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Rising antibiotic resistance: growing concern

Abstract

In the 20th century, antibiotics were regarded as a "wonder drug," but due to overuse, bacteria have become resistant to them, giving rise to highly resistant superbugs that can live in the presence of drugs intended to stop them from multiplying. There are several mechanisms behind antimicrobial resistance. Antibiotic resistance can typically be acquired by drug-susceptible bacteria by genetic mutation or gene transfer, with horizontal gene transfer (HGT). Antibiotic resistance can be prevented by using them targeted in their least concentration. Making nano biomolecules could improve antimicrobial therapy's effectiveness and address problems with current methods of infection control. Antimicrobial peptides, bacteriophage therapy, probiotic therapy, and the use of phytochemicals are all essential antibiotic alternatives that should be employed to limit antibiotic consumption. Implementing new regulations, reviving research projects, and pursuing crisis management strategies all require coordinated efforts.

Keywords: rising resistance, antibiotics, management strategies, drug resistance

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Introduction

Antibiotics have contributed significantly to significant advancements in surgery and medicine, in addition to saving the lives of many patients. By altering the course of bacterial infections, antibiotics have also aided in extending predicted life spans.[1] In the 20th century, antibiotics were regarded as a "wonder drug," but due to overuse, bacteria have become resistant to them, giving rise to highly resistant superbugs that can live in the presence of drugs intended to stop them from multiplying.[2] Antibiotic-resistant microbes pose serious dangers to public health, healthcare systems, and global wellbeing.[3] They are responsible for more than 25% of healthcare-associated infections in healthcare settings, which might result in 10 million fatalities by 2050.[4] They may restrict available therapies and raise the death rate of those with compromised immune systems. Slow advancements in the development of innovative antibiotics are making the issue worse.[5] Further, antibiotic resistant microorganisms can cause huge economic burden due to risk of pandemic. Antibiotics are frequently used in livestock and agriculture to treat infectious diseases, prevent infections, and maintain and improve the health of animals and plants that are crucial to industry.[6] Antibiotic resistance spreads and evolves as a result of the careless use of antibiotics in the development of food-producing plants and animals. Furthermore, the expansion of resistant bacteria and resistance genes in human-associated, animal-associated, and environmental microbiomes in food production systems is another factor that exacerbates the issue.[7]

In the late 1950s and early 1960s, it was discovered that the enteric bacteria *Shigella*, *Escherichia coli*, and *Salmonella* were resistant to a variety of antimicrobial treatments. However, their influence was minimal. The 1970s saw the rapid discovery of ampicillin resistance in *Neisseria gonorrhoeae* and *Haemophilus influenzae*.[3] Antibiotic resistance is a widely acknowledged issue in the clinical and health sectors, but it is particularly serious in poorer nations due to subpar public health systems, the prevalence of infectious diseases, and the usage of antibiotics without a doctor's or veterinarian's prescription.[5]

Mechanism behind antibiotic resistance

There are several mechanisms behind antimicrobial resistance[8,9] for instance, A barrier to some types of chemicals is provided by the LPS (lipopolysaccharide) layer in gram negative bacteria. Because of this, certain bacteria have inbuilt resistance to specific classes of powerful antimicrobial medicines. Further, *Mycoplasma* and similar types of bacteria, which lack a cell wall, are consequently inherently resistant to all medications that target the cell wall, such as -lactams and glycopeptides.[10] However, the two main pathways for the development of antibiotic resistance are considered to be vertical evolution (mutations that result in inheritable antibiotic tolerance that can be passed on to offspring) and horizontal evolution (acquisition of inheritable antibiotic-resistance genes from other bacteria through conjugation, transduction, or transformation).[5,11,12]

Genetics behind antibiotic resistance

Antibiotic resistance naturally arises when bacteria evolve and modify their behavior to withstand the effects of antibiotics. Antibiotic resistance emerges and spreads due to DNA mutation, vertical gene transfer (VGT), and horizontal gene transfer (HGT). Mutation in DNA could affect the targets' original structure, decreasing the affinity between medicines and targets. For instance, Fluoroquinolones suppress bacteria by interacting with the A subunit of DNA gyrase; however, mutations in the gyrA gene result in bacterial resistance to these drugs.[13] Some bacteria develop the enzymes necessary to chemically alter or degrade antibiotics, rendering them ineffective. Among these are beta-lactamases, which can hydrolyze and render inactive beta-lactam medicines like penicillins and cephalosporins. Furthermore, another typical mechanism of induced resistance is the multidrug-efflux pump. Bacteria can develop efflux pumps, which are specialized transport proteins that actively pump antibiotics out of the bacterial cell before they can exert their effect. This decreases the intracellular concentration of the antibiotic, making it less effective.[14] Antimicrobial resistance has rapidly evolved throughout various bacterial species with significant human and veterinary health implications as a result of the expansion of mobile genetic elements[15] such plasmids, transposons, and integrons.[16]

