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An Introduction to Actinobacteria

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Abstract

Actinobacteria, which share the characteristics of both bacteria and fungi, are widely distributed in both terrestrial and aquatic ecosystems, mainly in soil, where they play an essential role in recycling refractory biomaterials by decomposing complex mixtures of polymers in dead plants and animals and fungal materials. They are considered as the biotechnologically valuable bacteria that are exploited for its secondary metabolite production. Approximately, 10,000 bioactive metabolites are produced by Actinobacteria, which is 45% of all bioactive microbial metabolites discovered. Especially *Streptomyces* species produce industrially important microorganisms as they are a rich source of several useful bioactive natural products with potential applications. Though it has various applications, some Actinobacteria have its own negative effect against plants, animals, and humans. On this context, this chapter summarizes the general characteristics of Actinobacteria, its habitat, systematic classification, various biotechnological applications, and negative impact on plants and animals.

Keywords: Actinobacteria, Characteristics, Habitat, Types, Secondary metabolites, Applications, Pathogens

1. Introduction

Actinobacteria are a group of Gram-positive bacteria with high guanine and cytosine content in their DNA, which can be terrestrial or aquatic. Though they are unicellular like bacteria, they do not have distinct cell wall, but they produce a mycelium that is nonseptate and more slender. Actinobacteria include some of the most common soil, freshwater, and marine type, playing an important role in decomposition of organic materials, such as cellulose and chitin, thereby playing a vital part in organic matter turnover and carbon cycle, replenishing the supply of nutrients in the soil, and is an important part of humus formation. Actinobacterial

colonies show powdery consistency and stick firmly to agar surface, producing hyphae and conidia/sporangia-like fungi in culture media.

Actinobacteria produce a variety of secondary metabolites with high pharmacological and commercial interest. With the discovery of actinomycin, a number of antibiotics have been discovered from Actinobacteria, especially from the genus *Streptomyces*. They are widely distributed in soil with high sensitivity to acid and low pH. Actinobacteria have a number of important functions, including degradation/decomposition of all sorts of organic substances such as cellulose, polysaccharides, protein fats, organic acids, and so on. They are also responsible for subsequent decomposition of humus (resistant material) in soil and for the earthy smell of freshly ploughed soils, producing a number of antibiotics like streptomycin, terramycin, aureomycin, and so on. This chapter gives an overview about the types of Actinobacteria, their habitat, systematic classification and various biotechnological applications, and their ill effects on plants and animals.

2. Habitat of Actinobacteria

2.1. Terrestrial environment

Soil remains the most important habitat for Actinobacteria with streptomycetes existing as a major component of its population. According to numerous reports, *Streptomyces* was encountered to be the most abundant genus isolated in each of the study. Terrestrial Actinobacteria have various interesting antimicrobial potentials. Oskay et al [1] isolated Actinobacteria that had capability of producing novel antibiotics with high antibacterial activity. In anoxic mangrove rhizosphere, Actinobacterial species such as *Streptomyces*, *Micromonospora*, and *Nocardioform* were found to be abundant, which is 1000 to 10000 times smaller than arable lands because of tidal influence [2]. Similarly, *Nocardia* isolated from mangrove soil produced new cytotoxic metabolites that strongly inhibited human cell lines, such as gastric adenocarcinoma [3]. Desert soil is also considered as an extreme terrestrial environment where only certain species, especially wherein Actinobacteria, often use *Microcoleus* as a source of food. There are several reports showing 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 dessert soil (Wadi El Natrun, Egypt; Wadi Araba, Egypt), and subtropical dessert soil (Thar, Rajasthan), where *Streptomyces* sp. were dominant followed by the other organisms, such as *Nocardia*, *Nocardiopsis*, and Actinomycetes [4]. In the study of Nithya et al [5], 134 morphologically distinguished culturable Actinobacteria were isolated from 10 different desert soil samples, and the isolates were found to have varying level of antibacterial activity against bacterial pathogens. Equally, Actinobacteria play a major part in rhizosphere microbial community in the turnover of recalcitrant plant organic matter, and thus the rhizosphere region is considered as one of the best habitats for isolation of these microorganisms. Priyadharsini et al [6] in her study isolated 45 morphologically distinct colonies from 12 different paddy field soils and observed their ability to inhibit the growth of *Cyperus rotundus*. The isolates include *Streptomyces* sp., *Streptoverticillium* sp.,

Actinomadura sp., *Kitasatosporia* sp., *Nocardiopsis* sp., *Pseudonocardia* sp., and *Kibdelosporangium* sp.

2.2. Aquatic environment

Actinobacteria are widely distributed in aquatic habitats, which may sometimes be washed in from surrounding terrestrial habitats. It is vitally important that the numbers and kinds of Actinobacteria are interpreted in the light of information on organisms, such as *Thermoactinomyces* and *Rhodococcus coprophilus*, which are known to be good indicators of the terrestrial component of Actinobacterial propagules in water and sediments. The resistant endospores of *Thermoactinomyces* are produced in self-heating composts, overheated fodders, and surface soil, but they can be washed into aquatic habitats where they are deposited in muds and sediments. It has been assumed that these thermophiles are unable to grow at ambient temperatures in most aquatic habitats. Similarly, the resting coccal stage of *R. coprophilus* passes into freshwater and marine habitats, where it can survive but probably does not grow.

2.2.1. Freshwater

Cross [7] in his study evidenced that Actinobacteria can readily be isolated from freshwater sites. Some of the major type of Actinobacteria dwelling in freshwater include *Actinoplanes*, *Micromonospora*, *Rhodococcus*, *Streptomyces*, and the endospore-forming *Thermoactinomyces*. *Actinoplanes* are commonly found in soils, rivers, and lakes, and the spore vesicles of these organisms have the ability to withstand prolonged desiccation, but they release their motile spores for dispersal when rehydrated [8]. The zoospores are motile by means of a tuft of flagella exhibiting chemotaxis and require an exogenous energy source. *Micromonospora* are also considered to be a common freshwater Actinobacteria and found to be indigenous to such habitats where they turnover cellulose, chitin, and lignin. Numerous reports confirmed the presence of *Micromonospora* in streams, rivers, and river sediments and considered them to be an integral part of the aquatic microflora. Johnston & Cross [9] found that streptomycetes failed to grow in a various lakes, notably in the deeper mud layers where micromonosporae were found to be predominant, whereas another study of AI-Diwany et al [10] showed a significant correlation between micromonosporae and thermoactinomycetes isolated from the River Wharfe in West Yorkshire, where increased number of micromonosporae was found in the adjoining soil. A study revealed that *Micromonospora* spores were washed into freshwater habitats where they can remain dormant for several years [7]. Though streptomycetes spores are also continually washed into freshwater and marine habitats, there is only little evidence that they can be active in such environments. The existence of aquatic streptomycetes has been claimed, but AI-Diwany et al [10] found a high degree of correlation between counts of streptomycetes, fecal *Streptococci*, and *Rhodococci*. Other inhabitants of freshwater include *Actinomadura madurae*, *Mycobacterium kansasii*, and *Arthrobacter*, *Corynebacterium*, and *Nocardia* species. The concentration of hydrophobic spores and hyphae at the water/air interface can increase the number of streptomycetes, micromonosporae, and *Rhodococci* in foam on river water. Evidence clearly

shows that Actinobacteria can become active in freshwater ecosystem in the presence of suitable substrates and conditions for growth rather than specifically adapting themselves to live in such environment.

2.2.2. Marine

When comparing the Actinobacterial diversity in terrestrial environment, the greatest biodiversity lies in the oceans. The marine environment is an untapped source of novel Actinobacteria diversity and thus of new metabolites. Marine Actinobacteria dwelling in extremely different environment produce different types of bioactive compounds compared with terrestrial ones. Marine Actinobacteria 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. *Rhodococcus marinonascens*, the first marine Actinomycete species to be characterized, supports the existence of marine Actinobacteria. Members of the genera *Dietzia*, *Rhodococcus*, *Streptomyces*, *Salinispora*, *Marinophilus*, *Solwaraspora*, *Salinibacterium*, *Aeromicrobium marinum*, *Williamisia maris*, and *Verrucosipora* have been designated as indigenous marine Actinobacteria [11–15]. Grossart et al [16] have illustrated that Actinobacteria account for approximately 10% of the bacteria colonizing marine organic aggregates and that their antagonistic activity might be highly significant in maintaining their presence, which affects the degradation and mineralization of organic matter. The presence of indigenous marine Actinobacteria in the oceans and the distribution of marine Actinobacteria in different marine environments and habitats are confirmed by various recent researches. Innagi et al [17] isolated various marine Actinobacteria, such as *Dietzia maris*, *Rhodococcus erythropolis*, and *Kocuria erythromyxa*, from a sub-seafloor sediment core collected at a depth of 1225 meters off Hokkaido. Jensen et al [14] isolated five new actinomycete phylotypes from marine sediments collected around the island of Guam. Similarly, Actinobacteria were also isolated from samples collected at the deepest abyss, the Challenger Deep off the Marianas, at a depth of 10,923 meters [15]. Unusual Actinobacteria, belonging to *Micrococceae*, *Dermatophilaceae*, and *Gordoniaceae* have been isolated from sponges. Dhanasekaran et al [18] isolated 17 Actinobacteria from soil samples belonging to the saltpan regions of Cuddalore, Parangipettai, and screened for primary antibacterial activity among which *Streptomyces* spp. and *Saccharomonospora* sp. collected showed promising antimicrobial activity against different bacteria. An antibacterial methyl-substituted β -lactam compound was isolated and characterized from *Streptomyces noursei* DPTD21 in saltpan soil of Parangipettai Porto Novo in Cuddalore district, Tamil Nadu, by Dhanasekaran et al [19]. In another study, soil and sediment samples were collected from different locations in Muthupet mangrove region, and Actinobacteria were isolated viz *Streptomyces* sp. CC17 and SM13, *Streptosporangium* sp. SH15, and *Micropolyspora* sp. S22, which showed highest larvicidal activity against *Anopheles* mosquito larvae [20]. All the above-stated Actinobacteria isolated from marine environments, such as the deep sea floor, marine invertebrates and marine snow, sea shore soil, and deep sea sediments, represent unique ecosystems that cannot be found anywhere else in the world. Equally, these isolates produce various novel metabolites, which are listed in Table 1. Even with the limited screening efforts that have been dedicated to date to marine Actinobacteria, the discovery rate of novel secondary metabolites

from marine Actinobacteria has been recently exceeded terrestrial counterparts, as evident by the isolation of many new chemical entities from marine Actinobacteria.

