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MICROBIAL PIGMENTS NOVEL THERAPEUTIC AGENTS FOR COMBATTING INFECTIONS AND DISEASES

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Abstract:
Within the healthcare industry, the rise of infectious diseases is expected to be one of the main causes of death. Despite the fact that there are many medications on the market, recently discovered microorganisms with multidrug resistance (MDR) prevent existing medications from working as intended. This has led to the need for developing novel medications, which takes time, money, and labor, as well as increased antibiotic dosage therapies. MDR bacteria are a significant problem due to their increased prevalence and growth, which can be attributed to the misuse of antimicrobials. Antimicrobial drug resistance is being prevented via novel techniques. The main uses of natural products derived from bacteria for the treatment of autoimmune diseases, cancer, infections, allergies, and other conditions that pose a risk to public health are reviewed in this paper. We also go into detail on the biological activities of bacterial secondary metabolites that have been found, including their antiviral, antibacterial, antifungal, and antioxidant properties. These activities are particularly important in the modern day due to the rise of drug-resistant microbial infections. Antimicrobial resistance is one of the biggest concerns to world health today and a major barrier to the treatment of infectious diseases. We will talk about in this essay. Innovative Therapeutic Agents for Fighting Infections and Diseases: Microbial Pigments.

Keywords:
Microbial Pigments, Novel Therapeutic, Infections, Diseases, Secondary Metabolites, Antibacterial, Antifungal, Antiviral, Antioxidant, Bio-Pigments, Chemotherapy

Introduction:

Microbial Pigments

Under the umbrella of microbial autecology, bio-pigment manufacturing from bacterial species is being carried out worldwide with great interest. These substances, also known as "bioactive pigmented molecules," come in a wide variety and can be produced by both Gram-positive and Gram-negative bacterial species. The intricate process of "quorum sensing" mediates the production of these pigments in the marine environment. Alternatively, exposure to various stress conditions in external settings might promote the production of these pigments. The process by which individual bacterial cells can communicate with other members of their colony to perform out constitutive duties, such as secreting a variety of distinct chemical substances, is known as quorum sensing. These substances can support their competence,

survival, bioluminescence, biofilm development, sporulation, and other processes. [1]
Because of their advantageous qualities and biological activities, bio-pigments can be generated by activating the regulatory quorum sensing mechanisms of these species. Because of this, they are widely used in a variety of bio-medical and bio-industrial sectors, including the food, pharmaceutical, textile, and cosmetic industries. Furthermore, by using straightforward gene-editing techniques, they are easy to harvest in big quantities. Scientists are turning their attention to naturally derived, non-toxic, and environmentally friendly pigment replacements due in large part to growing consumer concerns about the safety and quality of industrial products.
Microbial communities provide immense potential for generating a wide range of captivating visual characteristics, including fluorescence and bioluminescence emission, magnetosome formation, bioactive metabolite production, and various colors for scientific purposes. In short, via controlling biogeochemical and ecological processes, microbial communities, whether directly or indirectly, play a significant integrated role in the biosphere. Regardless of their place in the ecosystem, microorganisms aid mankind in many ways. One such benefit is the creation of color by a variety of bacteria, which has received much-needed attention recently. However, there are still many unexplored sources for the investigation of several unidentified pigmented compounds.

Microbial pigments have been highlighted as being important in a variety of applications, including textiles, food, cosmetics, and pharmaceuticals. These chemicals are also well-known for their cytotoxic, antioxidant, antimicrobial, antimalarial, anticancer, and antitumor properties. [2]

