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Actinomycetes: Potential and Applications

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Abstract: Actinomycetes are considered as one of the most diverse groups of filamentous bacteria proficient of thriving into different types of ecological niches due to their bioactive potential. They make up the most promising source of wide range of important enzymes, some of which are produced on an industrial scale, but many other remained to be harnessed. Actinomycetes are well known for their metabolic versatility that is frequently accompanied by the production of primary and secondary metabolites of economic importance. Members of many genera of Actinomycetes have potential for use in the bioconversion of underutilized agricultural and urban wastes into high-value chemical products. The main focus of this review is to the highlight the various applications and uses of actinomycetes in various fields.

Key words: ***Actinomycetes, Secondary Metabolite, Antimicrobial, Enzymes.***

I. INTRODUCTION

"Actinomycetes" name has been derived from Greek "atkis" (a ray) and "mykes" (fungus), possessing the characteristics of both bacteria and fungi (Das et al., 2008). Actinomycetes are spore forming gram-positive bacteria, present aerobically in nature. They represent one of the largest taxonomic units among the18 major lineages currently recognized within the domain bacteria (Ventura et al., 2007). Actinomycetes have successfully produced large number of important secondary metabolite such as antibiotics compounds including streptomycin, actinomycin and tetracycline (Barrios-Gonzalez et al., 2005). Actinomycetes help in degrading a wide range of hydrocarbons, pesticides, aliphatic and aromatic compounds. They perform microbial transformations of organic compounds, a field of great commercial value.

Actinomycetes make upto the 80% of the world's antibiotics commonly made from the genera *Streptomyces* and *Micromonospora*. *Streptomyces* sp. have been recognized as the most prolific producers of bioactive metabolites with wide range of useful activities .Actinomycetes also play an important role in plant biotechnology as strains with antagonistic activity against plant pathogens are useful in bio control. Actinomycetes produce bioactive secondary metabolites which includes antibiotics, antitumor agents, and immunosuppressive agent sand enzymes. These metabolites are known to possess antibacterial, antifungal, antioxidant, neuritogenic, anti-cancer,anti-

algal, anti-helmintic, anti-malarial and anti-inflammatory properties (Kekuda *et al.,* 2010; Ravi kumar *et al.,* 2011).

The anti-infective turn-over of Actinomycetes is over 79 billion US dollars in 2009 that includes almost 166 antibiotics and derivatives such as the β-lactam peptide antibiotics, the macrolide polyketide erythromycin, tetracyclines, aminoglycosides, daptomycin and tigecycline. Actinomycetes continue to play a highly significant role in drug discovery and development. Actinomycetes have proved their ability to produce a variety of bioactive secondary metabolites and for this reason, the discovery of novel antibiotic and non-antibiotic lead molecules through microbial secondary metabolite screening is becoming increasingly important.

II. Occurrence And Habitat Of Actinomycetes

Actinomycetes form thread-like filaments are the most abundant organisms present. Actinomycetes are widely distributed in soil, compost, fodder, leaf litter, water and other environments. They are often considered as the prokaryotic equivalent of fungi. They grow as hyphae like fungi and are responsible for the characteristically "earthy" smell of freshly turned healthy soil (Sprusansky et al., 2005). They play an important role in recycling of complex organic material. They effectively compete with other microbes and survive under harsh and unfavourable environmental conditions.

Soil is the best source of Actinomycetes and mostly studies have been focussed and concentrated on soil ecosystem. They are found abundantly in all soils, cultivated and uncultivated, fertile and infertile, in various regions throughout the world. (Barakate et al., 2002). Soil Actinomycetes depend on the pH as a major environmental factor determining the distribution and activity. Acidic soils with pH below 5.0 consist of Neutrophiles that occur in less number, whereas acidophilic streptomycetes are present abundantly. Compost consists of many active mesophilic Actinomycetes. Recently, the studies have been carried out in aquatic habitats such as freshwater and marine situations. Many investigators considered Actinomycetes as part of indigenous micro flora in marine habitats, whereas others considered them as wash-in components that survive in marine and littoral sediments as spores. The species from marine habitats has shown salt tolerance. The studies on occurrence, survival and activity of Actinomycetes in certain extreme habitats are available. The acidophilic and aciduric *Streptomycetes* are widespread in acidic soils. Actinomycetes have been reported from various extreme environments like thermal spring, marine sediments and crater lakes (soda lakes). Lonar Lake, a crater formed by meteoritic impact, offers a unique ecological niche. The lake water is salty and alkaline (pH 9.5 to 10.0) due to high content of sodium carbonate (Thakkar &Ranade, 2002).

