REVIEW PAPER

Microbiology

POTENTIAL OF ACTINOMYCETES AS BIOREMEDIATING AND BIOCONTROLLING AGENTS

KEY WORDS: Actinomycetes, bioremediation, secondary metabolite production.

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ABSTRACT

Bioremediation and antibiotic resistance are one of the hot areas of research due to increased level of toxic compounds added to the environment and adaptation of defence mechanisms in microbes to current use antibiotics. Technologies in bioremediation are continuously being improved using naturally occurring microorganisms to clean residues and contaminated areas from toxic organic compounds. In most of the publications, Actinomycetes, types of filamentous bacteria are discussed separately as they play a major role in decomposition. They are widely distributed in soils and manmade environment such as compost heaps. As degradation agents, actinomycetes are important in the degradation of soil organic materials into humus. They secrete a range of enzymes that can completely degrade all the components. They are known for the production of bioactive secondary metabolites. The rapid development of drug resistance strains of pathogens has increased the demands for inventions of novel drugs and antibiotics. For this reason, many researchers have vigorously involved in isolation and screening of actinomycetes from diverse and even unexplored habitats, for their production of antibiotics. The potential of actinomycetes as bioremediation and secondary metabolite production has open exciting avenues in the field of biotechnology and biomedical research.

1 Introduction:

Actinomycetes are ubiquitous group of microbes widely distributed in natural ecosystems around the world (Srinivasan *et al*., 1991). Actinomycetes are gram-positive bacteria showing a filamentous growth like fungi. They are aerobic and widely spread in nature. They are predominant in dry alkaline soil (Jeffrey, 2008). Actinomycetes DNA are rich in G+C content with the GC % of 57 - 75% (Lo *et al*., 2002). These Gram Positive bacteria have been placed within the phylum Actinobacteria, class Actinobacteria, subclass Actinobacteridae, order Actinomycetales which currently consists of 10 suborders, more than 30 families and over 160 genera (Chavan *et al*., 2013). They morphologically resemble fungi and physiologically resemble bacteria (Sultan *et al*., 2002). Like fungi Actinomycetes form threads, filaments, or strands, which spread throughout a compost heap or soil. Actinomycetes have been well known for the production of bioactive secondary metabolites which had antibacterial, antifungal, antiparasitic, anticancer and immunosuppressive activities (Berdy, J., 2005, Jemimah *et al*., 2011, Nonoh *et al*., 2010, Chavan *et al*, 2013, Olano *et al*, 2009) Many of the presently used antibiotics such as streptomycin, gentamicin, rifamycin, erythromycin are the product of actinomycetes (Jeffrey, 2008). The metabolic approach of actinomycetes not only yields an interesting area for research but also provides possibility of commercialization of metabolites generated in the process. They produce enzymes such as cellulose, lipase, amylase and protease which are of industrial importance such as, food, fermentation, textile industries (Sharma *et al*., 2014). They are also reported to produce plant growth promoting hormone (Gopalkrishnan *et al*, 2011). They are well known as degraders of toxic materials and thus are used in bioremediation. They play important role in the recycling of organic carbon and are able to degrade complex polymers (Goodfellow and Williams, 1983).

2 Occurrence and habitat:

Actinomycetes are the most abundant free living saprophytes that form thread-like filaments in the soil. They grow as hyphae like fungi responsible for the characteristically "earthy" smell of freshly turned healthy soil. The actinomycetes exist in various habits in nature and represent a ubiquitous group of microbes widely distributed in natural ecosystems around the world (Chamikara, P., 2016). Actinomycetes are widely distributed in soil and ocean. There are many reports for isolation of actinomycetes from terrestrial soils (Jeffrey, 2008; Iyer and Subramanyam, 2014; Salim *et al*, 2017), marine ecosystem (Attimarad *et al*., 2012; Mohseni *et al*, 2013), mangrove ecosystem (Mangamuri *et al*., 2012; Abidin *et al*., 2016), composts (Workie and Abate, 2016), vermicomposts (Gopalkrishnan *et al*., 2011) Environmental factors influence the type and population of actinomycetes in soil. They are found both at mesophillic (25- 30°C) and thermophillic (40°C) environments (Haseena *et al*, 2016). The pH is also a major environmental factor determining the distribution and activity of actinomycetes. Most of the actinomycetes grow at optimum pH around 7. Vasavada *et al*. (2006) showed that pH, salinity, use of media and carbon and nitrogen sources affect the growth and antibiotic production by actinomycetes. Many mesophillic actinomycetes are active in compost in initial stages of decomposition. However the capacity for self-heating during decomposition provides ideal conditions for thermophillic actinomycetes (Chavan *et al*, 2013). Actinomycetes diversity can also be influenced by the diversity of plant species grown on that particular soil. Since different plants produce different chemical metabolite, so in order to survive the microbes (actinomycetes in this case) need to adapt to the environment (Oskay *et al*; 2004).

