Antibiotics An Effective Tool, Their Categories and Action Mechanism Against Microbial Infection.

Fareha Fatima[1], Dr. Krishna Kumar Prajapati[2]*

[1]Research Aspirant in M.R.D. life Sciences Lucknow[1].
[2*]Assistant Professor, Department of Zoology, Marwar Business School, Gorakhpur. Deen Dayal Upadhyay Gorakhpur University, Gorakhpur. Email Id: krishnaprajapati90@hotmail.com

Abstract
Many antibiotics originate from microorganisms like bacteria, fungi, and molds, although today some are partly or fully synthesized in laboratories. The introduction of antibiotics revolutionized modern medicine by drastically reducing deaths caused by bacterial infections, and many of today's antibiotics are still based on these natural substances. Although people in ancient times were aware that some molds and plant extracts had antibacterial properties, the modern era of antibiotics truly began in the early 20th century, highlighted by Alexander Fleming's groundbreaking discovery of penicillin in 1928. Antibiotics are generally categorized by their mode of action such as disrupting bacterial cell wall formation, inhibiting protein production, interfering with DNA or RNA synthesis, or blocking essential metabolic functions. The method of administration whether oral, topical, or by injection can also influence how resistance develops. Antibiotics with similar chemical structures often share similar properties, including their effectiveness, side effects, and potential for allergic reactions. Antibiotics can work in two main ways: they can be bactericidal meaning they directly kill bacteria, or bacteriostatic, meaning they stop bacterial growth. These drugs are grouped into different classes, each targeting specific bacterial structures or processes. However, bacteria continuously adapt and develop resistance mechanisms that weaken or block the effects of these drugs. These mechanisms involve altering the antibiotic's target site, decreasing drug entry by modifying cell membrane permeability, generating enzymes that deactivate the antibiotic, and employing efflux pumps to remove the drug from the cell.

Keywords: Antibiotics, Antibacterial effects, Bactericidal, Disrupting, Bacterial components, Antibiotic's target site.

Introduction

Antibiotics are vital tools in the fight against infectious diseases in humans, animals, and across sectors like livestock farming and aquaculture. However, their increasing accumulation in soil and water ecosystems has raised concerns about potential harm to native microbial communities [1]. These compounds, which are naturally occurring and function as defense mechanisms, are capable of killing or inhibiting harmful microorganisms even at very low concentrations. Most antibiotics are derived from microorganisms such as bacteria, fungi, and molds, although some are now partially or fully synthesized through chemical means. Bacillus species, for instance, are common soil dwellers due to their ability to produce durable endospores and secrete potent antibiotics like bacitracin, which help them outcompete other microbes [2].

Originally, all antibiotics were obtained from living organisms, which are found virtually everywhere, thrive in environments where competition is intense. In such settings, bacteria often produce antibiotics as secondary metabolites compounds not essential for survival but beneficial for gaining a competitive edge. These metabolites are now widely used in commercial antibiotic production. The traditional method of cultivating the antibiotic-producing microbes under optimal growth conditions and then extracting the desired compounds is still in practice. A study by Olga Viloreiyna (2018) [3] focused on isolating marine bacteria and testing their ability to produce antibiotics effective against common clinical pathogens like *Pseudomonas spp.*, *Escherichia coli*, *Bacillus subtilis*, and *Proteus spp.* Out of 36 tested isolates, four demonstrated strong antibacterial properties. One isolate, CW 602, produced antibiotics when grown alongside *Pseudomonas*, while another, CW 401, did so in the presence of *Bacillus*. The antibiotic activity of these bacterial extracts was evaluated using the disc diffusion method.

Growing concern exists regarding the persistence and degradation of antibiotics in soil, along with their impact on the structural, genetic, and functional diversity of microbial communities. One of the major consequences of this issue is the rising occurrence of antibiotic-resistant bacteria, which represents a significant global health risk. Bacteria can develop resistance through various mechanisms, either naturally or through acquisition. Intrinsic resistance refers to a microorganism's inherent ability to resist certain antibiotics, often because the drug cannot effectively penetrate the bacterial cell or due to specific structural traits of the cell membrane [4]. Variations in the chemical structure of the antibiotic can also influence the degree of resistance. In contrast, acquired resistance develops when bacteria that were once sensitive become resistant as a result of genetic mutations or the uptake of resistance genes via horizontal gene transfer, allowing them to survive exposure to antibiotics that previously inhibited their growth [4].

History of Antibiotics

The introduction of antibiotics revolutionized modern medicine, significantly reducing deaths from bacterial infections. Although ancient societies recognized that some molds and plant extracts had antibacterial properties, the true onset of the antibiotic era took place in the early 20th century with Alexander Fleming's landmark discovery of penicillin antibiotic in 1928. However, it wasn't until the 1940s that penicillin was produced in large quantities and became widely accessible, leading to the successful treatment of numerous infections that had once been deadly. Following to this, numerous antibiotics were discovered, primarily from soil-dwelling microorganisms such as *Streptomyces* and *Bacillus* species. The origins of antimicrobial drugs date back to the late 1890s, when German scientists Rudolph Emmerich and Oscar Low developed pyocyanase, the first known antibiotic, extracted from the bacterium *Pseudomonas aeruginosa*. This substance demonstrated notable efficacy against illnesses like cholera and typhus and was regarded as safe for human treatment [5]. These natural compounds became the foundation for many of the antibiotics still in use today. Remarkably, the use of substances with antibiotic properties can be traced back over 2,500 years to ancient China, where moldy soybeans were applied to treat skin infections such as furuncles and carbuncles. The first antibiotic to be used in modern medicine was Salvarsan, introduced in 1910 [6]. Since then, numerous antibiotics with various mechanisms of action have been identified, and the wide range of antimicrobial agents available today offers strong defense against a broad array of pathogens [7]. Despite their tremendous benefits, the widespread and sometimes inappropriate use of antibiotics has led to the emergence of antibiotic-resistant bacteria, posing a serious global health threat. This challenge has reignited scientific efforts to find new antibiotics, explore natural sources, and design alternative antimicrobial approaches. The introduction of antibiotics significantly reduced the threat posed by once-fatal diseases such as plague and syphilis and allowed for effective treatment of conditions like tuberculosis [8].

