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Actinomycetes as Antimicrobial Agents: An Overview

Nalinee Kumari[1*], Rekha Mithal[2] and Ekta Menghani[3]

[1,3]Department of Biotechnology JECRC University Jaipur, India
[2]Chemistry JECRC College Jaipur, India
E-mail: [1]nalineek9@gmail.com

Abstract—*Actinomycetes show very interesting characteristics as they are aerobic, spore forming gram-positive bacteria, belonging to the order Actinomycetales characterized with substrate and aerial mycelium growth1.They have high (G+C) ratio of the DNA. It represents one of the largest taxonomic units among the 18 major lineages currently known within the domain bacteria.The name "Actinomycetes" was derived from Greek "atkis" (a ray) and "mykes" (fungus), having characteristics of both Bacteria and fungi. The actinomycetes are potential producers of antibiotics and of other therapeutically helpful compounds. The bioactive secondary metabolites produced by actinomycetes includes antibiotics, antitumor agents, immunosuppressive agents and enzymes. Antimicrobial agents are natural or synthetic chemical substances which have the capability of inhibiting or terminating whole metabolic cell activity. These chemical molecules are classified depending upon their targets. They can also be referred to as broad or narrow spectrum depending on its mode of action towards the targets. They include cell wall synthesis, protein synthesis and also DNA replication. The major class of antibacterial agents are the β-lactams (including penicillins, cephalosporins, monobactams, and carbapenems), aminoglycosides, tetracyclines, sulfonamides, macrolides (such as erythromycin), quinones and glycopeptides (vancomycin).*
Therefore, in present research work attempts were made to search for those actinomycetes having Novel antimicrobial activity against multidrug resistant pathogens causing various infections.

Keywords: *Actinomycetes, Multidrug resistant, Erythromycin, β-lactams, Antimicrobial agents.*

1. INTRODUCTION OF ACTINOMYCETES

Production of various natural drugs and other bioactive metabolites has been paid a great attention. Streptomycin was discovered from a Streptomyces in 1945 by Selman A. Waksman, to promote the development, utilization and taxonomy of actinomycetes properties in the world[1]. Sir Alexander Fleming first discovered the antibiotic penicillin from the mould *Penicillin notatum* in 1929 at St. Mary's hospital in London. He observed that *Penicillin notatum* destroyed a staphylococcus bacterium in culture. Penicillin has bactericidal activity to many of gram-positive bacteria and acts by inhibiting transpeptidation thus preventing new cells from forming walls[2]. This antibiotic belongs to the beta-lactam family.

2. SECONDARY METABOLITES FROM ACTINOMYCETES

Microbial metabolites have been considered always as great concern in the discovery of antimicrobial agents. Today novel compounds with therapeutic applications are waiting to be discovered from the secondary metabolites, especially produced by actinomycetes. Actinomycetes have the potential to produce secondary metabolites with various biological activities[3].

Actinomycetes especially Streptomyces species are widely known as industrially important microorganisms as they are a rich source of numerous valuable bioactive natural products with potential applications[4] and are prolific manufacturers of secondary metabolites, various of which have commercial importance as antibiotics, anti-parasitic and antifungal agents, herbicides, pesticides, anticancer or immunosuppressive agents and as industrially important enzymes. 70% have been isolated from Actinomycetes bacteria and out of which 75% and 60% are used in medicine and agriculture in that order. Secondary metabolites, to a great extent, are species-specific and in contrast to primary metabolites, often accumulate in considerable quantity, which is a main factor in their commercial importance[2]. Actinomycetes have wonderful financial significance as the secondary metabolites produced by them such as antibiotics, other medicinal compounds, toxins, pesticides and animal and plant growth factors. The best identified secondary metabolites produced by Actinomycetes are the antibiotics. Antibiotics are really referred as the 'wonder drugs' for their effectiveness against pathogenic microorganisms. Secondary metabolites are not essential for vegetative growth of the producing organisms but they play a role as differentiation compounds conferring adaptive roles, such as, functioning as defense compounds or signaling molecules in biological interactions. They are produced at the end of the exponential growth phase and their syntheses critically depend on the growth conditions provided

them. Production is usually affected by the source of nutrient such as carbon or nitrogen . They are structurally varied and most of them have biological activities, such as antimicrobial agents, toxins, pesticides, ionophores, bio regulators, and quorum signaling. These bioactive metabolites are greatly used as antimicrobial agents for the treatment of various diseases[5]. Secondary metabolites isolated by actinomycetes exhibit a great number of miscellaneous and multipurpose biological effects. The order actinomycetales are well-known producer of bioactive metabolites with a path record of over 10,000 antimicrobial agents in medical use.