3 Structure:

Actinomycetes are characterized by the formation of normally branching threads or rods. The hyphae are generally non-septate. The sporulating mycelium may be branching or non-branching, straight or spiral shaped. The spores are spherical, cylindrical or oval. (Chamikara, P., 2016). Morphologically they resemble fungi may be due the adaptation to same habitat their cell wall composition is similar to that of gram positive bacteria. Due to their filamentous nature and cultural characteristics they have been placed in separate group other than common bacteria.

4 Cultural characteristics:

Actinomycetes show different cultural characteristics when grown on agar surface. Shirling and Gottlieb, (1976) suggested different media for the International Streptomyces Project (ISP) to distinguish and characterize actinomycetes at different level and have been used by many researchers to isolate actinomycetes from soil and other natural habitats such as starch casein agar [SCA] (Kuster and Williams, 1964, Duddu *et al*, 2016, Lekshmi *et al*, 2014), actinomycete isolation agar [AIA] (Pattnaik and Reddy, 2012 Pandey *et al*, 2011), glycerol asparagine agar [GAA] (Pridham and Lyons, 1961, Low *et al*, 2015), Oatmeal Agar [OMA] (Low *et al*, 2015), yeast malt extract Agar [ISP2] (Mohseni *et al*, 2013). They branch and form network of hyphae growing on both on the surface of the agar (aerial mycelium) and under the surface of agar (substrate mycelium). Their growth is characterized by small compact, soft to hard colonies tenaciously adhering to the medium, the surface being either flat or elevated (Sathi *et al*, 2001). The outer zones of the colonies are smooth but fringes of minute hyphae are observed under the low power microscope (Muiru *et al*., 2008). The colour of the the aerial mycelium can range from white, creamy white, chalky, powdery, brown, gray to pinkish and violet and substrate mycelium may vary from brown , yellow to orange (Arifuzzman; Mohseni *et al*, 2013; Jeffrey, 2008, Salim *et al*, 2017, Amit, 2011). They are also reported to form concentric rings on aging (Sathi *et al*, 2001). Many cultures on the surface appears same but they are different when seen from the reverse side of the plate, may be due differences in substrate hyphae. They are found to be pigment producing; blackish brown, yellow to orange, brown orange, brown red (Shirling and Gottlieb, 1966; Mohseni, *et al*, 2013). Many cultural characteristics of actinomycetes have been employed for the purpose of their classification such as actinomycetes are grown on tyrosine agar (ISP7) show melanin pigment production (Pridham *et al*, 1957; Duddu *et al*, 2016), ability to utilize various carbon sources for energy which is determined by their growth on carbon utilization medium [ISP 9] (Pridham and Gottlieb, 1948).

5 Classification of Actinomycetes:

The "Bergey's Manual of Systematic Bacteriology - 2nd edition" for Actinobacteria classification has five volumes, which contain internationally recognized names and descriptions of bacterial species. Classification of Actinobacteria has been rearranged (See table 1). In Volume 5, the phylum Actinobacteria is divided into six classes, namely Actinobacteria, Acidimicrobiia, Coriobacteriia, Nitriliruptoria, Rubrobacteria, and Thermoleophilia. The class Actinobacteria is further divided into 16 orders that are Actinomycetales, Actinopolysporales, Bifidobacteriales, Catenulisporales, Corynebacteriales, Frankiales, Glycomycetales, Jiangellales, Kineosporiales, Micrococcales, Micromonosporales, Propionibacteriales, Pseudonocardiales, Streptomycetales, Streptosporangiales, and Incertae sedis. In the order of abundance in soils, the common genera of Actinobacteria are *Streptomyces* (nearly 70%), *Nocardia*, and *Micromonospora*, although *Actinoplanes*, *Micromonospora*, and *Streptosporangium* are also generally found (Ranjani, 2016). At present, the molecular identification is based on 16S rDNA sequences, which is most significant for Actinobacteria

