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Short Communication

# Antimicrobial Agents: Current Status and Future Challenges

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## Introduction

Microorganisms are known to exist almost everywhere on Earth including water, air, and soil. They are also found in plants and animals. Various types of microorganisms, such as bacteria, fungi, viruses, or protozoa frequently interact with human beings in many ways. They cause either a beneficial or harmful effects in their host organisms. Harmful microbes, also known as pathogens such as bacteria, a virus, fungi or protozoa cause numerous communicable diseases that spread from one person to another. The principal cause of human deaths in the world is primarily due to these pathogenic microbes. They invade our body and multiply rapidly by suppressing defense mechanisms of host cells. The design of microbial genome allows them to overcome host cell defense barriers [1]. Microbes survive in host cells through a wide range of molecular mechanisms, including inactivation of enzymes, modification of the target, formation of biofilms, bypassing the pathways, repair mechanisms, and intracellular localization. The best way to control diseases is to fight against the pathogens and kill them.

An antimicrobial agent is a natural, synthetic or semisynthetic substance with the ability of inhibiting or destroying the growth of pathogens. Antimicrobial agents may cause meager or no harm to the host. The discovery of antibiotics in the 20$^{th}$ century has certainly improved the state of human health forever [2]. Antimicrobial agents are widely used in the treatment and prevention of infectious diseases. Since from the discovery of the first antibiotic drug Penicillin, the management of death causing infections have improved significantly [3]. Antimicrobial agents can destroy pathogens by inhibiting cell wall synthesis, DNA replication or protein synthesis, and altering intermediary metabolic activities. The discovery of many new antibiotic drugs and their wide application has prompted the microbes to evolve and develop antibiotic resistance properties. This is due to the fact that microbes demonstrate great flexibility and adaptability to various environments because of their remarkable genomic flexibility and ability to exchange their genetic content with different species [4]. This suggests that scientists should keep trying to develop novel key molecules, though it is tough to do. The inappropriate use of antimicrobials throughout the world is the main cause for the development of several resistance strains of microbes.

The emergence and spread of these multi-drug resistant strains is a global challenge and is a great threat in the effective treatment of several infectious diseases [3]. Both Gram-positive and Gram-negative bacteria have evolved with antimicrobial resistance. Some of the resistant strains of Gram-positive bacteria include, Vancomycin-Resistant Enterococci (VRE), Methicillin-Resistant *Staphylococcus aureus* (MRSA), and Penicillin-Resistant *Streptococcus pneumoniae* (PRSP). Some examples of Gram-negative bacteria include fluoroquinolone resistance in *Escherichia coli*, carbapenem resistance in *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, cephalosporin resistance in the Enterobacteriaceae and many more. Antimicrobial resistance is developed through the mutations in genes or due to the exchange of genetic information and recombination among other related or different species.

A variety of approaches are employed to mitigate the problem of multi-drug resistance among microbes can be potentially overcome by developing novel antimicrobial drugs using various sources. Natural products obtained from different sources including animals, algae, plants, bacteria, and fungi have shown effective antimicrobial activities and still remains as the major source of antimicrobial agents [5,6]. However, the chemical compound structure and functional relationships is yet to be understood in detail for many natural lead molecules. The diverse class of polyphenolic compounds obtained from plants exhibits a great diversity in their structures and therefore, their antimicrobial effectiveness against pathogens also differs significantly [7]. There are number of antimicrobials such as fusidic acid, pleuromutilins, and novobiomycin obtained from several antibiotic-producing microorganisms including bacteria and fungi. Many of the antibiotics when chemically modified exhibits superior antimicrobial properties. For example, Oritavancin a vancomycin derivative is effective against vancomycin-resistant Gram-positive bacteria. Administration of antibiotics in combination exhibit a superior synergistic inhibitory effect is an another classical approach against pathogens. Alternatively, the use of hybrid antimicrobial agents such as quinalactams formed by the chemical linkage of fluoroquinolones and cephalosporins can be more effective. Several peptides such as gramicidin and bacitracin are developed as novel agents to disturb the cell membrane architecture of the pathogens. Studies are also in focus to inhibit the bacterial attachment for instance, the use of oligosaccharides. Some of the agents including lincosamides, macrolides, and oxazolidinones inhibit protein synthesis in a number of bacteria. Recent advances in genomic sequencing in many pathogens assisted in identifying a large number of crucial genes responsible for pathogenicity and this could be the potential new targets of antimicrobials. Recent studies have witnessed the use of recombinant bacteriophages against bacteria [8]. The application of nanotechnology has revolutionized the modern medical world. Various types of nanoparticles have proved to be very effective alternatives against multidrug-resistance human pathogens [3].




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In addition, the development of a new delivery mechanisms might further maximize the levels of antimicrobials at the infection site and increase the antimicrobial effectiveness without causing toxic effect to the host. Modern technologies and information is far superior when compared to earlier decades and thus, certainly benefited scientists in developing effective new drug molecules using the available resources. In general, antimicrobials are relatively not harmful compared to any other drugs used for treating human diseases. However, toxic effect of any new antimicrobials should undergo clinical testing before its commercial use [9]. Despite the discovery of several novel antimicrobials, the clinical evaluation of these new agents are significantly reduced due to lack of funds and thus, new antimicrobial agents in the phase of development has reduced drastically in the recent years. This further raises fear of effective treatments against serious pathogens in the near future. More research efforts should be undertaken to discover novel antimicrobial agents against multidrug-resistant pathogenic microbes that are increasing relentlessly all over the world. The problem of drug resistance is a serious global concern in the healthcare system. The scientists are normally engaged in the development of novel molecules to tackle with this problem. However, more collaborative efforts should be initiated between various scientific groups and government funding agencies in order to control the emergence of multi-drug resistance in microbes.

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