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A Review on Mangrove Actinobacterial Diversity: The Roles of *Streptomyces* and Novel Species Discovery

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Abstract : In the class *Actinobacteria*, the renowned genus *Streptomyces* comprised of a group of uniquely complex bacteria that capable of synthesizing a great variety of bioactive metabolites. Streptomycetes are noted to possess several special qualities such as multicellular life cycle and large linearized chromosomes. The significant contribution of *Streptomyces* in microbial drug discovery as witnessed through the discovery of many important antibiotic drugs has undeniably encourage the exploration of these bacteria from different environments, especially the mangrove environments. This review emphasizes on the genus *Streptomyces* and reports on the diversity of actinobacterial population from mangroves at different regions of the world as well as discovery of mangrove-derived novel *Streptomyces* species. Overall, the research on diversity of *Actinobacteria* in the mangrove environments remains limited. A total of 19 novel *Streptomyces* spp. isolated from mangroves between the year 2009 - early 2019, notably from China, India, Malaysia, and Thailand. Hence, it will be worthwhile to encourage the study of these bacteria from mangroves of different locations.

Keywords: *Streptomyces*; actinobacteria; mangrove; environment; forest

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INTRODUCTION

The phylum *Actinobacteria* is among the earliest lineages within the prokaryotes which appears to exist since 2.7 billion years ago[1]. Being one of the major lineages in the domain *Bacteria*, this phylum consists of many genera which contributed to its vast diversity with reference to the morphological and physiological variations as well as metabolic abilities[2-4]. In the recent road map of phylum *Actinobacteria* revised by Ludwig *et al.* (2012)[5], this phylum currently comprises 6 classes, namely "*Actinobacteria*", "*Nitriliruptoria*", "*Acidimicrobiia*", "*Coriobacteriia*", "*Thermoleophilia*", and "*Rubrobacteria*". The largest class "*Actinobacteria*" consists of 15 orders, including order *Streptomycetales* that contains only the family *Streptomycetaceae*, where the type genus *Streptomyces* within this family is undeniably one of the most extensively studied genera in the phylum *Actinobacteria*[5-7]. The class *Actinobacteria* can be categorized into two groups: (1) the *Streptomyces* which represents the dominant genus, and (2) the non-*Streptomyces* genera (e.g. *Sinomonas* spp., *Mumia* spp., *Microbacterium* spp. etc.) which also known as rare *Actinobacteria*[8-13].

The genus *Streptomyces* was first introduced by Professor Dr. Selman Abraham Waksman and Professor Dr. Arthur Trautwein Henrici in the year 1943[14]. The name *Streptomyces* means "twisted fungus" in Greek and it is given due to its morphology which appears to be similar to that of filamentous fungi; *Streptomyces* is derived from the combination of *Actinomyces* which means "ray fungus" in Greek and *Streptothrix* which means "twisted hair" in Greek[14,15]. This genus is made up of a group of aerobic, Gram-positive, non-motile, and multicellular filamentous microorganisms that are commonly found in soil, often recognized as persistent soil saprophytes[16-19]. Besides, most of the members of *Streptomyces* produce a characteristic earthy odour due to the production of geosmin[7,20]. This group of bacteria has been greatly explored for their pharmaceutically important natural antibiotics or other bioactive compounds, and industrially useful enzymes[1,17,21]. As a result of the continuous efforts in isolation and screening of *Streptomyces* for their biologically active secondary metabolites, the genus *Streptomyces* presently contains 848 species and 38 subspecies that are validly identified (http://www.bacterio.net/streptomyces.html, accessed on 15th January 2019)[22].

UNIQUE FEATURES OF *Streptomyces*

Streptomyces bacteria are uniquely complex microorganisms, primarily well-known as prolific producers of secondary metabolites with bioactivities such as antimicrobial, anticancer, antioxidant, and immunosuppressive activities[19,20,23,24]. Production of secondary metabolites is not essential for bacterial growth, but it is crucial to facilitate the defence mechanisms of the hosts as to ensure survival during unfavourable environmental conditions[6]. It is remarkable that streptomycetes can generate secondary metabolites with various interesting bioactivities and extraordinary chemical diversity, although the roles play by these molecules in the survival of the host are still not fully understood other than the antibiotics which benefit the host by thwarting the growth of competing microbes in unfavourable environment[18,25].

