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THERMOPHILIC ACTINOMYCETES ARE POTENTIAL SOURCE OF NOVEL BIOACTIVE COMPOUNDS: A REVIEW

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ABSTRACT

Actinomycetes are one of the most efficient groups of microorganisms in terms of producing commercially important bioactive compounds such as enzymes, antibiotics and pigments. Among its various genera, *Streptomyces, Saccharopolyspora, Amycolatopsis, Micromonospora, Actinoplanes* are the major producers of industrially important biomolecules. Several species have been isolated and screened from variety of terrestrial and aquatic habitats in the past decades. Consequently the chances of isolating a novel strain of actinomycetes which could provide novel biomolecules has considerably reduced. However there is still an urgent need for discovering novel secondary metabolites to combat the problem of arising number of resistant pathogenic bacteria and increasing need of more efficient enzymes in pharmaceutical industries. For this reason, searching the less or unexplored ecosystems might lead to the discovery of novel bioactive compounds. Studies in recent years showed that the existence of actinomycetes has been reported in the unexplored extreme habitats. Among them thermophilic actinomycetes are reported to be efficient producers of new secondary metabolites that show a range of biological activities including antibacterial, antifungal and extracellular enzyme production.

KEYWORDS: Thermophilic Actinomycetes, Bioactive Compounds, Drug Resistance.

INTRODUCTION

Infectious diseases are the major cause of deaths worldwide accounting for almost 13.3 billion deaths, which constitute of about 25% of all the major causes of deaths per year. At present, resistance to the drugs used in the treatment of many infectious diseases is increasing, and microbial infections are being found to be responsible for more life threatening diseases than previously thought. The reasons for the increase in incidence of infectious diseases are not fully understood but one such possible reason is the emergence of multidrug resistant pathogens. [1]

Changing pattern of diseases and the emergence of resistant bacterial strains against currently useful antibiotics continuously put demand on the drug discovery scientists to search for novel antibiotics. [2] Although some novel compounds are under investigation, there is still an urgent unmet medical need for the development of novel antimicrobial compounds and microbial natural products still appear as the most promising source for drug identification. [3, 4]

To obtain antimicrobials from natural microbial flora, scientists are trying to investigate unexplored habitats for novel Actinomycetes as the possible candidates for the discovery of new antimicrobial compounds. The recent discovery of novel primary and secondary metabolites from taxonomically unique populations of extremophilic Actinomycetes suggest that, these organisms could add a new dimension to microbial natural product research. [5]

Actinomycetes perform significant biogeochemical roles in terrestrial soils and are highly valued for their unparalleled ability to produce biologically active secondary metabolites. They are responsible for the production of about half of the discovered bioactive secondary metabolites [6] that includes antitumor agents, [7] antibiotics [8, 6] and immunosuppressive agents and enzymes. [9]

A search of recent literature revealed that 4607 patents have been issued on Actinomycetes related products and processes. [6] The number of antimicrobial compounds reported from species of this genus per year increased almost exponentially for about two decades, followed by a steady rise to reach a peak in the 1970s and with a substantial decline in the late 1980s and 1990s.

In the past two decades, however, there has been a decline in the discovery of new lead compounds from common soil-derived Actinomycetes, as culture extracts usually yield unacceptably high number of previously described metabolites. The immense biotechnological ability of Actinomycetes had led to exhaustive surveys of cultivars from normal terrestrial habitats and an associated increase in the number of known compounds being rediscovered due to a high rate of redundancy in the strains isolated. For this reason, searching the less or unexploited ecosystems for Actinomycetes might lead to the discovery of novel bioactive compounds including those that can act against drug-resistant pathogens. [10]

Actinomycetes

The name “Actinomycetes” is derived from Greek “atkis” (a ray) and “mykes” (fungus), and has features of both bacteria and fungi. [11] Like fungi they form mycelia network of branching filaments but like bacteria they have thin cell wall containing muramic acid.