3. General characteristics of Actinobacteria

Actinobacteria comprises a group of branching unicellular microorganisms, most of which are aerobic-forming mycelium known as substrate and aerial. They reproduce by binary fission or by producing spores or conidia, and sporulation of Actinobacteria is through fragmentation and segmentation or conidia formation. The morphological appearance of Actinobacteria (Figure 1) is compact, often leathery, giving a conical appearance with a dry surface on culture media and are frequently covered with aerial mycelium.

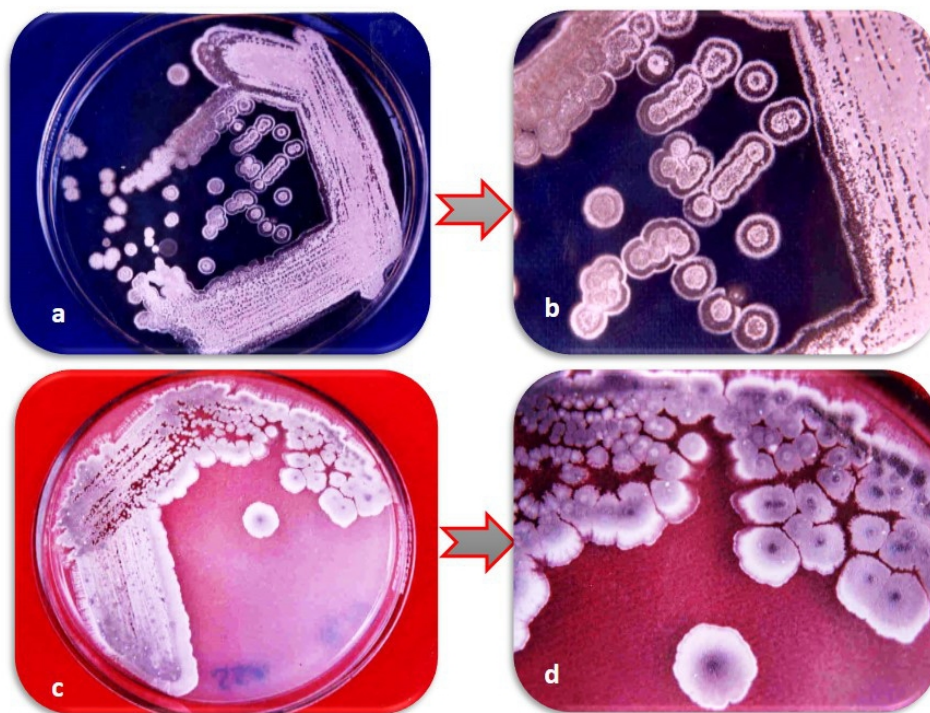


Figure 1. Appearance of Actinobacteria isolates on Starch casein agar plate. a, c Plate view of the Actinobacterial isolates. b, d Morphology of individual colonies.

3.1. Aerial mycelium

The aerial mycelium is usually thicker than the substrate mycelium (Figure 2a). The aerial mycelium shows sufficient differentiation that a miscellaneous assortment of isolates can be segregated into a number of groups having similar morphological characteristics under fixed condition. This is designated as one of the most important criteria for the classification of the genus *Streptomyces* into species, comprising structure (cottony, velvety, or powdery), formation of rings or concentric zones, and pigmentation.

3.2. Substrate mycelium

The substrate mycelium of Actinobacteria varies in size, shape, and thickness (Figure 2b). Its color ranges from white or virtually colorless to yellow, brown, red, pink, orange, green, or black.

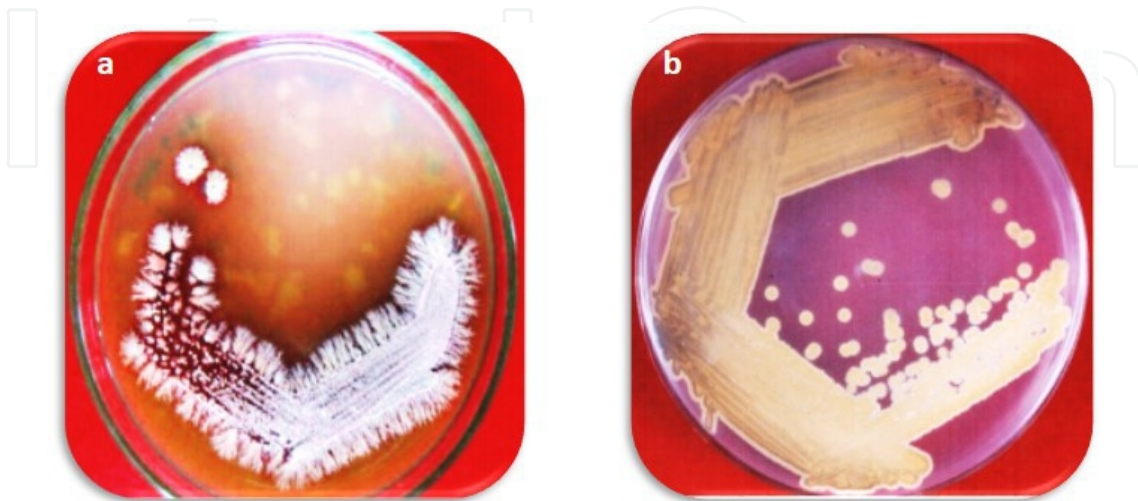


Figure 2. Abundant growth of Actinobacterial isolate on starch casein agar medium. a. Aerial mycelium. b. Reverse side of plate showing substrate mycelium.

3.3. Morphological appearance

Morphology has been an important characteristic to identify Actinobacteria isolates, which was used in the first descriptions of *Streptomyces* species (Figure 3). This is made using various standard culture media, including International *Streptomyces* Project (ISP). For nonstreptomycetes or rare Actinobacteria, strains maintained on ATCC Medium No.172 (NZ-amine glucose starch agar) (American Type Culture Collection, 1982) were used. Various morphological observations, including germination of spores, elongation and branching of vegetative mycelium, formation of aerial mycelium, color of aerial and substrate mycelium, and pigment production, have been used to identify Actinobacteria [21]. Light microscopy was used to study the formation of aerial mycelium and substrate mycelium, and scanning electron microscopy (Figure 4) was used to study the spores, the spore surface, and spore structure.

4. Systematics of Actinobacteria

In the Bergey's Manual of Determinative Bacteriology, Actinobacteria are included in several sections of volume four. All Actinobacteria are included under the order Actinomycetales. The order Actinomycetales is divided into four families—Streptomycetaceae, Actinomycetaceae, Actinoplanaceae, and Mycobacteriaceae [23]. The "Bergey's Manual of Systematic Bacteriology—2nd edition" for Actinobacteria classification has five volumes, which contain interna-

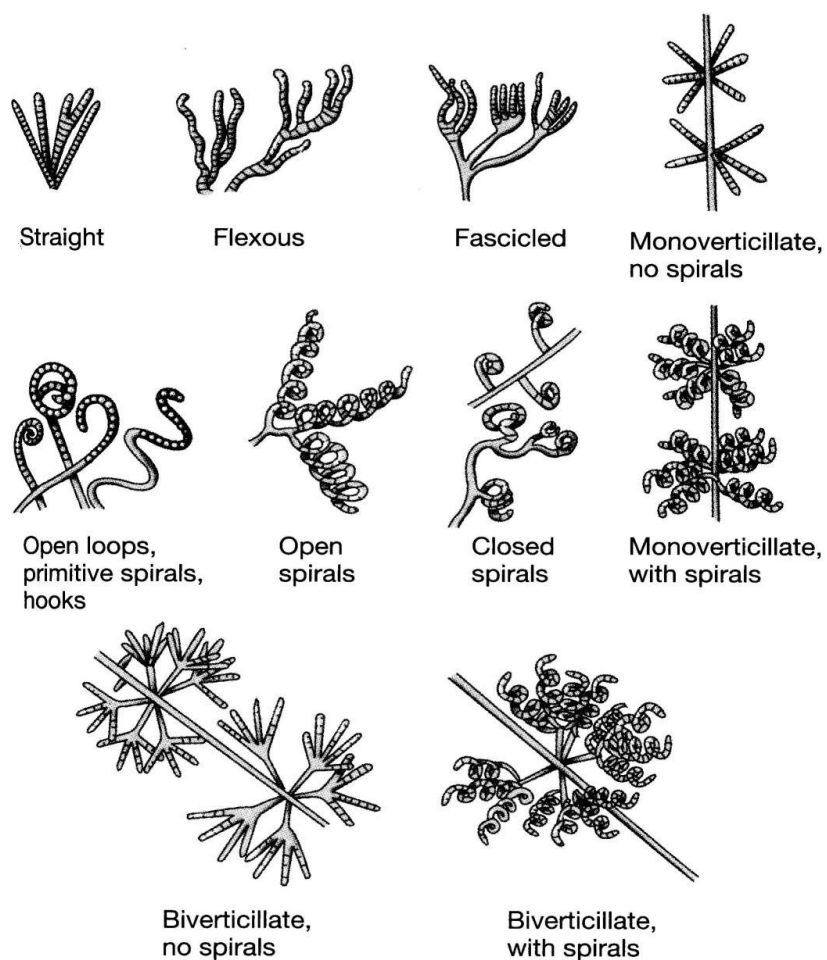


Figure 3. Type of spore-bearing structure in streptomycetes [22].

tionally recognized names and descriptions of bacterial species. Classification of Actinobacteria has been rearranged as follows:

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 5

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, Jiangel-

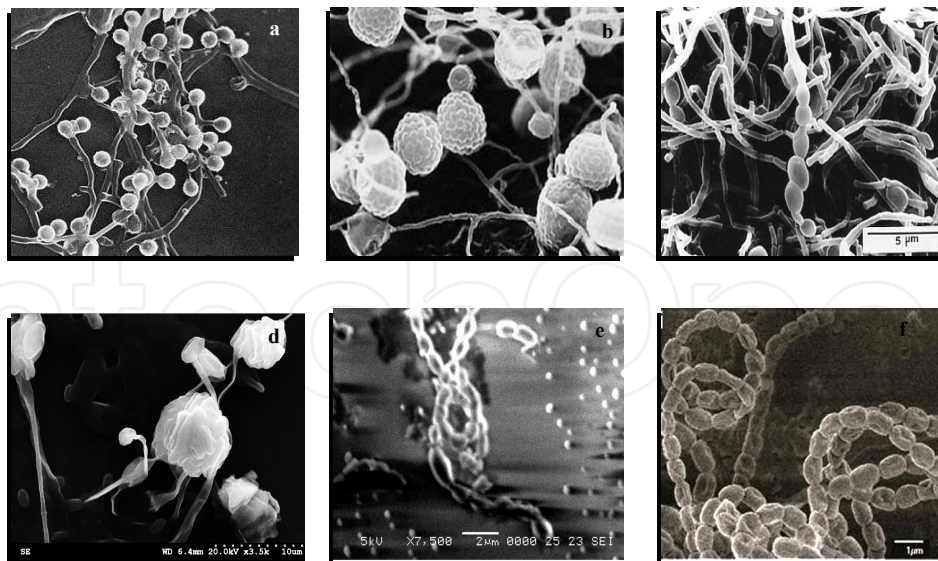


Figure 4. Scanning electron photographs of various Actinobacterial isolates. a. *Micromonospora* sp. b. *Streptosporangium* sp. c. *Saccharopolyspora* sp. d. *Actinosynnema* sp. e. *S. noursei* DPTD21. f. *Streptomyces* sp. JD9.

ales, 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 encountered. At present, the molecular identification is based on 16S rDNA sequences, which is most significant for Actinobacteria identification [24].

5. Types of Actinobacteria

5.1. Thermophilic Actinobacteria

Number of studies has been carried out by the researchers to confirm the existence of extremophilic and extreme tolerant soil Actinobacteria (acid tolerant and alkali tolerant, psychrotolerant and thermotolerant, and halotolerant and haloalkalitolerant or xerophilic). Mesophilic Actinobacteria can grow at an optimal temperature from 20°C to 42°C, among which thermotolerant species exist, which can survive at 50°C. Moderately thermophilic Actinobacteria have an optimum growth at 45°C–55°C [29], whereas strictly thermophilic Actinobacteria grow at 37°C–65°C with the optimum temperature at 55°C–60°C [25]. Incubation temperatures of 28°C, 37°C, and 45°C are considered optimal for isolation of soil mesophilic, thermotolerant, and moderately thermophilic Actinobacteria. *Thermoactinomyces*, which is presently excluded from the order Actinomycetales, are described as thermophilic forms depending on its phenotypic and molecular genetic characteristics, as well as among some species of *Thermomonospora*, *Microbispora*, *Saccharopolyspora*, *Saccharomonospora*, and *Streptomyces*.

5.2. Acidophilic Actinobacteria

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 [26, 27]. It has been shown that acidophilic Actinobacteria consistently form two distinct aggregate taxa (namely, the neutrotolerant acidophilic and strictly acidophilic cluster groups) based on numerical phenetic data; members of the two groups share common morphological and chemotaxonomic properties [26]. Also some members of the strictly acidophilic group form a distinct taxon, such as the genus *Streptacidiphilus*, which has been assigned to the revised family Streptomycetaceae, together with the genera *Kitasatospora* and *Streptomyces*.

5.3. Halophilic Actinobacteria

Halophilic Actinobacteria are categorized into different types based on their growth in media containing different concentrations of salt. Extreme halophiles grow best in media containing 2.5–5.2 M salt, whereas borderline extreme halophiles grow best in media containing 1.5–4.0 M salt, moderate halophiles grow best in media containing 0.5–2.5 M salt, and finally halotolerants that do not show an absolute requirement to salt for growth but grow well up to often very high salt concentrations and tolerate 100 g/l salt (equivalent to 1.7 M NaCl) at least. Seawater, saline soils, salt lakes, brines, and alkaline saline habitats are considered as the best habitats for isolating halophilic Actinobacteria. Generally, most of the halophilic Actinobacteria have been isolated from saline soils. Halophilic Actinobacteria isolated from marine environments are assigned to a few genera, including *Micromonospora*, *Rhodococcus*, and *Streptomyces* [28]. The other group includes *Dietzia*, *Salinispora*, *Marinophilus*, *Solwaspora*, *Salinibacterium*, *Aeromicrobium*, *Gordonia*, *Microbacterium*, *Mycobacterium*, *Nocardiosis*, *Pseudonocardia*, *Actinomadura*, *Saccharopolyspora*, *Streptosporangium*, *Nonomuraea*, *Williamsia*, and *Verrucosipora* [28–31].

5.4. Endophytic Actinobacteria

Endophytic Actinobacteria are defined as those that inhabit the internal part of plants, causing apparently no visible changes to their hosts. These Actinobacteria play specific roles, for instance, protecting the host plants against insects and diseases. Endophytic Actinobacteria constitute a large part of the rhizosphere, which are also found inside plants in which the extensively studied species are from the genus *Frankia*, nitrogen-fixing bacteria of nonleguminous plants [32], and a few species of the genus *Streptomyces* that are phytopathogens. Generally, the endophytic Actinobacteria include *Streptomyces*, but the genera *Streptoverticillium*, *Nocardia*, *Micromonospora*, *Kitasatospora*, *Pseudonocardia*, *Microbispora*, *Kibdelosporangium*, *Actinopolyspora*, *Nocardioides*, *Brevibacterium*, *Actinomadura*, *Glycomyces* *Plantactinospora*, *Polymorphospora*, *Promicromonospora*, and *Streptosporangium* are also found in the plants, such as *Palicourea longifolia*, *Calycophyllum acreanum*, *Monstera spruceana*, *Croton lechleri*, *Cantua buxifolia*, *Siparuna crassifolia*, and *Eucharis cyaneosperma*.

5.5. Symbiotic Actinobacteria

About 15% of the world's nitrogen is fixed naturally by the symbiotic relationships between various species of the *Frankia* belonging to the family of Actinobacteria. The plants that form symbiotic relationships with *Frankia* are called actinorhizal plants. Researchers have found over 160 plants that have Actinobacteria as their host, including alders, Russian olive, bayberry, sweet fern, bitterbrush, and cliff rose. The *Frankia* have the ability to provide most or all of the host plant's nitrogen needs. Numerous *Frankia* species including *Casuarina* isolates form nitrogen-reducing (NIR) vesicles *in vitro* and *in planta* [33]. These nitrogen-fixing bacteria and their host plants are often pioneer species on young nitrogen-deficient and disturbed soils such as moraines, volcanic flows, and sand dunes.

5.6. Endosymbiotic Actinobacteria

An endosymbiont is any organism that lives within the body or cells of another organism. Endosymbiosis process is sometimes obligate, that is, either the endosymbiont or the host cannot survive without the other. Members of the phylum Actinobacteria have been identified as abundant members of sponge-associated microbial communities. *Mycobacterium* along with *Micrococcus*, *Micromonospora*, *Microbacterium*, *Brevibacterium*, *Kocuria*, *Corynebacterium*, *Rhodococcus*, *Brachybacterium*, *Rubrobacter*, *Streptomyces*, *Dietzia*, *Salinispora*, *Actinokineospora*, *Gordonia*, *Arthrobacter*, *Nocardiopsis*, and *Rothia* species were found to live as endosymbionts in marine sponges *Callyspongia aff. Implexa*, *Aplysina aerophoba*, *Sphaciospongia vagabunda*, *Hemimycale culumella*, *Hyrtios erecta*, *Dysidea tupha*, *Callyspongia sp.*, *Dysidea avara*, *Amphimedon sp.*, and *Negombata magnifica*. However, the Actinobacterial endosymbionts have also been reported in other group of animals, such as *Hylobates hoolock*, *Rhinopithecus roxellanae*, *Rhinopithecus bieti*, *Panthera tigris altaica*, *Panthera tigris tigris*, *Panthera tigris amoyensis*, *Ailurus fulgens*, *Cavnlvara zlrsideae*, *Ursus thibetanus*, *Cervus elaphus*, *Elaphurus davidianus*, and *Vicugna pacos*.

5.7. Gut Actinobacteria

Though Actinobacteria are found in various diverse habitats, some are also known to form intimate associations with invertebrates and vertebrates. Symbiotic interactions are essential mainly for the survival and reproduction because they play a crucial role in nutrition, detoxification of certain compounds, growth performance, and protection against pathogenic bacteria. Many studies have shown that some symbiotic Actinobacterial species, that is probiotics, control bacterial diseases in livestock, poultry, and aquaculture. They also take part in host health by converting the feedstuffs into microbial biomass and fermentation end products that can be utilized by the animal host. Tan et al [34] isolated *Streptomyces*, *Nocardiopsis*, and *Oerskovia* from healthy goat feces. Similarly, Latha and Dhanasekaran [35] isolated 87 Actinobacterial cultures from different feces of goat and chicken collected from various locations in Pudukkottai and Tiruchirappalli Districts, Tamil Nadu, among which 45 isolates were selected for the screening of antibacterial activity and extracellular digestive enzyme production. The ability of the probiont *Streptomyces sp. JD9* from gut of chicken possesses all the characteristics needed to satisfy the indigenous Actinobacterial probiont for enhanced broiler production [36].