Actually, there are several notable features of *Streptomyces* that could account for their complex secondary metabolism. One of the unique features of streptomycetes is their multicellular life cycle involving complex morphological changes. Upon spore germination, they grow by tip extension and the development of a network of branched filaments known as the substrate mycelium (vegetative phase) is initiated. As they age, aerial multinucleated mycelium is formed which subsequently experience synchronous cell division leading to the generation of monoploid compartments where each will differentiate into resistant spores (reproductive sporulation phase) (Figure 1)[18,26,27]. According to the observation on agar plate media, the substrate mycelium of *Streptomyces* grows into and across the surface of agar plate through extension and branching, whilst the aerial mycelium erected on top of the substrate mycelium that appears above the surface of agar plate with granular, powdery, floccose or velvety appearance[26,28]. Apparently, the morphological differentiation event in *Streptomyces* is related to the sensing of essential nutrients depletion[18,27]. Meanwhile, *Streptomyces* starts to produce secondary metabolites when encountering nutritional deficiencies in a stressful environment and this process is referred to physiological differentiation[29]. Therefore, there is a close association between morphological differentiation and physiological differentiation in the life cycle of *Streptomyces*. During the shifting phase from vegetative to aerial growth and sporulation, metabolic development is activated and thus many interesting secondary metabolites are produced to ensure the survival of *Streptomyces* in stressful environments[27,29,30]. Furthermore, many of the *Streptomyces* isolates can produce diverse pigments or pigmented secondary metabolites that responsible for the colour of substrate and aerial mycelia of *Streptomyces* colonies on agar plate media[26,30].

Another distinctive feature of *Streptomyces* is that members of this genus have linearized chromosomes, commonly with a large size of over 8 Mbp and a high G+C content of approximately 67-78 mol %[32-34]. In the year 2002, the first complete genome sequence of *Streptomyces* was reported - a model actinomycete, *Streptomyces coelicolor* A3(2) with a genome size of 8,667,507 bp, thus, became the largest completely sequenced bacterial genome at that moment[35]. In the following year, the complete genome sequence of an industrial strain *Streptomyces avermitilis* was reported to consist of 9,025,608 bp[36]. Since then, many *Streptomyces* strains have been subjected to whole genome sequencing to at least the draft stage and these genome sequences are publicly available[37]. These evidences show that the genome size of *Streptomyces* is at least almost two times larger as compared with other well-studied bacteria such as *Bacillus subtilis* with genome size of 4,214,810 bp, and *Escherichia coli* K-12 with genome size of 4,639,221 bp[20,38,39]. The large genome size correlates with the ability of *Streptomyces* to produce large amount of diversified secondary metabo-

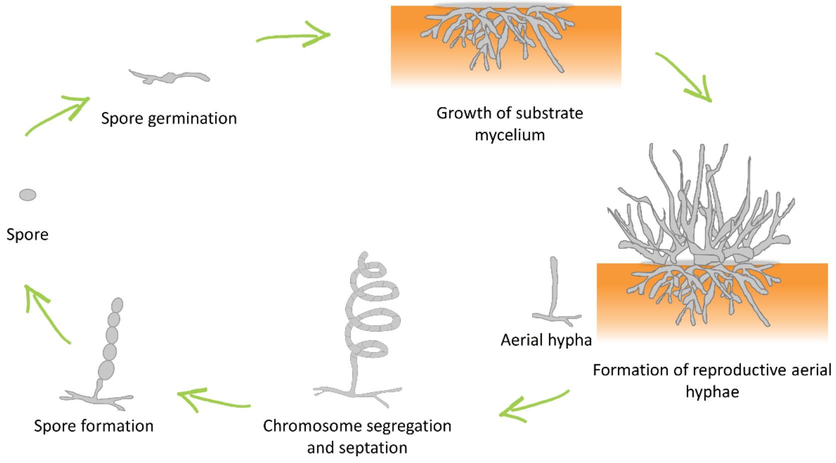


Figure 1. Schematic representation of the life cycle of *Streptomyces* (adapted from Barka *et al.* (2016)[31]).

lites. For instance, Bentley *et al.* (2002)[35] reported that the genome of *Streptomyces coelicolor* A3(2) was found to contain over 20 gene clusters related to/involved in the biosynthesis of secondary metabolites. Besides, Ikeda *et al.* (2003)[36] noted the presence of over 30 biosynthetic gene clusters *Streptomyces avermitilis* associated to various secondary metabolites. Therefore, these special features of *Streptomyces* have contributed to the complexity of the organisms, causing them to be capable of producing a vast array of interesting or novel bioactive secondary metabolite.

