Chapter 7
Natural Products in the Fight Against Multi-Drug-Resistant Bacteria:
Natural Antibiotics and Resistance

Mümtaz Güran
Eastern Mediterranean University, Turkey

ABSTRACT

It is well recognised that the antimicrobial resistance crisis has approached critical levels, and current treatment options are very limited, especially in the treatment of infections caused by resistant bacteria. Thus, ongoing research is focused on the development of new molecules which have broader antimicrobial activity. However, the advancements in drug development studies using synthetic compounds has led to a lack of success. Also, economic and regulatory issues have formed a challenge as well. Therefore, research has focused again on natural products. A large number of natural products and natural product-derived compounds are still in various stages of clinical development. Here, current research on the potential uses of natural products or their templates as viable sources of new drug candidates have been discussed to construct an understanding towards the goal of development of new antimicrobials to overcome resistant pathogens.

INTRODUCTION

The life before antibiotics was dark and the discovery of antibiotics has shined upon the darkness of humanity and saved many lives. Average lifespan of a human being has increased significantly after the introduction of antibiotics. But, after a century of gains in the war against infectious diseases, the humanity is losing ground again. Common bacteria, parasites and fungi are developing widespread immunity to our best weapons.

Since its development, the humanity thought that penicillin will be a magic bullet for the infectious diseases. It has been used extensively and irresponsibly together with other following antimicrobials. Since many decades, there is a tremendous effort throughout the world to overcome the global antibiotic resistance. But now, medical authorities are raising concerns that treatment options in certain infectious diseases are narrowing because of alarming global antibiotic resistance problem. As new antimicrobial drugs are developing, the need for newer ones grow as well.

The looming public health crisis of antimicrobial-resistance have been evaluated by Centers for Disease Control and Prevention (CDC) and a report on antimicrobial resistance and its impact on various sectors in United States of America (USA) which highlights the scope of the problem have been published (CDC, 2013). CDC estimates that in the United States, more than two million people are infected every year with antibiotic-resistant bacteria, ending with at least 23,000 deaths as a result. From an economic standpoint, an economic burden of $18,000 -- 29,000 of medical costs per patient in a single year have been reported for USA in the year of 2000 which is similar in many geographies (Thabit et al., 2015). For example, high burden of antimicrobial drug resistance in Asia have been reported for various pathogens, namely; Methicillin-Resistant *Staphylococcus aureus* (MRSA), Vancomycin Resistant *S. aureus* (VISA), Vancomycin resistant *Enterococcus* (VRE), macrolide and penicillin resistant *Streptococcus pneumoniae*, Extended Spectrum Beta- Lactamase Producer *Escherichia coli* and *Klebsiella pneumoniae*, Carbapenem Resistant Enterococci (CRE), Multi drug resistant (MDR) *Pseudomonas aeruginosa* and *Acinetobacter* spp. are mentioned as superbugs of the 21st century (Lai et al., 2014).

As a result, the emergence of pathogens with different mechanisms of resistance has intensified the challenges associated with infection control and treatment strategies. Therefore, as prudent use of antimicrobials is not at the intended level, development of novel antimicrobial molecules remains as the main strategy to overcome the present narrow pass. In this context, many products have been studied to develop antimicrobials and the major sources of chemical diversity for starting materials were mainly natural products because of their abundant scaffold diversity (Mishra & Tiwari, 2011). Before, the pharmaceutical companies were using crude plant extracts to produce relatively simple therapeutic formulations but nowadays

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