6. Applications of Actinobacteria

Actinobacteria are well recognized for their production of primary and secondary metabolites that have important applications in various fields. They are also a promising source of wide range of important enzymes, which are produced on an industrial scale. A large fraction of antibiotics in the market is obtained from Actinobacteria. They produce enzyme inhibitors useful for cancer treatment and immunomodifiers that enhance immune response. They have the ability to degrade a wide range of hydrocarbons, pesticides, and aliphatic and aromatic compounds. They perform microbial transformations of organic compounds, a field of great commercial value. Members of many genera of Actinobacteria can be potentially used in the bioconversion of underutilized agricultural and urban wastes into high-value chemical products. Actinobacteria are also important in plant biotechnology as strains with antagonistic activity against plant pathogens are useful in biocontrol. Their metabolic potential offers a strong area for research. Here, we have a brief description about important applications of Actinobacteria (Figure 5).

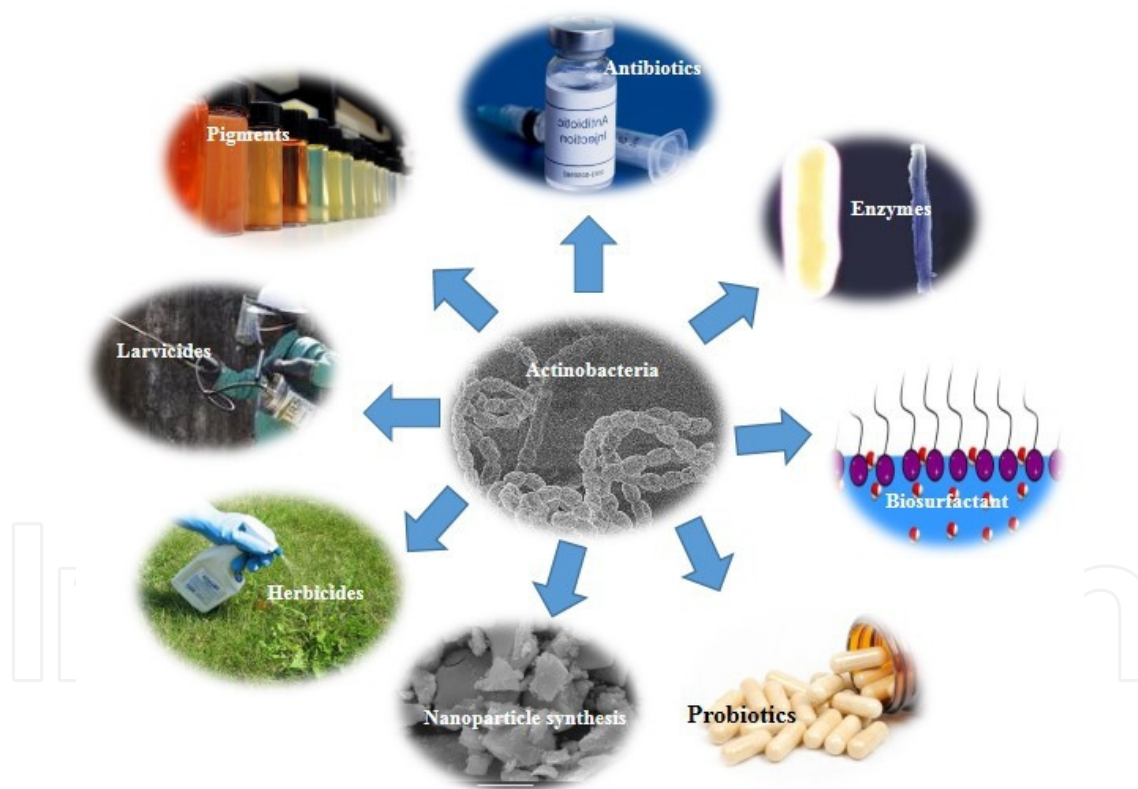


Figure 5. Biotechnological applications of Actinobacteria.

6.1. Antimicrobials

Actinobacteria hold a significant role in producing variety of drugs that are extremely important to our health and nutrition. Recently, diseases due to multidrug-resistant patho-

genic bacteria are sturdily increasing, and thus search for new antibiotics is effective against the multidrug-resistant pathogens. Natural products having novel structures have been observed to possess useful biological activities [37]. Nature always remains the richest and the most versatile propitious source for new antibiotics, though there is considerable progress within the fields of chemical synthesis and engineered biosynthesis of antibacterial compounds. Toxic nature of certain antibiotics led to their limited usage although thousands of antibiotics have been discovered till date. To get through this problem, search of new antibiotics that are more effective and that do not have any toxic side effects is in progress. As already mentioned, one of the major healthcare problems is the antibiotic resistance. One approach to solve this problem is to search for new antibiotics with new mechanism of action. Figure 6 shows that a majority of antibiotics are derived from microorganisms, especially from the species Actinobacteria. Almost 80% of the world's antibiotics are known to be derived from Actinobacteria, mostly from the genera *Streptomyces* and *Micromonospora* [38, 39].

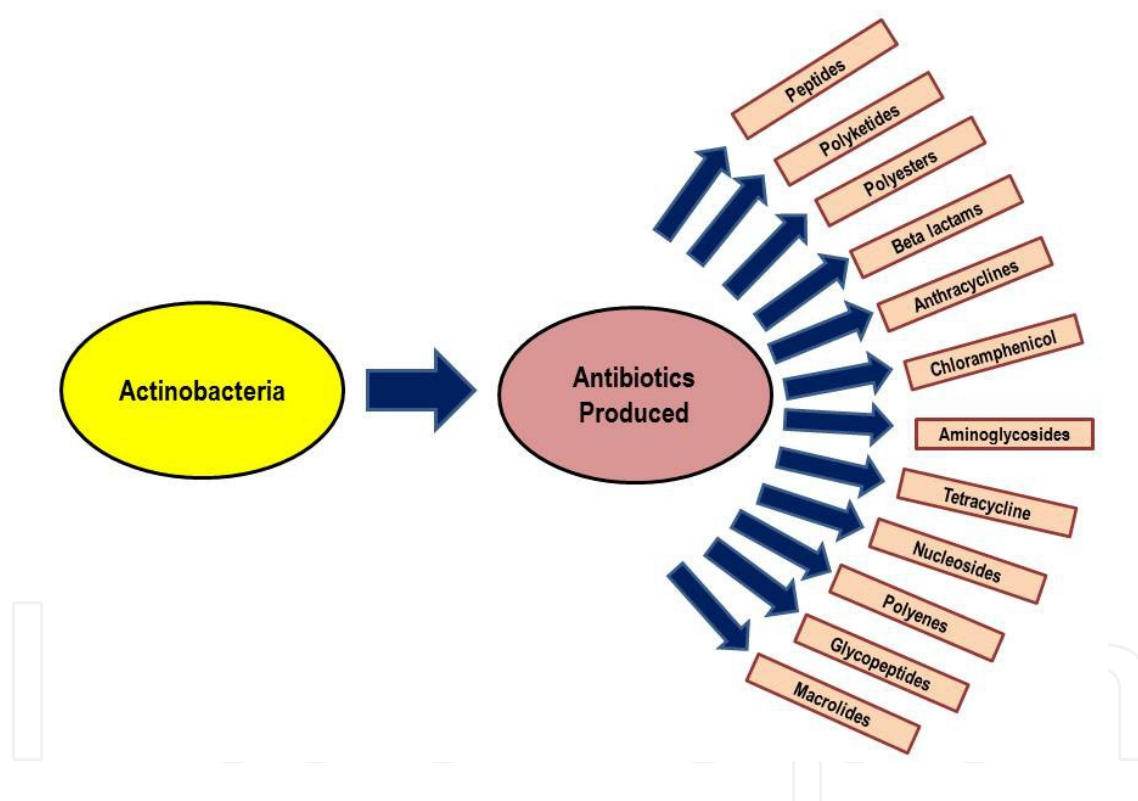


Figure 6. Antibiotics from Actinobacteria.

Particularly, *Streptomyces* species produce around 7600 compounds, many of which are secondary metabolites that are potent antibiotics, which has made streptomycetes the primary antibiotic-producing organisms exploited by the pharmaceutical industry [40, 41]. The reason behind the ability of the genus *Streptomyces* to produce commercially significant compounds remains supreme because of the extra large DNA complement of these bacteria [42]. It has been estimated that the last five decades have seen the discovery of more than 12,000 antibiotics, out of which the Actinobacteria yielded about 70% of them and the remaining 30% are products

of filamentous fungi and nonActinobacteria. The antibiotics from Actinobacteria are differentiated into several major structural classes, such as aminoglycosides (e.g., streptomycin and kanamycin), ansamycins (e.g., rifampin), anthracyclines (e.g., doxorubicin), β -lactam (cephalosporins), macrolides (e.g., erythromycin), and tetracycline. *Streptomyces* strains have produced many of the antibiotics known to humans, which appears that these organisms produce antibiotics to kill off potential competitors [43]. One of the first antibiotics used is streptomycin produced by *Streptomyces griseus* [44]. Indeed, different *Streptomyces* species produce about 75% of commercially and medically useful antibiotics. In the course of screening for new antibiotics, several studies are oriented toward isolation of streptomycetes from different habitats. Different conditions of nutrition and culturing may affect the ability of *Streptomyces* cultures to form antibiotics, and hence the medium constitution together with the metabolic capacity of the producing organism greatly affects antibiotic biosynthesis.

Antagonistic Actinobacteria produce a variety of antibiotics that vary in chemical nature, in antimicrobial action, in toxicity to animals, and in their chemotherapeutic potentialities. Some of the antibiotics that have been isolated so far from Actinobacteria are crude preparations, whereas others have been crystallized, and considerable information has been gained concerning their chemical nature, which includes lysozyme, actinomycin, micromonosporin, streptothricin, streptomycin, and mycetin. Some Actinobacteria produce more than one antibiotic substance (e.g., *S. griseus*), as well as the same antibiotic may be produced by different species of Actinobacteria (e.g., actinomycin, streptothricin). A given antibiotic may, therefore, be identical, even when produced by different Actinobacteria, as shown by its chemical composition and antibiotic spectrum. Table 1 represents the list of antibiotics produced by various Actinobacteria with excellent antimicrobial application (Table 1).

