

Antibacterial and Antifungal effect of Halophilic *Nocardiopsis* Species

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Abstract- Multidrug-resistant strains of microorganisms are nowadays a serious threat to mankind health. With the irregular use of antibiotic drugs, the pathogenic strains of several bacteria, virus and fungi have become resistant to a specific drug. The growing demand for such novel antibiotics is now at a peak level. Thus a rare and a potent halophilic actinomycetales have been found, namely *Nocardiopsis* species. *Nocardiopsis* have gained a much attention in the field of biotechnology and also their unique characteristic is observed in ecological parameter. They are a potent resource of antibiotics, anti-toxin, anti-cancer and immunomodulator like bioactive compounds. Our main aim in this review paper is to highlight those members of *Nocardiopsis* species that are effective antimicrobial producers and are effective against multidrug-resistant strains of bacteria, and fungi. With these supportive pieces of information, this paper will highlight the need for antimicrobial products that are being produced by *Nocardiopsis* species.

Keywords: *Nocardiopsis*, halophilic actinomycetes, multidrug-resistant strains, rare halophiles.

I. INTRODUCTION

Nocardiopsis species comes under the order Actinomycetales of phylum actinobacteria. They have a potent role in producing antimicrobial substances. *Nocardiopsis* grows in the presence of oxygen. Unlike *Mycobacterium*, they lack mycolic acid and hence cannot give acid-fast staining test. High G: C amount is present in their DNA. Being actinomycetes, they possess substrate aerial mycelia harbouring long chain of spores. They are halotolerant in nature and are found in marine and soil associated with high saline conditions. Meyer firstly described it in 1976. They exhibit coarsely grooved colony morphology. Nowadays multidrug-resistant Gram-negative pathogens and Gram-positive pathogens are a serious threat for urinary tract infections as they have modified themselves in secreting β -lactamase and their derivatives like enzymes which degrades side chains of β -lactam antibiotics like penicillin, cephalosporin, monobactam etc. *Pseudomonas aeruginosa* and *Klebsiella pneumonia* are the dreadful UTI's disease-causing multidrug-resistant bacteria as they have developed into producing extended-spectrum β -lactamase (ESBL) proteins. Multidrug-resistant microorganisms are now a serious threat to human health globally.

About half of the carriers of ESBL are existing in the Southeast part of Asia. A bacterium is said to be multidrug resistance if it is resistant to more than one antibiotic. Resistant to antibiotics occur either by cross-resistance mechanism or by the accumulation of a resistance gene on a plasmid containing microorganism. Cross-resistance includes single pumping of several antibiotic molecules out of the cell. Therefore, treatment of multi-drug resistant microorganisms are nowadays much difficult due to no availability of specific drug against it. Bacteria that are found in hospital and cattle farms are regularly exposed to antibiotics and therefore multidrug-resistant strains evolved and spread further. Therefore novel antimicrobial compounds are isolated from a range of different kind of microorganisms which are growing in adverse conditions are therefore an effective solution against multi-drug resistant microorganisms.

Hence bacterial species of the genera *Nocardiopsis* comes at emerging novel microorganisms that are halotolerant antimicrobial producing gram-positive bacteria. Antibiotics such as Naphthospiroones, griseusin, cancer cell killing pendolmycin were isolated from *Nocardiopsis* species. Our main aim in this review paper is to discuss several halophilic *Nocardiopsis* species that can produce potent antimicrobial compounds that are much sensitive against pathogenic bacteria and fungi. Today 70% of the earth's ecosystem is covered with marine water bodies and a range of halophilic Actinomycetes producing potent secondary metabolite compounds and drugs. These potent secondary metabolite compounds can tolerate extreme temperature, pH, stress, salinity. Marine actinomycetes are much potent than terrestrial actinomycetes. *Actinomycetes* are gram-positive, filamentous, bioactive molecules producing organisms. These halophilic antibacterial bioactive molecules are much effective than antibacterial compounds that are produced by mesophilic non-halophilic microorganisms.

