Chapter 9
Ancient Pediocin to Innovative Antimicrobial

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ABSTRACT

Multi-drug resistance among patients suffering from infectious diseases has reached such proportions as to render them ineffective. WHO has to put out advisories time and again as to regulate their use. The presently available antibiotics are targeted at inhibiting vital biochemical pathways of pathogens, like nucleotide, protein, or cell wall synthesis in a very specific manner. Antibiotics have been rendered ineffective due to chemical modification, gene mutation, or transport mechanisms employed by pathogens. The novel approach to this problem can be naturally occurring antimicrobial peptides like bacteriocins produced by food grade bacteria. Pediocins produced by pediococcal strains have been found to inhibit a broad spectrum of pathogens by mechanisms that are robust enough to withstand development of resistance. Thus, these pediocins are attractive molecular precursors to develop novel antimicrobials. However, their application as such poses challenges that can be overcome with developing innovative technologies of chemical modifications and delivery strategies.

DOI: 10.4018/978-1-7998-0307-2.ch009

INTRODUCTION

The emergence of Multi Drug Resistant pathogens in last few decades is posing a real threat to the world community. With emerging new pathogenic diseases, the repertoire of drugs suddenly seems to be woefully inadequate. This scenario becomes scarier when we factor in lack of reported novel antimicrobials in the pharmaceutical research pipelines. A cause of concern is also an increasing population living in closely packed clusters in cities and increased mobility, creating conditions conducive to quick spread of infectious agents as well as their antimicrobial resistance.

Such is the extent of the problem that in 2017, World Health Organization (WHO) published its first ever list of antibiotic-resistant "priority pathogens" –basically cataloguing 12 families of bacteria which were identified as greatest threat to human health. So much so that WHO further prioritized them into critical, high and medium based on the urgency to develop novel antibiotics specially for pathogens spreading in hospitals, threatening the medical fraternity itself (Table 1). ESKAPE is the acronym of six such antibiotic resistant species of pathogenic bacteria, the six species are ***E****nterococcus faecium*, ***S****taphylococcus aureus*, ***K****lebsiella pneumoniae*, ***A****cinetobacter baumannii*, ***P****seudomonas aeruginosa* and ***E****nterobacter.*

Table 1. WHO prioritization of antibiotic resistant pathogens (WHO, 2017)

Priority 1: CRITICAL	Priority 2: HIGH	Priority 3: MEDIUM
Acinetobacter baumannii, carbapenem-resistant *Pseudomonas aeruginosa*, carbapenem-resistant *Enterobacteriaceae*, carbapenem-resistant, extended spectrum β-lactamase (ESBL) producing	*Enterococcus faecium*, vancomycin-resistant *Staphylococcus aureus*, methicillin-resistant, vancomycin-intermediate and resistant *Helicobacter pylori*, clarithromycin-resistant *Campylobacter* spp., fluoroquinolone-resistant *Salmonellae*, fluoroquinolone-resistant *Neisseria gonorrhoeae*, cephalosporin-resistant, fluoroquinolone-resistant	*Streptococcus pneumoniae*, penicillin-non-susceptible *Haemophilus influenzae*, ampicillin-resistant *Shigella* spp., fluoroquinolone-resistant

BACKGROUND

In order to curb this spread, a few restrictions were imposed on widespread use of antibiotics and only the permitted antibiotics and other chemicals to be used in feed supplements were allowed. However, the non-compliance with these regulations at