Actinobacteria and Environmental Adaptations

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Actinobacteria are among the secondary metabolites producers and hold high pharmacological and commercial interest. It has great capability to produce secondary metabolites such as immunomodulators, antibiotics, anti-cancer drugs, growth factors, anthelminthic enzymes and herbicides.describes the historical isolation of bioactive compounds from Actinobacteria from the first isolation by Selman Waksman.

Keywords: microbial ecology ; aquatic and marine environments ; drug-resistant pathogens ; natural products ; VOSviewer software

1. Introduction

Global demand for new chemotherapeutic compounds and antibiotics with high bioactivity and low toxicity has increased recently due to the emergence of life-threatening microorganisms and multidrug resistance agents among viruses, bacteria and fungi [1]. Additionally, the detection of secondary metabolites molecules with unique modes of action established various therapeutic agents' strategies for treating many illnesses [2]. To be more specific, endophytic Actinobacteria are microorganisms that represent a new production source of a large number of secondary metabolites, including alkaloids, beta-lactams, sulfonamides, aminoglycosides, glycopeptides, siderophores, quorum-sensing molecules, immunosuppressants, polyene macrolides, saccharides, pyrazoloisoquinolinones, butenolides, nucleosides and degradative enzymes [3]. In fact, it has been reported that more than 10,000 various bioactive compounds have been discovered from Actinobacteria [4].

Endophytic microbes refer to a group of microorganisms, mostly fungi and bacteria, that exist in the host plant's intracellular space. It usually causes no obvious harmful effect or symptoms of the disease and could produce various associations such as trophobiotic communalistic, mutualistic and symbiotic co-existence [5]. Endophytes in woody plant hosts could exist within host tissues and protect host plants against herbivores and other pathogenic microorganisms [6]. ActinobacteriaActinobacteria are Gram-positive bacteria with high guanine and cytosine (G + C) content in their genomes, and they are classified into 6 classes, 79 families of 46 orders and 10 fresh families of 16 new orders based on phylogeny using 16S rRNA sequences. The Actinobacterial classes consist of *Thermoleophilia, Rubrobacteria Nitriliruptoria, Coriobacteria, Actinomycetia* and *Acidomicrobiia Salam* et. al. [7]. Actinobacteria have ubiquitous characteristics. They are present in diverse ecosystems on the earth such as endophytically with plants and in terrestrial and aquatic environments. An abundance of Actinobacteria species have been recorded in ordinary, extraordinary and extreme environments with high or low temperatures, high radiation, acidic/alkaline pH, salinity, low levels of available moisture and nutrients [8].

The genus *Streptomyces* is a Gram-positive bacteria. It is the largest genus of the phylum Actinobacteria, which has complex growth and can produce various secondary metabolites [8]. In addition, there are more than 800 Streptomyces species that have been found to date (see http://www.bacterio.net/ Streptomyces .html (accessed on 20 August 2020) [9]. Streptomyces is the major microbial genus of the most antibiotic-producing bacteria in the microbial world discovered so far, where streptomycin, gentamycin, rifamycin, chloramphenicol and erythromycin are produced by *Streptomyces* [10].

Actinobacteria have a large number of secondary metabolite biosynthetic gene clusters. Biosynthetic gene clusters (BGCs) are known as genes comprising locally clustered groups encoding a secondary metabolite biosynthetic pathway. In addition, BGCs contain genes encoding all enzymes required to produce secondary metabolites and pathway-specific regulatory genes. The Actinobacteria have diverse physiology and metabolic flexibility with high potential to produce novel bioactive compounds and enzyme production [11].

2. Mechanism of Bioactive Compounds from Actinobacteria against Drug-Resistant Pathogens

Once scientists provide new antimicrobial drugs, the microorganism starts to adapt themselves against these drugs, which become ineffective at some points. This is primarily due to changes that occur inside the microorganism, especially bacteria, due to the interaction of numerous organisms through their environment and surroundings. These changes may occur for various reasons: mutations, selective pressure, gene transfer and phenotypic change [12]. For example, gene mutation occurs when bacteria reproduce, leading to the development of bacteria with genes that help them resist antibiotics. In addition, the mutation leads to alter the target and modification of the drug-receptor site in the target site [13].

Moreover, selective pressure means that bacteria carrying resistance genes hold up and multiply so that new resistance bacteria become the predominant type. The selective pressure leads to a lack of entry and decreased cell permeability. In addition, it leads to greater exit and active efflux pump [14]. Bacteria unnecessarily replicate to transmit their antibiotic resistance gene. Instead, it is passed across various types of bacteria resistance determinants through horizontal gene transfer making the bacterium resistant [15]. Besides this, phenotypic change suggests that the bacteria can change some of their properties to become more resistant to common antibiotics using the enzymatic inactivation of the antibiotics or by synthesising resistant metabolic pathways [16]. Other mechanisms, by modulation of methicillin-resistance of penicillin-binding protein (PBP2a) synthesis, were regulated by two genes known as MecI and MecR1 proteins. When existing, the signalling or regulatory proteins of the plasmid-mediated staphylococcal β-lactamase gene bla-Z system are working.