Thus *Nocardiopsis* species have evolved to a much extent for producing antibacterial compounds and now comes under a wide area of interest for researchers. Nowadays, medical science field are in much need of such antibiotics due to evolvement of multi-drug resistant microorganisms and also development of chemical based synthetic antimicrobial agents is a tedious task and is less effective. *Nocardiopsis* and *Streptomyces* are the important genera for the production of antiviral, anti-parasitic, antitumor like secondary metabolites during their static phase of growth.

2.1 HABITAT FOR HALOPHILIC *NOCARDIOPSIS* SPECIES

Halophilic actinomycetes of genera *Nocardiopsis*, *Microbacterium*, *Streptomonospora*, *Streptosporangium*, *Actinopolyspora* and *Marinophilus* etc. are recovered from the hypersaline environment such as saline and alkaline water bodies, high salinity like dead sea and black sea, salty ponds and lakes.

2.2 MEDIUM FOR ISOLATING *NOCARDIOPSIS* IN VITRO

Humic acid and their derivatives and vitamin containing medium are favourable culture for isolation of *Nocardiopsis*. The role of humic acid is that it help in the diffusion of the pigment secreted this genus and hence making it easy for morphological identification. They also enhanced sporulation in the medium which retains the viability of the cells during unfavourable conditions.

2.3 MECHANISM FOR TOLERATING HIGH SALINITY

As *Nocardiosis* species are halo tolerant in nature, they survive by two mechanisms in high saline condition- high salt in and low salt, organic solutes-in methods. They are classified into moderate halophilic actinomycetes (15%) and extreme halophilic *actinomycetes* (30%). Assimilation of inorganic salts and organic weight with low molecular weight generally balance osmotic potential and intracellular salt levels.

2.4 NOCARDIOPSIS SPECIES PRODUCING ANTIBACTERIAL COMPOUNDS

Similarly antibiofilm effect of *Nocardiosis* species GRG-1 (KT 235640) has been evaluated against biofilm-forming gram-negative bacteria causing UTI's (Rajivgandhi et al., 2019). This strain produces pyrrolo 1,2-β pyrazine-1, 4-dione hexahydro-3-(2-methylpropyl) antibiotic which prevents bacterial bio film production and its viability against *E.coli* and *P. mirabilis*.

Griseusin D, an antibiotic was isolated from an alkaliphilic *Nocardiosis* species. It was a kind of pyranonaphthoquinone antibiotic. The structure of griseusin D determined as 5-one-4-hydroxy-12- methoxygriseusin by the assay of spectroscopic analysis, related to standard information and single-crystal X-ray method (Li, 2007).

An antibiotic WA-52-A is isolated from *Nocardiosis dassonvillei* from Wadi Araba, Egypt which comes under class macrolide that mainly includes erythromycin, roxithromycin that are helpful in the cure of lungs, dermal tissue, genital , *Helicobacter pylori* infections (Ali et al., 2009). A thiopeptide TP-1161 was isolated from marine sediment derivative *Nocardiosis* species by microwell plate fermentation method which is structurally and biologically characterized (Engelhardt et al., 2010).

Similarly, *Rhodococcus*, *Sacharomonospora*, *Micromonospora*, *Streptomyces*, *Streptosporangium* isolates were extracted from the marine sediment that shows antimicrobial property like *Nocardiosis* species. The largest arrayed includes 7 *Nocardiosis* isolates and is categorized into 4 sub clusters nearer the closest type strains, *Nocardiosis exhalans*, *Nocardiosis alba*, *Nocardiosis listeri*, and *Nocardiosis umidischolae*. A similar *Nocardiosis* species associated with a marine sponge produced a lipopeptide biosurfactant compound that increases the bioavailability of hydrophobic substrate through solubilizations or desorption (Gandhimathi et al., 2009).

Some rare actinomycetes are isolated from Algerian Sahara of genera *Nocardiosis* and *Saccharothrix* on humic acid and Vitamin B agar medium that shows characteristic antimicrobial property against bacteria (Quadri, 2016).

