

New perspectives on antibacterial drug research

Review Article

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Abstract: Bacterial resistance to commonly used antibiotics is constantly increasing. Bacteria particularly dangerous for human life are methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus faecium* and fluoroquinolone-resistant *Pseudomonas aeruginosa*. Hence, there is an incessant need for developing compounds with new modes of action and seeking alternate drug targets. In this review, the authors discuss the current situation of antibacterial medicines and present data on new antibiotic targets. Moreover, alternatives to antibiotics, such as bacteriophages, antimicrobial peptides and monoclonal antibodies, are presented. The authors also draw attention to the valuable features of natural sources in developing antibacterial compounds. The need to prevent and control infections as well as the reasonable use of currently available antibiotics is also emphasized.

Keywords: Bacterial resistance • Antibacterial compound • Drug discovery • Target • Antimicrobial peptides

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1. Introduction

The use of antibiotics, especially the excessive and indiscriminate use, both in medicine and veterinary science has contributed to the emergence of drug resistant organisms. Antimicrobial drug resistance constitutes a growing problem worldwide [1]. Infections caused by resistant pathogens result in increased mortality and morbidity among human and animal populations. In addition, pathogenic microorganisms, including *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Clostridium difficile*, contribute to many hospital-acquired infections. Gram-negative bacteria are traditionally more difficult to destroy than Gram-positive bacteria as they contain an outer membrane that constitutes an extra barrier for antibacterial compounds. The latest reports from the American and European disease associations claim that there are only a few antibiotics in the clinical pipeline that are more effective in targeting Gram-negative bacteria than existing pharmaceuticals on the market [1]. In the surveillance report titled "Antimicrobial resistance surveillance in Europe" made by the European Centre for Disease Prevention and Control, the authors show a general, Europe-wide increase in antimicrobial resistance in Gram-negative

pathogens (*Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*) [2].

In this review, the authors will discuss the present status of bacterial resistance to antibiotics, especially of bacterial species that cause serious hospital and community-acquired infections. Furthermore, the review presents antibiotics that are currently on the market and summarizes novel promising discoveries in drug development. The authors will also refer to new antibacterial targets and other alternatives to antibiotics.

2. How antibiotics became outdated?

The lack of new and effective antibacterial compounds is due to several factors. First of all, it is difficult to find new antibacterial compounds with good pharmacological profiles and low toxicity for the host. Furthermore, from an economic point of view, pharmaceutical companies are more interested in developing drugs for chronic conditions than for short-term treatments. Moreover, it is preferable when antibiotics target multiple species. In addition, bacteria tend to develop resistance to antimicrobials which restricts their use and consequently causes drug sales decline [3]. Finally, the chemical structures of antibiotics, especially those derived from

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