Pathogenicity of Pigmented Microbes

Some of the colors produced by specific microbes are known to improve pathogenicity and virulence, regardless of the use of microbial pigments in various applications. P. aeruginosa is frequently highly beta hemolytic on sheep blood agar and is capable of producing a variety of diffusible pigments, including the green pigment pyocyanin. Melanin production seems to be associated with the virulence and pathogenicity of some bacterial (like Vibrio cholerae) and fungal (like Aspergillus fumigatus and Cryptococcus neoformans) species for their respective animal or plant hosts. Skin and soft tissue infections are commonly caused by Mycobacterium marinum, and certain Bacillus species have also been identified as pathogens. One well-known cause of nosocomial infections of the urinary system and wounds is Serratia marcesens. Other pigmented substances that may have virulence activities include golden staphyloxanthin, porphyrin, and granadaene, which are generated by Staphylococcus aureus, Porphyromonas gingivalis, and Streptococcus agalactiae, respectively.
Chromobacterium violaceum, which produces vitexin, is an opportunistic pathogen that can kill both humans and animals through septicemia from skin lesions that have numerous liver and lung abscesses. Orange pigmentation in Stenotrophomonas maltophiliais has recently been identified. This species is another new human pathogen that causes deadly infections in humans. Rutabagas, cauliflower, and cabbage illnesses are caused by the phytopathogenic bacteria Xanthomonas campestris. Fish furunculosis in salmonids appears to be caused by chemicals that resemble melanin and produce Aeromonas salmonicida. Pyocyanine is a pigmented exotoxin that Pseudomonas aeruginosa produces. It causes people to have chronic

lung infections, specifically cystic fibrosis. [3]

Infections by Pathogenic Microbes:

A multitude of microorganisms or microbes pose a threat to human, animal, and plant life, causing a wide range of illnesses that cause significant morbidity and mortality. Microorganisms known as pathogenic bacteria are responsible for infectious illnesses. The pathogenic bacteria that cause diseases like anthrax, TB, and plague; the protozoa that cause diseases like toxoplasmosis, malaria, and sleeping sickness; and fungi that cause diseases like candidiasis, ringworm, and histoplasmosis are among the implicated organisms. However, pathogenic viruses—which are not living things—cause other illnesses including the flu, yellow fever, and AIDS. Pathogenic bacteria are linked to numerous serious illnesses that affect people around the world, such as food-borne illnesses like Salmonella, Campylobacter, and Shigella, as well as pneumonia brought on by Streptococcus and Pseudomonas bacteria. Infections including tetanus, typhoid fever, diphtheria, syphilis, and leprosy are also brought on by pathogenic bacteria. Every type of parasite has a unique way of interacting with its host. microbes that cause skin infections, pneumonia, meningitis, and other surface infections, such as Streptococcus or Staphylococcus species. However, a large number of organisms that live on the skin, nose, urinary tract, colon, and other normal human body parts do not cause illness. However, occasionally these developed into opportunistic parasites and caused illnesses. Only host cells allow obligatory intracellular parasites like Chlamydia and Rickettesia to proliferate. Certain organisms, like Mycobacterium avium, Burkholderia cenocepacia, and Pseudomonas aeruginosa, are parasitic when an individual has cystic fibrosis cells or immunological suppression. [4]

Review of Literature:

Microorganisms, terrestrial vertebrates and invertebrates, mammals, marine organisms, and terrestrial plants are among the many natural sources of secondary metabolites. These compounds represent a unique class of medicines that can be used to treat a wide range of ailments due to their structural and chemical diversity. Between 2900 and 2600 BCE, in ancient Mesopotamia, the earliest natural items discovered to enhance human health were first documented. Owing to the previous achievements of natural goods, major pharmaceutical companies made investments in this established field (Maher 2020), and over 60% of authorized small-molecule medications have a natural product connection. [5]

Fungal infections are a prime example of these often disregarded illnesses. The prevalence of fungal infections has been steadily increasing over the past few decades, despite notable advancements in medicine. Additionally, the prolonged therapeutic use of antifungal medications in patients has resulted in the multi-drug resistant fungal strains, such as the extremely aggressive Candida auris, emerging. Clinical mycology is a dynamic and constantly shifting science. A novel treatment for autoimmune and malignant diseases has exposed new risk factors for atypical mycoses. Antifungal medications (echinocandin, triazoles) have been shown to successfully lower the incidence of invasive fungal diseases in cancer patients and transplant recipients; however, they have also raised the risk of non-fumigatus Aspergillus sp. infections in these patients (Husain and Camargo, 2019). [6]

