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"Search for Antimicrobial Agents Produced by the Soil Actinomycetes"

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Abstract

Actinomycetes are biotechnologically important bacteria which are well exploited for secondary metabolites. Screening, isolation and characterization of capable strains of actinomycetes producing potential secondary metabolites has been a most important area of research by many groups worldwide for many years. Actinomycetes are the foundation of the antibiotics industry and hold a significant role in producing variety of drugs that are extremely vital to our health and nutrition. Research has been demonstrate that a large number of antimicrobial agents have been produced from the soil. One of the first antibiotics used is streptomycin produced by *Streptomyces griseus.* Among Actinomycetes, approximately 7600 compounds are produced by *Streptomyces* species. The actinomycetes are a group of gram-positive bacteria that exhibit characteristics of both bacteria and fungi. The genus *Streptomyces* is responsible of the synthesis of the majority of antimicrobial agents with clinical importance example:- Amphotericin, Erythromycin, Streptomycin, Tetracycline, and Rifamycin. Another group of gram-positive bacteria present in soil and responsible for the production of antimicrobial agents with clinical and agricultural importance is genus *Bacillus.* Especially in hospitals, there are strains of *Staphylococcus* bacteria that are resistant to, not just one, but nearly all known antibiotics. The search for Novel antimicrobial agents with clinical importance is significant since many clinical pathogens such as *Mycobacterium tuberculosis*, *Streptococcus pneumoniae***,** and *Staphylococcus aureus* are developing resistance to routine used antimicrobials. Therefore, in present research work attempts were made to isolate actinomycetes having antimicrobial activity against multidrug resistant pathogens causing various infections/diseases.

Keywords: Actinomycetes, Antimicrobial agents, MDR

Introduction To 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 A. Waksman, to promote the development, utilization and taxonomy of actinomycetes properties in the world. Sir Alexander Fleming first discovered the antibiotic 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. Actinomycetes are potential producers of many antimicrobial compounds[1]. Research has been demonstrate that a large number of antimicrobial agents have been produced from the soil and aquatic systems[2]. Most of the actinomycetes are free living and abundantly distributed in natural environment .They are found in both terrestrial and aquatic environment and have high tolerance in adverse condition of the environment. For the study of microbial diversity use of molecular techniques has been brought a great achievement in the microbial ecology like in the soil[3]. A range of bioactive secondary metabolites produced by actinomycetes with various biological activities includes; antibiotics, antifungal, antibacterial, antiparasitic, immunosuppressive agents, enzymes etc. Actinomycetes species have been found well known saprophytic organisms that decompose the organic matter, especially they degrade the biopolymers that includes starch, chitinin soil, and lignocellulose. Various antimicrobial compounds have been isolated from the actinomycetes such as, aminoglycosides, anthracyclines, macrolides b- lactams, peptides, polyene, actinomycins tetracyclines etc.

Antimicrobial Agents

The first antibacterial agent prontosil was derived in 1935 by Gerhard Domagk.[4, 5] Protonsil was the first of the "sulfa" drugs discovered and this discovery was lead 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 with in 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[6]. 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.

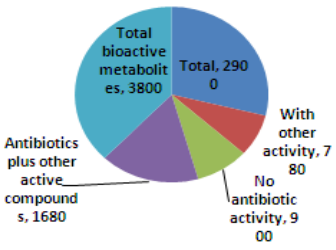
Soil Antimicrobial Agent Producing Microbes

Microorganisms like gram positive and gram negative bacteria and fungi have the capability to synthesize various types of antimicrobial agents but the major sources of

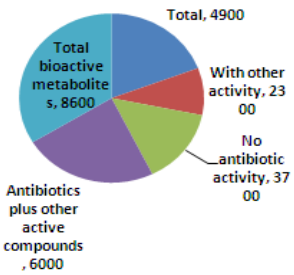
antimicrobial agents are the actinomycetes and they are to cultivable producers that are present in the soil[7]. The actinomycetes are a group of gram-positive bacteria that show characteristics of both bacteria and fungi. They produce filamentous structures which forms pseudo-mycelia. They are spore forming microorganisms and have cell wall, flagella and ribosomes like in bacteria. 10% - 33% of the total bacteria present in soil is of bacteria, especially the genera *Streptomyces* and *Nocardia* present in a great number[8]. Streptomyces produces a number of antimicrobial agents that have clinical and agricultural importance included as amphotericin, erythromycin, streptomycin tetracycline, and rifamycin[9]. Bacillus is the another group of organism that have the ability of producing antimicrobial agents in the growth curve of their life cycle having clinical and agricultural significance.

