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Review Article

Persepectives on Extremophilic Actinobacteria - A Review

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Abstract

Actinobacteria are considered as the most potential and biotechnologically viable prokaryotes because of their ability for the production of bioactive metabolites. They have immense biosynthetic prospect that remains unopposed without a competent organism from other microbial collections. But the prospect of finding highly potential actinobacteria from ambient habitats is reduced due to the wide exploitation for antibiotic production. So attention has been diverted to the unexploited extremophilic habitats such as marine sediments, mangroves, deserts, rocks, glaciers, etc. Extremophilic actinobacteria are competent producers of new secondary metabolites that show a wide range of antagonistic activities against bacteria, fungi, cancer and also exhibit insecticidal and enzyme inhibition. This review is an attempt to explore extremophilic actinobacteria that may form the source for the synthesis of novel drugs that could be used to combat resistant pathogens and also for xenobiotic degradation

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Introduction

Extremophiles are organisms competent enough to grow under extreme conditions that are particularly antagonistic to humans and to the majority of the known microorganisms as far as temperature, pH, and salinity parameters are concerned (Horikoshi et al, 2010). They have been isolated from habitats characterized by hydrostatic pressure, aridity, radiations, high temperatures, extreme pH values, high salt concentrations, and high solvent/metal concentrations, and it is well authenticated that these organisms are capable of thriving under extreme conditions better than any other organism living on Earth. Extremophiles have also been explored as far as the search for life on other planets is concerned (Stan-Lotter,2007). They are fascinating tools for the study of basic and applied science due to their unique structural and physiological features which help them to thrive in extremely selective environmental conditions. These properties are often attributed to specific biomolecules (DNA, lipids, enzymes, osmolites, etc.) that have been used as novel sources for biotechnological applications (Canganella and Wiegel, 2011). Actinobacteria which is a large phylum in the microbial community exhibits wide diversity in their habitat (Al-Shaibani et al, 2021). Many of the genera in this phylum have been isolated from extremophilic conditions. Generally, they are mostly aerobic, gram-positive to gram-variable with high G+C content, having mycelial or nonmycelial growth, and occupies diverse ecological niche (Amin et al,2020). Though many *Actinobacteria* produce a mycelium, which is a nonseptate and slenderer-like filamentous fungus, and many of them reproduce by sporulation (Chater and Chandra, 2006). However, the comparison to fungi is only superficial: like all bacteria, actinobacteria cells are thin with a chromosome that is organized in a prokaryotic nucleoid and a peptidoglycan cell wall; and the cells are susceptible to antibacterial agents (Smith, 2005).

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Actinobacteria mostly inhabit in soil, freshwater, and marine habitats playing an important role in the degradation of organic compounds, such as cellulose and chitin, thereby playing a vital part in biogeochemical cycles, replenishing the supply of nutrients in the soil, and aiding in humus formation (Anandan et al,2016). A phylogenetic study based on 16S rRNA classifies actinobacteria into six classes i.e., Acidimicrobia, Corniobacteria, Nitriliruptoria, Rubrobacteria, Thermoleophilia, and Actinobacteria (Sen et al. 2014). The class Actinobacteria contains 16 orders and the order Actinomycetales is now restricted to the members of the family *Actinomycetaceae*, and the other suborders that were previously part of this order are now designated to specific orders (Salam et al, 2020). This phylum is recognized as a producer of a wide variety of secondary metabolites with different activities including herbicides, antifungals, antitumor or immunosuppressant compounds, and anthelmintic agents (Manivasagan et al., 2014). However, the phylum has adapted to a wide range of ecological environments (Goodfellow and Williams, 1983) that are of adverse conditions such as acidic/alkaline pH, low or high temperatures, salinity, high radiation, low levels of available moisture, and nutrients (Zenova et al, 2011). This is possible due to their high metabolic and physiological flexibility in terms of several surviving strategies such as the production of enzymes, chaperones, varied nutrient adaptations, antibiosis, etc. (Mukhia et al,2021). Based on the different extremophile habitats they can be classified as alkaliphilic, thermophilic, acidophilic, radio-tolerant, halophilic, etc.

Thermophiles

Thermophilic actinobacteria flourish at relatively high temperatures ranging from 40 to 80°C (Shivlata and Satyanarayana,2015, Tortora et al., 2007). They are widespread, and commonly found in moldy hay (Corbaz et al., 1963), self-heating plant residues, cereal grains, sugar cane bagasse (Suihko et al., 2006), decaying vegetable materials, and compost heaps (Henssen and Schnepf, 1967). They can be strictly thermophilic and moderately thermophilic in nature. The former can grow in the temperature range between 37 and 65°C, but optimum proliferation takes place at 55–60°C. The moderately thermophilic actinobacteria thrive at 28–60°C and require 45–55°C for optimum growth (Jiang and Xu, 1993). Another group known as thermotolerant actinobacteria can survive at temperatures up to 50°C (Lengeler et al., 1999). Some examples of thermophilic actinobacteria are *Amycolatopsis ruanii and Amycolatopsis thermalba Thermopolyspora, Thermomonospora, Thermotunica, Thermocatellispora, Thermobispora, Acidothermus, Acidimicrobium, and Thermoleophilum.*