3. MARINE ACTINOMYCETES

It has been discovered that actinomycetes are distributed in the different marine ecosystems and culture dependant and independent methods have demonstrated that native marine actinomycetes exist in the oceans. They show diversity among other actinomycetes. Many of which have potential to develop therapeutic agents with novel activity. In the recent study the actinomycetes were isolated from Caspian Sea sediments at a depth of 5-10 m. Out of them some strains were used for the antibacterial activities using Kirby-Bauer disk diffusion method. Hydrolytic exo-enzymatic (amylase and protease) activities were performed. Antibiotic susceptibility tests were performed against some test organisms. As a result marine actinomycetes were found potent source of bioactive compounds and antibiotics[6]. Marine actinomycetes have been isolated for the production of enzymes. L- glutaminase enzyme produced by various microorganisms but the actinomycetes have been found to produce a large amount of L- glutaminasen enzyme at different conditions. The favourable conditions for the maximum production was at temperature 30^0 c, pH 7, salinity 3.5% and time 96 hrs at 480 nm.

4. METABOLITES PRODUCED BY MARINE ACTINOMYCETES

Although the exploitation of marine Actinomycetes as a source for discovery of novel secondary metabolites is at an early stage, numerous novel metabolites have been isolated in the past few years. Abyssomicin C is a novel polycyclic polyke- tide antibiotic produced by a marine Verrucosispora strain. It is a potent inhibitor of para-aminobenzoic acid biosynthesis and, therefore, inhibits the folic acid bio-synthesis at an earlier stage than the well-known synthetic sulfa drugs[7]. Abyssomicin C possesses potent activity against Gram-positive bacteria, including clinical isolates of multiple-resistant and vancomycin-resistant Staphylococcus aureus. Abyssomicin C or its analog has the potential to be developed as antibacterial agent against drug-resistant pathogens. Diazepinomicin (ECO-4601) is a unique farnesylated dibenzodiazepinone produced by a Micromonospora strain[8]. It possesses antibacterial, anti-inflammatory and antitumor activity. It has a broad spectrum of in vitro cytotoxicity and has demonstrated in vivo activity against glioma, breast and prostate cancer in mouse models. The preclinical development of ECO- 4601 as an anticancer agent has been completed by Ecopia Bio-Sciences Inc. Ecopia filed Clinical Trial Application (equivalent to Investigational New Drug application in the USA) for ECO-4601 in Canada on 3 January 2006. Salinosporamide A (NPI-0052) is a novel b- lactone-g-lactam isolated from a fermentation broth of a new obligate marine Actinomycete, Salinispora tropica. NPI-0052 is an orally active proteasome inhibitor that induces apoptosis in multiple myeloma cells with mechanisms distinct from the commercial proteasome inhibitor anticancer drug Bortezomib[9]. NPI-0052 is being developed by Nereus Pharmaceuticals, Inc. and is scheduled to enter clinical studies for treatment of cancer in humans in 2006. NPI-0052 represents the first clinical candidate for the treatment of cancer produced by saline fermentation of an obligate marine actinomycete. In addition to the production of NPI-0052, Salinispora tropica strains also produce two unprecedented macrolides, sporolides A and B. Sporolides A and B appear to be synthesized from two different polyketides, containing a large number (23 out of 24 carbon skeleton) of oxidized carbons. This, in part, contributes to the highly unusual structures of the sporolides. Even though sporolides have not demonstrated any biological activity in the few antimicrobial and anticancer screens tested, these structures demonstrate the tremendous potential of marine actinomycetes.

