Chapter 8
Alternative Therapies: Toolbox to Combat Antibiotic-Resistant Bugs

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ABSTRACT

Antibiotic resistance is one of the leading public health concerns across the globe. Antibiotics are losing their effectiveness, leading to uncertainty in available treatment options to clinicians. Resistance to antibiotics is at an all-time high, and there is a pressing demand to look for alternative antimicrobial candidates other than antibiotics. Alternative therapies include use of bacteriophages, lytic proteins, nanoparticles, phytochemicals, quorum quenchers, and other antibacterial or antivirulent agents that can eradicate bacterial infection alone or in conjunction with antibiotics. Alternative therapies can replace or lower the effective antibiotic dose, which can help to tackle antibiotic resistance as well as counter its side effects. For sustainable development of antimicrobials against drug resistant bugs, novel alternative strategies need to be explored in the near future. Alternative therapies can help researchers to construct a toolbox containing a variety of antimicrobial agents, which can be used alone, in combination with other agents, or in rotation.

DOI: 10.4018/978-1-7998-0307-2.ch008

ANTIMICROBIAL RESISTANCE

Antibiotic resistance is a state when microorganisms show resistance to an antibiotic upon exposure. Antibiotic resistance is a global problem which can cross international boundaries and spread between continents in recent times. Various forms of resistance spread with astonishing speed which could not be paralleled by the development of novel antimicrobial products. Researchers have described antibiotic resistant microorganisms as "nightmare bacteria" that can "pose a catastrophic threat" to global population. The problem is so serious that majority of pathogenic bacteria such as *Streptococcus pneumoniae, Mycobacterium tuberculosis, Acinetobacter baumannii, Neisseria gonorrhoeae, Klebsiella pneumoniae, Enterococcus faecium, Staphylococcus aureus, Pseudomonas aeruginosa*, and species of *Enterobacter, Shigella* and *Salmonella* are now resistant to most of the available antibiotics (Nathan, 2014). Perhaps the single biggest public health threat today is antibiotic resistance (Laxminaraya et al, 2013). For instance gonorrhea, was treatable with penicillin in the 1970s but now has become resistant even to third generation oral cephalosporins (Fernandes et al, 2017). Drug resistance causes 25 000 deaths per year ("ECDC/ EMEA Joint Technical Report", 2009). Similarly, in same epoch in the USA and China, resistance caused 100 000 and 80 000 deaths, respectively (Prestinaci et al, 2015). Antibiotic resistance can lead to escalating costs and deterioration of health care systems. Patients suffering from drug resistant nosocomial (hospital acquired) bloodstream infections or infection following consumption of food contaminated with antibiotic resistant pathogens experience longer recovery and a higher occurrence of septicemia and mortality (Angulo et al,2004).

There are several reasons that contribute towards antimicrobial resistance crisis. These includes overuse of antibiotics, inappropriate prescription, extensive non-clinical use, and slow development of newer antibiotics. The overuse and misuse of antibiotics in clinical practice clearly leads the evolution of antibiotic resistance. A number of epidemiological studies have established a direct correlation between antibiotic utilization and emergence of drug resistant bacterial strains. In bacteria, genes which confer antibiotic resistance can be inherited from closely related or from nonrelated on the mobile genetic elements which primarily includes plasmids (Reed et al, 2014). Antibiotics are poorly regulated and easily available over the counter without a proper prescription (Michael et al, 2014). Poor regulatory system results in antibiotic misuse due to their easy availability and low cost. Faultily prescribed antibiotics have dubious therapeutic effects and may expose patients to the possible complications of antibiotic treatment (Murthy et al, 2015). Subinhibitory antibiotic concentrations can also promote the development of antibiotic resistance by supporting genetic alterations (Viswanathan et al, 2014). The antibiotics used in farm animals are ingested by humans when they consume such foods (Golkar et al, 2014). Even