ROLES OF *Streptomyces* IN MICROBIAL DRUG DISCOVERY

The search for antibacterial agents from *Streptomyces* had in fact began since the early 1940s, before the reclassification of *Actinobacteria* and the introduction of genus *Streptomyces*. Pioneered by Professor Dr. Selman A. Waksman, who ventured into the discovery of antagonistic soil-inhabiting microbes towards pathogenic bacteria with his team of scientists[40]. The outcome of their investigation led to the isolation of first antibiotic designated as actinomycin, a specific bacteriostatic and bactericidal agent, produced by *Streptomyces antibioticus* (formerly known as *Actinomyces antibioticus*)[20,41,42]. A few years later, Waksman and his team achieved a breakthrough in *Streptomyces* research, which was the discovery of streptomycin as a cure for many diseases[40,43]. Streptomycin was the first discovered broad-spectrum antibiotic for effective treatment of tuberculosis caused by *Mycobacterium tuberculosis* – a deadly pathogen. Streptomycin was derived from *Streptomyces griseus*, the first *Streptomyces* to be utilized for industrial production of this antituberculosis drug[1,25,40,43,44]. From this event, Professor Selman A. Waksman was awarded with the Nobel Prize in Physiology or Medicine in 1952 for his successful discovery of streptomycin[6].

Eventually, scientists intensified the search for antibiotics from *Streptomyces*. Consequently, *Streptomyces* has become the producers of over 75% of the commercially valuable antibiotics applied in human and veterinary medicines[45]. A variety of antibiotics belonging to different classes can be sourced from *Streptomyces*, for instances: clavulanic acid (class: β-lactam) from *Streptomyces clavuligerus*[46], neomycin (class: aminoglycoside) from *Streptomyces fradiae*[47], vancomycin (class: glycopeptide) from *Streptomyces orientalis*[48], and tetracycline (class: tetracycline) from *Streptomyces aureofaciens*[49].

After a period of more than 50 years since the amazing achievement of Professor Selman A. Waksman, streptomycetes continue to surprise the scientific community by their ability in synthesizing functionally and structurally varied bioactive compounds. These bacteria have relentlessly showcasing their significance in the drug discovery and development. Recently, Professor Satoshi Omura and Professor William Cecil Campbell were bestowed with the Nobel Prize of Physiology or Medicine in 2015 for the successful discovery of avermectin (which later chemically modified to ivermectin) from *Streptomyces avermitilis*. Avermectin is a strong anthelmintic agent effective against many nematodes, arachnids, and insects. The semisynthetic derivative ivermectin is an effective treatment for onchocerciasis (river blindness) and lymphatic filariasis (elephantiasis) in human[50-52]. To date, researchers are still actively searching for bioactive *Streptomyces* strains around the world due to their enormous potential in producing effective drug candidates and many efforts have been put to further explore the potential of these organisms in producing other clinically important compounds (examples: anticancer, antioxidant etc.) in addition to antibiotic agents[53].

OCCURRENCE OF *Streptomyces* FROM DIFFERENT HABITATS

Terrestrial and aquatic environments

Member of *Streptomyces* are ubiquitous in soil and aquatic sediments, existing either in a metabolically active state or relatively inactive state in the form of spores. *Streptomyces* is among the significant microbial populations in most terrestrial soils, thus, the soil is the most extensively studied habitat as a rich source of streptomycetes[54]. Additionally, streptomycetes have a substantial role in soil ecology through their involvement in biodegradation. These organisms are capable of degrading recalcitrant polymers present in soil and plant litter, such as lignocelluloses, chitin, and keratin[54,55]. Soil-derived streptomycetes have been the producers of pharmaceutically important bioactive compounds and valuable enzymes. Therefore, *Streptomyces* of terrestrial soil origin has been greatly exploited in many drug screening programs for the past decades. Moreover, it is common to find *Streptomyces* in marine environments where they were frequently assumed to be derived from spores that wash-in from adjacent terrestrial habitats[54]. Nevertheless, several studies have proven the existence of indigenous marine *Streptomyces*, although their distributions and ecological roles remain elusive[56-59]. There are also evidences for the presence of *Streptomyces* in other aquatic environments such as freshwater lakes and rivers[54,60,61].