Actinomycetes as Producers of Antibiotics

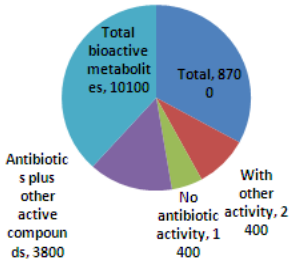
Any chemical or natural origin, which kill or inhibit the growth of other cells and have low molecular weight molecules produced by microorganisms as secondary metabolites. Actinomycetes are the potential producers of antibiotics especially from the genera Streptomyces and Micromonospora[10] and the number of compounds from Streptomyces species is 7600. Out of 12000 antibiotics that are discovered from the last 5 decades 70 % are from actinomycetes and 30% from fungi and other bacteria[12]. The antibiotics obtained from actinomycetes sort into several major structural classes such as amino glycosides, ansamycins, anthracyclines, β-lactam, macrolides and tetracycline. There are a number of antibiotics which is produced by streptomyces[9].They all have clinical importance and have antibacterial, antifungal, antiparasitic antiviral activities.. The streptomycin antibiotic was isolated from *Streptomyces griseus*[11]



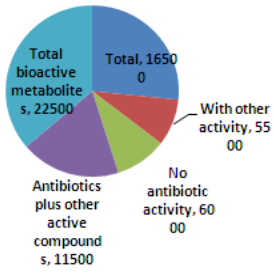
Source-Actinomycetes



Source-Bacteria



Source-Fungi



Total

Resistance to Antimicrobial Agents

The overuse of the antibiotics has caused an increasingly multiple drug resistant strains (MDR) they includes streptococcus, pseudomonas and staphylococcus. The search for novel antimicrobial agents with their clinical importance is very necessary as increase in the number of resistant pathogens like Mycobacterium tuberculosis, Enterococcus, Pseudomonas sp, streptococcus pneumoniae and staphylococcus aureus[13]. It has been reported in new England journal of medicine researchers identified bacteria to be resistant to currently all available antibiotics. Microorganisms have acquired resistant through a number of ways. Bacteria can also acquire resistant to antimicrobial agents by genetic events like: mutation, conjugation, transformation, transduction.[13, 14]

The Need for Novel Antimicrobial Agents

The occurrence of drug resistant bacteria is rising at an alarming rate in both developing and developed countries. From this statement alone, it should be clear that the need for the development of novel antimicrobial agents is of greatest significance. In the present antibacterial drug pipeline, there is only a minute spark of expectation 36. Some experts call this time the "dawn of the post-antibiotic era due to this quick increase in resistant bacteria together with the slow development of novel agents"40. There is an urgent need for the new antibiotics because of the unavoidable rise of resistance. Three classes of antibiotic-resistant pathogens are emerging as major threats to public health. The first class of pathogen is *methicillin resistant Staphylococcus aureus* MRSA. It is investigated that because of MRSA approximately 19,000 deaths occur per year in the United States. The growing frequency of MRSA increases the likelihood that vancomycin-resistant *Staphylococcus aureus* (VRSA), which is same as of MRSA but more complicated to treat than that of MRSA.

Conclusions

There are thousands of antimicrobial metabolites that are recognized until now and the number of all known natural products is around one million. Most of them derived from Actinomycetes. It is an obvious question where is the border in the diversity of natural products? Where is the limit or is there any limit at all, in the continuous increase in the number of Novel microbial compounds. The reinvestigation of the known natural or microbial compounds and specially the whole microbial population with at extensive range, more selective, sensitive and specific methods, especially in the light of the expanding knowledge of microbial genetics and acquired knowledge about various genomes, would be fruitful. In all means, in the future we will discover more and more Novel functions; new activities of the microbial metabolites will understand their real role and function and will develop the area of their practical utilization.

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