Antibiotic compound	Application	Actinobacteria
1,8-Dihydroxy-2-ethyl-3-methylanthraquinone	Antitumor	<i>Streptomyces</i> sp.
1-Hydroxy-1-norresistomycin	Antibacterial; anticancer	<i>Schisandra chinensis</i>
2-Allyloxyphenol	Antimicrobial; food preservative; oral disinfectant	<i>Streptomyces</i> sp.
Anthracyclines	Antitumor	<i>S. galileus</i>
Arenicolides A–C	Mild cytotoxicity	<i>Salinispora arenicola</i>
Arenimycin	Antibacterial; anticancer	<i>S. arenicola</i>
Avermectin	Antiparasitic	<i>Streptomyces avermitilis</i>
Bafilomycin	ATPase inhibitor of microorganisms, plant and animal cells	<i>S. griseus</i> , <i>Streptomyces halstedii</i>
Bisanthraquinone	Antibacterial	<i>Streptomyces</i> sp.
Butenolides	Antitumor	<i>Streptoverticillium luteoverticillatum</i>
Carboxamycin	Antibacterial; anticancer	<i>Streptomyces</i> sp.
Chinikomycins	Anticancer	<i>Streptomyces</i> sp.

Antibiotic compound	Application	Actinobacteria
Chloramphenicol	Antibacterial, inhibitor of protein biosynthesis	<i>Streptomyces venezuelae</i>
Cyanospraside A	Unknown	<i>Solieria pacifica</i>
Daryamides	Antifungal; anticancer	<i>Streptomyces</i> sp.
Frigocyclinone	Antibacterial	<i>S. griseus</i>
Glaciapyrroles	Antibacterial	<i>Streptomyces</i> sp.
Hygromycin	Antimicrobial, immunosuppressive	<i>Streptomyces hygrosopicus</i>
Lajollamycin	Antibacterial	<i>Streptomyces Nodosus</i>
Lincomycin	Antibacterial, inhibitor of protein biosynthesis	<i>Streptomyces lincolnensis</i>
Marinomycins A–D	Antimicrobial; anticancer	<i>Marinispora</i>
Mechercharmucins	Anticancer	<i>Thermoactinomyces</i> sp.
Mitomycin C	Antitumor, binds to double-stranded DNA	<i>Streptomyces lavendulae</i>
Pacificanones A & B	Antibacterial	<i>S. pacifica</i>
Piericidins	Antitumor	<i>Streptomyces</i> sp.
Proximicins	Antibacterial; anticancer	<i>Verrucosipora</i> sp.
Rapamycin	Immunosuppressive, antifungal	<i>S. hygrosopicus</i>
Resistoflavin methyl ether	Antibacterial; antioxidative	<i>Streptomyces</i> sp.
Saliniketal	Cancer chemoprevention	<i>S. arenicola</i>
Salinispyrone	Unknown	<i>S. pacifica</i>
Salinispyrone A & B	Mild cytotoxicity	<i>S. pacifica</i>
Salinosporamide A	Anticancer; antimalarial	<i>Salinispora tropica</i>
Salinosporamide B & C	Cytotoxicity	<i>S. tropica</i>
Sesquiterpene	Unknown	<i>Streptomyces</i> sp.
Staurosporinone	Antitumor; phycotoxicity	<i>Streptomyces</i> sp.
Streptokordin	Antitumor	<i>Streptomyces</i> sp.
Streptomycin	Antimicrobial	<i>S. griseus</i>
Streptozotocin	Diabetogenic	<i>S. achromogenes</i>
Tetracyclines	Antimicrobial	<i>Streptomyces achromogenes</i> <i>Streptomyces rimosus</i>
Tirandamycins	Antibacterial	<i>Streptomyces</i> sp.
Valinomycin	Ionophor, toxic for prokaryotes and eukaryotes	<i>S. griseus</i>
ZHD-0501	Anticancer	<i>Actinomadura</i> sp.
Elaiomycins B and C	Antitumor	<i>Streptomyces</i> sp. BK 190
N-[2-hydroxyphenyl]-2-phenazinamine (NHP),	Anticancer; antifungus	<i>Nocardia dassonvillei</i>
Chromomycin B, A2, A3	Antitumor	<i>Streptomyces coelicolor</i>

Antibiotic compound	Application	Actinobacteria
1,4-dihydroxy-2-(3-hydroxybutyl)-9, 10-anthraquinone 9, 10-anthrac	Antibacterial	<i>Streptomyces</i> sp. RAUACT-1

Table 1. List of antibiotics produced from Actinobacteria

6.2. Enzymes

A wide variety of biologically active enzymes are produced by both marine and terrestrial Actinobacteria (Figure 7; Table 2). They secrete amylases to the outside of the cells, which helps them to carry out extracellular digestion. This enzyme is of great significance in biotechnological applications such as food industry, fermentation, and textile to paper industries because of their ability to degrade starch [45]. Another important aspect of Actinobacteria is the production of cellulases, which are a collection of hydrolytic enzymes that hydrolyze the glucosidic bonds of cellulose and related cello-digosaccharide derivatives. Lipase is produced from various Actinobacteria, bacteria, and fungi and is used in detergent industries, foodstuff, oleochemical, diagnostic settings, and also in industries of pharmaceutical fields [46]. Many Actinobacteria have been isolated from various natural sources, as well as in plant tissues and rhizospheric soil. Biological functions of Actinobacteria mainly depend on sources from which the bacteria are isolated. Actinobacteria, particularly streptomycetes, are known to secrete multiple proteases in the culture medium [47]. Similarly, Actinobacteria have been revealed to be an excellent resource for L-asparaginase, which is produced by a range of Actinobacteria, mainly those isolated from soils, such as *S. griseus*, *Streptomyces karnatakensis*, *Streptomyces albidoflavus*, and *Nocardia* sp. [48, 49]. The roots and rhizomes of several Thai medicinal plants such as lemon grass (*Cymbopogon citratus*) and ginger (*Zingiber officinale*) have long been used in Thai traditional medicine for stomach ache and asthma treatment. Rhizosphere soil of these plants may be an attractive Actinobacterial source, which has the ability to produce novel secondary metabolites. Enzymes such as catalase, chitinase, and urease are also produced from Actinobacteria. Interestingly, keratinase, an enzyme that degrades the poultry chicken feather, has been successfully produced from *Nocradiopsis* sp. SD5 isolated from feather waste in Tamil Nadu, India [50]. Similarly, Actinobacteria isolated from chicken and goat gut showed the presence of various enzymes such as amylase, protease, phytase, and lipase [35].

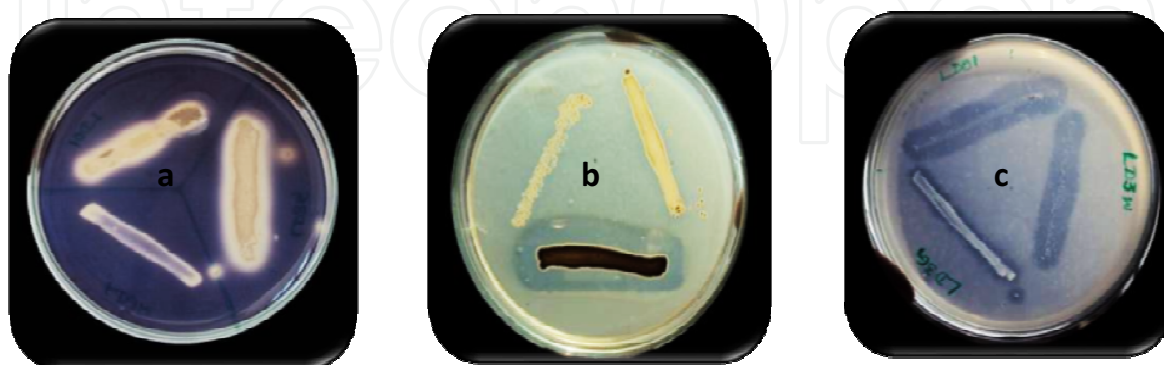


Figure 7. Different types of enzymes produced by Actinobacteria. a. Amylase. b. Protease. c. Lipase. The zone of inhibition around the inoculated Actinobacteria confirms the production of particular enzyme.

Enzyme	Actinobacteria	Use	Industry of application
Protease	<i>Thermoactinomyces</i> sp., <i>Nocardiopsis</i> sp., <i>Streptomyces</i> <i>pactum</i> , <i>Streptomyces</i> <i>thermoviolaceus</i> , <i>Streptomyces</i> sp.	Detergents	Detergent
		Cheese making	Food
		Clarification- low calorie beer	Brewing
		Dehiding	Leather
		Treatment of blood clot	Medicine
Cellulase	<i>Streptomyces</i> sp., <i>Thermobifida</i> <i>halotolerans</i> , <i>Streptomyces</i> sp., <i>Thermomonospora</i> sp., <i>Streptomyces</i> <i>ruber</i>	Removal of stains	Detergent
		Denim finishing, softening of cotton	Textile
		Deinking, modification of fibers	Paper and pulp
Lipase	<i>Streptomyces griseus</i>	Removal of stains	Detergent
		Stability of dough and conditioning	Baking
		Cheese flavoring	Dairy
		Deinking, cleaning	Textile
Xylanase	<i>Actinomadura</i> sp., <i>Streptomyces</i> spp.	Conditioning of dough	Baking
		Digestibility	Animal feed
		Bleach boosting	Paper and pulp
Pectinase	<i>Streptomyces lydicus</i>	Clarification, mashing	Beverage
		Scouring	Textile
Amylase	<i>Streptomyces</i> sp., <i>Streptomyces</i> <i>erumpens</i> , <i>Nocardiopsis</i> sp. , <i>Thermobifida fusca</i> , <i>Nocardiopsis</i> sp.	Removal of stains	Detergent
		Softness of bread softness and volume	Baking
		Deinking, drainage improvement	Paper and pulp
		Production of glucose and fructose syrups	Starch industry
		Removal of starch from woven fabrics	Textile
Glucose oxidase	<i>Streptomyces coelicolor</i>	Strengthening of dough	Baking
Keratinase	<i>Nocardiopsis</i> sp. SD5	Feather degradation	Animal feed
Phytase	<i>Streptomyces luteogriseus</i> R10	Phytate digestibility	Animal feed

Table 2. Enzymes and their industrial applications

6.3. Bioherbicides

Another interesting application of the Actinobacteria is the use of their secondary metabolites as herbicides against unwanted herbs and weeds. *Streptomyces saganonensis* produce herbicides and herbimycins that control monocotyledonous and dicotyledonous weeds. Anisomycin, which is produced by *Streptomyces* sp., is a type of growth inhibitor for annual grassy weeds such as barnyardgrass and common crabgrass and broad-leaved weeds; anisomycin can destroy the ability of the plants to synthesize chlorophyll. 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. Anisomycin can make small seedlings of barnyardgrass and common crabgrass die above 50 ppm and inhibit radicle growth below 12.5 ppm. Its synthetase may accumulate ammonia and control photosynthetic phosphorylation, causing plant death [51]. *S. hygrosopicus* produce carbocyclic coformycin and hydantocidin, which can decrease synthetase of acetylsuccinate by increasing the content of ATP and hold back the synthesis of protein [52]. In addition, phthoxazolin, hydantocidin, and homoalanosin from *Streptomyces* sp. can control several weeds [53]. Dhanasekaran et al [54] reported that *Streptomyces* sp. had the ability to inhibit the growth of *Echinochilora crusgalli*. Similarly, *Streptomyces* sp. KA1-3, KA1-4, KA1-7, and KA23A were found highly effective against *C. rotundus* [55]. Herbicidal activity of the bioactive compounds *N*-phenylpropanamide and *N* (naphthalene-1-yl) propanamide from *Streptomyces* sp. KA1-3 [56, 57] was also evaluated.