Actinomycetes are Gram-positive, free living, saprophytic bacteria widely distributed in soil, water and colonizing plants show marked chemical and morphological diversity but form a distinct evolutionary line of organisms. [12]

Taxonomy

Actinomycetes belong to the class Actinobacteria (Kingdom: Bacteria, Phylum: Firmicutes, Class: Actinobacteria, Subclass: Actinobacteridae). Actinomycetes are divided into eight diverse families such as, Actinomycetaceae, Mycobacteriaceae, Actinoplanaceae, Frankiaceae, Dermatophilaceae, Nocardiaceae, Streptomyceteceae, Micromonosporaaceae which comprise sixty three genera. [13]

Biological aspects

They are a group of heterogeneous, aerobic, filamentous bacteria with high G+C content. They form branching filaments or hyphae that may persist as a stable mycelium or may break up into rod shaped or coccoid shaped elements. When grown on agar surface, the Actinomycetes branch forming a network of hyphae growing both on the surface and under the surface of the agar. The on-surface of the hyphae is called an aerial mycelium and the under surface hyphae is called as substrate mycelium. Actinomycetes sometimes reproduce asexually; the asexual mode of reproduction is accomplished by spores or conidia formation. Actinomycetes cell wall composition varies greatly among different groups and this characteristic is effortlessly exploited to identify the novel genera of actinobacteria. [14]

Ecological occurrence

Actinomycetes are among the most widely distributed groups of microorganisms in nature. Very few natural habitats are entirely free from them. In some of the habitats, as in soils, in lake water and in lake bottoms, in composts, they lead a normal existence. In other substrates, as in sea water and in dust, they are only in a transitory state.

Actinomycetes are found abundantly in all soils throughout the world such as alkaline soil, desert soil, soils from salt pans to under the snow caps. Actinomycetes constitute a large part of the microbial population of the soil. They also occur on plant residues and upon and in various foodstuffs, such as fruits, vegetables, milk and milk products, and cacao.

Commercial Importance of Actinomycetes as producers of secondary metabolites

The microbial secondary metabolites are the low molecular mass products of secondary metabolism. J.D. Bu’Lock in 1961 was the first to explicitly introduce the term ‘secondary metabolite’ in microbiology. Microbial secondary metabolites are not essential for vegetative growth of the producing organisms. They are biosynthesized from one or more general (primary) metabolites by a wider variety of pathways. They are mainly produced by a relatively restricted group of bacteria and fungi, but their intergeneric, interspecific, and intraspecific variation is extremely high. Actinomycetes are the biotechnologically valuable bacteria which are well exploited for various secondary metabolites, including antibiotics, pigments and enzymes.

Most of the known antibiotics, about 80% of total, are produced by Actinomycetes mainly *streptomyces*, which have a non-motile, saprophytic lifestyle in a complex habitat, such as terrestrial soil, where they lead an intensive social life and are subject to great competition with other inhabitants. Actinomycetes have broad metabolic capabilities and can produce huge variety of enzymes and antibiotics which have great use in various biotechnological applications, especially in the food and pharmaceutical industries.

Antibiotics

The first antibiotic isolated and crystallized was Actinomycin (1940). This was followed by isolation of Streptomycin (1942). However the word antibiotic was discovered by Alexander Fleming in 1928.

The discovery of streptomycin, an amino-glycoside antibiotic from *Streptomyces griseus* led to increase interest in Actinomycetes as a potential source of antibacterial antibiotics. [15] Among Actinomycetes, *Streptomyces* is a unique genus for antibiotics as they produce over two thirds of clinically useful antibiotics of natural origin. Some of the commercially useful antibiotics isolated from Actinomycetes species are summarized below **(Table no. 1)**.

Antibiotics are generally classified as broad spectrum antibiotics (effective against large number of bacterial pathogens) and narrow spectrum antibiotics (effective against small number of bacterial pathogens).

