

## A Review on Mode of Action of Antibiotics : Paved the Path to Evolution of Antibiotic Resistance and their Mechanisms in Phytobacterial Disease Management

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**ABSTRACT:** One of the most important public health issues is the crisis of antimicrobial-resistant microorganism infections. In the production of antibiotic resistance bacterium, common agricultural methods are involved. Biopesticides are non-pathogenic living bacteria, considered safe to consume, utilised for the treatment of pests. In high concentrations, application of bacterial pesticides on crops increases the chance of unintentional contributions to movement and production within the surrounding area of antimicrobial resistance genes. The existence and the manifestations are currently unclear in clinically important antibiotic resistance genes. In this case, a multi-bioinformatic- and microbiological mix is utilised to define the resistance of large-scale biopesticides and to verify the presence in many biopesticide products of putative antimicrobial resistance genes. Our data show that biopesticide products are clinically significant repositories of antimicrobial resistance genes, which resist several kinds of drugs.

**Keywords:** Antibiotics, resistance, mechanisms, phytobacterial management.

### INTRODUCTION

#### Definition of Antibiotics and Antibiotic Resistance:

A compound produced by a microbe with killing or growth-inhibiting activity against other microbes” (Waksman, 1973). The discovery and deployment of antibiotics in plant disease management were soon referred as ‘Silver bullets’ in managing the diseases. However, the use of antibiotic has been decreased due to the antibiotic resistance development, “microbial survival despite exposure to antibiotics designed to kill them or to impede their growth” (Barbosa *et al.*, 2000). To frame this review, the understanding of little history of antibiotics and subsequent development of resistance of microorganisms (Bacteria) to antibiotics is essential.

#### Timeline of deployment of antibiotics and succeeding development of antibiotic resistance:

The scenario shows that the introduction of any novel antibiotics had followed by significant resistance to that antibiotic in the last few years. For instance, the deployment of sulphonamides and penicillin in 1930 and 1940 showed significant resistance to the mentioned antibiotics in the following years, 1940 and 1945, respectively (Clatworthy *et al.*, 2007).

#### Beginning and development of Antibiotic resistance elements:

Antibiotic resistance that is determined in microorganism pathogens has according to be grown up from 3 major resources; the escape through horizontal gene transfer of natural resistance genes encoded by the antibiotic-producing microbes, the presence and

supreme movement of resistance genes living among the microbiome to pathogenic organisms underneath antibiotic selection, and mutations encoding target-site alterations (Sundin and Wang 2018).

- *Streptomyces rimosus* carries multiple tetracycline resistant determinants, including *otr A*, *otr B*, & *otr C* through antibiotic resistance genes (Sundin and Wang 2018).

- Kasugamycin resistance in *Acidovorax avenae* sub sp. *Avenae* and *Burkholderia glumae* was conferred likely acquired by HGT and for *Erwinia amylovora* (McGhee and Sundin 2012) through spontaneous mutation.

#### Mode of action of Antibiotics and Antibiotic resistance mechanisms:

##### Mechanisms of Antibiotic Resistance:

(a) **Inactivation of antibiotics:** To inactivate and degrade the antibiotics, Bacteria may produce enzymes. Eg. Penicillin resistance in *Streptomyces rimosus* due to the production of the enzyme - lactamase that inactivates the antibiotic by hydrolysing the - lactam ring.

(b) **Target site modification:** The molecules that are usually sure by an antibiotic are usually altered or replaced and so primarily eliminates the antibiotic target in microorganism cells.

Eg. Structural changes in r RNA of some gram positive bacteria modulates the macrolides target sites and thus bacteria continues to produce proteins.

**(c) Immunity and Bypass:** By altering the membrane permeability, the entry of the antibiotic into bacterial cells can be eliminated.

Eg. Tetracycline resistance to *Streptococcus* is predominately due to ribosomal protection encoded by tet genes.

There are five super families of microbial efflux systems viz. NorM, multi- antimicrobial extrusion protein family (MATE), QacA major facilitators (MFS), LmrA, ATP- binding cassettes (ABC), MexAB, QacC small multidrug resistance family (SMR), resistance- nodulation cell division (RND) these Eps are responsible for the export of antibiotics before they find their intercellular targets. For instance EP is an effective mechanism of macrolide resistance in *Streptococcus pyogenes* and the resistance is encoded by the *mefA* gene and is specific for 14 and 15-membered macrolides (Sharma *et al.*, 2019).

**(d) Biofilm formation:** Biofilm is made by a complex aggregation of microbes, whereby the cells are embedded matrix of extracellular compound substance (EPS) that may be a major virulence issue related to augmented antibiotic resistance, reduced phagocytosis and overall persistence of the microorganisms.