Natural products have been vital to the discovery and development of antibiotics since ancient times. One successful approach to finding new antimicrobial compounds has involved drawing on traditional knowledge or historical sources, which often help direct researchers to specific geographic areas or target soil-based investigations [9]. Although the history of antibiotic production spans less than a hundred years, it has had a profound impact on medicine. Thousands of years ago, humans had limited protection against infectious diseases, many of which caused catastrophic epidemics and resulted in millions of deaths. Over time, a variety of antimicrobial agents have been discovered, each working through distinct mechanisms. Today, it is widely recognized that modern antimicrobial treatments provide significant protection against most pathogens [7]. Antimicrobial compounds have been utilized for centuries, in forms ranging from naturally occurring substances to chemically synthesized medications. The advancement of microscopy and research methodologies allowed scientists to identify, isolate, and culture infectious bacterial species. This progress led to the recognition of these microbes not only as disease-causing agents but also as producers of biologically active compounds. One of the most significant milestones in human history was the discovery of antibiotics.

Categories of Antibiotics

Antibiotics can be classified in various ways, most commonly based on their chemical structure, mode of action, or spectrum of activity. They are typically grouped according to how they interfere with bacterial functions by inhibiting cell wall formation, blocking protein synthesis, disrupting nucleic acid replication, or interfering with key metabolic pathways. The main classes of antibiotics include β-lactams (such as penicillins and cephalosporins), macrolides, tetracyclines, aminoglycosides, and fluoroquinolones. Moreover, antibiotics are often described as broad spectrum, acting against a wide range of bacteria, or narrow-spectrum, effective against specific bacterial types. This classification system aids in selecting the most appropriate treatment and helps in managing antibiotic resistance. In general, antimicrobial agents are essential for preventing and treating infections, with antibiotics primarily categorized by their molecular structure, mechanism of action, and spectrum of activity [10].

Understanding to the widespread occurrence of antibiotic resistance, its significant clinical impact, the underlying causes, and the mechanisms by which bacteria resist various antibiotics is crucial. Furthermore, studying the ways in which bacteria develop resistance either through genetic mutations or horizontal gene transfer provides insight into how certain strains gain resistance to multiple classes of antibiotics [11].

1. **Beta-lactams-** Beta-lactum (β-lactums) are a group of antimicrobial drugs distinguished by a highly reactive ring structure made up of three carbon atoms and one nitrogen atom. Therapeutic drug monitoring (TDM) is often advised for beta-lactams, especially in critically ill patients, to manage fluctuations in drug levels [12]. These antibiotics act by targeting proteins vital for constructing the bacterial cell wall, leading either to the death of the bacteria or the inhibition of their growth. They specifically attach to enzymes known as penicillin-binding proteins, which are responsible for cross-linking peptide chains during the formation of peptidoglycan, a key structural component of the bacterial cell wall. By binding to these enzymes, the antibiotics disrupt peptidoglycan synthesis, resulting in cell wall damage, cell lysis, and ultimately bacterial death. Beta-lactum (β-lactams) comprise a large class of antibiotics that kill bacteria by preventing cell wall formation. Research has explored bacterial resistance to these drugs and evaluated the effectiveness of newer β-lactam antibiotics, such as amoxicillin and ceftazidime, particularly when combined with quantum dots [13]. Key members of the beta-lactam class include penicillins, cephalosporins, monobactams, and carbapenems (Figure 1).

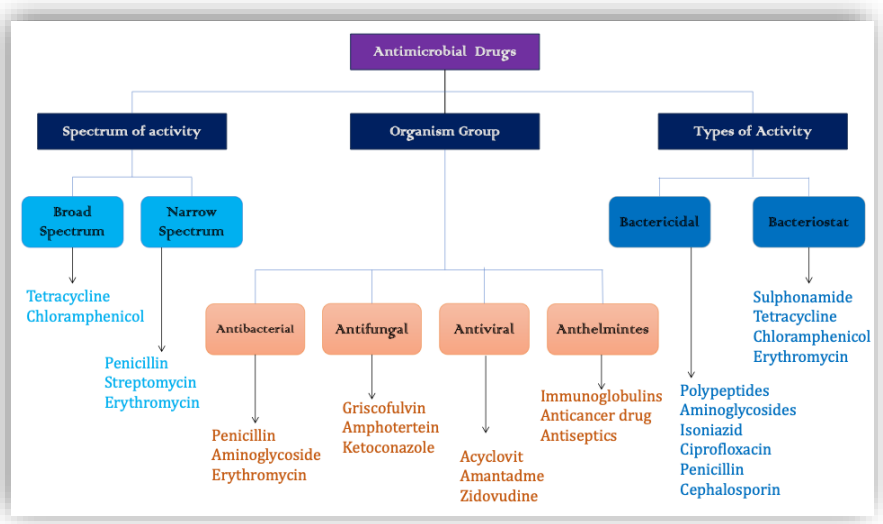

Figure 1: Various categories of antibiotics can be distinguished based on their spectrum of activity, types of organism they target and their mode (type) of action.