Many mesophilic Actinomycetes show activity in the compost in the initial stages of decomposition. However, the capacity for self-heating during decomposition provides ideal conditions for obligate or facultative thermophilic Actinomycetes. Some genera like thermo-actinomycetes and Saccharomonospora are strictly thermophilic. Animal manure is an ideal choice for growth of thermophilic actinomycetes.

III. Role Of Actinomycetes As Potential Producer Of Antibiotics

Actinomycetes are important sources of compounds for drug discovery and have attracted considerable pharmaceutical, chemical, agricultural and industrial interest. Actinomycetes are best known for their ability to produce antibiotics. Two third of today's antibiotics are obtained from Actinomycetes. The discovery of antimicrobial agents from Actinomycetes led to a breakthrough in the world of medicine, due to their tremendous contribution in saving human from infectious diseases. Actinomycetes hold a significant role in producing variety of drugs that are extremely important to

our health and nutrition (Magarvey *et al.,* 2004).Waksman and Woodruff reported the isolation of actinomycin, the first actinomycetes produced antibiotic to be obtained in a crystalline form. After this discovery, the attention of other investigators all over the world turned towards detailed scrutiny of the actinomycetes in screening programmes. It was followed by the discovery of streptothricin (1942) and streptomycin (Schatz, A. et al, 1944). The chemotherapy of tuberculosis was made possible with streptomycin. Until 1974 antibiotics of actinomycete origin were almost exclusively confined to Streptomyces.

Recently efforts have been made to target and explore rare actinomycetes like *Actinomadura, Actinoplanes, Ampullariella, Actinosynnema* and *Dactylosporangium* for the search of new antibiotics. Target directed screening is being used for screening of antibiotic producing actinomycetes. Molecular biological techniques have helped on large scale in finding new antibiotics from Actinomycetes. During recent decades, we have seen an increasing number of reports on the progressive development of bacterial resistance to almost all available antimicrobial agents. Search for new antibiotics effective against multidrug resistant pathogenic bacteria is presently an important area of antibiotic research. Majority of antibiotics are derived from microorganisms especially from the species actinomycetes (Bérdy, 1995). Almost 80% of the world's antibiotics are known to come from Actinomycetes, mostly from the genera Streptomyces and Micromonospora (Jensen *et al.,* 1991; Hassan *et al.,* 2011).

Among Actinomycetes, around 7600 compounds are produced by *Streptomyces* species. The most frequent producers, the *Streptomyces* species produces 7600 compounds (74% of all actinomycetales), while the rare actinomycetes represent 26%, altogether2500 compounds. In this group *Micromonospora, Actinomadura, Streptoverticillium, Actinoplanes, Nocardia, Saccharopolyspora* and *Streptosporangium.* Many of these secondary metabolites are potent antibiotics, which has made streptomycetes the primary antibiotic-producing organisms exploited by the pharmaceutical industry (Ramesh *et al.,* 2009; Jensen *et al.,* 2007). The capacity of the members of the genus *Streptomyces* to produce commercially significant compounds, especially antibiotics, remains unsurpassed, possibly because of the extra-large DNA complement of these bacteria (Kurtböke, 2012). The antibiotics from actinomycete sort into several major structural classes such as amino glycosides (e.g., streptomycin and kanamycin) (Nanjawade et al., 2010), ansamycins (e.g., rifampin) (Floss and Yu, 1999), anthracyclines (e.g., doxorubicin) (Kremer and Van Dalen, 2001), β-lactam (cephalosporins) (Kollef, 2009), macrolides (e.g., erythromycin) and tetracycline (Harvery and Champe, 2009). Secondary metabolites produced by actinomycetes exhibit a great number of diverse and versatile biological effects, first of all antimicrobial activities. The order actinomycetales are renowned producer of bioactive metabolites with record of over 10,000 antimicrobial agents in clinical use (Demain, 2009). The secondary metabolites produced by actinomycetes reveal multifarious biological activities such as antibacterial, antifungal, antiviral, anticancer, antiprotozoal, anticholesterol, anti-ageing, antihelminth and immunosuppressant.