Table no. 1: Some clinically important antibiotics from Actinomycetes

S. No.	Antibiotic	Organism	Active against
1	Amphotericin B	*Streptomyces nodosus*	Fungi
2	Erythromycin	*Streptomyces erythreus*	Gram positive bacteria
3	Neomycin	*Streptomyces fradiae*	Broad spectrum
4	Streptomycin	*Streptomyces griseus*	Gram negative bacteria
5	Tetracycline	*Streptomyces rimosus*	Broad spectrum
6	Vancomycin	*Streptomyces orientalis*	Gram positive bacteria
7	Gentamicin	*Micromonospora purpurea*	Broad spectrum
8	Rifamycin	*Streptomyces mediterranei*	Tuberculosis
9	Tetracycline	*Streptomyces aureofaciens*	Broad spectrum
10	Actinomycin	*Streptomyces chrysomallus*	Broad spectrum
11	Actinorhodin Methylenomycin Undecylprodigiosin Perimycin	*Streptomyces coelicolor*	Broad spectrum
12	Chloramphenicol	*Streptomyces venezuelae*	Broad spectrum

Actinomycetes are very well known producers of antibiotics which are widely used in industries for large scale production so they are highly significant in their commercial aspects.

Enzymes

In nature, a wide variety of microorganisms exist that secretes extracellular enzymes that can degrade many polymer compounds. Actinomycetes produce many enzymes which are or could be applied in biotechnology, clinical chemistry and medical therapy. From traditional times, they are well known as antibiotic producers and now a days being explored on large for the production of industrial enzymes also. A variety of enzymes of commercial importance are known to be produced by the Actinomycetes such as protease, amylase, catalase, cellulose and carbohydrases. They all are commonly hydrolases in nature. [16]

Actinomycetes may provide enzymes for many biotechnological processes. Thus, glycosidases of all kinds are exploited for the degradation of plant biomass and very active proteases serves as additives to detergents or are used in tanning industry. Glucose isomerases have been successfully used to obtain fructose-heavy syrups. Moreover bacteriolytic and mycolytic enzymes from Actinomycetes may be used for beer and wine clarification or serves as non-toxic food preservatives. Enzymes produced by Actinomycetes also seem to be very promising as immobilized preparations for routine clinical diagnostic tests. [17]

Detergent, textile, pulp and paper industries, organic synthesis and biofuels industry are the major consumers of hydrolytic enzymes. The demand for more stable enzymes in many industrial applications is growing rapidly today, which can be satisfied if Actinomycetes from diverse and extreme environments are isolated and studied for enzyme production.

Enzymes are biocatalysts that perform variety of chemical reactions and are commercially used in many industries such as food, detergent, pharmaceuticals, diagnostics and fine chemicals. Almost 75% of all industrial enzymes are hydrolytic in nature of which carbohydrases, proteases and lipases dominate the enzyme market, accounting for more than 70% of all enzyme sales. [14]

Pigments

Pigments could be defined as natural colour substances produced by plants, animals and microorganisms such as bacteria, fungi, algae and Actinomycetes. Though pigments were primarily used as a colouring agent in various industries, from the past decade, researchers have focused the usage of pigments from colouring agents to antioxidants in pharmaceutical and food industries. [16]

Naturally they are colourful organisms which produce variety of intracellular and extracellular pigments including melanin with different biological functions. Actinomycetes are known to produce diverse variety of pigments **(Table no. 2)** which are of two types such as, diffusible pigments (the pigments which diffuse from the organism into the agar medium) and non-diffusible pigments (pigments stays with the organisms and do not diffuse into the agar medium).

Table no. 2: Varieties of pigments produced by Actinomycetes

S. No.	Pigment produced	Actinomycetes genus
1	Melanin	*Streptomyces* [18]
2	Carotenoids	*Streptomyces griseus, Streptomyces setonii, Streptomyces coelicolor* [19]
3	Violacein	*Chromobacterium violaceum* [20]
4	Prodigiosin	*Serratia, S treptoverticillium rubrireticuli, Streptomyces longisporus* [21]
5	Anthracyclin glycoside	*Streptomyces galilaeus, Streptomyces melanogenes, Streptomyces peucetius* [22]
6	Naphthoquinone	*Streptomyces coelicolor* [23]
7	Phenoxazinone	*Streptomyces parvullus* [24]

Extreme Environments

Any environmental condition that can be perceived as beyond the normal acceptable range is an extreme condition. Extreme is a relative term, which is viewed, compared to what is normal for human beings. Extreme environments include high temperature, pH, pressure, salt concentration, and low temperature, and also conditions having high levels of radiation, harmful heavy metals and toxic compounds.