2. **Penicillin:** Penicillin, the first discovered antibiotic, was identified by Alexander Fleming in 1929 and later found to belong to a broader group of related antibiotics known as the penicillins. This category encompasses a variety of drugs, including Penicillin-G, Penicillin-V, Oxacillin, Dicloxacillin, Methicillin, Nafcillin, Amphicillin, Amoxicillin, Carbenicillin, Piperacillin, Mezlocillin and Ticarcillin [14]. Most of these antibiotics share the "-cillin" suffix, indicating their classification. Although Fleming originally isolated Penicillin-G from the mold *Penicillium notatum*, a related species, *Penicillium chrysogenum*, is now more commonly used in large-scale production because it yields higher quantities. Producing penicillin via microbial fermentation is much more economical compared to chemical synthesis from raw materials. Penicillin G was not only the first penicillin to be produced but also the first antibiotic to be manufactured and applied in medical treatments.

Although Alexander Fleming discovered Penicillin G in the 1920s, it was not until 1945 that researchers including Ernst Chain, Edward Abraham, Norman Heatley, and Howard Florey expanded understanding of the fungus's growth conditions and proved its clinical effectiveness. Penicillin G has a relatively limited spectrum of activity, being primarily effective against Gram-positive bacteria such as streptococci, as well as a few Gram-negative organisms like *Treponema pallidum*, the causative agent of syphilis, and meningococci. Despite its restricted range, its discovery marked a crucial turning point that ushered in the modern antibiotic era. As with many biological systems, bacteria have evolved defense mechanisms, including the production of enzymes capable of deactivating antibiotic.

Some antibiotics, including ampicillin, carbenicillin, and amoxicillin, have been semi-synthetically modified by changing their side chains. These modifications help the drugs resist breakdown by certain bacterial enzymes and improve their ability to penetrate bacterial cell walls, enhancing their effectiveness, especially against Gram-negative bacteria. A well-known example is Augmentin, which combines amoxicillin with clavulanic acid, a non-antibiotic compound. Clavulanic acid inhibits beta-lactamase enzymes also called penicillinases that some bacteria produce to deactivate beta-lactam antibiotics. By blocking these enzymes, clavulanic acid boosts and extends amoxicillin's antibacterial activity, allowing Augmentin to work against bacteria that produce beta-lactamase [15].

3. **Cephalosporin:** Cephalosporins are a group of antibiotics that are structurally and functionally similar to penicillins and are especially effective in treating healthcare-associated infections caused by carbapenem resistant Gram-negative bacteria [16]. The first cephalosporin antibiotic was discovered in 1945 by Giuseppe Brotzu from the fungus *Cephalosporium acremonium*. Cephalosporins are among the most frequently prescribed antibiotics, making up roughly one-third of all antibiotic prescriptions in the UK's National Health Service. Cefiderocol is a newer siderophore cephalosporin designed to target Gram-negative bacteria, including carbapenem-resistant strains. Its molecular structure is similar to ceftazidime and cefepime, which allows it to withstand degradation by β-lactamase enzymes. This development represents a recent advancement in the cephalosporin class, providing a novel strategy for treating resistant Gram-negative infections.

Cephalosporins are a group of antibiotics characterized by a core structure of 7-aminocephalosporanic acid and a variety of side chains, some containing 3,6-dihydro-2H-1,3-thiazine rings. Certain cephalosporins, such as cefiderocol, feature a catechol group on the C-3 side chain, which binds iron and mimics natural siderophores, thereby enhancing bacterial uptake of the drug [16]. The structural diversity of cephalosporin side chains enables these antibiotics to target different penicillin-binding proteins (PBPs), penetrate the blood-brain barrier, resist degradation by penicillinase enzymes, and efficiently enter Gram-negative bacteria through ion channels. Cephalosporins are widely used to treat infections caused by penicillinase-producing and methicillin-sensitive *Staphylococci* and *Streptococci*, as well as *Proteus mirabilis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Haemophilus influenzae*, *Enterobacter*

aerogenes, and some *Neisseria* species [17]. They are classified into five generations, with each successive generation generally showing increased activity against Gram-negative bacteria (Table 1).

4. **Macrolides:** Macrolides were first discovered in 1952 by the Philippine Island scientist J. M. McGuire [18], who identified them as a metabolic byproduct of the soil-dwelling fungus *Saccharopolyspora erythraea*, previously called *Streptomyces erythraeus* [19]. Macrolides have a wider spectrum of activity compared to penicillins and are often prescribed as alternatives for patients with penicillin allergies. They work by inhibiting bacterial protein synthesis, which can either halt bacterial growth or cause bacterial cell death. These antibiotics tend to accumulate in the body since they are metabolized by the liver and excreted into the bile, allowing for reabsorption and recycling. Due to their potential to provoke inflammation, clinicians frequently advise using them at low doses [19] (Figure 1).

While macrolides are typically classified as broad-spectrum antibiotics, some bacteria, including *Streptococcus pneumoniae*, have developed resistance to them. Notable macrolides include erythromycin, azithromycin, and clarithromycin [20]. Structurally, macrolides feature large macrocyclic lactone rings containing 14, 15, or 16 atoms, along with distinctive deoxy sugars such as L-cladinose and D-desosamine. Macrolides exert their antibacterial action by attaching to bacterial ribosomes, where they prevent the addition of amino acids to growing polypeptide chains, thereby halting protein synthesis.