Living organisms

Furthermore, some streptomycetes exist as symbionts instead of free-living soil bacteria. They create a symbiotic relationship with other organisms such as plants and invertebrates, whereby these interactions can either be beneficial or parasitic in some cases[62]. Streptomycetes that associated with plants could lead a pathogenic or endophytic lifestyle. While the presence of phytopathogenic *Streptomyces* species are scarce, but one of the most notable phytopathogenic streptomycetes is *Streptomyces scabies*. *Streptomyces scabies* is the primary causative agent of common scab disease in potato and other crops including beet and radish[63]. As for endophytic *Streptomyces* species, they could live as plant commensals whilst occasionally provide certain beneficial properties to their hosts such as protection from phytopathogens or plant growth promotion. Also, studies have demonstrated that endophytic streptomycetes could be attractive biocontrol agents due to their ability in generating antibacterial or antifungal agent that can eradicate phytopathogens [19,62,64].

There are several *Streptomyces* species have been found to form protective mutualistic symbioses with insects such as European beewolf, Southern pine beetles, and attine ants, in which basically the *Streptomyces* offers protection to its host or host's resources against pathogens through the production of antibiotics, in return, the host feeds the *Streptomyces*[62,65-67]. Apart from forming symbioses with insects, many reports have revealed the associations between *Streptomyces* species and marine sponges as well as cone snails though the symbiotic relationships between these organisms remain inconclusive as further studies are required to address these queries[62,68,69].

Other unique environments

Interestingly, *Streptomyces* bacteria happen to be widely distributed in extreme and underexplored environments such as deserts[70], caves[71], hot springs[72], mangroves[33,73], mountain plantations[55], Arctic and Antarctic regions[74,75]. These environments are often characterized by certain fluctuations in environmental conditions, extreme high/low temperature, acidic/alkaline pH, limitation of nutrients, or high radiation[1]. Existence of *Streptomyces* in these unusual environments have demolished the traditional paradigm pertaining the restricted predominance of *Streptomyces* in terrestrial soil and aquatic environments. It is relatively unsurprising that streptomycetes can occur in these environments because they can exist for an extended period as resting arthrospores; these spores are resistant to water and high temperatures, also, they will germinate when sufficient nutrients are available[16,54]. These bacteria also possess physiological and metabolic flexibility that could trigger the production of secondary metabolites to facilitate their survival under extreme conditions[1,74].

EXPLORATION OF *Streptomyces* FROM UNDEREXPLORED MANGROVE

Recent drug discovery research seeks to discover novel and useful bioactive compounds by emphasizing on the screening of *Streptomyces* species from uncommon and underexplored areas. There is increasing evidence that bioprospecting of *Streptomyces* from dynamic environment like the mangroves are producing positive outcomes[6]. Similarly, mangroves have been regarded as one of the rich resources for isolating *Streptomyces* bacteria, which also includes novel *Streptomyces* species[76]. There has been increasing number of mangrove-derived *Streptomyces* strains exhibiting potent bioactivities such as antimicrobial, anticancer, and antioxidant[20,77-81]. It is possible that mangrove streptomycetes have unique metabolic capacity on the synthesis of bioactive secondary metabolites. Therefore, it is worthwhile to pursue new groups of *Streptomyces* from less investigated ecological systems such as the mangroves in hopes to unearth novel and/or useful bioactive compounds from these organisms.

The mangrove environment

The mangroves stand out as an exceptional type of forest distributed along the intertidal zone between the terrestrial and the sea of tropical and subtropical regions around the world[82]. Mangroves are described as assemblage of trees and shrubs adapted to thrive in dynamic environmental settings of extreme tides, high salinity, high temperature, and high sedimentation[82,83]. Despite those harsh environmental conditions, these "rainforests of the seas" are very productive and biologically significant ecosystems, for which they provide a superb nursery habitat for a wide range of flora and fauna[84]. Of course, mangrove forests offer invaluable benefits towards human society besides sustaining biodiversity. These wetland forests provide ecosystem goods that are vital to sustain human well-being, which cover food source (e.g. fish, shrimps), boat building materials, furniture, firewood, and traditional medicine[85]. Mangrove forests also provide protection by buffering salinity changes, stabilizing shorelines through reducing coastal erosion, and minimizing severe impact of natural disasters like floods, tidal waves, hurricanes, and tsunamis[82,86,87].