The important antibiotics from actinomycetes include Penicillin, Cephalosporins, Tetracyclines, Fattiviracins, Cephamycins, Quinolone, Macrolides, Aminoglycosides, Sulphonamides, Lincomycin and clindamycin, Phencomycin, Fluostatins, Oligomycin, Rifampin, Sparsomyin,anthracyclines, chloramphenicol, nucleosides, peptides and polyethers.

Table 1: Some clinically important antibiotics from actinomycetes.

Antibiotic	**Produced by**	**Activity**	**Reference**
Sagamicin	*Micromonosporasagamiensis*	Antibacterial	(Okachi*et al.,* 1974)
Amiclenomycin	*Streptomyces lavendulae*	Antibacterial	(Okami *et al.,* 1974)

Methylenomycin	*Streptomyces violaceoruber*	Antibacterial	(Haneishi*et al.,* 1974)
Roseoflavin	*Streptomyces davawensis*	Antibacterial	(Matsui *et al.,* 1979; Grill *et al.,* 2008)
Minosaminomycin	*Streptomyces sp.*	Antibacterial	(Hamada *et al.,* 1974)
Libramycin	*Streptomyces sp.*	Antifungal	(Yahagi *et al.,*1974)
Candihexin	*Streptomyces viridoflavus*	Antifungal	(Martin and McDaniel, 1974)
Nanaomycin	*Streptomyces rosa*	Antifungal	(Omura*et al.,*1974)
Purpuromycin	*Actinoplanesianthinogenes*	Antifungal	(Coronelli*et al.,*1974)
Zorbonomycin	*Streptomyces bikiniensis*	Antifungal	(Argoudelis*et al.*1971)
Validamycin	*Streptomyces hygroscopicus*5008	Antifugal	(Wu *et al.,*2012)
Rosamicin	*Micromonospora Rosaria*	Antibacterial	(Anzai*et al.,*2009)
Rifamycin	*Micromonosporarifamycinica*	Antibacterial	(Huang *et al.,* 2008; Huang *et al.,* 2009)
Platenomycin	*Streptomyces platensis*	Antibacterial	(Furumai*et al.,*1973)
Lincomycin	*Streptomyces lincolnensis*	Antibacterial	(Michalik*et al.,* 1975)
Azalomycin	*Streptomyces hygroscopicus*	Antifungal	(Arai and Hamano,1970)
Azalomycin	*Streptomyces malaysiensis*	Antifungal	(Cheng *et al.,*2010)
Streptimidone	*Streptomyces sp.*	Agricultural	(Chatterjee *et al.,*1995)
Kinamycin	*Streptomyces murayamaensis*	Antibacterial	(Gould *et al.,* 1998)
Kuwaitimycin	*Streptomyces kuwaitinensis*	Antibacterial	(Shimi*et al.,* 1973)

Sarkomycin	*Streptomyces sp.*	Antitumor	(Umezawa*et al.,* 1954)
Salinomycin	*Streptomyces albus*	Antiparasite	(Naidenova*et al.,* 2001)
Antimycin	*Streptomyces antibioticus*	Antifungal	(Xu *et al.,* 2011)
Antimycin	*Streptomyces lucitanusus*	Antifungal	(Han et al., 2012)
Tomaymycin	*Streptomyces achromogenes*	Antiviral	(Arima*et al.,* 1972)
Erythromycin	*Actinopolyspora sp.*	Antibacterial	(Huang *et al.,* 2009)
Rapamycin	*Streptomyces Hygroscopicus*	Anti-proliferative immunosuppressant	(Garrity*et al.,* 1993)
Myomycin	*Nocardia sp*	Antibacterial	(French *et al.*,1973)
Lomofungin	*Streptomyces lomondensis*	Antifungal	(Bergy, 1969; Das *et al.,* 2012)
Sclerothricin	*Streptomyces scleogranulatus*	Antifungal	(Kono*et al.,* 1969)
Spoxamicin	*Streptosporangiumox azolinicum*	Antitrypanosomal	(Inahashi*et al.,* 2011)
Avermectin	*S. avermitilis*	Antiparasitic	(Kitani*et al.,* 2011)