5. **Monobactams**: Monobactams, a subgroup of beta-lactam antibiotics, were initially discovered by Sykes and colleagues from the bacterium *Chromobacterium violaceum*. Unlike most other beta-lactams, monobactams are characterized by a single beta-lactam ring that is not fused with any additional ring structures [21]. The sole monobactam approved for clinical use is aztreonam, which has a narrow spectrum, targeting primarily aerobic Gram-negative bacteria such as *Neisseria* and *Pseudomonas*. It is commonly prescribed for infections like pneumonia, septicemia and urinary tract infections caused by these bacteria. Monobactams, however, are ineffective against Gram-positive bacteria and anaerobes, and are typically administered via injection and inhalation [22].
6. **Tetracyclines:** Tetracycline was initially discovered in 1945 by Benjamin Duggar, who isolated it from a soil bacterium of the *Streptomyces* genus [23]. The earliest antibiotic in this class was chlortetracycline, also known as Aureomycin. Tetracyclines are characterized by a structure containing four hydrocarbon rings, and their names generally end with "-cycline." They are commonly categorized into generations based on their method of production. First-generation tetracyclines including tetracycline, chlortetracycline, oxytetracycline, and democlocycline, are produced naturally through biosynthesis. Second-generation tetracyclines such as doxycycline, lymecycline, meclocycline, methacycline, minocycline and rolitetracyclines are developed using semi-synthetic techniques. Third-generation tetracyclines like tigecycline**,** are fully synthetic [24]. These antibiotics mainly function by targeting bacterial ribosomes, thereby inhibiting protein synthesis.

   Tetracyclines inhibit bacterial protein synthesis by blocking the addition of amino acids to the elongating polypeptide chain at the ribosome. For best absorption, it is recommended that these antibiotics be taken at least two hours before or after meals. One recognized side effect is tooth discoloration in young children. Despite this, tetracyclines have been widely employed to treat a range of infections, including malaria, elephantiasis, amoebic infections, and rickettsial diseases [24]. They were once highly regarded by healthcare providers for their broad-spectrum activity. However, their clinical usefulness has diminished over time due to the emergence of resistant bacterial strains [25].
7. **Glycopeptide:** Glycopeptide antibiotics (GPAs) were originally obtained from natural sources, but over the past two decades, semi-synthetic forms have been created to improve their antimicrobial potency and pharmacokinetic characteristics [26]. Naturally occurring glycopeptides consist of a cyclic heptapeptide (seven amino acids) linked to two sugar units, which is the origin of the term "glycopeptides." Grace Yim and colleagues (2014) [27] provide detailed structural illustrations of various glycopeptide types. These antibiotics exert their action by forming five hydrogen bonds with the peptide backbone of their bacterial targets. In some cases, chemical modifications such as the addition of chlorine atoms or sugar groups are introduced during synthesis to enhance binding affinity, as observed with oritavancin [28]. Furthermore, incorporating a lipophilic side chain can improve antibacterial activity and prolong the drug's half-life.
8. **Oxazolidinones:** Oxazolidinones are a relatively recent class of fully synthetic antibiotics, with linezolid being the first approved for medical use in 2000. While their exact mechanism is not completely understood, they are known to inhibit bacterial protein synthesis by binding to the P site of the 50S ribosomal subunit [29]. Oxazolidinones are effective against a broad range of Gram-positive bacteria, including strains resistant to methicillin, vancomycin, and penicillin, as well as some anaerobic species. Linezolid is frequently used to treat respiratory and skin infections caused by Gram-positive pathogens [30]. These antibiotics are especially valuable in surgical infections due to their excellent tissue penetration and accumulation in sites such as bone, lungs, vegetations, hematomas, and cerebrospinal fluid [31].
9. **Sulphonamides:** Sulphonamides are acknowledged as the first class of antibiotics used therapeutically and remain important in both human and veterinary medicine [32]. These drugs are effective against a broad spectrum of Gram-positive and Gram-negative bacteria, including *Nocardia, E. coli, Klebsiella, Salmonella, Shigella,* and *Enterobacter*, as well as *Chlamydia trachomatis* and certain protozoa. They are commonly prescribed for infections such as tonsillitis, septicemia, meningococcal meningitis, bacillary dysentery, urinary tract infections [32]**.** Research also suggests that sulfonamides may have potential in inhibiting cancer-causing agents [33]. The original antibacterial sulphonamides are fully synthetic antimicrobial compounds characterized by the presence of a sulfonamide functional group (Table 1).

Sulphonamides are typically considered bacteriostatic agents, meaning they inhibit bacterial growth rather than directly killing the bacteria. However, early research by Henry (1943) [34] suggests that under certain conditions such as high drug concentrations or environmental stressors they can exhibit bactericidal activity. These stressors may include adverse growth conditions, extreme temperatures, exposure to antibodies, or harmful proteolytic byproducts. While sulfonamides are effective against a range of infections, their use requires caution due to potential toxicity and side effects, which can include urinary tract problems, hemolytic anemia, porphyria, and hypersensitivity reactions [35].