The latest update on global distribution of mangroves was reported in the 2010 World Atlas of Mangroves, with the inputs from several organizations including the International Tropical Timber Organization (ITTO), International Society for Mangrove Ecosystems (ISME), Food and Agriculture Organization (FAO), United Nations Environment Programme (UNEP), and others. It was estimated that the mangrove area was a total of 152,361 km^2 found in 123 countries and territories, based on satellite imagery captured in year 1999 – 2003[88,89]. The distribution of mangroves in each region is summarized in the chart illustrated in Figure 2. The largest proportion of mangroves is found in Southeast Asia, where Indonesia, Malaysia, and Myanmar are the top three mangrove-rich countries within this region[82,89].

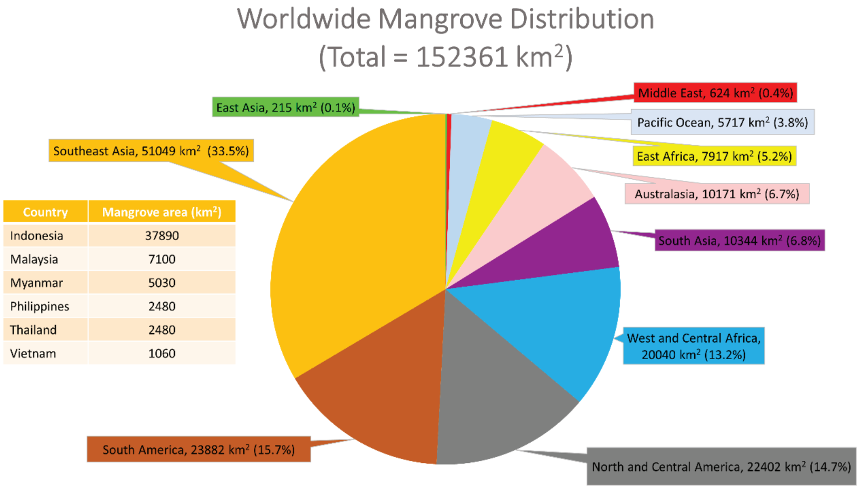
BACTERIAL DIVERSITY OF MANGROVE

Mangroves have a highly diverse microbial community comprising numerous different species of fungi and bacteria. In the mangrove sediments, bacteria are the primary decomposers of organic residues and the main contributors in the carbon cycle. Many of them are associated with ecologically important roles such as nitrogen fixation, phosphate solubilising, sulphate reducing, enzyme producing, photosynthetic anoxygenic, and methanogenic[90,91]. Based on previous research findings, the bacterial assemblages which dominated the mangrove ecosystems include phyla *Proteobacteria*, *Actinobacteria*, *Firmicutes*, *Bacteroidetes*, *Chloroflexi*, *Acidobacteria*, *Cyanobacteria*, *Nitrospirae*, *Fusobacteria*, and *Planctomycetes*[92-96].

Given the fact that bacteria control the nutrient availability in the environment, so the abundance of these bacteria present in mangroves could result in an increased amount of nutrient levels in the sediments, thereby controlling vegetation patterns, stimulating growth of many organisms, and promoting species diversity[91,97,98]. Above all, the periodic tidal flushing and constant fluctuation in salinity could induce changes in metabolic pathways in microorganisms for their adaptation to the mangrove environment. Henceforth, these factors could encourage the advent of "new" species that have the potential to produce uncommon metabolites which may be compelling to the pharmaceutical and biotechnology industry[45,94,99].

Diversity of *Actinobacteria* in mangrove

Actinobacteria are important soil inhabitants and the exploration of *Actinobacteria* in mangroves has been gaining attention from researchers around the world due



Country	Mangrove area (km^2)
Indonesia	37890
Malaysia	7100
Myanmar	5030
Philippines	2480
Thailand	2480
Vietnam	1060

Figure 2. The global distribution of mangrove (information obtained from ITTO (2012))[89].

to their incredible contribution to drug discovery. In the recent years, there are several reports regarding the diversity of *Actinobacteria* in mangroves, mainly from the East Asia, South Asia, and Southeast Asia regions.