5. ANTIMICROBIAL AGENTS

The first antibacterial agent prontosil was derived in 1935 by Gerhard Domagk and was the first of the “sulfa” drugs discovered and this discovery was escorted in the antibiotic era. Bacteriostatic agents are those agents which inhibit the growth of microorganisms for example tetracycline, inhibit the growth and multiplication of bacteria. Exposure to a bacteriostatic agent, cells in a susceptible population stop dividing. However if the agent is removed, the cells once again multiply. Bactericidal agents, are those agents which not only inhibit the growth but also trigger pathways within the cell that causes death of microorganisms for example fluoroquinolones. The actions of bactericidal drugs are irreversible so once susceptible cells are exposed to a bactericidal agent, they die[10]. Antimicrobial agents are the chemical compounds that inhibits or kill the microorganisms. They are natural synthetic chemical compounds which have the capacity of interfering in the metabolic activity of the organisms. They can be divided on the basis of their activity as broad spectrum and narrow spectrum antibiotics.

Natural products are secondary metabolites that are only produced by certain microorganisms and are frequently large, elaborated organic molecules that require complex enzymatic synthesis. Several antimicrobial agents are known; but, not all of them can be used because of their antimicrobial activity they can be toxic to human beings. Antimicrobials have to be non-toxic, non-allergenic, effective and selective, chemically stable, active against possibly more than one bacterium and

should be low-priced. The ratio between the therapeutic effect and the toxic effect in the human body is described by the drugs therapeutic index (TI)[11]. Antibacterial agents or antibiotics belong to a much larger group of compounds that known as antimicrobial agents. Antibiotics are not only natural compounds, produced by microorganisms but also are chemically modified molecules or man-made synthetic molecules.

They can also be classified based upon their mechanism of action. The four classes are:- 1) protein inhibitors, 2) DNA RNA inhibitors, 3) cell wall inhibitors, 4) folate inhibitors[12].

REFERENCES

[1] Waksman, S.A., The actinomycetes, vol. 2. Classification, identification and descriptions of genera and species. The Williams & Wilkins Co., Baltimore. (1961)

[2] Fleming A., on the antibacterial action of cultures of a Penicillium, with a special Reference to their use in the isolation of *B. influenze*, "*Br. J.Exp. Pathol*."**10:**226-236 (1929)

[3] Marinelli F, Marcone GL, Microbial secondary metabolites. Comprehensive biotechnology second edition. Burlington, *American: Academic Press*; 285-297 (2011)

[4] Miyadoh, S., Research on antibiotic screening in Japan over the last decade. A producing microorganism approach, "*Actinomycetologica*" **9**:100-106 (1993)

[5] Sanchez S, Demain AL. Metabolic regulation of fermentation processes. "*Enzyme and Microbial Technology"*,**31**:895-906 (2002)

[6] Mojtaba M., Hamed N., Javad H., Aboulghasem R., Screening of Antibacterial Producing Actinomycetes from Sediments of the Caspian Sea "*Int J Mol Cell Med Spring*" **2(6)**(2013)

[7] Bister B, Bischoff D, Strobele M, Riedlinger J, Reicke A, Wolter F, Bull AT, Zahner H, Fiedler H-P, Sussmuth RD: Abyssomicin C–a polycyclic antibiotic from a marine Verrucosispora strain as an inhibitor of the p-aminobenzoic acid/tetrahydrofolate biosynthesis pathway. "*Angew Chem Int Ed Engl"*, **43**:2574-2576 (2004)

[8] Charan RD., Schlingmann G., Janso J., Bernan V., Feng X., Carter GT: Diazepinomicin, a new antimicrobial alkaloid from marine Micromonospora sp."*J Nat Prod*",**67**:1431-1433 (2004)

[9] Chauhan D., Catley L., Li G., Podar K., Hideshima T., Velankar M., Mitsiades C., Mitsiades N, Yasui H, Letai A et al.: A novel orally active proteasome inhibitor induces apoptosis in multiple myeloma cells with mechanisms distinct from Bortezomib. *Cancer Cell* **8**:407-419 (2005)

[10] Stephen J. Cavalieri et al., Marie B., Coyle Coordinating Editor, *Manual of antimicrobial susceptibility testing*, "*American society for Microbiology"* (2005)

[11] Gable R.S., Comparison of acute lethal toxicity of commonly abused psychoactive substance *"Addiction*" **99**, 686-696*,* (2004)

[12] Walsh, C., Antibiotics: actions, origins, resistance. American Society for Microbiology Press: Washington DC, "*Protein Sci.***" 13(11)**: 3059–3060 (2004)