10. **Aminoglycosides:** Streptomycin, the first discovered antibiotic in the aminoglycoside group, was isolated in 1943 [36]. Aminoglycosides have been widely used to target *Mycobacterium tuberculosis*, the bacterium that causes tuberculosis in humans. Structurally, they consist of three amino sugers connected by glycosidic bonds and are typically derived from soil-dwelling Actinomycetes. These antibiotics have broad activity and function by inhibiting bacterial protein synthesis through binding to a specific ribosomal subunit. They are particularly effective against aerobic Gram-negative rods and certain Gram-positive bacteria. Streptomycin, the first discovered aminoglycoside, was extensively used to treat diseases such as bubonic plague, tularemia and tuberculosis. Although highly effective, streptomycin was later found to have significant toxicity, prompting the development of safer aminoglycosides that preserved strong antibacterial activity. This resulted in newer drugs like gentamicin, neomycin, tobramycin, and amikacin. Gentamicin, known for its lower toxicity, is commonly prescribed for infections caused by Gram-negative rods such as *Escherichia*, *Pseudomonas*, *Shigella*, and *Salmonella*. Tobramycin is particularly useful in treating infections caused by *Pseudomonas* species, especially in patients with cystic fibrosis [37].
11. **Quinolones:** Quinolones were first discovered in the early 1960s with the identification of nalidixic acids, which emerged as an unexpected byproduct during the development of quinine-based antimalarial drugs. These antibiotics work by interfering with bacterial DNA replication and transcription. From the original compound, two main subgroups have since developed: quinolones and naphthyridones. Notable examples include cinoxacin, norfloxacin, ofloxacin, ciprofloxacin, temafloxacin, sparfloxacin, nalidixic acids and enoxacin. Quinolones generally possess a core structure of two fused rings, although newer generations have added a third ring, expanding their activity to a wider range of bacteria, including certain anaerobic strains that were previously resistant. Since the discovery of nalidixic acid, various chemical modifications have led to the development of many powerful antibiotic variants. Although naming within this drug class can be complex [38], a common identifying feature is the suffix “oxacin,” seen in drugs such as floxacin, ciprofloxacin, and levofloxacin.

    Chemical modifications have greatly enhanced the bioavailability, potency, and spectrum of activity of these drugs, making them highly effective for treating various infections, including urinary tract, respiratory, and systemic infections [39]. However, despite these advancements, safety concerns remain for certain quinolones, resulting in the withdrawal of specific drugs such as grepafloxacin, sparfloxacin, temafloxacin, and trovafloxacin from clinical use [38]. While ongoing research continues to improve our understanding of their in vitro effectiveness and pharmacodynamics, the exact mechanisms behind their toxicity are still not fully understood.

Table 1: A historical overview of various antibiotics, including their discovery year, mechanism of action, and the bacterial species that have developed resistance to them.

S. N.	Antibiotics	Discovery year	Action mechanism	Species Resistant
1.	Penicillin	1928	Destroy bacterial cell wall structure	*Staphylococcus*
2	Sulphonamycin	1932	Inhibit bacterial folic acid synthesis process	*Straptococcus*
3	Streptomycin	1943	Inhibit bacterial protein synthesis	*M. tuberculosis*
4	Tetracycline	1948	Inhibit bacterial protein synthesis	*Shingella*
5	Erythromycin	1952	Inhibit bacterial protein synthesis	*Straptococcus*
6	Vancomycin	1953	Inhibit bacterial cell wall synthesis	*Staphylococcus*
7	Ampicillin	1961	Inhibit bacterial cell wall synthesis	*H. influenzae*
8	Quinolones	1962	Inhibit bacterial DNA gyrase enzyme activity	*K. pneumoniae*
9	Gentamycin	1963	Inhibit bacterial protein synthesis	*Enterococcus*
10	Cefalotin	1964	Inhibit bacterial cell wall synthesis	*E. coli*
11	Clindamycin	1966	Inhibit bacterial protein synthesis	*Staphylococcus*
12	Fosfomycin	1969	Inhibit bacterial MurA enzyme activity	*E. coli*
13	Ceftriaxone	1978	Inhibit bacterial cell wall synthesis	*Neisseria*
14	Azithromycin	1980	Inhibit bacterial protein synthesis	*Neisseria*
15	Ciprofloxacin	1980	Inhibit bacterial DNA gyrase enzyme activity	*Serrtia*
16	Daptomycin	1984	Destroy bacterial cell wall	*Staphylococcus*
17	Levofloxacin	1985	Inhibit bacterial DNA gyrase enzyme activity	*Pneumococcus*
18	Ceftaroline	2010	Inhibit bacterial cell wall synthesis	*Staphylococcus*
19	Tobacobactum	2014	Inhibit bacterial cell wall synthesis	*Pseudomonas*
20	Avibactum	2015	Inhibit bacterial cell wall synthesis	*Klebsiella*

Action mechanism of antibiotics

Over the past two decades, antimicrobial resistance (AMR) has become a significant global health threat. Although the introduction of antibiotics marked a major medical breakthrough, their widespread and improper use in both human and veterinary medicine has substantially accelerated the worldwide spread of AMR [40]. The way antibiotics are administered whether via injection, orally, or topically also influences the development of resistance. Antibiotics with similar chemical structures tend to have similar effectiveness, side effects, and allergic reaction risks. Antimicrobials work through various mechanisms: some kill bacteria (bactericidal), while others inhibit bacterial growth (bacteriostatic). Antibiotics are classified into different groups, each targeting specific bacterial processes or components. However, bacteria continuously evolve resistance mechanisms that undermine or neutralize the effectiveness of these drugs [11] (Figure 2).