Hence, focusing on the virulence characteristics of pathogenic bacteria is one strategy to counteract the rise of antibiotic resistance. Bacteria produce certain chemicals or structures known as virulence factors, which give them the ability to penetrate, colonize, and survive in host cells. This reduces virulence only, not viability, if they are eliminated. By causing harm to the host or by eluding the host's immune system, virulence factors contribute to disease. Consequently, anti-virulence medications possess the ability to reduce the emergence and spread of antibiotic resistance as well as the requirement for antibiotics. This is accomplished without affecting the survival of the bacteria and while protecting the helpful, commensal microbiota. Adhesion and attachment inhibitors, toxin inhibitors, secretion inhibitors, communication and signaling inhibitors, and other groups are some of the additional categories into which these anti-virulence medications are divided. (Gómez et al., 2022). [7]

Objectives:

- To Study Microbial Pigments Novel Therapeutic Agents for Combatting Infections and Diseases.
- Conventional Antibiotics to Combination Therapy
- Controlling infections and detecting microbes

Research Methodology:

The overall design of this study was exploratory. The research paper is an effort that is based on secondary data that was gathered from credible publications, the internet, articles, textbooks, and newspapers. The study's research design is primarily descriptive in nature.

Result and Discussion:

Microbes:

Single-celled microorganisms are known as microbes. Only a microscope can see them because they are so tiny that thousands of them can fit on the tip of a needle. Since microbes can dwell anywhere in the environment, they are also regarded as microscopic organisms. While some of them can withstand intense heat, others do well in the cold. While some microbes need oxygen to survive, others do not. Certain types of infectious illnesses are predominantly caused by certain bacteria. Microbes are classified into various classes, including bacteria, viruses, fungi, and parasites. Microbes are the cause of a number of prevalent infections. For instance, viruses, bacteria, fungi, or protozoa can all cause influenza. Bacteria are the cause of Inflammatory Bowel Disease. The cause of onychomycosis is fungi. A virus is the cause of Severe Acute Respiratory Syndrome (SARS). Protozoa are the cause of babesiosis. The cause of protothecosis is algae. Archea is the source of gastrointestinal endogenous (Figure 1). [8]

