity but may also cause adverse effects. Examples of quinolones include nalidixic acid, ciprofloxacin, levofloxacin, and trovafloxacin. Streptogramin antibiotics consist of two groups: polyunsaturated macrolactones (streptogramins A) and cyclic hexadepsipeptides (streptogramins B). Alterations to group B structural units have primarily involved modifying the 3-hydroxypicolinoyl and other related molecules. Dalfopristin is a water-soluble group A derivative obtained through Michael addition of aminothiols to the dehydroproline ring of pristinamycin IIA. This modification results in quinupristin, which impairs polypeptide chain expansion by inhibiting aminoacetyl-tRNA binding to ribosomes and preventing peptide bond formation. In contrast, group B building blocks promote disconnection of peptidyl-tRNA and may interfere with the removal of completed polypeptides from the ribosome. Sulphonamides possess a sulphonamide functional group, which grants them medicinal importance and antibacterial properties, including sulfadiazine. The structural unit of sulphonamides is based on a basic structure containing a sulphonamide group. Tetracyclines, comprising hydrocarbon-containing compounds with an octahydrotetracene-2-carboxamide skeleton, are derived from Streptomyces bacteria and feature semi-synthetic derivatives like oxytetracycline and doxycycline. Nitroimidazoles contain a basic imidazole ring and primarily feature the nitro group at position 6 in metronidazole, with varying positions also present in benznidazole. The mode of action for these antibacterial agents varies, targeting key processes such as cell wall synthesis, membrane function, protein synthesis, and nucleic acid synthesis. The process of stopping bacterial growth involves inhibiting peptidoglycan layer synthesis by targeting its cell walls. This is achieved through cell wall inhibitors, which cause new bacteria to lack a peptidoglycan layer even when they're growing in the presence of these agents. β-Lactam drugs, including penicillin derivatives and cephalosporins, are primary antibiotics that inhibit bacterial growth by working as false molecules for D-alanyl-D-alanyl transpeptidases, resulting in a disrupted peptidoglycan synthesis. Additionally, autolytic enzyme inhibitors become inactive, leading to the activation of lytic enzymes that facilitate bacterial division in an isotonic environment. Other antibiotics like bacitracin and vancomycin also target early stages of peptidoglycan synthesis. However, Gram-negative bacteria often exhibit reduced susceptibility due to their outer membrane blocking antibiotic entry. Factors such as receptor availability, lipid composition, and crosslinking influence the effectiveness of these drugs. Resistance occurs when bacterial enzymes called β-lactamases (e.g., penicillinases) inactivate these antibiotics. The cytoplasmic membrane serves as a selective barrier controlling internal cell composition; its disruption can lead to macromolecule outflow and cell death. To prevent this, targeted chemotherapy agents must selectively target the bacterial cell membrane. Polymyxins are cyclic peptides with hydrophobic tails that show specificity for polysaccharide molecules in Gram-negative bacteria's outer membranes. They work by disrupting osmotic balance, causing molecule discharge from the cell interior, inhibiting respiration, and increasing water permeability. The process of protein synthesis is a crucial function in both bacterial and human cells. However, it's a prime target for antibiotics aimed at combating infectious diseases caused by pathogenic bacteria. The thickness of Gram-positive bacteria cell walls hinders the effectiveness of polymyxins, making them less potent against these types of bacteria [19]. Protein synthesis inhibitors, on the other hand, can target multiple stages of protein synthesis, such as initiation and elongation, to disrupt bacterial protein production. Several classes of antibiotics have been developed to inhibit protein synthesis. Aminoglycosides bind to the 30S ribosomal subunit, altering its structure and disrupting normal protein synthesis steps. Macrolides, tetracyclines, streptogramines, phenicols, oxazolidinones, and ketolides work by binding to different ribosomal subunits or stages of protein synthesis, ultimately leading to cell death. In addition to targeting protein synthesis, antibiotics can also inhibit nucleic acid synthesis. The difference in enzymes responsible for DNA and RNA synthesis between eukaryotic and prokaryotic cells enables the development of selective antibiotics with reduced toxicity to human cells. Antibacterials can be categorized into DNA inhibitors and RNA inhibitors, with the latter affecting bacterial transcription by binding to RNA polymerase and preventing gene expression. This ultimately leads to cell death. Antibacterial drugs target different stages of DNA synthesis, including initiation, elongation, and termination. Quinolones, such as nalidixic acid and ciprofloxacin, inhibit DNA gyrase, a topoisomerase responsible for cutting chromosomal DNA parts. Other antibacterials, like nitrofurantoin and metronidazole, work by creating metabolites that bind to DNA strands, leading to cell damage. Recent antibacterial agents have been listed in Table 4, but the classification of antibacterials is still evolving. A proposed categorization into five principal categories could provide a clearer understanding of these agents' characteristics and therapeutic nature. This classification system can be useful for future research, academic purposes, and healthcare applications. This compilation of articles provides an overview of antibiotic classes, mechanisms of action, and resistance to antibiotics. Carbon and Isturiz discuss the factors that contribute to pneumococcal resistance to beta-lactams, highlighting the importance of selecting narrow-spectrum antibacterials. King et al. introduce the quinolone antibiotics and their classification, while Kotra et al. explore the mechanisms of action and resistance of aminoglycosides. Zhanel et al. provide a comparative review of the carbapenems, a group of beta-lactam antibiotics with broad-spectrum activity. Hof discusses the macrolides, a group of antibiotics that target bacterial protein synthesis. Floss and Yu examine the mode of action, resistance, and biosynthesis of rifamycins. Hamilton reviews the beta-lactams, discussing their variations in chemical structure and surprising biological effects. Cunha explores the use of aminopenicillins in urology. Benveniste and Davies investigate the structure-activity relationships among aminoglycoside antibiotics. Zhu et al. examine the structure-activity relationships of macrolides against Mycobacterium tuberculosis, while Emami et al. discuss recent developments in quinolone research. Mast and Wohlleben review streptogramins, a group of antibiotics that inhibit bacterial protein synthesis. Barrière et al. provide an overview of recent developments in streptogramin research, while Bugg et al. discuss the assembly of bacterial cell walls as an attractive antibacterial target. Newton reviews the mechanisms of antibiotic action, highlighting their targets and networks. Kohanski et al. explore how antibiotics kill bacteria, from targeting specific pathways to disrupting entire networks. Swaney et al. investigate the oxazolidinone linezolid's mechanism of action in inhibiting protein synthesis initiation. Rai et al. summarize recent advances in antibacterial drugs, highlighting the development of new classes and mechanisms of action. 