Bacteria can acquire resistance through multiple mechanisms, including altering the antibiotic's target site, decreasing cell wall permeability to block drug entry, producing enzymes that break down the antibiotic, and employing efflux pumps to remove the drug from the cell. A thorough understanding of how antibiotics work and how bacteria develop resistance is essential for creating new antibiotics or more effective drug combinations. Antibiotics are widely utilized due to their various modes of action, which include inhibiting cell wall synthesis, damaging cell membranes, interfering with protein and nucleic acid production, and disrupting key metabolic processes [41]. Macrolides, a significant class of antibiotics, are frequently used in clinical practice due to their ability to block bacterial protein synthesis. These drugs feature a large macrocyclic lactone ring attached to sugar molecules, such as amino or deoxy-sugars, and act by binding to the bacterial 50S ribosomal subunit, thereby inhibiting proper protein synthesis [42].

Despite medical progress, antibiotics continue to be essential for treating numerous infectious diseases. They are particularly effective against bacterial infections such as those affecting the respiratory tract, skin, and certain sexually transmitted diseases. Antibiotics work by killing bacteria, relieving symptoms and preventing the transmission of infections. However, widespread and improper use of antibiotics has created significant problems. Excessive and incorrect use is a key factor driving the emergence of multidrug-resistant bacteria, posing a serious global health threat to both patients and healthcare professionals [41].

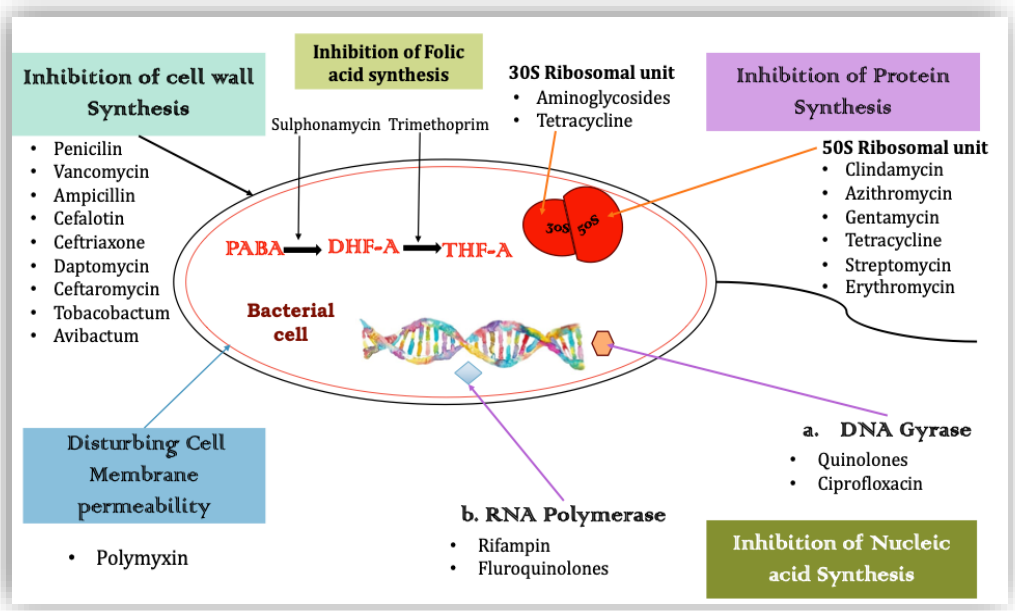

Figure 2: The site of action mechanism of different types of antibiotics against bacterial cell.

Antibiotics are naturally occurring, low-molecular-weight organic compounds produced by microorganisms, capable of inhibiting the growth or metabolic activity of other organisms at low concentrations. In many cases, the immune system eliminates bacteria before they multiply enough to cause noticeable symptoms, with white blood cells playing a central role by detecting and destroying harmful bacteria. Even when symptoms develop, the immune system continues to fight the infection and aid recovery. Antibiotics are effective solely against certain bacterial infections, including strep throat, urinary tract infections, and infections caused by *E. coli*. Notably, outer membrane vesicles (OMVs) from *E. coli* MG1655 have been shown to shield *Pseudomonas aeruginosa* NCTC6751 and *Acinetobacter radiodioresistens* MMC5 from antibiotics that target bacterial membranes [43] (Figure 2).

Besides white blood cells, cytokines secreted by epithelial cells in the skin and mucosal tissues play a crucial role in initiating a type 2 immune response to harmless allergens. This response activates and recruits type 2 T helper (TH2) cells, type 2 innate lymphoid cells (ILC2s), M2 macrophages, and eosinophils, which together help protect the body against bacterial infections [44]. Furthermore, bacteria secrete outer membrane vesicles (OMVs) that serve both protective and defensive functions, particularly against antibiotic exposure. These vesicles not only protect the bacteria that produce

them but can also shield other bacterial species from the growth-inhibiting effects of specific antibiotics, underscoring their role in inter-bacterial communication and defense [43] (Table 1; Figure 2).

Conflicts of interest

The authors declare that they have no conflicts of interest of any kind.