Acidophiles

Mostly, actinobacteria grow in soils with a neutral pH. They grow best at a pH between 6 and 9, with maximum growth around neutrality. However, a few strains of *Streptomyces* have been isolated from acidic soils (pH 3.5) (Kim et al, 2003). Other Acidophilic Actinobacteria, which are common in terrestrial habitats such as acidic forest and mine drainage soil, grow in the pH range from about 3.5 to 6.5, with optimum rates at pH 4.5 to 5.5 (Poomthongdee et al,2015). For instance, *Streptacidiphilus anmyonensis* sp. nov., *Streptacidiphilus rugosus* sp. nov., *Streptacidiphilus melanogenes* sp. nov. (Cho et al, 2008) grow well in acidic soil. Acidophilic and acid-tolerant actinobacteria have been studied as promising strains in biotechnology.

Xerophiles

The organisms which can grow in xeric or desert conditions are known as xerophiles. Desert soil is also considered an extreme terrestrial environment where certain species of actinobacteria, often use *Microcoleus, a cyanobacterium* as a source of food (Anandan et al,2016). The distribution of actinobacteria in various locations, such as sandy soil (Cario, Egypt; Falmouth, MA), black alkaline soil (Karnataka, India), sandy loam soil (Keffi Metropolis, Nigeria; Presque Isle, PA), alkaline desert soil (Wadi El Natrun, Egypt; Wadi Araba, Egypt), and subtropical desert soil (Thar, Rajasthan), where *Streptomyces sp*. were dominant followed by the other organisms, such as *Nocardia, Nocardiopsis*, and *Actinomycetes* (Cundell and Piechoski,2016) are reported. The novel isolate recovered from a desert soil sample collected in Beni-Abbes (southwest Algeria) and named Nonomuraea sp. (Badji et al,2007) *Streptomyces youssoufiensis* sp.nov., was isolated from a Moroccan phosphate mine by Hamdali et al, 2011.In 2019, Nafis et al reported the isolation of different actinobacterial genera (*Streptomyces, Nocardioides, Saccharomonospora, Actinomadura*, and *Prauserella* from Moroccan desert soil of Merzouga, Draasfar mining sites which exhibits plant growth promoting activities. Bioactive compounds have also been identified in actinobacterial isolates from the Algerian Saharan desert (Badji et al., 2006), Atacama Desert (Rateb et al., 2011), Egyptian desert (Koberl et al., 2011), Qinghai-Tibet Plateau (Ding et al., 2013), and Thar desert (Thumar et al., 2010). Saccharothrix sp. PAL54A strain isolated from Saharan soil in Ghardaïa produced the known chloramphenicol (Aouiche et al,2012); therefore, it is the first production of this antibiotic by a Saccharothrix species. Currently, the focus has been diverted to extremophilic actinobacteria with the hope that these organisms would add a novel dimension to antimicrobial products research (Zitouni et al., 2004, Vijayakumar et al., 2012, Dhanasekaran et al., 2014).

Psychrophiles

Psychrophiles (cold-loving organisms) are the most plenteous organisms on earth in terms of biomass, diversity, and distribution (Margesin et al,2008). Actinobacteria phylum has been reported as one of the more abundant microbial groups in different Antarctic regions (Cary et al., 2010; Pearce et al., 2012). It has been observed that very old permafrost contains an increased amount of Actinobacteria (Willerslev et al., 2004). Antarctic actinobacteria isolates belonging to genus *Arthrobacter*, *Streptomyces,* and *Rhodococcus* exhibited antifungal activities (Santos et al,2020). The genus *Arthrobacter* was isolated from alpine permafrost in China (Bai et al., 2006). The psychrophilic and psychrotolerant actinobacteria of *Nocardiopsis* and *Streptomyces* were isolated from the water samples of the Polar Frontal region of the Southern Ocean (Sivasankar et al,2014). Psychrophiles are subjected to temperature fluctuations and frequent freeze-thaw events. This has led to the evolution of a number of adaptation mechanisms with regard to reproduction, metabolic activities, survival, and protection strategies in these organisms (Teufel et al,2018). The actinobacterial isolates that were adapted to growth at low temperatures and alkaline conditions, produce a wide range of extracellular enzymes such as proteases, amylases, and cellulases (Zhang et al, 2007). Culture-dependent and culture-independent molecular methods and the emerging fields of genome and proteome analyses will provide further new insights into a psychrophilic lifestyle (Margesina and Miteva, 2011).