Table 1: Classification of Actinobacteria

The Archaea and the Deeply Branching and Phototrophic Bacteria	Volume 1
The Proteobacteria	Volume 2
The Firmicutes	Volume 3
The Bacteroidetes, Spirochaetes, Tenericutes (Mollicutes), Acidobacteria, Fibrobacteres, Fusobacteria	Volume 4
The Actinobacteria Volume	Volume 5

identification (Wang *et al*., 1999).

6 Actinomycetes in Bioremediation and secondary metabolite production:

Microorganisms that play a role in composting and vermicomposting include bacteria, fungi and actinomycetes. Bacteria break down or metabolise raw organic material and use it as an energy source. Fungi and actinomycetes clean up what the bacteria leave behind. They decompose toughest things – starches, cellulose and proteins to break down. Bacteria and fungi secrete enzymes that break down complex organic compounds, and then they absorb the simpler compounds into their cells (Pattnaik and Reddy, 2012). As degradation agents, actinomycetes are important in the degradation of soil organic materials into humus. Some actinomycetes secrete a range of enzymes that can completely degrade all the components of lignocelluloses such as lignin, hemicellulose and cellulose (Limaye *et al*, 2017). Because of their ability to secrete enzymes they are effective in attacking raw plant tissues and softening them for other microbes The use of microbes, which are able to degrade cellulose and hemicellulose, are important because of high percentage of these cellulose and hemicellulose contents in plant biomass (Jeffrey, 2007). The compost microbial population is highly dominated by actinomycetes. Presence of actinomycetes can potentially serve as an indicator of compost maturity and they also participate in suppressing of pathogens in the curing stage (Steger *et al*, 2007; Tang *et al*, 2006) which is accompanied by the presence of pleasant earthy smell due to release of a chemical "geosmin" by them (Wilkins, 1996). Other than saprophytes actinomycetes have been continuously reported as most prolific producers of microbial bioactive secondary metabolites for potential agricultural, pharmaceutical and industrial applications (Gesheva and Gesheva, 2000; Balachandran *et al*, 2012; Dasari *et al* 2012; Abidin *et al*, 2016) such as antibiotics, enzymes, antitumors agents, biopesticises, plant growth promoting hormones. *Among actinomycetes, around 7,600 compounds are produced by Streptomyces species* (Berdy, 2005). *Streptomyces* – derived antibiotics used as antibacterial agents include Streptomycin by S. *griseus,* neomycin by S. *fradiae*, Kanamycin by S. *kanamyceticus.* tetracycline by S. *rimosus*, chloramphenicol by S. *venezuelae*. (Sharma *et al*, 2014). Members of this group are producers in addition, of clinically useful antitumor drugs such as Anthracyclines (Aclarubicin, Daunomycin and Doxorubicin), Peptides (Bleomycin and Actinomycin D), Aurelic acids (Mithramycin), Enediynes (Neocarzinstatin), Antimetabolites (Pentostatin), Carzinophilin, Mitomycins and others (Newman and Cragg, 2007, Olano *et al*, 2009, Sharma *et al*, 2014). They are also known for their use as herbicides against unwanted herbs and weeds. *Streptomyces saganonensis* produce herbicidines and herbimycins that controls monocotyledonous and dicotyledonous weeds. Similarly, bialaphos, a metabolite of *Streptomyces viridochromogenes*, is widely used to control annual and perennial grassy weeds and broad-leaved weeds by inhibiting glutamine synthesis (Ranjani, 2016). They produce bactericidal and fungicidal metabolites to control plant diseases. Polyoxin B and D were isolated as metabolites of *Streptomyces cacaoi* var. *asoensis* in 1965 by Isono *et al* can control rice sheath blight caused by *Rhizoctonia solani* (Sharma *et al*, 2004). Similarly Dapiramicin produce by *Micromonospora* sp. *is* effective against Rice root disease (Ranjani, 2016). Until 1974 antibiotics of actinomycete origin were almost exclusively confined to Streptomyces. Recently efforts have been made to explore rare actinomycetes like Actinomadura, Actinoplanes, Ampullariella, Actinosynnema and Dactylosporangium for the search of new antibiotics (Khanna *et al*, 2011; Chavan *et al*, 2013). Molecular biological techniques have helped on large scale in finding new antibiotics from actinomycetes. With the advancement of technology in molecular study, primers had been developed by researchers to target specifically the 16SrRNA sequence of the actinomycetes (Schwieger and Tebbe, 1998; Wang *et al*., 1999). Identification of actinomycetes to genus level has been a great advancement in the area of identification as that the ability to obtain thegenus of the actinomycetes in just a few hours is now possible. A wide variety of biologically active enzymes are produced by both marine and terrestrial Actinobacteria. Actinomycetes secrete amylases to the outside of the cells to carry out extracellular digestion of - amylase starch degrading amylolytic enzymes is of great significance in biotechnological applications such as food industry, fermentation and textile to paper industries (Pandey *et al*. 