Reference

1. Mariusz C, Agnieszka M, Zofia PS. Antibiotics in the Soil Environment-Degradation and Their Impact on Microbial Activity and Diversity. Front Microbiol. 2019 Mar 8:10:338. doi: 10.3389/fmicb.2019.00338. eCollection 2019.
2. Musliu A, Salawudeen W. Screening and Isolation of the Soil Bacteria for Ability to Produce Antibiotics. European Journal of Applied Sciences 4 (5): 2012., 211-215.
3. Olga VK, Irina AG, Svyatoslav VL, Anastasia MK, Elena PM, Victoria AS, Artem VB, Natalia OD. Effect of probiotics on the basis of Bacillus subtilis and Bifidobacterium longum on the biochemical parameters of the animal organism. Environ Sci Pollut Res Int. 2018 Jan;25(3):2175-2183. doi: 10.1007/s11356-017-0534-9. Epub 2017 Nov 7.
4. Abduleziz JH, Netsa BS, Ibsa AO. Literature Review on Antibiotics. Clinical Medicine and Health Research Journal, Vol. 2 No. 4 (2022), 23 August 2022, Page 174-182.
5. Ronald B. Mycophenolic Acid: A One Hundred Year Odyssey from Antibiotic to Immunosuppressant. Chemical ReviewsSeptember 26, 2000., Vol 100/Issue 10.
6. Mathew IH, Andrew WT, Barrie W. Antibiotics: past, present and future. Curr Opin Microbiol. 2019 Oct:51:72-80. doi: 10.1016/j.mib.2019.10.008. Epub 2019 Nov 13.
7. Antoniadis A, Legakis NI, Tselentis I, Mavridis A, Maniatis A. 2000. Medical Microbiology, 3rd Edition ed. vol. 1. 2000; Athens: Publications Paschalidis.
8. Kotsiftopoulos C, Kourkouta L, Papageorgiou M. The use of antibiotic medicine Monograph. Saarbrucken Germany: 2014; Lap Lambert Academic.
9. Cordell GA, Farnsworth NR, Beecher CW, Soejarta DD, Kinghorm AD, Pezzuto JM, Wall ME, Wani MC, Cobb RO, Neil MJR, Tait M, Harris TJR. Novel strategies for the discovery of plant derived anticancer agents. 1994; 63-83.
10. Calderon CB, Sabundayo BP. Antimicrobial classifications: Drugs for bugs. In: Schwalbe R, Steele-Moore L & Goodwin AC (eds). Antimicrobial susceptibility testing protocols. CRC Press, Taylor and Frances group. 2007, ISBN 978-0-8247-4100-6.
11. Manar AM, Amal JF, Mohammed A, Wael M, Merin G, Sadananda A, Sanjay R, Darshan DD, Chitra J, Sajith V, Aftab AK, Jilani S, Poojdev J. Antimicrobial resistance, mechanisms and its clinical significance. Dis Mon. 2020 Jun;66(6):100971.
12. Rekha PM, Aadith A, Sue JL, Lorena R, Trisha NP, Andrew AU, Anton YP. Beta-Lactam Antibiotic Therapeutic Drug Monitoring in Critically Ill Patients: A Systematic Review and Meta-Analysis. Clin Infect Dis. 2022 Nov 14;75(10):1848-1860. doi: 10.1093/cid/ciac506.
13. Sandeepta KV, Jyoti K, Tikendra KV, Jadhav, SK, Rekha N, Manmohan LS. Antibacterial Activity of CdTe/ZnS Quantum Dot-β Lactum Antibiotic Conjugates. J Fluoresc. 2024 Mar;34(2):833-846. doi: 10.1007/s10895-023-03316-x. Epub 2023 Jun 30.
14. Mariya L, Giulia P. Penicillin's Discovery and Antibiotic Resistance: Lessons for the Future? Yale J Biol Med. 2017 Mar 29;90(1):135–145.
15. Uto LR, Gerriets V. Clavulanic Acid. In: StatPearls. Treasure Island (FL): StatPearls Publishing, Updated 2023 May 29.
16. Takafumi S, Kenji Y. Cefiderocol: Discovery, Chemistry, and In Vivo Profiles of a Novel Siderophore Cephalosporin. Clin Infect Dis. 2019 Nov 13;69(Suppl 7):S538-S543. doi: 10.1093/cid/ciz826.
17. Afroj AS, Sachin JA. Cephalosporins: A Comprehensive Review and Anticipated Directions for the Future, *J. Pharmaceutics and Pharmacology Research,* 2023; 6(6); DOI: 10.31579/2693-7247/137.
18. Bunch RL, Mcguire JM. Erythromycin, Its Salts, and Method of Preparation. 2,653,899. U.S. Patent. 1952 September 29.
19. Katheleen NM, Hossein B, David MO, Woondong J, Shelly MS, Todd MB, Raymond PP, Ursula AM, Kellu LR, Xiaoyan Z, Jose FP, Rodrigo RS, Michael JB. Phase 1 dose-escalation study of mirvetuximab soravtansine (IMGN853), a folate receptor α-targeting antibody-drug conjugate, in patients with solid tumors. Cancer. 2017 Aug 15;123(16): 3080-3087.doi: 10.1002/cncr.30736. Epub 2017 Apr 25.
20. Alvarez Elcoro S, Enzler MJ. The macrolides: erythromycin, clarithromycin, and azithromycin. Mayo Clin Proc. 1999 Jun;74(6): 613-34.doi: 10.4065/74.6.613.
21. Wells JS, Trezo WH, Principe PA, K. Bush KN. Georgopapadakou, Bonner DP, Sykes RBS. SQ 26,180, a novel monobactam. I Taxonomy, fermentation and biological properties. J Antibiot (Tokyo). 1982 Feb;35(2):184-8. doi: 10.7164/antibiotics.35.184.
22. Katayama N, Nozaki Y, Okonogi K, Ono H, Harada S, Okazaki H. Formadicins, new monocyclic beta-lactam antibiotics of bacterial origin. I. Taxonomy, fermentation and biological activities. J Antibiot (Tokyo). 1985 Sep;38(9):1117-27. doi: 10.7164/antibiotics.38.1117.
23. Andres RS, Roy SR, Phillip JS. Tetracycline and other tetracycline-derivative staining of the teeth and oral cavity. Int J Dermatol. 2004 Oct;43(10): 709-15.doi: 10.1111/j.1365-4632.2004. 02108.x.