An alkalophilic *Nocardiosis dassonvillei* OPC-15 was isolated from Mino City, Osaka, Japan which can produce 1,6-Dihydroxyphenazine after incubation for 6 days at 27°C. *Nocardiosis dassonvillei* was the first that can produce phenazine antibiotic (Tsujiyo et al., 1988). A halotolerant HR-4 strain belonging to the genus *Nocardiosis* showed antibacterial effect against gram-positive bacteria as well as antifungal one. The novel strain shows more than 95% similarity with *Nocardiosis rosea*. The unique natural compound was named as 7-deoxy-8-O-methyltetrangomycin having a unique arrangement which belongs to class angucyclinones (Rabia-Boukhalfa et al., 2017).

2.5 NOCARDIOPSIS SPECIES PRODUCING ANTIFUNGAL COMPOUNDS

Nocardiosis ZoA1 shows antifungal activity against *Pythium myriotyllum* and also a better antibiofilm activity compared to the present antibiotics. Scanning electron microscope has revealed anti-fungal activity against *Pythium myriotyllum* and various phytopathogens. The antimicrobial compound from *Nocardiosis ZoA1* was tested against *Staphylococci* CoNS, a lab isolated coagulase negative bacteria. Interestingly; it had shown high antimicrobial activity as compared to vancomycin, ciproflaxacin and gentamycin with a zone of inhibition of 25mm against *Staphylococcus capitis* (Sabu, 2017).

Nocardiosis gilva YIM 90087 is a halophilic *actinomycete* which had shown antifungal activity against three plant infectious fungi of genus *Fusarium* by secreting a novel antifungal compound called p-terphenyl. Members of genus *Fusarium* causes head blight of potato name disease. The antifungal p-terphenyl consists of a benzothiazole group which provides the antifungal compound its functionality. It was also studied that the minimum inhibitory concentration of this compound against the three infective fungi was in the range of 8-128 µg/ml. (Tian, 2013).

(Chen, 2018) studied the halophilic, filamentous *actinomycetes* TRM20105 strain which is isolated from the cotton field of an endorheic basin called Tarim Basin which is situated in the northwest part of China. The strain TRM20105 has exhibited antifungal activity against *Candida albicans* in a fermentation broth. After performing 16S rDNA phylogenetic assay, it was confirmed to be a member of genus *Nocardiosis*. It was judged approximately to be a actinomycetes because scanning electron microscope imaging had revealed toruliform spores and aerial filamentous mycelium structure of the colony.

Chitin, being the abundant polymer is present in the cell wall of pathogenic fungi and crustaceans. Chi A and B are the chitin degrading enzymes produced by an alkaliphile namely *Nocardiosis prasina* OPC-131. Although this paper have discussed about characterization of chitinase genes (Tsujiyo, 2003).

II. CONCLUSION

As stated above informations, our conclusive information related to antibacterial and antifungal compounds derived from *Nocardiosis* can be summarized. It can be stated that Griseusin D, pyrazine, WA-52, TP-1161 showed antibacterial activity. OPC-15 strain of *Nocardiosis* shows antibacterial and antifungal activity. Similarly, potent antifungal compounds are also produced by *Nocardiosis ZoA1* that revealed anti-fungal activity against *Pythium myriotyllum* as it showed high antimicrobial activity as compared to vancomycin, ciproflaxacin and gentamycin with a zone of inhibition of 25mm against *Staphylococcus capitis*. The antibiotic p-terphenyl exhibited fungicidal activity against three pathogenic fungi that cause *Fusarium* head blight. Strain TRM20105 showed antifungal activity against *Candida albican*. As highlighted above information, researchers from both industrial and academic background should focus on marine-derived halophilic *Nocardiosis* species as they are a potent tool for various primary and secondary metabolites like antimicrobial and antifungal production of commercial use. Commercial production of such antimicrobial compounds can be a effective tool against multidrug resistant pathogenic microorganisms. Not only humans, but plants that are also affected by phytopathogens can be treated well with the derived products of this genus. Hence, it can be concluded that halophilic *Nocardiosis* species are a good source for antimicrobial compounds. If systematic screening and proper molecular characterization are done then it will motivate us to extract more unique species of this genus with appreciable antimicrobial compounds of choice.

III. REFERENCES

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