IV. ACTINOMYCETES AS A SOURCE FOR INDUSTRIAL ENZYMES V.

Actinomycetes are one of the ubiquitous dominant groups of gram positive bacteria. They constitute a significant component of the microbial population in most soils and can produce extracellular enzymes which can decompose various materials. Their enzymes derived from actinomycetes are more attractive than enzymes from other sources because of their high stability and unusual substrate specificity. Novel enzymes can be obtained from the Actinomycetes that are found in extreme habitats which carry huge commercial potential. Screening of Actinomycetes is done on regular basis for the production of novel bioactive compounds. A wide array of enzymes and their products applied in biotechnological industries and biomedical fields has been reported from various genera of actinomycetes. Since there is vital information available due to the advent of genome and protein sequencing data, actinomycetes have been continuously employed of the production of proteases, cellulases, chitinases, amylases, xylanases, and others (Divya Prakash et al., 2013).

V. BIOSURFACTANTS FROM ACTINOMYCETES

Bio-surfactants are defined as surface-active molecules produced by living cells. They are mainly produced by those microorganisms having some influence on interfaces. Biosurfactants are biodegradable molecules with high specificity; they are amphiphilic and non-toxic in nature (Zajic and Panchal, 1976; Cooper and Zajic, 1980). They can withstand and thrive in extreme conditions of temperature, pH and salt concentration (Desai, 1987; Drouin and Cooper, 1992). The molecules have the ability to decrease the surface tension, critical micelle concentration and interfacial tension (Banat, 1995). The surfactant character of molecules is due to their mixed hydrophilic and hydrophobic nature. All surface-active compounds constitute the emulsion secreted by the cell to facilitate the uptake of insoluble substrate. Emulsan a bioemulsifier produced by Acineotobacter species is the only known product in the market. Actinomycetes play major role in production of bioemulsifiers. Trehalosedimycolates produced by Rhodococcus erythropolis has been extensively studied by Wagner and his group. Biosurfactants have many advantages over their chemically synthesized counterparts. They are highly specific, less toxic and biodegradable. They are effective at extreme conditions of temperature, pH and salinity. They are easy to synthesize from cheaper and renewable feed stocks. A list of important biosurfactants produced from Actinomycetes is given in Table 2.

Table: 2 Types of Biosurfactants produced from Actinomycetes

Biosurfactant	**Microorganism**	**Surface Tension (m N/m)**
Glycolipids:		
Glycolipids	Rhodococcusaurantiacus	26
Glycolipids	Rhodococcus sp. 5AT7	30
Pentasaccharide lipids	Nocardiacorynebacteroids	26
Trehalosetetraester	Rhodococcuserythropolis	26
Trehalosedicorynomycolate	Rhodococcuserythropolis	32-36
Lipopeptides/ Aminolipids:		
Lipopeptide	Streptomyces canus	-
Peptidolipids 'Na'	Nocardia asteroids	-
Fatty acids/ Neutral lipids:		
Fatty acids + Neutral lipids	Nocardiaerythropolis	32
Others:		
Biosurfactant types I and II	Nocardia sp.L-417	29
Phosphatidylethanolamines	Rhodococcuserythropolis	30

VI. ROLE OF ACTINOMYCETES IN TRANSFORMATION OF XENOBIOTICS

Xenobiotics are man-made compounds, frequently halogenated hydrocarbons that are extremely difficult for microbes to breakdown in the environment. Transformation of xenobiotics is defined as the structural modification of components foreign to an organism's metabolism, which occur in its chemical environment. The most characteristic reactions in transformation of xenobiotics are oxidative, reductive, hydrolytic, dehydration and condensation. The ability of actinomycetes to perform a variety of microbial conversions of organic compounds is an important factor in the complicated processes of biodegradation of pollutants in soil and water and in the biodegradation of bio-pesticides, oil spills, chemical waste decomposition and the like.