Furthermore, homogeneous tolerance is based on mutations at a different locus of genetics. Furthermore, other external and internal causes affect the development of methicillin resistance [17]. The mechanism of anti-bacterial resistance is demonstrated in **Figure 1**.

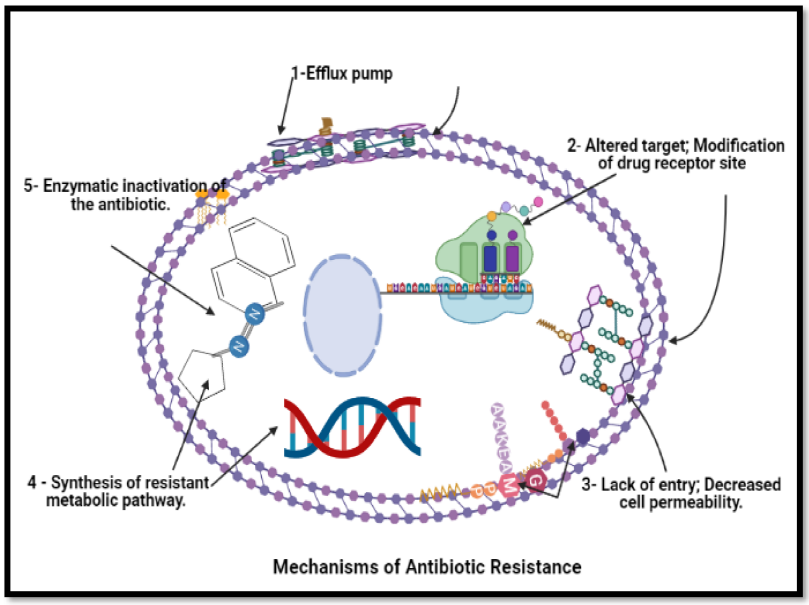

Figure 1. Mechanism of anti-bacterial resistance to avoid killing by antimicrobial molecules. N.B.: BioRender was used to draw these scientific figures.

3. Conclusions and Future Prospects

There is a global demand for new chemotherapeutic agents and antibiotics that are extremely active and have low toxicity and environmental effects. The drug resistance in viruses, fungal and bacteria, as well as the emergence of life-threatening microorganisms, have become higher than before. This is due to the wrong usage of dose and time of medication administration, increasing the requirement of new and active compounds that assist and relieve all the aspects of the human condition. Actinobacteria have been isolated from different ecosystems, including several medicinal plants from the terrestrial and rhizosphere environment, hot springs as thermophilic Actinobacteria, deep-sea sediments, marine sponges and alkalines line soil. Several previous published works reported that Actinobacteria are understudied phylogenetic groups with high biosynthetic potential. This type of bacteria was found to have the greatest number of biosynthetic gene clusters in its genomes. There are more opportunities to investigate new resources and other biological characteristics of previously inaccessible natural products extracted from Actinobacteria as interest grows in bioactive molecules from drug formulation with minimal side effects. This group represents the new resource of bioactive compounds due to its ability to grow in multisectoral environments.

We focused on the emphasis and the connection between finding new resources and novel strategies to search for potential bioactive compounds isolated from phylum Actinobacteria. In addition, this review highlighted some limitations in today's research regarding a new source for bioactive compounds isolated from Actinobacteria. For example, most previous publications concentrated only on the endophytic Actinobacteria, excluding other environments such as thermophilic, alkaliphilic and haloalkaliphilic Actinobacteria. Note that many other biodiversities and multidisciplinary environments represent important and new resources of potentially bioactive compounds. As a result, it appears that certain new techniques and methodologies for a thorough investigation of bioactive natural compounds are required. This includes, for example, the discovery of novel structure–activity relationships in nature, which has become increasingly important for the synthesis inspiration of natural bioactive product compounds. This results in increased diversity with less complexity and a good knowledge of isolation processes.

To address the challenges of biodiversity and promote future sustainable use of natural resources, a multidisciplinary perspective is required to find, describe and convey nature's richness. This is necessary for identifying novel bioactive chemicals from Actinobacteria. Moreover, this review summarised the new bioactive compounds isolated from Actinobacteria and their applications in industrial, agricultural and environmental protection, pharmaceutical bioactive compounds and pharmaceutically related biomolecules. This includes superordinate metabolites that act as inhibitory or killing agents against pathogens that affect humans and animals, including resistant bacteria, fungi, viruses and several protozoa. They can also produce an anti-cancer and several enzymes for active degradation and meeting industrial demands worldwide. Therefore, continuous selective isolation and screening studies on the characterisation and identification of novel potential bioactive compounds from Actinobacteria are required. This is to create commercially viable, long-term and cost-effective production methods. Their metabolic flexibility and abundance also provide a novel, strong pathway for the bioremediation of organic wastes and contaminants.