24. Domenico F. Classification Framework and Chemical Biology of Tetracycline-Structure-Based Drugs. Antibiotics (Basel). 2012 Jun 12;1(1): 1-13.doi: 10.3390/antibiotics1010001.
25. Chopra I, Roberts M. Tetracycline antibiotics: mode of action, applications, molecular biology, and epidemiology of bacterial resistance. Microbiol Mol Biol Rev. 2001 Jun;65(2):232-60; second page, table of contents. doi: 10.1128/MMBR.65.2.232-260.2001.
26. Francoise VB. Glycopeptides in clinical development: pharmacological profile and clinical perspectives. Curr Opin Pharmacol. 2004 Oct;4(5): 471-8.doi: 10.1016/j.coph.2004.04.006.
27. Grace Y, Maulik NT, Kalinka K, Gerard W. Glycopeptide antibiotic biosynthesis. J Antibiot (Tokyo). 2014 Jan;67(1): 31-41.doi: 10.1038/ja.2013.117. Epub 2013 Nov 13.
28. Norris EA, Thalia IN. Mechanism of action of oritavancin and related glycopeptide antibiotics. FEMS Microbiol Rev. 2003 Jan;26(5): 511-32.doi: 10.1111/j.1574-6976.2003.tb00628.x.
29. Bulent B, Peter CA. Oxazolidinones: activity, mode of action, and mechanism of resistance. Int J Antimicrob Agents. 2004 Feb;23(2):113-9. doi: 10.1016/j.ijantimicag.2003.11.003.
30. Robert CM. Linezolid: the first oxazolidinone antimicrobial. Ann Intern Med. 2003 Jan 21;138(2): 135-42. doi: 10.7326/0003-4819-138-2-200301210-00015.
31. Kuter DJ, Tillotson GS. Hematologic effects of antimicrobials: focus on the oxazolidinone linezolid. Pharmacotherapy. 2001 Aug;21(8): 1010-3. doi: 10.1592/phco.21.11.1010.34517.
32. Hekster CA, Vree TB. Clinical pharmacokinetics of sulphonamides and their N4-acetyl derivatives. Antibiot Chemother (1971). 1982:31:22-118. doi: 10.1159/000400131.
33. Pranjal J, Chinnaduraj S, Sushil KS. Sulphonamides: Deserving class as MMP inhibitors? Eur J Med Chem. 2013 Feb:60:89-100. doi: 10.1016/j.ejmech.2012.10.016. Epub 2012 Nov 1.
34. Henry J. The Mode of Action of Sulfonamides. Bacteriol Rev., 1943 Dec;7(4):175-262. Doi: 10.1128/Br.7.4.175-262.1943.
35. Christopher GS, Stephen AT. Sulfonamide hypersensitivity. Immunol Allergy Clin North Am. 2004 Aug;24(3):477-90, vii.doi: 10.1016/j.iac.2004.03.011.
36. Girish BM, Lakshmi B. Antibacterial agents from actinomycetes - a review. Front Biosci (Elite Ed). 2012 Jan 1;4(1):240-53. doi: 10.2741/373.
37. Crozier DN, Khan SR. Tobramycin in treatment of infections due to *Pseudomonas aeruginosa* in patients with cystic fibrosis. J Infect Dis. 1976 Aug:134 Suppl: S187-90. doi: 10.1093/infdis/134.supplement_1.s187.
38. Domagala JM. Structure-activity and structure-side-effect relationships for the quinolone antibacterials. J Antimicrob Chemother. 1994 Apr;33(4):685-706. doi: 10.1093/jac/33.4.685.
39. Shilpakala SR, Raghavachari R, Ramesh E, Malathi R. In vitro activity of a new quinoline derivative, ER-2, against clinical isolates of *Mycoplasma pneumoniae* and *Mycoplasma hominis*. Antimicrob Agents Chemother. 2009 Dec;53(12):5317-8. doi: 10.1128/AAC.00746-09. Epub 2009 Sep 8.
40. Maurizio F, Paola R, Valerio G. Antimicrobial resistance: A global emerging threat to public health systems. Crit Rev Food Sci Nutr. 2017 Sep 2;57(13):2857-2876.
41. Aleksandra B, Aleksandra K, Leszek P. Antibiotics and Bacterial Resistance-A Short Story of an Endless Arms Race. Int J Mol Sci. 2023 Mar 17;24(6):5777. doi: 10.3390/ijms24065777.
42. George PD. The macrolide antibiotic renaissance. Br J Pharmacol. 2017 Sep;174(18):2967-2983. doi: 10.1111/bph.13936. Epub 2017 Aug 10.
43. Heramb MK, Nagaraj R, Medicharla V J. Protective role of *E. coli* outer membrane vesicles against antibiotics. Microbiol Res. 2015 Dec: 181:1-7. doi: 10.1016/j.micres.2015.07.008. Epub 2015 Aug 1.
44. Zsolt IK, Willem VV, Nóra KGS, Milena S, Liam OM, Mübeccel A, Cezmi AA. Cellular and molecular mechanisms of allergic asthma. Mol Aspects Med. 2022 Jun:85:100995. doi: 10.1016/j.mam.2021.100995. Epub 2021 Aug 5.