6.4. Probiotics

Probiotics are the live microbial adjunct that has a beneficial effect on the host by various means, such as modifying the host associated or ambient microbial community, by ensuring the improved use of the feed or enhancing its nutritional value, by enhancing the host response towards disease, or by improving the quality of its ambient environment. Despite several other important applications, marine Actinobacteria have been given its attention for their use as probiotics. The potential of Actinobacteria against shrimp pathogenic *Vibrio* spp. made marine Actinobacteria as potential probiotic strains due to their ability to degrade macromolecules, such as starch and protein, in culture pond water; the production of antimicrobial agents; and the formation of heat- and desiccation-resistant spores [58]. Recently, a few studies were made on the possible use of marine Actinobacteria in disease prevention against aquatic pathogens. Das et al [59] in their preliminary study reported the use of *Streptomyces* sp. on the growth of black tiger shrimp. An antibiotic product extracted from marine Actinobacteria was incorporated into feed to observe the *in vivo* effect on white spot syndrome virus in black tiger shrimp. Again, You et al [58] reported the activity of marine actinomycete as a potential organism against biofilms produced by *Vibrio* spp. and recommended the use of Actinobacteria to prevent the disease caused by *Vibrio* spp. In another study, Latha et al [36] screened 18 of the Actinobacteria isolated from chicken for probiotic properties, and the results revealed that *Streptomyces* sp. JD9 was the potent isolate with well-distinct probiotic properties.

6.4.1. Aggregative peptide pheromones

Aggregation is one of the most important criteria for the selection of a good probiotic candidate, which is the process of reversible accumulation of cells with one or more strains. For this aggregating process to take place, pheromone production is one of the main criteria that involves defense against predators, mate selection, and in overcoming host resistance by mass attack. In particular, sex pheromone peptides in culture supernatants have been shown to promote aggregation not only with the same species but also with related species [60–62]. Thus, the auto-aggregating ability of a probiotic is a prerequisite for colonization of the gastrointestinal tract, whereas coaggregation provides a close interaction with pathogenic bacteria. Though there are a number of studies in accordance with peptide pheromone-mediated signaling, it is lacking in the case of Actinobacteria, and thus a novel report on isolation and purification of diffusible aggregation promoting factor, that is, pheromones from potent Actinobacterial probiont *Streptomyces werraensis* LD22 isolated from the gut region of goat, were described by Muthu Selvam et al [63]. The results clearly portray that Actinobacterial strain *S. werraensis* LD22 secretes a heat-stable, acidic pH-resistant, low molecular weight peptide pheromone that promotes the aggregation propensity and enhances the biofilm forming ability of other Actinobacterial isolates.

6.5. Biosurfactants

Biosurfactants are the microbially derived compounds that share hydrophilic and hydrophobic moieties that are surface active. When compared with chemically derived surfactants, biosurfactants are independent of mineral oil as a feedstock; they are readily biodegradable and can be produced at low temperatures. Biosurfactants can be applied in various areas, such as the nutrient, cosmetic, textile, varnish, pharmaceutical, mining, and oil recovery industries [64–66]. The lipopeptide antibiotic daptomycin is an Actinobacterial biosurfactant that has already entered the market and is used in the treatment of diseases caused by Gram-positive pathogens and has been marketed as Cubicin by Cubist Pharmaceuticals. Diverse types of biosurfactants or bioemulsifiers have been described to be produced within the class *Actinobacteria*. Among the best described biosurfactants are glucose-based glycolipids, most of which have a hydrophilic backbone consisting of glycosidic-linked glucose units forming a trehalose moiety.

6.6. Vitamins

Vitamin B₁₂ as it exists in nature may be produced by bacteria or Actinobacteria [67]. Isolation of vitamin B₁₂ from Actinobacteria fermentations [68, 69] stirred up considerable interest in possible production of vitamin by microbial fermentations. Addition of cobalt salts to the media apparently acts as a precursor for all Actinobacteria to produce vitamin. As cobalt is a rather effective bactericidal agent, this precursor must be added carefully. The fermentations producing the antibiotics streptomycin, aureomycin, grisein, and neomycin will produce some vitamin B₁₂ as well if the medium is supplemented with cobalt without apparently affecting the yields of antibiotic substances. Several other studies suggested that some Actinobacteria

that are non-antibiotic-producing cultures produce more of this vitamin than those producing antibiotics. Actinobacteria have been shown to produce other water soluble vitamins, with special studies on production of thiamine and the pteroylglutamic acid derivative that is active in promoting the growth of certain strains of *Leuconostoc citrovorum* and coenzyme A.

6.7. Pigments

As synthetic dyes have some limitations such as usage of hazardous chemicals for their production, creating worker safety concerns and generation of hazardous wastes, microbe-oriented pigments are of great concern. Specially, Actinobacteria are characterized by the production of various pigments on natural or synthetic media (Figure 8) and are considered as an important cultural characteristic in describing the organisms. Any phenotypic changes induced by environmental influences will help Actinobacteria as they boast distinctive colony morphologies and produce variety of pigments and aerial branching filaments called hyphae, which give them a characteristic fuzzy appearance. These pigments usually comes in various shades of blue, violet, red, rose, yellow, green, brown, and black, which may be dissolved into the medium or it may be retained in the mycelium. The pigments produced by *Streptomyces* may be either endopigments (bound to certain cell structures) or exopigments (excreted into the surrounding medium). Sometimes different antibiotics produced by the Actinobacteria are considered as pigments. Since the formation of pigment is influenced by the pH of the medium, aeration, temperature of the growth, and carbon and nitrogen sources, only a little is known about the exact chemical nature of pigments. Its formation is also linked to respiratory mechanisms, defense mechanisms, and ultraviolet protection. These microbes also have the ability to synthesize and excrete dark pigments, melanin or melanoid, which are considered to be a useful criterion for taxonomical studies. The textile industry produces and uses approximately 1.3 million tonnes of dyes, pigments, and dye precursors, valued at around \$23 billion, almost all of which are manufactured synthetically. Table 3 provides a list of pigments from different Actinobacteria.



Figure 8. Diffusible pigment produced by various Actinobacteria in starch casein agar medium.

Pigment	Class	Actinobacteria
Rhodomyacin	Anthracycline glycoside	<i>Synodontis violaceus</i> DSM 40704
Actinomycin	Phenoxazinone	<i>Streptomyces</i> sp.
III Undecylprodigiosin	Prodigiosin	<i>Streptomyces longispororuber</i> DSM 40599
IV Metacycloprodigiosin		
Granaticin	Naphthoquinone	<i>Streptomyces litmocidin</i> DSM 40164

Table 3. Pigments from Actinobacteria

6.8. Nanoparticle synthesis

Nanoparticles are of great scientific interest as they bridge the gap between bulk materials and atomic or molecular structures. Generally, the chemical methods are low cost for high volume; however, their drawbacks include contamination from precursor chemicals, use of toxic solvents, and generation of hazardous byproducts. Hence, there is an increasing need to develop high-yield, low-cost, nontoxic, and environmentally benign procedures for synthesis of metallic nanoparticles. Therefore, the biological approach for synthesis of nanoparticles becomes important. In fact, Actinobacteria are efficient producers of nanoparticles, which show a range of biological properties, namely antibacterial, antifungal, anticancer, antibiofouling, antimalarial, antiparasitic, and antioxidant. *Streptomyces* and *Arthrobacter* genera have been studied as possible “nanofactories” for the development of clean and nontoxic methods of the synthesis of silver and gold nanoparticles. A recent example of silver nanoparticle synthesis from an Actinobacteria *Streptomyces* sp. GRD was performed by Gopinath et al [70]. Ranjani et al [71] observed the diversity of silver nanoparticle synthesizing Actinobacteria from marine environment and showed that 25 isolates of 49 synthesized silver nanoparticles, the genus of which includes *Streptomyces* sp., *Nocardiopsis* sp., *Kitasatosporia* sp., *Actinopolyspora* sp., *Thermoactinomyces* sp., *Actinomadura* sp., *Kibdelosporangium* sp., *Saccharopolyspora* sp., and *Thermomonospora* sp. Table 4 shows the synthesis of nanoparticles using various genera.