References

1. Carvalho, I.T.; Santos, L. Antibiotics in the aquatic environments: A review of the European scenario. Environ. Int. 2016, 94, 736–757.
2. Ribeiro, I.; Girão, M.; Alexandrino, D.; Ribeiro, T.; Santos, C.; Pereira, F.; Mucha, A.; Urbatzka, R.; Leão, P.; Carvalho, M. Diversity and Bioactive Potential of Actinobacteria Isolated from a Coastal Marine Sediment in Northern Portugal. Microorganisms 2020, 8, 1691.
3. Qi, D.; Zou, L.; Zhou, D.; Chen, Y.; Gao, Z.; Feng, R.; Zhang, M.; Li, K.; Xie, J.; Wang, W. Taxonomy and Broad-Spectrum Antifungal Activity of Streptomyces sp. SCA3-4 Isolated From Rhizosphere Soil of Opuntia stricta. Front. Microbiol. 2019, 10, 1390.
4. Girão, M.; Ribeiro, I.; Ribeiro, T.; Azevedo, I.C.; Pereira, F.; Urbatzka, R.; Leão, P.; Carvalho, M.F. Actinobacteria Isolated From Laminaria ochroleuca: A Source of New Bioactive Compounds. Front. Microbiol. 2019, 10, 683.
5. Kandel, S.L.; Joubert, P.M.; Doty, S.L. Bacterial Endophyte Colonization and Distribution within Plants. Microorganisms 2017, 5, 77.
6. Frank, A.C.; Guzmán, J.P.S.; Shay, J.E. Transmission of Bacterial Endophytes. Microorganisms 2017, 5, 70.
7. Salam, N.; Jiao, J.-Y.; Zhang, X.-T.; Li, W.-J. Update on the classification of higher ranks in the phylum Actinobacteria. Int. J. Syst. Evol. Microbiol. 2020, 70, 1331–1355.
8. Passari, A.K.; Chandra, P.; Leo, V.V.; Mishra, V.K.; Kumar, B.; Singh, B.P. Production of potent antimicrobial compounds from Streptomyces cyaneofuscatus associated with fresh water sediment. Front Microbiol. 2017, 8, 68.
9. Li, L.-Y.; Yang, Z.-W.; Asem, M.D.; Fang, B.-Z.; Salam, N.; Alkhalifah, D.H.M.; Hozzein, W.N.; Nie, G.-X.; Li, W.-J. Streptomyces desertarenae sp. nov., a novel actinobacterium isolated from a desert sample. Antonie Leeuwenhoek 2019, 112, 367–374.
10. Bérdy, J. Bioactive Microbial Metabolites. J. Antibiot. 2005, 58, 1–26.
11. Shivlata, L.; Satyanarayana, T. Thermophilic and alkaliphilic Actinobacteria: Biology and potential applications. Front. Microbiol. 2015, 6, 1014.
12. Yamaguchi, M.; Goto, K.; Hirose, Y.; Yamaguchi, Y.; Sumitomo, T.; Nakata, M.; Nakano, K.; Kawabata, S. Identification of evolutionarily conserved virulence factor by selective pressure analysis of Streptococcus pneumoniae. Commun. Biol. 2019, 2, 96.
13. Lee, W.; Do, T.; Zhang, G.; Kahne, D.; Meredith, T.C.; Walker, S. Antibiotic Combinations That Enable One-Step, Targeted Mutagenesis of Chromosomal Genes. ACS Infect. Dis. 2018, 4, 1007–1018.

14. Schwarz, S.; Loeffler, A.; Kadlec, K. Bacterial resistance to antimicrobial agents and its impact on veterinary and human medicine. Adv. Vet. Dermatol. 2017, 8, 95–100.
15. Touchon, M.; Sousa, J.A.M.D.; Rocha, E.P. Embracing the enemy: The diversification of microbial gene repertoires by phage-mediated horizontal gene transfer. Curr. Opin. Microbiol. 2017, 38, 66–73.
16. Kapoor, G.; Saigal, S.; Elongavan, A. Action and resistance mechanisms of antibiotics: A guide for clinicians. J. Anaesthesiol. Clin. Pharmacol. 2017, 33, 300–305.
17. Uma Maheswari, R. Phenotypic and Genotypic Characterisation of Vancomycin Resistant Staphylococcus aureus among MRSA Isolates in a Tertiary Care Hospital. Master's Thesis, Tirunelveli Medical College, Tirunelvel, India, 2019. Available online: http://repository-tnmgrmu.ac.in/id/eprint/11129 (accessed on 23 August 2019).