Members of the genera Nocardia and Streptomyces have ability to perform highly selective chemical modifications of complicated compounds of natural and synthetic origin. Nocardia strains have been found to degrade aromatic hydrocarbons by hydroxylation. Actinomycetes have the ability to hydroxylate aliphatic chains of hydrocarbons in the terminal and sub terminal position and subsequently followed by shortening of the transformed chains. Actinomycetes are able to degrade certain pesticides. The herbicide, dalapon, 2, 2-dichloropropionic acid was degraded by Nocardia strains isolated from soil (Desai JD, 1987). Actinomycetes indigenous to soil and water are probably the first line of attack on hydrocarbon molecules, as these compounds are not broken down by the majority of microorganisms. Actinomycetes are able to degrade certain pesticides and herbicide. The herbicide such as Dalapon, 2,2,-dichloropropionic acid can be degraded by Nocardia strains isolated from soil and DDT (1,1,1-trichloro-2,2-Di-4-chlorophenyl-ethane) can be de-chlorinated by *Streptomyces aureofaciens, Streptomyces cinnamoneous* and *Nocardia erythropolis.*

VI. ROLE OF ACTINOMYCETES IN SOIL FERTILITY AND AGRICULTURAL PRODUCTION

Actinomycetes are involved in all processes that contribute to soil fertility such as nutrient cycling, decomposition of various compounds, formation of beneficial soil humus and in the biological control of plant pathogens, insects and weeds (Kennedy, 1999; Heuer et al. 1997a). The Actinomycetes is growing slowly compared to the true bacteria, so are not competitors, their number decreases with increasing concentration of organic nutrients by the pressure of biological competition with other groups and when nutrients are in low concentration at the beginning, the placement mineralization of plant debris dominate due to reduced carbon and nitrogen source of competition is reduced because the antibodies are heterotrophs depend on the availability of organic compounds, carbon and then the remaining single complex, such as organic acids, sugars and certain polysaccharides such as starch, insulin, chitin, lipids, proteins and long chain aliphatic hydrocarbons and aromatic Actinomycetes mineralize cellulose in pure culture a slow rate of decomposition, also degrade proteins. Free-living actinomycetes have additionally been concerned in the improvement of plant growth byproduction of plant growth-producing substances like auxins and gibberellin-like compounds (Persello-Cartieaux et al., 2003, Bloemberg et al., 2001). It also leads to decrease in root length and increase in root hair formation, so enhancing the potential of the plant to absorb soil nutrients. Besides, there are several developmental processes in which auxin plays a role, together with embryo and fruit development, organogenesis, vascular tissue differentiation, root patterning, elongation and tropistic growth, apical hook formation and apical dominance (Paciorek et al., 2006; Dobbelaere et al., 1999; Bennett et al., 1998). Actinomycetes are known to be durable organisms and thus appropriate for soil applications. The spores of most Actinomycetes endure desiccation and show slightly higher resistance to dry or wet heat than vegetative cells.

Microscopic and microbiological analysis of soil and fertilizer indicates that Actinomycetes (Gutierrez-lugo et al., 1999; Meyer. J, 2000) are of lesser impact than bacteria and fungi but are involved in mineralize some polysaccharides resistant plant and animal tissue, but not immediately respond to organic carbon enrichment, not compete with real bacteria or fungi with simple carbohydrates, but if the compounds are resistant to mineralization. Participate in the formation of humus by the oxidation of plant debris and leaves from the organic portion of soil, some kinds of Ac to grow in culture synthesize complex molecules that are essential in the fraction of humus in soil. Perform the mineralization of green manure, straw and manure at high temperatures which dominate the genre as Thermo Actinomycetes, Streptomyces, the surface of these materials may be white or gray by the activity typical of that group. Plant pathogens, *Streptomyces scabies* and *S. Ipomoeae* are pathogens, causing scab of potato, sweet potato and smallpox (Alexander. M, 1977). There are those who associate with N2 fixing trees in plant roots and Frankia to solve problems of reforestation and land degradation, with actions such as the plant growth promoting bacteria with potential use as biological inoculants (Sturtz .A.V. et al., 2000).