2000). The production of cellulases by actinobacteria which are a collection of hydrolytic enzymes that hydrolyze the glucosidic bonds of cellulose and related cello-digosaccharide derivatives (Ito, 1997). In the current industrial processes, cellulolytic enzymes are employed in the color extraction from juices, detergents causing color brightening and softening, biostoning of jeans etc.(Zhou *et al*, 2001). Lipase produced from actinobacteria has broad applications in the food, pharmaceutical and detergent industries. They have also been used in biotechnological industries for the synthesis of biopolymers and biodiesel (Jaeger *et al*., 2002). Proteases are the most important group of the enzymes produced commercially and industrial purpose. The microbial protease represents 60% of the worldwide market of industrial enzyme (Lekshmi *et al*., 2014) such as in detergents, cheese making and clarification – low calaorie beer. Actinomycetes have been revealed to be an excellent resource for L-asparaginase (DeJong 1972, Narayana *et al*. 2007). There are many literatures pertaining to various aspects of isolation, screening and characterization of antibiotic and other secondary metabolites producing actinomycetes from soil, ocean and ecofriendly degradation of solid waste. Limaye *et al*., (2017) successfully isolated potent thermo tolerant and alkali tolerant actinomycetes strains from marine environment, hot springs, composts, lake sediment, soil on Actinomycete Isolation Agar (HiMedia) and screened for xylanase, laccase, cellulase production. The consortium of selected actinomycete applied for biodegradation of domestic agro waste by composting and treatment of paper mill effluent. First time the laccase production by *Streptomyces rochei* was reported here. The results were promising regarding degradation of domestic waste and paper fill effluent by inoculum of selected actinomycetes strains. Duddu *et al*., (2016) showed that actinomycetes isolated from Kaplupudda plastic waste dumping yard were found to be most promising microrganisms for the production of antibacterial and antifungal agents. Haseena *et al*., (2016) reported actinomycetes in weed compost, Ayurvedic herbal waste compost, coir pith compost, saw dust compost on 10th day of composting. The species among actinomycetes were *Streptomyces celluloflavus* and *Streptomyces albicans*. Workie and Abate et.al, (2016) showed the actinomycetes isolated from mushroom compost exhibit antifungal activity against test organism *Candida albicans* Meignanalakshmi *et al*., (2013) for the first time reported cellulase producing actinomycetes from slaughter house waste. They isolated a gram positive, spore forming and motile actinomycete bacterium and screened for cellulase production by Congo Red Assay and species are identified based on 16s rRNA analysis. Anusuya and Geetha (2012) reported presence of thermophillic actinomycetes from banana waste compost. They isolated them on starch casein agar and studied morphological characteristics and enzymatic activity. They showed the production of alpha amylase. The genus *Streptomyces* were shown to exhibit high alpha amylase production. Kumar et.al, (2012) in their study screened actinomycetes from earthworm castings for their antimicrobial activity and industrial enzymes. They were able to isolate and characterize Streptomyces (dominant) followed by Streptosporangium Saccharopolyspora and Nocardia. Besides there were other genera like Micromonospora, Actinomadura, Microbispora, Planobispora were also isolated in low frequency. In the view of antimicrobial activity as well as enzyme production capability the genus Streptomyces was dominant. Gopalakrishnan et.al, (2011) indicated that the selected actinomycetes isolated from herbal vermicompost have the potential for biological control of *Fusarium* wilt disease in chickpea. Jeffrey (2008) reported isolation of actinomycetes from soils is the potential microbes which can be used as biocontrol and bioremediation agents. Rajan *et al*, 2012 showed actinomycetes isolated from marine environment found to have cytotoxicity and antioxidant properties. Cytotoxic activity of isolate on HeLa cells suggested that the strain could be clinically important and need to be investigated further for the anticancer properties. Arifuzzaman *et al*, 2010 showed that actinomycetes isolated from soil samples of sunderbans were found to have antibacterial activity which showed potential as a source of antibiotics for pharmaceutical interest. Mohseni *et al*, 2013 in their investigation revealed that the marine actinomycetes of Caspian Sea Sediments were potent source of novel antibiotics and bioactive compounds. Oskay *et al*. (2004)also reported that the ability of actinomycetes isolated from Turkey's farming soil have the ability to inhibit *Erwinia amylovora* a bacteria that cause fireblight to apple and *Agrobacterium tumefaciens* a causal agent of Crown Gall disease.