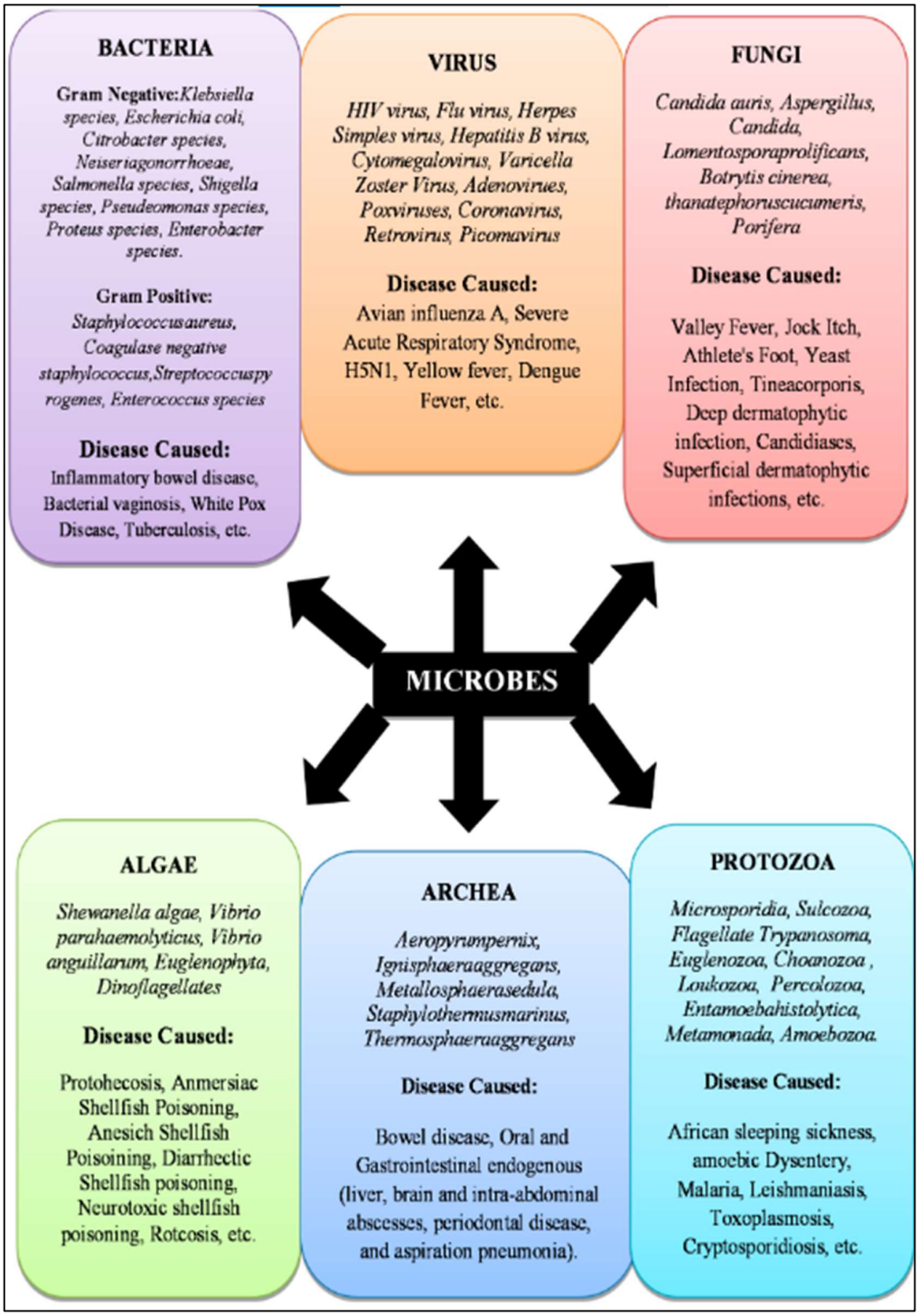

Figure 1. Infectious microbial species. [9]

Infectious Microbial Species

The pathogen's kind and strain determine how a disease manifests and affects the human body. Generally speaking, the immune system offers great protection against infectious pathogens. But microbes might become more powerful than the immune system's ability to fight them off. An infection is hazardous in these circumstances. Some microbes do not cause harm to the

body, but others produce toxins or other hazardous compounds that do. This variance explains why certain infections are mild and barely noticeable, while others could be serious and even fatal. Because bacteria, viruses, fungi, and parasites are all distinct types of microbes, there are a variety of methods in which an infection can spread. These variations arise from the microbe's genetic makeup, structure, function, and size as well as its mode of impact on the body. [10]

Conventional Antibiotics to Combination Therapy:

- **Antibiotics Groups and Their Mode of Action:**

Antibiotics are categorized into groups according to their major mechanism of action, targets, and class of molecules. Examples of antimicrobial targets are protein synthesis, cell membranes, cell walls, DNA or RNA synthesis, and biological metabolic compound production, as indicated in Table 1.

