J. Mountain Res. P-ISSN: 0974-3030, E-ISSN: 2582-5011 DOI: https://doi.org/10.51220/jmr.v19-i2.10
Vol. 19(2), (2024), 85-95

A Comprehensive Review on Actinomycetes Distribution, Novel Bioactive Compounds and Their Implementation in The Field of Agronomy And Medical

Vaishali Negi[1] • Parul Sharma[1*] • Amreen[2] • Geeta Rawat[1]

[1]*Department of Microbiology, Dev Bhoomi Uttarakhand University, Manduwala, Dehradun-248007, Uttarakhand, India.*
[2]*Department of Zoology, Dev Bhoomi Uttarakhand University, Manduwala, Dehradun-248007, Uttarakhand, India*

*Corresponding Author: parulsharma1291@gmail.com

Received: 09.07.2024 Revised: 03.10.2024 Accepted: 10.10.2024

Abstract: Actinomycetes, particularly *Streptomyces*, thrive in extreme ecosystems and are key producers of diverse secondary metabolites with pharmaceutical and agricultural applications. These metabolites exhibit antibiotic, enzymatic, antiviral, and antitumor activities, contributing to half of all known secondary metabolites. In medicine, they yield immunosuppressants, antivirals, and hypertension treatments. In agriculture, they support sustainable farming through siderophores, phosphate solubilization, growth hormone synthesis, nitrogen fixation, and natural insecticide production. This review highlights recent advancements in actinomycetes research, emphasizing their pivotal roles across industries.

Keywords: Bioactive compounds • Niches • Actinobacteria • Therapeutic use • Agriculture

Introduction

Actinomycetes are free-living gram-positive, filamentous, saprophytic and spore-forming bacteria belonging to the order Actinomycetal and phylum Actinobacteria, which produce approximately 20,000 bioactive compounds (Alenazi et al, 2023)**.** Owing to the presence of true aerial hyphae and their ability to form spores, they were mistakenly classified as fungi. Their deoxyribonucleic acids comprise of significant amount of guanine and cytosine (Bawazir et al, 2019). However, some new species that do not follow this norm have been discovered (Sutaria et al, 2021). Actinomycetes are distinguished by their wide variety and their capability to synthesize new compounds. They produce around half of the researched beneficial secondary metabolites, including enzymes, antibiotics, and compounds that fight against cancer and inflammation (Mohan and Rajamanickam (2018); Elmallah et al, (2020)). Except unicellular *Mycobacterium* and *Corynebacterium*, most of the actinomycetes are saprophytic microorganisms in nature with complex lifecycles (Prudence et al, 2019)

Actinomycetes are an essential class of major compounds makers that are used in pharmacology and biotechnology because they synthesize secondary metabolites and other valuable compounds, such as antibiotics, anticancer medicines, immunosuppressive agents, and nutritive materials (Ngamcharungchit and Chaimusik, 2023). They also play a major role in reducing environmental pollution and are well-known for their bioremediation abilities. Pesticides and other xenobiotics compounds have been successfully bioremediated by actinomycetes (Sutaria et al, 2021). Improved plant growth has been achieved through the production of plant growth hormones by actinomycetes. One of the growth hormones synthesized by actinomycetes, Indole-3-acetic acid, promotes cell proliferation, elongation, and differentiation (Meena et al, 2017). Recent studies have revealed rare actinomycetes that produce a diverse array of natural substances.

However, extracting and cultivating them poses challenges. These microorganisms are cosmopolitans in habitats such as soil, mangrove forests, deserts, mountains, and plants. As of 2022, actinomycetes have been isolated from over 220 genera, with more than 50 taxa producing 25,000 bioactive compounds (Ezeobiora et al, 2022).

Habitats and niches of actinomycetes

Actinomycetes are extensively ecologically diverse around the planet, in variety of ecosystem including terrestrial, marine, plants, insects and caves (Ngamcharungchit and Chaimusik, 2023) (Table 1). Their presence has been observed in extreme environments, particularly in cryophilic regions such as soil samples from Antarctica and even in desert environments (Chaudhary et al, 2013).

Terrestrial biome

Soil: A wide range of soil types have been used to isolate most unusual actinomycetes. They are found in cultivated and uncultivated soils, as well as in both barren and productive soils. It has been possible to isolate more than 90% of actinomycete genera from soil (McCarthy and Williams, 1990). The earthy fragrance of soil can be attributed to them (Zenova et al, 2011). The pH has a significant impact on actinomycetes growth and activity. In acidic soils, acidophilic and acididuric *Streptomyces* are more prevalent (Infanta and Santhi, 2021).