Extremophile

An extremophile (Latin *extremus* meaning “extreme” and Greek *philia* meaning “love”) is an organism that thrives in physically or geographically extreme conditions that are detrimental to most life on earth. [25] In contrast, organism that lives in more moderate environments may be termed mesophiles or nuetrophiles. Microbial communities are found in most diverse conditions, including extremes of temperature, pressure, salinity and pH. In order to survive under such conditions, these organisms have developed adaptive features to function under extreme conditions. These microorganisms, referred as extremophiles, grow optimally under one or more environmental extreme, while polyextremophiles grow optimally under multiple extremes. The extremophiles can grow optimally in some of the earth’s most hostile environments of temperature (-2ºC to 15ºC; Psychrophiles; and 60ºC to 115ºC; Thermophiles), salinity (2-5M NaCl; Halophiles), pH (<4 Acidophiles and >9; Alkaliphiles), anaerobicity (Methanogens), and/or pressure (Barophiles). [26]

Thermophilic environment

Although habitats with elevated temperatures are not as widespread as temperate or cold habitats, a variety of high temperature, natural and man-made habitats exist. These include volcanic and geothermal areas with temperatures often greater than boiling, sun-heated litter and soil or sediments reaching 70°C, and biological self-heated environments such as compost, hay, saw dust and coal refuse piles. In thermal springs, the temperature is above 60°C, and it is kept constant by continual volcanic activity.

Besides temperature, other environmental parameters such as pH, available energy sources, ionic strength and nutrients influence the diversity of thermophilic microbial populations. The best known and well-studied geothermal areas are in North America (Yellowstone National Park), Iceland, New Zealand, Japan, Italy and the Soviet Union. Hot water springs are situated throughout the length and breadth of India, at places with boiling water (e.g. Manikaran, Himachal Pradesh). [27]

A REVIEW OF THERMOPHILIC ACTINOMYCETES

A thermophile is an organism capable of living at temperatures at or near the maximum for the taxonomic group of which it is a part. [28] Some thermophilic Actinomycetes can survive temperature upto 70 ^{o}C. Such conditions prevail in the areas close to volcanoes or hot springs and deserts.

Survival of Thermophilic Actinomycetes

The membrane lipids of thermophiles contain more saturated and straight chain fatty acids than mesophiles. This allows thermophiles to grow at higher temperatures by providing the right degree of fluidity needed for membrane function. Histone-like proteins that bind DNA have been identified in hyperthermophiles, and these may protect DNA.

Taxonomic distribution

Thermoactinomycets belong to genus *Thermoactinomyces, Thermomonospora, Microbispora, Saccharopolyspora* and *Streptomyces*. [29] Among these thermophilic Actinomycetes, the genus *Thermoactinomyces* has industrial and clinical importance. Some *Thermoactinomyces* strains are known as potent protease producers. [30]

In recent years, researchers have shown great interest in thermophilic Actinomycetes because of their economic potential, either in useful biological processes such as biodegradation, or in the production of antibiotics and enzymes.

Natural Habitats

Some microbiologically diverse and specialized habitats for the isolation of Thermophilic Actinomycetes are desert soil, hot springs, volcanic eruptions and thermal industrial waste.

Desert soil

Deserts are apparently lifeless due to lack of moisture yet there appear a number of microhabitats that are inhabited by microorganisms. Since stress allows only the tolerant forms to grow, the microorganisms not only dominate such habitat but also grow sufficiently to impart special visible features to the habitat. Along with soil there are various other sources such as patina (desert varnish), cryptobiotic crusts, playas and rhizospheres are rich in microbial populations in desert habitats.