Table 1. Antibiotics class and mode of action. [11]

Antibiotic Class	Mechanism of Action
Beta lactams: carbapenems, cephalosporins, monobactam, penicillin, glycopeptides	Inhibit cell wall synthesis
Lipopeptides	Depolarize cell membrane
Aminoglycosides, tetracyclines Chloramphenicol, macrolides	Inhibit protein synthesis by binding to 30S ribosomal unit and 50S ribosomal unit
Quinolones	Inhibit nucleic acid synthesis
Sulfonamides, trimethoprim	Inhibit metabolic pathways

Controlling Infections and Detecting Microbes

- **Effects and mechanisms of antimicrobial therapies**

Chemotherapy: The use of artificial or natural small molecules, including antibiotics, to control the growth of certain pathogenic microorganisms is known as antimicrobial chemotherapy. Its methods of action often include the following: (i) blocking the formation of nucleic acids and cell walls; (ii) rupturing the integrity of cell membranes; (iii) producing oxidative stress; and (iv) interfering with metabolism by blocking the activity of enzymes and proteins. Since they were first discovered in the 1920s, antibiotics—both natural and synthetic—have been regarded as one of the most significant antimicrobial chemotherapeutic medicines on the international market. The evolution of antimicrobial resistance (AMR) has outpaced the discovery of new medications, despite the growing demand for antibiotics. In the meantime, plants' defensive mechanisms provide natural antimicrobials, particularly phytochemicals, that combat the invasion by different microorganisms. Certain substances, such as essential oils, phenolic acids, flavonoids, Saponin, anthraquinones, and alkaloids, have partially shown evidence of antiviral, antifungal, and antibacterial properties. [12]

Photo/sonodynamic therapy: PDT and SDT are non-invasive, antibiotic-independent treatment techniques that address microbial illnesses by utilizing light and sound, the two fundamental forms of energy. PDT and SDT, which have comparable modes of action, have attracted a lot of attention because of their quick elimination of a variety of microorganisms, including antibiotic-resistant strains (Figure 2A).

In general, the following three essential elements must be present for PDT/SDT to function appropriately: (i) the existence of oxygen molecules; (ii) exposure to light or ultrasound at a

certain wavelength; and (iii) a non-toxic dye called a photosensitizer (PS)/sonosensitizer (SS). To be more precise, when the sensitizers are exposed to radiation, the absorbed electrons change into a higher energy triplet state and interact with biomolecules in Type I and Type II pathways. This results in the production of radicals, also known as reactive oxygen species (ROS), and singlet oxygen (1O2) through energy transfer (Figure 2B). Since the microenvironment and the type of sensitizer utilized mostly determine the ratio between the Type I and Type II pathways, the type of radical generated can also be controlled in the meantime.