**Alternative approaches to Antibiotic resistances.**

**Efflux pump inhibitors (EPIs):**

Down regulating the expression of efflux pump genes by intrusive in genetic regulation; Redesigning antibiotics that aren't any longer recognized as substrates; Inhibiting the assembly of functional efflux pumps; interference the pump to avoid substrate binding to the active site; Collapsing the energy mechanism to blame for energizing these pumps (Sharma *et al.*, 2019).

**Table 1: List of EPIs derived from various sources.**

EPIs	Active against bacterial strain	Sources
Pheophorbide A	<i>Streptococcus aureus</i>	Plant source
Carnosol		
Carnosic acid		
Coumarins		
Essential oils (Salvia species)		
-Terpinene		
Tannic acid	<i>Streptococcus aureus</i> , <i>S. aureus</i> , <i>E.coli</i> and <i>Burkholderia pseudomallei</i>	Chemically synthesised
Cholecalciferol and alpha-tocopherol		
Phenothiazine and its derivatives		
Valinomycin		
EA-371 and EA-371	<i>Mycobacterium spp.</i> <i>P. aeruginosa</i>	Microbial sources

**Inhibition of biofilm formation:**

1. Transcinnamaldehyde, an aromatic organic compound of cinnamon bark such as carvacrol, thymol and geraniol, is known (Amalaradjou and Venkitanarayanan 2011)
2. Cymbopogon citratus and clove tree essential oils are amazing plants Antibiotics membrane activity against

and microbial biological membranes (Stavri *et al.*, 2007).

3. A portion of lemongrass oil strangled biofilm formation, disrupting preformed biofilms and targeting multiple microbial cells. Some macrolide antibiotics, such as azithromycin, suppress the QS of *P. aeruginosa* biofilm (Hoffman *et al.*, 2007)

**Some antibiotic resistance modifying compounds found in plants (Sibanda *et al.*, 2007).**

Compound	Plant source	Antibiotics potentiated	References
Ferruginol 5-Epispiferol	<i>Chamaecyparis lawsoniana</i>	Oxacillin, Tetracycline, Norfloxacin Tetracycline	Smith <i>et al.</i> , (2007)
2, 6-dimethyl-4-phenyl pyridine-3, 5-dicarboxylic acid diethyl ester	<i>Jatropha elliptica</i>	Ciprofloxacin, Norfloxacin, Pefloxacin, Acriflavine and Ethidium bromide	Lanfer-Marquez <i>et al.</i> , (2005)
Carnosic acid carnosol	<i>Rosmarinus officinalis</i>	Erythromycin	Oluwatuyi <i>et al.</i> , (2004)
Ethyl gallate	<i>Caesalpinia spinosa</i>	Lactams	Shibata <i>et al.</i> , (2005)
Methyl-1 - - acetoxy- 7- - 14 - dihydroxy- 8, 15- isopimaradien- 18-oate Methyl-1 - - 14- - diacetoxy- 7- -hydroxy- 8,15- isopimaradien- 18-oate	<i>Lycopus europaeus</i>	Tetracycline and Erythromycin	Gibbons <i>et al.</i> , (2010)
Epicatechin gallate Epigallocatechin gallate	<i>Camellia sinensis</i>	Norfloxacin, Imipenem, Panipenem L actams	Hu <i>et al.</i> , (2002); Zhao <i>et al.</i> , (2001)

## CONCLUSION

The study of antibiotic resistance mechanisms have shown that the EFFLUX pump is actively playing an important role in the development of bacterial antibiotic resistance. Therefore, the Passing Efflux was considered an attractive replacement to reduce the problem. Plants are the source of new antibacterial and resistant modified active ingredients. Many goals and strategies that disturb by combining antibiotic drugs with target websites and various measures that can benefit to reduce resistance development. Explore Replacement Systems (Flavonoids, Tannin Cumarins, V.V.) that inhibit the formation of biological membranes through higher education inhibitors are different approaches to reduce the antibiotic resistance.

## FUTURE SCOPE

Antibiotics have been produced, utilised, and safeguarded in ways that have led to our current predicament of escalating antibiotic resistance and declining new treatments, as expected. We must fundamentally alter our strategy if we are to avoid a post antibiotic era. Long-held assumptions and deeply held ideas must be challenged. We must push through our instinctive opposition and justifications (e.g., "that's not how we do things" and "that can't be done") that arise when we challenge established practises. There are a plethora of justifications. It's time to take action. To battle opposition, we'll need a unified national action plan in the end.

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