Preventive strategies

Antibiotic usage in high concentrations is one of the main causes of resistance because low concentrations have been found to be less effective. Researchers are working on methods to improve antibiotic effectiveness at low concentrations. The tailored distribution of antibiotics can be quite beneficial in this situation. For instance, these antibiotics can be administered in a targeted manner if they combine with metal nanoparticles. Additionally, conjugating antibiotics like amoxicillin, methicillin, ciprofloxacin, gentamicin, rifampicin, and vancomycin on the surface of nanostructures made of gold, silver, selenium, zinc oxide, iron oxide, and copper oxide can facilitate targeted drug delivery to the infected site and shield the antibiotics from microbial enzyme-mediated antibiotic degradation.[2]

Alternative strategies to fight bacterial infections

The fear that humanity is reentering the "preantibiotics" age is now quite serious, and modern medicine and biotechnology now place a high priority on the development of alternative anti infection methods.[17] Some of the alternative strategies to fight bacterial infections showing below.

Antimicrobial peptides

There are few strategies available for the treatment of bacterial infections without antibiotics. One of them is antimicrobial peptides.[18] These substances belong to diverse group of molecules and present in every organism, they have capability to modulate immune system and they also can kill bacteria by attacking their membrane directly. They are also the part of first line of defense in many eukaryotic organisms. Lactoferrin , protamine, α-poly-L-arginine, pleurocidin etc. are some of the examples of antimicrobial peptides.[19] A class of antimicrobial peptides known as bacteriocins are produced by bacteria and are effective at controlling clinically significant susceptible and drug-resistant pathogens. To be able to alter and enhance their physicochemical characteristics, pharmacological effects, and biosafety, bacteriocins have been researched.

Bacteriophage therapy

Bacteriophages are obligatory parasite of specific bacteria. A lytic phase, which is a component of the active phage lifecycle, causes the host bacteria to physically degrade so that offspring viruses can escape.[20] It has been more than a century since phage therapy, or the use of bacteriophage viruses to treat bacterial illnesses, was first developed. They were used to treat a variety of illnesses, such as mastoid infections, suppurating wounds, vaginitis, acute and chronic upper respiratory tract infections, and abscesses.[17]

Probiotic therapy

The gut is home to trillions of different microbes, including anaerobic bacteria, yeasts, viruses, and bacteriophages. The most prevalent groups are Firmicutes, Bacteroidetes, and Actinobacteria. Improving the composition of gut microflora not only help the individuals to improve their digestive system but also improve their capability to fight infections.[6] Probiotics are beneficial against a variety of pathological disorders because of their antibacterial action, including diarrhea, constipation, polycystic ovarian syndrome, ulcerative colitis, stress and anxiety, inflammatory bowel disease, breast cancer, and diabetes.[21] By stabilizing the intestinal permeability barrier and the gut microbiome, as well as by accelerating enteral antigen breakdown and changing their immunogenicity, probiotic bacteria may reduce inflammation.[22]

Phytochemicals

Research into natural compounds acting as effective antimicrobials has resurged as a result of the demand for new and effective antibacterial medicines.[23] Alkaloids, saponins, tannins, flavonoids, and steroids are examples of phytochemical substances that have been proven to be physiologically active and hence partly responsible for the antibacterial properties of plants, which explains their usage in traditional medicine. In this perspective, essential oils extracted from different plant species could be good candidate. For instance cinnamon oil exhibited strong antibacterial effects against carbapenem resistant nosocomial *Acinetobacter baumannii* and *Pseudomonas aeruginosa* bacteria.[24] Further, Essential oils from clove (*Syzygium aromaticum*) and thyme (*Thymus zygis*) increase susceptibility to colistin in the nosocomial pathogens.[25,26]

Future prospects

Antibiotic resistance management is a complicated and multifaceted subject that calls for the efforts of everyday people, healthcare workers, governments, and academics. It includes public awareness about risk of antibiotics overuse, adherence to rational antibiotic use, research in the field of developing new and effective antibiotics and global cooperation regarding adopting best practices to combat antibiotic resistant bacteria. Probiotics, antibodies, and vaccinations are examples of progressive alternative therapies that have produced encouraging results in studies that point to their potential as preventative or supplemental treatments in the future.[3] Without effective action, the consequences of antibiotic resistance could be devastating, leading to a return to a pre-antibiotic era where even simple infections could become life-threatening.

Author's contribution

Neha Singh and Khushboo Bange have equal contribution in conceptualization, draft writing, review, data validation and editing.

Data accessibility

Data information will be provided upon request.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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