Strains NT202^{T} and NT303 were isolated from scrubland and arid soil samples collected in Madurai, India, and Van, Turkey, respectively. The taxonomic positions of two thermophilic Actinomycetes were established in a polyphasic taxonomic study. The organisms were shown to have phenotypic properties typical of members of the genus *Amycolatopsis.* Genotypic and phenotypic data show that the two strains should be classified in the genus *Amycolatopsis* as a novel species, *Amycolatopsis eurytherma* sp. nov., [31]

The Atacama Desert of Chile, South America is one of the most extreme environments on Earth. Okoro *et al.* reported the first extensive isolations of Actinomycetes from soils at various locations within the Desert in the year 2009. The use of selective isolation procedures enabled Actinomycetes to be recovered from arid, hyper-arid and even extreme hyper-arid environments in significant numbers and diversity. Majority of isolates belonged to members of the genera *Amycolatopsis*, *Lechevalieria* and *Streptomyces*, a high proportion of which represent novel centres of taxonomic variation. The results of this study supported the view that arid desert soils constitute a largely unexplored repository of novel bacteria, while the high incidence of non-ribosomal peptide synthase genes in isolates recommend them as promising material in screening for new bioactive natural products. [4]

The soils of Mongolian desert steppes are periodically heated to high temperatures (50–60°C) and are characterized by intermittent modes of moistening and nutrient supply. Thermotolerant and thermophilic Actinomycetes were found in high abundance in this area. Among the thermotolerant members of the order Actinomycetales, *Streptomyces, Micromonospora, Actinomadura,* and *Streptosporangium* species were most widespread in desert soils. [32]

The taxonomic positions of two thermophilic actinomycetes isolated from an arid Australian soil sample were established to be members of the genus *Amycolatopsis*. It was proposed that the two isolates were classified in the genus *Amycolatopsis* as *Amycolatopsis thermophila* sp. nov., was *Amycolatopsis viridis* sp. nov., [33]

Similarly, the taxonomic positions of three thermophilic Actinomycetes isolated from arid soil samples of U.K. were established in the genus *Amycolatopsis*. It was proposed that the three isolates be classified as *Amycolatopsis granulosa* sp. nov., *Amycolatopsis ruanii* sp. nov. and *Amycolatopsis thermalba* sp. nov., [34]

Hot springs

Hot spring is a spring that is produced by the emergence of geothermally heated groundwater from the earth's crust. There are geothermal hot springs in many locations all over the crust of the earth.

The water issuing from a hot spring is heated by geothermal heat, i.e., heat from the Earth's mantle. In general, the temperature of rocks within the earth increases with depth. The rate of temperature increase with depth is known as the geothermal gradient. If water percolates deeply enough into the crust, it will be heated as it comes into contact with hot rocks. The water from hot springs in non-volcanic areas is heated in this manner.

A thermophilic Actinomycete, strain LA5^T, was isolated from a hot spring in Yunnan province, China. The isolate grew aerobically at temperatures of 50–75 ^{0}C. Phylogenetic analyses based on 16S rRNA gene sequences indicated that strain belonged to the genus *Planifilum*. Strain represented a novel species of the genus *Planifilum*, for which the name *Planifilum yunnanense* sp. nov was proposed. [35]

Hot spring sediment and soil samples total of twenty samples from West Anatolia in Turkey were investigated for the occurrence of thermophilic Actinomycetes. Strains were grown at 55 °C. Sixty-seven thermophilic Actinomycetes isolates were classified in *Thermoactinomyces thalpophilus* and *T. sacchari* species. Among these, maximum isolates were found to be extracellular protease producers. [36]

Volcanic crusts

A volcano is a rupture on the crust of a planetary mass object, such as the Earth, which allows hot lava, volcanic ash, and gases to escape from a magma chamber below the surface. Crusts formed due to volcanic eruptions are heated part of the earth and are very suitable environment for Thermophilic microbes to evolve. Although very studies showed the presence of actinobacteria in these areas but a decent research on such bacteria could be of great significance.