7 Conclusion:

Due to over-prescription and the improper use of antibiotics and excessive use of herbicides has led to the generation of resistance mechanisms in many bacterial and fungal pathogens and weeds. Thus, producing novel antibiotics as well as using integrative therapy is effective in the treatment of resistant pathogenic infections. So we need to screen more actinomycetes from different habitats, unexplored habitats for antimicrobial activity in the hope of getting some new actinomycetes strains that produce antibiotics, which have not been discovered yet and are active against drug resistance pathogens. The above mentioned findings have cleared that *Streptomyces* genera are dominant in them. Different generalized and advanced methods have been adopted to isolate rare actinomycetes from various sources like soil, marine and plant, composts. These methods include pretreatment (dry heat) enrichment (with $CaCO_3$, antibiotics) membrane. Marine and endophytic actinomycetes were isolated from unexplored habitats in search of unidentified species to find novel bioactive substances. The research is still continuing. In recent years using molecular identification methods it was found that the some of the isolated microorganisms are new species. The actinomycetes strains can be successfully isolated and applied for biodegradation of solid wastes. The consortium of selected actinomycetes strains may be further utilized in order to assess its commercial viability for biodegradation process. This expands the possibilities for their use in biotechnology and biomedical research.

Table 2: *Actinomycetes isolated from diverse ecological habitat*

S.No.	Habitat	Actinomycetes isolates	Secondary metabolite production	Author
1.	Kapuluppada plastic waste dumping yard soil	Streptomyces sp.	Antimicrobial and enzyme producing	Duddu et al., 2016
2.	Banana waste compost	Actinomadura, Streptomyces sp. Nocardia sp.	– amylase production	Anusuya .D and Geetha .M, 2012
3.	Slaughter house waste	Genus Actinomycetes	Cellulose production	Meignanalakshmi et al, 2013
4.	Urban waste compost and vermicompost	Streptomyces sp., Rhodococcus sp, Nocardia sp., Micrococcus sp., Microbacterium sp.	-	Pattnaik and Reddy, 2012
5.	Agriculture soils at Semongok, Sarawak	Streptomyces sp.	Antimicrobial	Jeffrey, L.S.H, 2008
6.	Herbal vermicompost	S.caviscabies,, S. globisporus, S. griseorubens	Plant growth promoters	Gopalakrishnan et al, 2014
7.	Mushroom compost, green waste.	Thermomonospora sp., Sacchromonospora sp., Streptomyces sp.	-	
8.	Soil	Streptomyces sahachiroi, neyagawaensis, Streptomyces, Streptomyces hygrostaticus	Antibacterial	Muiru et al., 2008
9.	Soil	Nocardia alba	Antibacterial	Salim et al, 2017
10.	Mangrove forest of Pahang, Malaysia	Streptomyces and Micromonospora	Antimicrobial	Abidin et al, 2016
11.	Sundarbans soil	Actinomyces, Nocardia, Streptomyces, Micromonospora.	Antibacterial	Arifuzzaman et al., 2010
12	Sediments of Caspian sea	Marine actinomycetes	Antibacterial	Mohseni et al., 2013.

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