The *Actinobacteria* population in mangrove forests of China of East Asia region was investigated by Hong *et al.* (2009)[100]. In the report, more than 2,000 actinomycetes were isolated from soil and plant samples obtained from eight mangrove sites. Furthermore, many of these actinomycetes exhibited biological activities such as growth inhibition of Human Colon Tumor 116 cells, antimicrobial activity against *Candida albicans* and *Staphylococcus aureus*, inhibition of protein tyrosine phosphatase 1B (PTP1B), caspase 3 and aurora kinase A. It was found that the bioactive strains were belonged to 13 genera and most of them were from the genus *Streptomyces* (Table 1). The study also revealed that most of the bioactive actinomycetes were originated from soil samples. On the other hand, a study conducted by Wei *et al.* (2010)[101] demonstrated that 77 out of 118 actinobacterial strains isolated from China mangrove plant samples exhibited antibiotic property and these bioactive strains were from the genus *Streptomyces*, *Micromonospora*, *Nocardia*, *Nocardiopsis*, *Saccharothrix*, and *Lentzea*.

In the South Asia region, one of the largest areas of mangroves is situated in India. A few researchers have reported the actinobacterial diversity in India's mangroves. For instance, the distribution of *A*ctinobacteria in mangrove forests of Sundarbans in India was examined by Mitra *et al.* (2008)[102] and the actinomycetes isolated from soil samples were found to belonged to 9 genera with potential antimicrobial activity. In addition, Rajkumar *et al.* (2012)[76] had unveiled the isolation of 116 actinomycetes belonging to 7 genera from sediment samples collected from five sites of Bhitarkanika mangroves (Table 1). These studies have showed that *Streptomyces* emerged as the most prevalent genus detected in the mangroves of India[76, 102].

As for the Southeast Asia region, Lee *et al.* (2014)[45] discovered a high level of diversity of *Actinobacteria* in mangrove forest located at Peninsular Malaysia. A total of 87 actinobacterial isolates from mangrove soil samples were identified to belong to 11 genera and 48 of these isolates exerted antibacterial activity to at least 1 of the 12 pathogens tested, which were *Bacillus subtilis*, *Bacillus cereus*, *Enterococcus faecalis*, *Staphylococcus epidermidis*, methicillin-resistant *Staphylococcus aureus*, *Klebsiella pneumonia*, *Klebsiella oxytoca*, *Salmonella typhi*, *Pseudomonas aeruginosa*, *Acinetobacter calcoaceticus*, *Yersinia pseudotuberculosis*, and *Aeromonas hydrophila*. Additionally, diversity of *Actinobacteria* in mangrove soil of Indonesia was reported by Retnowati *et al.* (2017)[103], for which they had revealed mangrove actinomycetes with antibacterial activity belonging to the genus *Amycolatopsis*, *Nocardiopsis*, *Streptomyces*, and *Saccharomonospora*. The studies on the actinobacterial population in mangroves of different locations are summarized and listed in Table 1.

Among the many genera of class *Actinobacteria*, there is no doubt that the genus *Streptomyces* is the most biologically active microorganisms. As a result, the exploration of *Streptomyces* in mangrove environments has been the centre of attraction, which subsequently lead to the discovery of novel species. Table 2 describes the discoveries of novel *Streptomyces* species isolated from several mangrove areas.

Meanwhile, there are some studies focusing on the diversity of only the rare *Actinobacteria*. The rare *Actinobacteria* are recognized as non-*Streptomyces* strains of actinomycetes and the frequency of isolation of these actinomycetes through conventional methods is often lower as compared to that of *Streptomyces*[108,109]. One of the examples include the study conducted by Naikpatil *et al.* (2011)[110] who investigated the rare *Actinobacteria* from mangrove sediments of Karwar, India. A total of 53 rare actinomycetes were isolated in the study and identified as *Actinoplanes*, *Actinomadura*, *Microbispora,* and *Micromonospora*. Another research led by Ismet *et al.* (2013)[111] described the diversity of rare actinomycetes in mangrove rhizosphere soil samples collected from several mangrove sites in Bangladesh. Rare actinomycetes belonging to *Actinomadura*, *Actinoplanes*, *Catellatospora*, *Longispora*, *Micromonospora*, *Microbispora*, *Nocardia*, *Nocardiopsis*, *Nonomuraea*, *Rhodococcus*/*Gordonia*, *Saccharomonospora*, *Streptosporangium*, and *Virgisporangium* were isolated from the soil samples.

Table 1. Actinobacterial diversity present in mangroves at East Asia, South Asia, and Southeast Asia regions.