Lithophiles

The actinobacterial community is known for its role in ecological succession as one of the pioneer communities. There is a growing interest in stone-dwelling actinobacteria which exhibit several adaptations to thrive in their habitat. The major family which has been isolated from stone niche is *Geodermatophilaceae*. *Geodermatophilaceae*, an actinobacterial family (Normand, 2006) which is endemic to the soil in the order *Geodermatophiliales* (Sen et al., 2014) that comprises three genera: *Geodermatophilus*, *Blastococcus*, and *Modestobacter* initially isolated from desert soils (Luedemann, 1968), seawater (Ahrens and Moll, 1970) and Antarctic regolith (Mevs et al., 2000), respectively. They grow despite unfavorable conditions associated with stone including limited sources of nutrients and water, high pH, and exposure to extreme variations in temperature, humidity, and irradiation. These stone-dwelling microbes are often resistant to extreme environments including exposure to desiccation, heavy metals, and UV & Gamma irradiation (Ding et al,2022). These early ambassadors of life may give new insights into the evolution of life.

Halophiles

Halophiles are present in the salt-rich environment such as deep marine sediments, mangroves, salt lakes, etc. The marine environment is an emerging source of novel actinobacteria and thus of new metabolites. *Rhodococcus marinonascene*, the first marine Actinomycete species to be characterized, supports the existence of marine Actinobacteria (Helmke and Weyland, 1984). Marine actinobacteria present in the extremely diverse environment produce different types of bioactive compounds compared with terrestrial ones (Ward and Bora, 2006, Makkar and Cross 1982). They had to adapt from extremely high pressure and anaerobic conditions at temperatures just below 0- 8 °C on the deep-sea floor to high acidic conditions at temperatures of over 8- 100°C near hydrothermal vents at the mid-ocean ridges (Bull et al,2005). Members of the genera *Dietzia*, *Rhodococcus, Streptomyces, Salinispora, Marinophilus, Solwaraspora, Salinibacterium, Aeromicrobium marinum, Williamsia maris,* and *Verrucosispora* are indigenously marine actinobacteria (Jenson et al, 2004). Currently, there has been a growing awareness of the potential value of marine water habitats as source of actinobacteria that produce useful metabolic products.

Another important source of a hypersaline environment is mangroves. Mangrove forests are the ecosystems prevalent in the tropics and subtropics; they make up over a quarter of the total coastline in the World (Saddhe et al,2016). They provide a habitat for different flora and fauna and also an abode of the microbial biome. The microbes in mangrove habitats not only produce primary and secondary metabolites but are also involved in soil organic matter decomposition and mineralization (Ghosh et al. 2011). In the anoxic mangrove rhizosphere, Actinobacterial species such as *Streptomyces*, *Micromonospora*, and *Nocardioform* were found to be abundant (Tan and Cao,2009). Similarly, *Nocardia* isolated from mangrove soil produced new cytotoxic metabolites that strongly inhibited human cell lines, such as gastric adenocarcinoma (Schneider,2009). There is an ongoing interest in the isolation and characterization of actinobacteria and in to study of the enzymatic adaptations present in them.

Cave Dwellers

Caves are rarely studied and contain different mineral formations, permafrost and previously unknown organisms that have evolved in the micro-environment with more or less constant temperature, humidity, air composition, and other parameters over extended periods of time (Culver DC, Sket B,2000). These ecosystems are of great interest to microbiologists, due to the presence of microorganisms, which have been subjected to evolutions in stable conditions for a long duration (Grady F,2005). Actinobacteria are reported to be a dominant microbial population in several cave ecosystems (Groth and Saiz-Jimenez, 1999; Cheeptham et al., 2013; Tomczyk-Zak and Zielenkiewicz, 2016; Ghosh et al., 2017). The majority of the novel actinobacteria were isolated from cave soils including 6 novel genera, *Antricoccus, Beutenbergia, Knoellia, Lysinibacter Spelaeicoccus* and *Sphaerimonospora* (Rangseekaew and Pathom-Aree, 2019). The genus *Hoyosella* was recovered from the complex biofilm on the ceiling and wall of Altamira cave, Spain (Jurado et al, 2009). The extreme conditions within the caves are supposed to create stress for the inhabiting microorganisms at the genetic level, leading to the evolution of new species (Tiwari and Gupta, 2013). Therefore, caves are considered a prospective source for the isolation of novel actinobacterial taxa.

Conclusion and Future Perspectives

Actinobacteria which is a primitive and prominent phylum among prokaryotes are distributed in a wide range of ecological niches. They are encountered with different lifestyles such as plant commensals, nitrogen-fixing symbionts, as well as animal and plant pathogens. Thus, they constitute a significant proportion of the telluric microflora which is of extensive interest to the scientific community. The studies have proven that extremophilic actinobacteria are efficient producers of new secondary metabolites which show a wide range of biological activities including antibacterial, antifungal, anticancer, and insecticidal properties and enzyme production.

The pure culture and isolation of microbes from their natural environment posed a severe constraint in the recent past. The advent of 16S RNA analysis and metagenomic studies are helping us to remove this drawback. Furthermore, actinobacteria with its diverse portfolio is an ideal group of organisms to study xenobiotic metabolism. This field is gathering momentum because of the increased efflux of xenobiotics by anthropogenic activities.

Yet, actinobacterial research for the most part is rather recent and knowledge of many members is still elusive. This review is an attempt to give a comprehensive account of actinobacteria, especially from extremophilic habitats based on the knowledge available today.

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