The taxonomic position of two Actinomycetes strains, LC2^T and LC11^T, isolated from a filtration substrate made from Japanese volcanic soil, was determined using a polyphasic approach. The strains grew at temperatures from 5 to 45 ^{o}C. A phylogenetic tree based on 16S rRNA gene sequences showed that the two strains formed a distinct evolutionary lineage within the genus *Amycolatopsis*. The isolates are proposed to represent two novel species for which the names *Amycolatopsis echigonensis* sp. nov. and *Amycolatopsis niigatensis* sp. nov. are proposed. [37]

Thermal Industrial waste

Some industries discard their waste products along with a stream of very hot water. This heated sludge of industries could be of great significance in order to find the thermophilic species, however there is still no concrete evidence available of studies conducted on such industrial waste for the isolation of Actinomycetes. But in future this prospect can also be explored in order to isolate thermoohilic Actinomycetes.

The taxonomic position of a group of moderately thermophilic Actinomycetes isolated from floor dust of a hemp factory in Lucknow, India, was determined to be the typical of members of the genus *Amycolatopsis.* It is clear from the combined datasets that the strains merit recognition as a new species of *Amycolatopsis* for which the name *Amycolatopsis sacchari* was proposed. [38]

Ten strains of thermophilic actinomycetes were isolated from waste and mushroom composts, as well as from the air of compost plants and a refuse incineration plant in Germany. 16s ribosomal DNA sequence data indicated that these organisms represent a new genus of the Order *Actinomycetales*, for which the name *Thermocrispum* was proposed. [39]

Isolation of novel Thermophilic Actinomycetes

A new species of thermophilic monosporic Actinomycete isolated from sugar cane bagasse, was described as *Thermoactinomyces sacchari* sp.nov., [40]

Actinomycetes isolated at 40 ^{0}C and/or 60 ^{0}C from hay samples from Harpenden, Hertfordshire included *Micrornonospora vulgaris, Thernopolyspora polyspora, T. glauca* sp.nov. *Streptomyces therrnoviolaceus,* S. *fradiae, S. griseojlavus,* S. *olivaceus* and *S . griseus*. [41]

Thermoactinomyces candidus, a new species isolated from home environments and other sources of New Brunswick, New Jersey. *Thermoactinomyces candidus*, was a New Species of Thermophilic Actinomycetes. [42]

A novel filamentous bacterium, strain SCSIO 10219^T, was isolated from a sediment sample collected from the South China Sea at a depth of 2105 m. Growth was observed at 25–35 °C (optimum 30 °C) and pH 5.0–8.0 (optimum pH 6.0–7.0). Phenotypic characterization and 16S rRNA gene sequence analysis indicated that strain belonged to the family *Thermoactinomycetaceae*, a novel species in a new genus, *Marininema mesophilum* gen. nov., sp. nov. was proposed. [43]

A novel strain IMMIB L-1269^T, originated from sputum of patients suspected with pulmonary tuberculosis. On the basis of its morphological, biochemical and chemical characteristics, the strain did not confirmed to be of any recognized taxon. On the basis of phenotypic and molecular phylogenetic evidence, it represented a novel genus and species, for which the name *Desmospora activa* gen. nov., sp. nov. was proposed. [44]

A thermophilic, strain, designated I3^T, grew at temperatures between 35 and 62 ^{0}C, with optimum growth at 50–55 ^{0}C. No growth was observed below 29 ^{0}C or above 65 ^{0}C. 16S rRNA gene sequence analysis assigned this Actinomycete to the family *Nocardioidaceae*, strain represented a novel species, for which the name *Thermasporomyces composti* gen. nov., sp. nov. was proposed. [45]

Production of Bioactive compounds

Two Thermophilic Actinomycetes strains were isolated and identified as *Thermomonospora fusca* strains. Random aliphatic-aromatic copolyesters synthesized from 1, 4-butanediol, adipic acid, and terephthalic acid (BTA) have excellent thermal and mechanical properties and are biodegradable. These Actinomycetes exhibited about 20-fold higher BTA degradation rates than usually observed in a common compost test. Thermophilic Actinomycetes obviously play an outstanding role and appear to dominate the initial degradation step. [46]