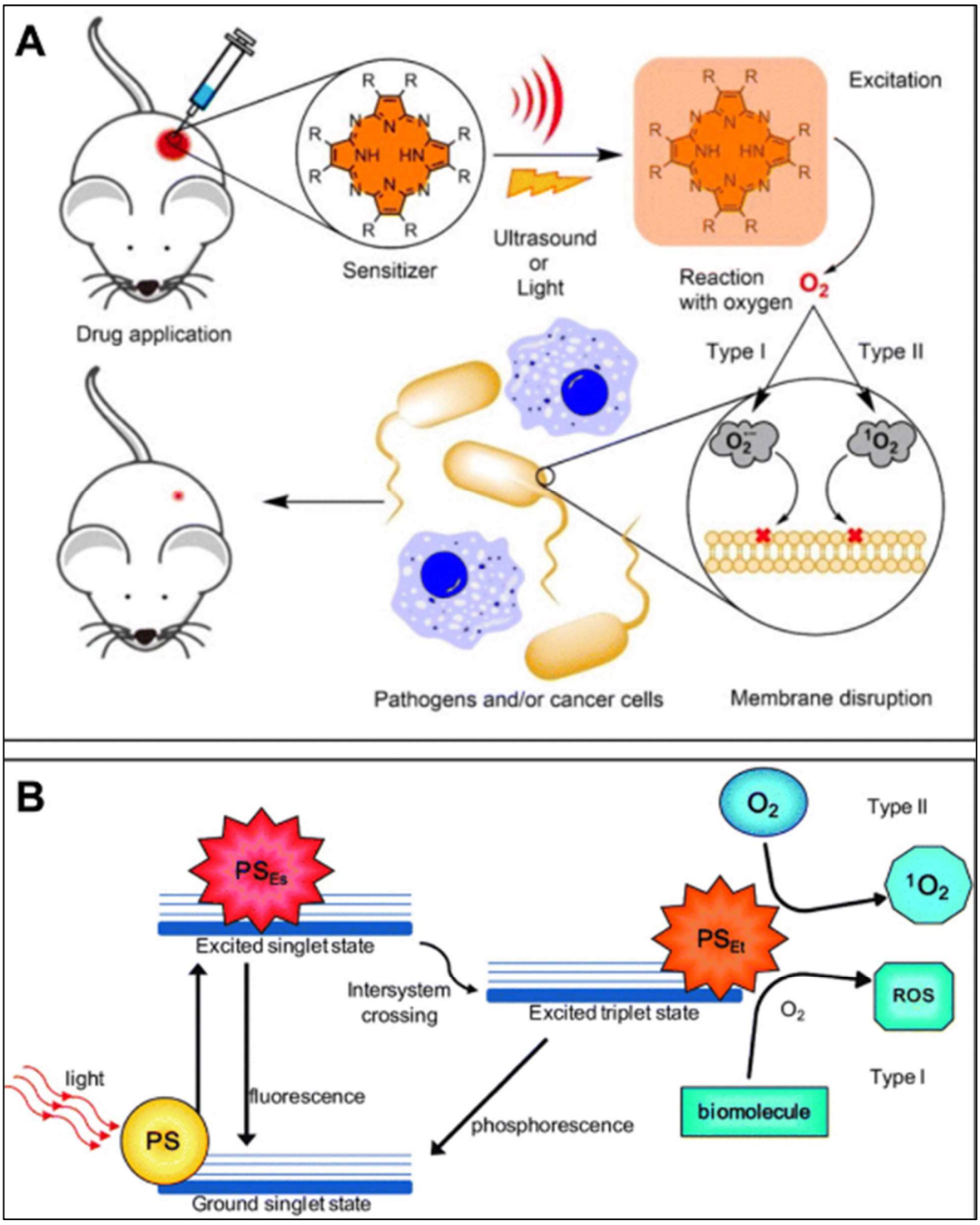

Figure 2 (A) Simplified mechanism of PDT and SDT. **(B) Schematic Jablonski's diagram showing the energy transfer and mechanism of action of Type I and Type II pathways in PDT. [13]**

Combined Therapy: Combined therapy has been used extensively to overcome the limitations of individual antimicrobial medications or techniques, as well as to maximize therapeutic outcomes through the acquisition of synergistic effects. Combined therapy often entails the

combination of two or more antimicrobial agents or therapeutic techniques. This helps improve treatment efficiency, decrease or reverse antibiotic resistance in bacteria, and raise susceptibility of the microbes to the treatments. Multi-antimicrobial drugs or sensitizers combined with nanoparticle-derived delivery systems are thought to be the best options for cooperating to effectively treat a range of infections caused by microorganisms. This is based on the design concepts. [14]

Conclusion:

Many natural, semi-synthetic, and synthetic antibiotics have been used for many years to effectively treat infections brought on by a variety of microorganisms, including bacteria. Almost all antibiotics used therapeutically interfere with some element of bacterial metabolism; their methods of action are well understood. Resistance to some of the therapeutically used antibiotics is a severe issue as a result of the early success of using antibiotics effectively and the underestimate of bacteria's capacity to withstand their effects. The focus of attention in recent years has been on how serious the issue is in clinical medicine. The issue also made it necessary to look for molecules that would be less likely to acquire resistance over time.

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