VIII. ENZYME INHIBITORS

Actinomycetes synthesise enzyme inhibitors of low molecular weight. Enzyme inhibitors have received increasing attention as useful tools, not only for the study of enzyme structures and reaction mechanisms but also for potential utilization in pharmacology (Vignardet, C.et. al., 1999). Umezawa reported the first low molecular weight enzyme inhibitor, by a streptomycetes strain. Since then more than 60 inhibitors have been reported including leupreptins, which inhibit papain, plasmin and trypsin. Antipain inhibits papain, chymotrypsin, trypsin and cathepsnin B. Enzyme inhibitors are finding possible uses in cancer treatment. e. g. revistin, an enzyme inhibitor from Streptomyces species inhibit reverse transcriptase. Streptonigrin and retrostatin synthesized by Streptomyces inhibit reverse transcriptase. Alistragin found in culture filtrates of *Streptomyces roseoviridis* which inhibits carboxypeptidase *B. Phosphoramiden*, which inhibits metallo-proteases is produced by *S. tanashiensi (*Goodfellow M. et al., 1988). Marine actinobacteria are the potential source for production of enzyme inhibitors (Stutzenberger F.J et al., 1987; Bode W et. al., 1992) reported different types of enzyme inhibitors viz. -glucosidase, N-acetyl--D-glucosaminidase, pyroglutamyl peptidase and - amylase inhibitors from marine actinobacteria.

IX. ROLE OF ACTINOMYCETES IN BIOREMEDIATION

Actinomycetes are popular for their powerful bioremediating properties. Actinomycetes are effective consumers of antibiotics and chemical complexes. They can degrade high doses of pesticides and chemical complexes. Petroleum hydrocarbons are widely used in our daily life as chemical compounds and fuel. Greater use of result, petroleum has become one of the most common contaminants of large soil surfaces and eventually is considered as a major environmental problem (Sanscartier et al., 2009).There are several ways in which hydrocarbons degraded in the environment. One mechanism through which they can be removed from the environment is Bioremediation. Bioremediation is the use of soil microbes to degrade pollutants to harmless substances (Collin, 2001).

Actinomycetes are the important group which effectively disintegrate and bioremediate the pesticides and other xenobiotics in the environment. Actinomycetes play important roles in the environmental fate of toxic metals with a multiplicity of physico-chemical and biological mechanisms effecting transformations between soluble and insoluble phases and produces significant levels of biosurfactants (Subhajit, 2012). Such mechanisms are important components of natural biogeochemical cycles for metals and metalloids with some processes being of potential application to the treatment of contaminated materials. Role of Actinomycetes in Bioremediation and stress related behaviour has been extensively studied by (Justin et al., 2008). Several Actinomycetes strains from composts are now being investigated to evaluate their capacity to degrade some petroleum hydrocarbons and to decolorize several synthetic dyes in order to reveal their potential application in bioremediation.

Actinomycetes possess many properties that make them good candidates for application in bioremediation of soils contaminated with organic pollutants. They play an important role in the recycling of organic carbon and are able to degrade complex polymers (Good fellow and Williams, 1983). Some reports indicated that Streptomyces flora could play a very important role in degradation of hydrocarbons (Radwan et al., 1998; Barabas et al., 2001). Many strains have the ability to solubilise lignin and degrade lignin-related compounds by producing cellulose- and hemi cellulose-degrading enzymes and extracellular peroxidise (Mason et al., 2001). In some contaminated sites Actinomycetes represent the dominant group among the degraders (Johnsen et al., 2002). Actinomycetes species have the capability to live in an oily environment. So we can apply these microorganisms in Bioremediation to deduct oil pollutants.

X. CONCLUSION

In present review we have summarized the up to date available information about the commercial potential of actinomycetes in knowledge on actinomycetes and their applications in different prospects. Furthermore actinomycetes have shown high potential to be a candidate for therapeutic treatment, more research is been carried out for the deeper understanding of their mechanisms and their therapeutic potential using metagenomics and other advanced approaches. Apart from this actinomycetes play an important role in several industries, their potential is much greater and their applications in future processes are likely to increase in the near future. In past different techniques and approaches were used against pathogenic agents with lower success rate due to increase in their morality rate and emergence of drug resistance. Actinomycetes are open to newer approaches that can include novel discovery strategies that can target new dimensions of microbial diversity.

XI.. REFERENCES

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