During a search antifungal antibiotics, 320 Actinomycetes strains were isolated from several Moroccan habitats including desert sand and thermal water. Many isolates from these regions showed strong activity against yeast, moulds and bacteria. One of the active Desert sand isolate was characterized to belong to taxonomic group *Streptomyces* microflavu. [47]

A novel species of Actinomycetes was isolated from Australian arid soils and genotypically and phenotypically merited the species status within the genus *Amycolatopsis*. Along with various biochemical activities, it was also shown to have antagonistic Activity against *B. subtilis* and *S. cerevisiae*. [48]

The enrichment and isolation of thermophilic bacteria capable of rubber [poly (*cis*-1, 4-isoprene)] degradation were isolated from different parts of Egypt. Taxonomic characterization of these isolates by 16S rRNA gene sequence analysis demonstrated closest relationships to *Actinomadura nitritigenes*, *Nocardia farcinica*, and *Thermomonospora curvata*. For all strains, optimum growth rates were observed at 50°C. [49]

An Actinomycetes strain, *Streptomyces hygroscopicus* subsp. *ossamyceticus* (strain D10) was isolated from Thar Desert soil, Rajasthan during the year 2006 and found to produce a yellow color pigment with antibiotic activity. The crude pigment was found to poses antimicrobial activity against drug resistant pathogens such as methicillin-resistant *Staphylococcus aureus,* vancomycin-resistant *Staphylococcus aureus,* extended spectrum β-lactamase producing cultures of *Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella* sp. Based on the results of chemical screening, the pigment was tentatively identified as group of sugar containing molecules. [50]

In a screening program to study the antimicrobial activities of desert Actinomycetes as potential producers of active metabolites, 75 Actinomycetes strains were isolated from the Egyptian desert habitats and tested. Out of the total isolates, 42.67% showed activity against the used test organisms. The most potent Actinomycetes strain, designated D332 was identified to genus *Streptomyces* where it formed a distinct phyletic line in the *Streptomyces* 16S rRNA gene tree. Strain D332 produced one major compound active against Gram-positive and Gram-negative bacteria and yeasts. [51]

Songara and kaur aimed to identify the thermal resistant Actinomycetes from the desert soil of Rajasthan, India. Isolate designated as stb-1 showed growth at high temperatures and was screened for antagonistic potentiality against gram positive and gram negative human pathogenic bacteria. According to the observation and phylogenetic analysis, the strain stb-1 was proved to belong to the genus *Streptomyces* with thermal resistance and antibiotic potentiality. [52]

During the course of the anti-infective drug discovery programme, Actinomycetes strain D25 was recovered from the Thar Desert soil, Rajasthan, India. Antimicrobial compound isolated from the strain D25 showed promising activity against multi drug resistant and extensively drug resistant *M. tuberculosis* isolates. Further 16s rRNA analysis confined the genus *Streptomyces* with 97% similarity to the closely related species *Streptomyces althioticus*. [53]

CONCLUSION

The potential biotechnological applications associated with Actinomycetes and their products is the major impetus that has driven extensive and intensive research efforts on diversity of Actinomycetes in extreme environments during the last decades.

The Actinomycetes have provided many important bioactive compounds of commercial value and are being routinely screened for novel bioactive substances. These searches have been remarkably successful, and approximately two third of naturally occurring antibiotics, have been isolated from Actinomycetes (mainly Streptomycetes). Actinomycetes are also known to produce enzymes of high commercial value. Yield of high quality antibiotics and enzymes require discovery of novel important metabolites for which novel Actinomycetes have to be isolated from variety of extreme habitats. Actinomycetes are able to grow well in such harsh and poorly explored environments. Also finding new species and novel bioactive compounds is comparatively easy considering the rarity in approach of extreme habitats. Species from hot and highly thermophilic environments provide products which could tolerate very high temperature and still show fairly good activity. This review concluded that the Actinomycetes found in extreme thermophilic environments can play a major role in pharmacological and biotechnological industry as they might produce novel bioactive compounds such as antibiotics and enzymes.

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