Actinobacteria	Nanoparticles
<i>Streptomyces</i> sp., <i>Thermoactinomyces</i> sp., <i>Nocardiopsis</i> sp., <i>Rhodococcus</i> sp., <i>Streptomyces albidoflavus</i> , <i>Streptomyces hygroscopicus</i> , <i>Streptomyces rochei</i>	Silver
<i>Streptomyces aureofaciens</i> , <i>Actinobacteria</i> , <i>Streptomyces glaucus</i> , <i>Streptomyces viridogens</i> , <i>Thermoactinomyces</i> spp., <i>Thermomonospora</i> spp., <i>Nocardia farcinica</i> , <i>Streptomyces hygroscopicus</i>	Gold
<i>Streptomyces</i> sp.	Zinc, copper, manganese

Table 4. List of nanoparticles synthesized using Actinobacteria

6.9. Bioremediation

Actinobacteria possess many properties that make them good candidates for application in bioremediation of soils contaminated with organic pollutants. In some contaminated sites, Actinobacteria represent the dominant group among the degraders [72]. They play an

important role in the recycling of organic carbon and are able to degrade complex polymers. Sanscartier et al [73] reported that the greater use of petroleum hydrocarbons that are widely used in our daily life as chemical compounds and fuel has become one of the most common contaminants of large soil surfaces and eventually is considered as a major environmental problem. Some reports suggests that *Streptomyces* flora could play a very important role in degradation of hydrocarbons [74, 75]. Many Actinobacterial strains have the ability to solubilize lignin and degrade lignin-related compounds by producing cellulose- and hemicellulose-degrading enzymes and extracellular peroxidase [76]. Actinobacteria species have the ability to live in an oily environment and thus they can be used in bioremediation to reduce oil pollutants. *Nocradiopsis* sp. SD5 degraded feather waste by producing keratinase enzyme [50].

6.10. Control of plant diseases

The worldwide efforts in the search of natural products for the crop protection market have progressed significantly, and Actinobacteria, especially genus *Streptomyces*, appear to be good candidates in finding new approaches to control plant diseases. The agroindustry shows a marked interest for Actinobacteria as a source of agroactive compounds of plant growth-promoting rhizobacteria (PGPR) and of biocontrol tools [77, 78]. About 60% of the new insecticides and herbicides reported in the past 5 years originate from *Streptomyces* [78]. Kasugamycin is a bactericidal and fungicidal metabolite discovered in *Streptomyces kasugaensis* [79], which acts as an inhibitor of protein biosynthesis in microorganisms but not in mammals, and its toxicological properties are excellent. To market the systemically active kasugamycin for control of rice blast *Pyricularia oryzae* and bacterial *Pseudomonas* diseases in several crops, Hokko Chemical Industries developed a production process. Polyoxin B and D were isolated as metabolites of *Streptomyces cacaoi* var. *asoensis* in 1965 by Isono et al [80] as a new class of natural fungicides. The ability of the polyoxins to interfere with the fungal cell wall synthesis by specifically inhibiting chitin synthase [81] makes them acceptable with regard to environmental considerations. Polyoxin B found application against a number of fungal pathogens in fruits, vegetables, and ornamentals. Polyoxin D is marketed by several companies to control rice sheath blight caused by *Rhizoctonia solani*. The validamycin family was detected by Takeda researchers in 1968 in a greenhouse assay when screening streptomycete extracts for activity against rice sheath blight. Validamycin A was found to be a prodrug, which is converted within the fungal cell to validoxylamine A, an extremely strong inhibitor of trehalase [82]. This mode of action gives validamycin A a favorable biological selectivity because vertebrates do not depend on the hydrolysis of the disaccharide trehalose for their metabolism. Inhibition of plant pathogenic *Rhizoctonia solani* under *in vitro* condition was assessed with the culture supernatant of *Streptomyces* sp., which showed that the tested Actinobacteria had the ability to reduce damping off severity in tomato plants. Table 5 represents some of the antibiotics produced by the Actinobacteria that suppresses various plant diseases.

Disease	Actinobacteria	Antibiotic produced
Potato scab	<i>Streptomyces melanosporofaciens</i> EF-76 and FP-54	Geldanamycin
Grass seedling disease	<i>Streptomyces violaceusniger</i> YCED9	Nigericin and guanidylfungin A
Root rot of Pea	<i>Streptomyces hygroscopicus</i> var. <i>geldanus</i>	Geldanamycin
Asparagus root diseases	<i>Streptomyces griseus</i>	Faeriefungin
Rice blast disease	<i>Streptomyces kasugaensis</i>	Kasugamycin
Broad range of plant diseases	<i>Streptomyces griseochromogenes</i>	Blasticidin S
Sheath blight of rice	<i>Streptomyces hygroscopicus</i> var. <i>limoneus</i> No. T-7545	Validamycin
Brown rust of wheat	<i>Streptomyces hygroscopicus</i>	Gopalamycin
Phytophthora blight of pepper	<i>Streptomyces violaceusniger</i>	Tubercidin
Phytophthora blight of pepper	<i>Streptomyces humidus</i>	Phenylacetic Acid
Damping-off of cabbage	<i>Streptomyces padanus</i>	Fungichromin
Rice sheath blight	<i>Streptomyces cacaoi</i> var. <i>asoensis</i>	Polyoxin B and D
Powdery mildew	<i>Streptoverticillium rimofaciens</i>	Mildiomyacin
Rice root disease	<i>Micromonospora</i> sp. SF-1917	Dapiramycin
Rice blast	<i>Micromonospora</i> sp. M39	2,3-dihydroxybenzoic acid, phenylacetic acid, cervinomycin A1 and A2
Blotch of wheat	<i>Streptomyces malaysiensis</i>	Malayamycin
Powdery mildew of cucumber	<i>Streptomyces</i> sp. KNF2047	Neopeptin A and B

Table 5. Plant disease suppression by antibiotics produced by Actinobacteria

6.11. Nematode control

It has been known for decades that effective control of plant-parasitic nematodes is dependent on chemical nematicides. Due to its ill effects with respect to the environmental hazards, hazardous nematicides have emphasized the need for new methods to control nematodes. Today, numerous microorganisms are recognized as antagonists of plant-parasitic nematodes. Especially, Actinobacteria have potential for use in biological control as they are known to produce antibiotics. The production of avermectins by a species of *Streptomyces* shows that soil-borne organisms can produce highly nematicidal compounds. *S. avermitilis* produces ivermectin, which has an excellent activity against *Wuchereria bancroftii* [83]. Similarly various other antiparasitic compounds are produced from different *Streptomyces* sp., *Salinispora* sp., and *Marinactinospora* sp., which includes *Milbemycin*, *Antimycin A9*, *Fervenulin*, *bafilolides*, *Valinomycin*, *Salinosporamide A*, *Kalafungin*, *Thiamycins*, and *Axenomycins*.

6.12. Enhancement of plant growth

Despite the well-documented history of *Streptomyces* in biocontrol and preliminary evidence of their capacity to enhance plant growth [84], *Streptomyces* species have been poorly investigated specifically for their potential as PGPR. While the beneficial effect of some strains of PGPR on particular crops is certain, the mechanisms employed by PGPR are unclear [85]. PGPR can affect plant growth in two general ways, either directly or indirectly. Indirect promotion occurs when PGPR lessen or prevent the harmful effects of one or more deleterious microorganisms. This is chiefly attained through biocontrol or the antagonism of soil plant pathogens. Specifically, colonization or the biosynthesis of antibiotics and other secondary metabolites can prevent pathogen invasion and establishment. Direct promotion of plant growth by PGPR occurs when the plant is supplied with a compound that is synthesized by the bacteria, or when PGPR otherwise facilitates plant uptake of soil nutrients. Merriman et al [86] reported the use of *S. griseus* for seed treatment of barley, oat, wheat, and carrot to increase their growth. The isolate was originally selected for the biological control of *Rhizoctonia solani*. Though the *S. griseus* isolate did increase the average grain yield, dry foliage weight, tiller number, and advanced head emergence for both wheat and oat over controls, the differences were not statistically significant. As a seed treatment for carrot, the isolate was more successful. Marketable yields were increased over controls by 17% and 15% in two separate field trials. Specifically, both trials also indicated an increased yield of large and very large grade carrots over controls [86]. El-Abyad et al [87] described the use of three *Streptomyces* spp. in the control of bacterial, *Fusarium* and *Verticillium* wilts, early blight, and bacterial canker of tomato. The isolates used were *Streptomyces pulcher*, *Streptomyces canescens*, and *Streptomyces citreofluorescens*. In addition, tomato growth was observed to be significantly improved with the antagonistic *Streptomyces* spp. as a seed coating. An increased availability of growth regulators produced by the inoculum was the reason proposed for the improvement in tomato growth, although this was not formally tested. The information available on streptomycetes as plant growth promoters is limited, so is the information describing the possibility of their direct growth promotion mechanisms. Like most rhizobacteria, it seems highly probable that streptomycetes are capable of directly enhancing plant growth.

6.13. Phytohormone production

The production of the plant hormone indole-3-acetic acid (IAA) and the pathways of its synthesis by various *Streptomyces* sp., including *S. violaceus*, *Streptomyces scabies*, *S. griseus*, *Streptomyces exfoliatus*, *S. coelicolor*, and *S. lividans*, were described by Manulis et al [88]. While prior works had reported IAA synthesis in *Streptomyces* spp., this was the first confirmation of its production using modern analytical methods, such as high-performance liquid chromatography (HPLC) and gas chromatography (GC)–mass spectrometry (MS), and Manulis et al [88] provided a detailed description of the IAA biosynthetic pathways in *Streptomyces*. Aldesuquy et al [84] studied the effect of streptomycete culture filtrates on the growth of wheat plants that showed significant increase in shoot fresh mass, dry mass, length, and diameter, displayed statistically with certain strains at varying sample times. *Streptomyces olivaceoviridis* had a pronounced effect on yield components (spikelet number, spike length, and fresh

and dry mass of the developing grain) of wheat plants. This activity may be due to, at least in part, an increase in bioavailable phytohormones that are PGPR produced since ail PGPR strains (*Streptomyces rimosus*, *Streptomyces rochei* and *S. olivaceoviridis*) produced substantial amounts of exogenous auxins (IAA), as well as gibberellins and cytokinins.