Region	Author	Country	Mangrove location	Source	Diversity of *Actinobacteria*
East Asia	Hong *et al.* (2009)[100]	China	i. Hainan Province: Danzhou, Haikou, Sanya and Wenchang ii. Guangdong Province: Shenzen and Zhanjiang iii. Fujian Province: Xiameng iv. Guangxi Province: Beihai	Soil and plant samples	*Actinoplanes*, *Actinomadura*, *Arthrobacter*, *Isoptericola*, *Microbacterium*, *Microbispora*, *Micrococcus*, *Micromonospora*, *Nocardia*, *Nonomuraea*, *Rhodococcus*, *Streptomyces*, and *Verrucosispora*.
	Wei *et al.* (2010)[101]	China	Guangxi Province: Shankou Mangrove Nature Reserve	Plant samples	*Lentzea*, *Micromonospora*, *Nocardia*, *Nocardiopsis*, *Saccharothrix*, and *Streptomyces*.
	Liao *et al.* (2010)[104]	China	Guangxi Province: Beihai	Soil samples	*Streptomyces* and *Nocardiopsis*.
	Jiang *et al.* (2018)[105]	China	Guangxi Zhuang Autonomous Region: Beilun Estuary National Nature Reserve	Plant samples	*Actinoplanes*, *Agrococcus*, *Amnibacterium*, *Brachybacterium*, *Brevibacterium*, *Citricoccus*, *Curtobacterium*, *Dermacoccus*, *Glutamicibacter*, *Gordonia*, *Isoptericola*, *Janibacter*, *Kineococcus*, *Kocuria*, *Kytococcus*, *Leucobacter*, *Marmoricola*, *Microbacterium*, *Micrococcus*, *Micromonospora*, *Mycobacterium*, *Nocardia*, *Nocardioides*, *Nocardiopsis*, *Pseudokineococcus*, *Sanguibacter*, *Streptomyces*, and *Verrucosispora*.
South Asia	Mitra *et al.* (2008)[102]	India	Indian Sundarbans: i. Bally jetty ii. Pakhiralaya 1 iii. Pakhiralaya 2 iv. Jamespore v. Dattar forest vi. Bally forest	Soil samples	*Actinomadura*, *Actinoplanes*, *Nocardia*, *Nocardiopsis*, *Micromonospora*, *Saccharopolyspora*, *Streptomyces*, *Streptosporangium*, and *Streptoverticillium*.
	Rajkumar *et al.* (2012)[76]	India	Sites of Bhitherkanika: i. Kola creek ii. Bhiterkkanika iii. Baguludia iv. Kalibhanchidia v. Thanidia	Sediment samples	*Actinomadura*, *Actinomyces*, *Actinopolyspora*, *Micromonospora*, *Nocardiopsis*, *Saccharopolyspora*, and *Streptomyces*.
	Karthikeyan *et al.* (2013)[106]	India	Tamil Nadu: Ennoor	Soil samples	*Actinokineospora*, *Actinopolyspora*, *Amycolata*, *Glycomyces*, *Microbispora*, *Microtetraspora*, *Micropolyspora*, *Nocardia*, *Nocardiopsis*, *Promicromonospora*, *Saccharothrix*, *Saccharopolyspora*, *Streptomyces*, *Streptoverticillium*, *Spirillospora*, and *Thermomonospora*.
Southeast Asia	Lee *et al.* (2014)[45]	Malaysia	Pahang: Tanjung Lumpur	Soil samples	*Gordonia*, *Leifsonia*, *Microbacterium*, *Micromonospora*, *Mycobacterium*, *Nocardia*, *Nocardioides*, *Sinomonas*, *Streptacidiphilus*, *Streptomyces*, and *Terrabacter*.
	Malek *et al.* (2015)[107]	Malaysia	Pahang: Tanjung Lumpur	Soil samples	*Actinophytocola*, *Gordonia*, *Micromonospora*, *Mycobacterium*, *Pseudonocardia*, *Rhodococcus*, and *Streptomyces*.
	Retnowati *et al.* (2017)[103]	Indonesia	Gorontalo Province: Torosiaje	Soil samples	*Amycolatopsis, Nocardiopsis, Streptomyces,* and *Saccharomonospora*.

Table 2. Mangrove-derived novel *Streptomyces* species published from year 2009 to early 2019.