6.14. Biolarvicides

Extensive use of chemical insecticides for controlling malaria, filaria, dengue, chickungunya, Japanese encephalitis, and other mosquitoes have resulted in hazards to the environment and caused development of resistance in vector mosquitoes. Accordingly, various biological control agents have gained importance with innumerable advantages over the chemical insecticides. At very low doses, these biolarvicides are highly effective against mosquito larvae and are completely safe to other nontarget organisms, environment, man, and wild life. Several varieties of microorganisms, including fungi, bacteria, and nematodes have been reported as strategies to biologically control the vectors. Specifically, Actinobacteria produce many important bioactive compounds of high commercial value and continue to be routinely screened for new bioactive substances. In a study made by Vijayan and Balaraman [89], extracellular secondary metabolites were produced from 35 different Actinobacterial isolates that showed high larvicidal activity against *Culex* and *Anopheles* mosquitoes. Dhanasekaran et al [20] reported that the isolates *Streptomyces* sp., *Streptosporangium* sp., and *Micropolyspora* sp. had high larvicidal activity against *Anopheles* mosquito larvae. Rajesh et al [90] synthesized silver nanoparticles from *Streptomyces* sp. GRD cell filtrate and observed larvicidal activity against *Aedes* and *Culex* vectors, which are responsible for the transmission of dengue and filariasis. Yet again, Rajesh et al [91] studied the larvicidal effect of Actinobacterial extracts against *Culex* larvae and found that 1000 ppm concentration of the isolate *Streptomyces* sp. KA13-3 showed 100% mortality and *Streptomyces* sp. KA25-A showed 90% mortality. Variety of other secondary metabolites from Actinobacteria, namely tetranectin [92], avermectins [93], macrotetrolides [94], and flavonoids [95] were found to be toxic to mosquitoes.

6.15. Odor and flavor compounds production

Actinomycetes have long been associated with musty odors in water but their actual contribution to odor in freshwater was unknown. But in late 1960s, secondary metabolites, geosmin and 2-methylisoborneol (MIB), were identified from actinomycete cultures [96] after which actinomycetes have gained considerable importance throughout the water industry as major sources of drinking water taste and odor. Gaines and Collins [97] studied the metabolites of *Streptomyces odorifer* and concluded that the earthy odor might be due to the production of a combination of trivial compounds, such as acetic acid, acetaldehyde, ethyl alcohol, isobutyl alcohol, isobutyl acetate, and ammonia. They emphasized that the other constituents contributing to the odor might also be produced. A number of odor-producing compounds have been identified from Actinobacteria (Table 6). Earthy odors in adequately treated water supplies cause concern among consumers, who may think water with these odors is unsafe to drink. These odors are the second most common cause of odor problems recorded by water utilities, behind chlorine.

Actinobacteria	Secondary metabolite	Odor type
<i>Streptomyces</i> sp.	Trans-1,10-dimethyl-trans-9-decalol (Geosmin)	Earthy
	1,2,7,7-tetramethyl-2-norbornanol	Musty
	6-ethyl-3-isobutyl-2-pyrone (mucidone)	Potato like
	2-isobutyl-3-methoxypyrazine or 2-isopropyl-3-methoxypyrazine	
<i>Actinomadura</i> sp.	(2-methylisoborneol)	Musty
<i>Thermoactinomyces</i> sp.	6-methyl-5-hepten-2-one	Potato like
<i>Pseudonocardia</i> sp.	Dimethyl trisulfide	Potato like
<i>Saccharomonospora</i> sp.		
<i>Thermoactinomyces</i> sp.		
<i>Thermomonospora</i> sp.		

Table 6. Odor-producing compounds from Actinobacteria

7. Harmful effects

7.1. Actinobacterial plant diseases

A number of significant plant diseases are caused by Actinobacteria. Actinobacteria currently assigned to the genus *Corynebacterium* [98] cause a variety of diseases (Table 7). Serodiagnosis has been used to detect and identify *Corynebacterium insidiosum* and *Corynebacterium sepedonicum*, but most of these Corynebacteria are still identified by inoculation tests in host plants. Most phytopathogenic Corynebacteria are considered to produce their antagonistic effects by the production of hormones, polysaccharides, and toxins, whereas the potential of some strains to form biosurfactants may help in attachment to the host. The taxonomy of the phytopathogenic Corynebacteria is unsettled, though some prefer to retain these organisms in the genus *Corynebacterium* [99]. Others accept that there is an overwhelming case for restricting *Corynebacterium* for animal pathogenic Corynebacteria and related strains and a consequent need to reclassify the plant pathogens. *Corynebacterium betae*, *Corynebacterium oortii*, and *Corynebacterium poinsettiae* are genetically identified with *Corynebacterium flaccumfaciens* [100] and have many properties in common with the genus *Curtobacterium* [100], which would serve as a suitable niche for them. *C. insidiosum* and *Corynebacterium michiganense*, also fell into a single genospecies, were recovered in a loose DNA homology group with *Corynebacterium nebraskense* and *Corynebacterium sepedonicum* and together with the latter probably from the nucleus of a new genus.

7.2. Actinobacterial human and animal diseases

Actinobacteria have proved to be the causal agents of many human and animal infections, which include a number of common and intensively studied diseases, such as diphtheria, tuberculosis, and leprosy. There is also a wide range of infections that are less well known;

<i>Arthrobacter ilicis</i>	B light of holly (<i>flex opaca</i>)
<i>C. betae</i>	Wilt and leaf spot of red beet (<i>Beta vulgaris</i>)
<i>C. flaccumfaciens</i>	Wilt of bean (<i>Phaseolus vulgaris</i>)
<i>C. insidiosum</i>	Wilt and stunting of alfalfa (<i>Medicago sativum</i>)
<i>C. michiganense</i>	Canker of tomato (<i>Lycopersicon esculentum</i>) and some other solanaceous plants
<i>C. nebraskense</i>	Wilt and blight of corn
<i>C. oortii</i>	Spot of tulip leaves and bulbs
<i>Corynebacterium Poinsettiae</i>	Stem canker and leaf spot of poinsettia (<i>Euphorbia pulcherrima</i>)
<i>Corynebacterium rathayi</i>	Gumming of cereals
<i>C. sepedonicum</i>	Wilt and tuber rot of potato (<i>Solanum tuberosum</i>)
<i>Nocardia vaccinii</i>	Galls and bud proliferation in blueberry plants (<i>Vaccinium</i>)
<i>Rhodococcus fascians</i>	Leaf gall in many plants, fasciation of sweet pea
<i>S. aureofaciens</i> <i>S. flaveolus</i> . <i>S. griseus</i>	Common scab of potato
<i>S. ipomoeae</i>	Sweet potato scab
<i>S. scabies</i> , <i>Streptomyces</i> sp.	Common and russet scab of potatoes, sugar beet, etc

Table 7. Plant diseases caused by Actinobacteria

some, like actinomycosis and nocardiosis, are proving to be more clinically significant than previously thought. In addition, it is becoming increasingly evident that *Actinomyces* play a role in the etiology of caries and periodontal disease. Following are the human and animal diseases caused by Actinobacteria (Table 8).

Disease	Actinobacteria	Site of infection
Actinomycetoma	<i>A. madurae</i> , <i>pellerieri</i> , <i>Nocardia asteroides</i> , <i>Nippostrongylus brasiliensis</i> , <i>N. otitidiscaviarum</i> , <i>Streptomyces somaliensis</i>	Feet, legs, upper extremities, and other sites
Actinomycosis	<i>Actinomyces bovis</i> , <i>Actinomyces israelii</i> , <i>Arachnia propionica</i>	Cervicofacial, thoracic, abdominal, and uterine regions
Bacterial kidney disease	<i>Renibacterium salmoninarium</i>	Kidney, liver, spleen, and other internal organs
Bovine farcy	<i>Mycobacterium farcinogenes</i> , <i>Mycobacterium senegalense</i>	Lymphatic system
Dermatophilosis & streptothricosis	<i>Dermatophilis congolensis</i>	Skin
Diphtheria	<i>Corynebacterium diphtheriae</i>	Throat, occasionally wounds
Endocarditis	<i>Oerskovia turbata</i> , <i>Rothia dentocariosa</i>	Endocardium

Disease	Actinobacteria	Site of infection
Equine pneumonia	<i>Rhodococcus (Corynebacterium) equi</i>	Lung
Hypersensitivity pneumonitis	<i>Micropolyspora jaeni</i> , <i>Saccharomonospora viridis</i> , <i>Thermoactinomyces vulgaris</i>	Lung
Leprosy	<i>Mycobacterium leprae</i>	Skin
Mycobacterioses	Several <i>Mycobacterium</i> Species	Lungs, lymph nodes, and skin
Pulmonary nocardiosis	<i>Nocardia asteroides</i> , rarely <i>N. brasiliensis</i> , possibly <i>Nocardiopsis dassonvillei</i>	Lung
Systemic nocardiosis	<i>Nocardia asteroides</i> , rarely <i>N. brasiliensis</i>	Lung, central nervous system, kidney, muscle, and other tissues
Superficial nocardiosis	<i>Nocardia asteroides</i> , <i>N. brasiliensis</i> , possibly <i>Nocardiopsis dassonvillei</i>	Any part of body surface, especially the extremities
Purulent infections including abscesses	<i>Actinomyces</i> , (<i>Corynebacterium</i>) <i>pyogenes</i> , <i>Corynebacterium pseudotuberculosis</i>	Abscess formation in various organs (brain, spinal cord, and joints)
Pyelonephritis in cattle	<i>Corynebacterium renale</i>	Kidney
Tuberculosis	<i>Mycobacterium tuberculosis</i>	Lung

Table 8. Human and animal diseases caused by Actinobacteria

8. Conclusion

Actinobacteria is one of the dominant groups of microorganisms that produce industrially important secondary metabolites. A wide range of antibiotics in the market is obtained from Actinobacteria. Products such as enzymes, herbicides, vitamins, pigments, larvicides, phyto-hormones, and surfactants are produced by these several genera of Actinobacteria, which are of great commercial value. They are capable of degrading a wide range of hydrocarbons, pesticides, and feather waste, and their metabolic potential offers a strong area for research. However, many of the rare genera of Actinobacteria have been neither discovered from unexplored locations nor employed for their biotechnological and industrial potential. Thus, studies on unique ecological environments could yield molecules that could become future harbingers of green technology.

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