No.	Strain name and designation	Mangrove sampling site	Source	Reference
1.	*Streptomyces avicenniae* MCCC 1A01535^{T}	National mangrove reserve in Fujian Province, China	Rhizosphere of mangrove plant *Avicennia mariana*	Xiao *et al.* (2009)[112]
2.	*Streptomyces xiamenensis* MCCC 1A01550^{T}	National mangrove reserve in Fujian Province, China	Sediment	Xu *et al.* (2009)[113]
3.	*Streptomyces sundarbansensis* MS1/7^{T}	Sundarbans mangrove forest, India	Sediment	Arumugam *et al.* (2011)[114]
4.	*Streptomyces shenzhenensis* 172115^{T}	Shenzhen, China	Sediment	Hu *et al.* (2011)[115]
5.	*Streptomyces sanyensis* 219820^{T}	Sanya, Hainan Province, China	Composite sediment	Sui *et al.* (2011)[116]
6.	*Streptomyces qinglanensis* 172205^{T}	Qinglan Harbour, Wenchang, Hainan, China	Composite soil	Hu *et al.* (2012)[117]
7.	*Streptomyces pluripotens* MUSC 135^{T}	Tanjung Lumpur mangrove forest in Pahang, Peninsular Malaysia	Soil	Lee *et al.* (2014)[33]
8.	*Streptomyces ferrugineus* HV38^{T}	Thailand	Soil	Ruan *et al.* (2015)[118]
9.	*Streptomyces mangrovisoli* MUSC 149^{T}	Tanjung Lumpur mangrove forest in Pahang, Peninsular Malaysia	Soil	Ser *et al.* (2015)[119]
10.	*Streptomyces gilvigriseus* MUSC 26^{T}	Tanjung Lumpur mangrove forest in Pahang, Peninsular Malaysia	Soil	Ser *et al.* (2015)[120]
11.	*Streptomyces mangrovi* HA11110^{T}	Dongzhaigang National Nature Reserve, Hainan, China	Soil	Wang *et al.* (2015)[121]
12.	*Streptomyces malaysiense* MUSC 136^{T}	Tanjung Lumpur mangrove forest in Pahang, Peninsular Malaysia	Soil	Ser *et al.* (2016)[78]
13.	*Streptomyces antioxidans* MUSC 164^{T}	Tanjung Lumpur mangrove forest in Pahang, Peninsular Malaysia	Soil	Ser *et al.* (2016)[122]
14.	*Streptomyces humi* MUSC 119^{T}	Tanjung Lumpur mangrove forest in Pahang, Peninsular Malaysia	Soil	Zainal *et al.* (2016)[123]
15.	*Streptomyces euryhalinus* MS 3/20^{T}	Lothian Island of Sundarbans mangrove forest, India	Sediment	Biswas *et al.* (2017)[124]
16.	*Streptomyces colonosanans* MUSC 93J^{T}	Mangrove forest in Kuching, Sarawak, Malaysia	Soil	Law *et al.* (2017)[125]
17.	*Streptomyces nigra* 452^{T}	Zhangzhou, Fujian Province, China	Rhizosphere soil of mangrove plant *Avicennia marina*	Chen *et al.* (2018)[126]
18.	*Streptomyces caeni* HA15955T	Sanya, China	Mud	Huang *et al.* (2018)[127]
19	Streptomyces monashensis MUSC 1J^{T}	Mangrove forest in Kuching, Sarawak, Malaysia	Soil	Law *et al.* (2019)[128]

CONCLUSION

Research on the diversity of microbial community in the class *Actinobacteria* originating from different environments and countries has been thoroughly conducted due to their ecological importance and astonishing biotechnological potential. Nevertheless, there is still limited knowledge pertaining the diversity of *Actinobacteria* in the mangrove environments given that there are over 150, 000 km^2 of mangroves distributed at many different parts of the world. It will be valuable to explore the diversity of *Actinobacteria* from mangrove given that they have been producers of numerous useful bioactive compounds and enzymes, especially from *Streptomyces*. The discovery novel *Streptomyces* in addition to bioprospecting of *Streptomyces* population from underexplored mangrove environments could therefore increase the chances of uncovering new sources of natural products for various applications.

Authors Contributions

The literature review and manuscript writing were performed by JW-FL, PP, N-SAM, SHW, B-HG, and L-HL. L-HL founded the research project.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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