Plants: Healthy plant tissues contain endophytic actinomycetes which are present without harming the plants (Narayana et al, 2008). They are an excellent source of bioactive compounds, lytic enzymes, and antibiotics (Helmke and Weyland, 1984). The *Frankia* genera of endophytic actinomycetes assist with nitrogen fixation, which plays vital role in the environment (Xu et al, 2007). Genera such as *Blastococcus, Saccharopolyspora, Dactylosporangium, Oerskovia, Promicromonospora, Actinocorallia, Dieizia*are isolated from endophytic habitants (Qin et al, 2009)

Aquatic ecosystem:

Nearly 70% of earth ecosystem is covered by the oceans which is residence for varieties of living organisms including bacteria like actinomycetes that may be found in the depth of the ocean`s surface and its depths. They produce secondary metabolites for their survival in these habitats. In marine ecosystem, symbiotic connection between microbes and marine creatures have been documented. These microbial marine symbionts are substantial producers of bioactive natural marine products (Sarkar and Suthindhiran, 2022).

Hostile environment

In harsh ecosystems, microorganisms that can thrive in extreme conditions such as extreme temperatures, pH levels, and high pressure are referred to as extremophile (Macelroy, 1974), while those capable of surviving in such conditions are termed extremotolerant. Actinomycetes are extremophilic bacteria can be found in diverse habitats such as in salty seas, oceans and alkaline soil (Jiang et al, 2016). Actinobacteria isolated from extreme environments are rich source of drugs which has its potential value in the fields of agriculture, industry, and medicine (Sayed et al, 2019).

3. Novel bioactive compounds of actinomycetes

Actinomycetes are prolific producers of bioactive compounds, encompassing a diverse range of molecules with significant biological activities. These metabolites have a wide range of applications in drugs, agrochemicals, biofuels, and food additives (Fig 1)

Antibiotics: Secondary metabolites synthesized by actinomycetes, fungi and bacteria are known as antibiotics utilized to suppress and sometimes eliminate the proliferation of microorganisms. (Adegboye and Babalola, 2013). Around 75% of secondary metabolites, including antibiotics, originate from the order Streptomycetes, which alone accounts for 45% of bioactive metabolite production. These species are utilized in medicine, industry and agriculture

J. Mountain Res. P-ISSN: 0974-3030, E-ISSN: 2582-5011 DOI: https://doi.org/10.51220/jmr.v19-i2.10
Vol. 19(2), (2024), 85-95

(Bentley et al, 2002; Barke et al, 2010; Bano et al, 2019). Antifungal activities are exhibited by streptomycetes, *Streptomyces mediocidicus* ATCC23936 synthesizes mediomycins A, B, whereas *Streptomyces malaysiensis* DSM4137 produces antibiotics cethromycin (Hussain et al, 2002). Polyketides are natural products have garnered significant attention in the pharmaceutical industry due to their therapeutic applications. Polyketides include erythromycin (antibacterial), nystatin (antifungal), and avermectin (antiparasitic). All of these antimicrobial agents are produced by *Streptomyces* species, which are considered as a potent producer of antibiotics (Hasani et al, 2014).

.

Table 1. Distribution of actinomycete strains across various habitats

Habitat	Area	Strains	References
Terrestrial	**Hypersaline soil**	*Nocardia sp., Streptomyces alboflavus, Micromonospora sp., Streptomyces griseoflavus*	(Selim et al, 2021)
	Plants (endophytes)	*Nocardia, Nonomuraea, Pseudonocardia, Plantacttinospora, Streptomyces, Wangella,*	(Ngamcharunchit and Chaimusik (2023) ; Masand et al, 2015)
Aquatic	**Marine sediment**	*Agromyces marinus, Anylotatopsis flava, Saccharmonospora oceani, Kocuria indica, Saccharopolyspora, Streptosporangium, hermoactin*	(Ezeobiora et al, 2022)
	Sea sediment	*Myceligeneras cantabricum, Pseudonocardia sediminis, Microbacterium enclense, Zhihenglivella*	(Cho et al, 2013)
Extreme	**Hostile environment**	*Saccharomononospora, Thermoactinomyces, Thermobifida, Thermonospora*	(Meklat et al, 2011)
	Caverans	*Micribispora thailandensis.nov, Nonomuraean sp.nov, Stretomyces sp., Nocardioidae, Agromyces, Rhodococcus*	(Farda ,2023)

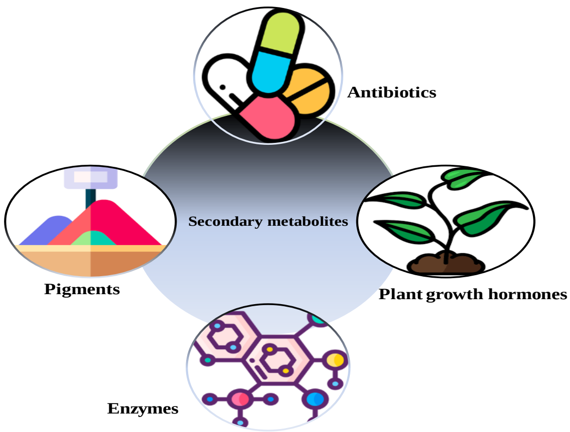

Fig. 1 Diversity of secondary metabolites produced by actinomycetes.

DOI: https://doi.org/10.51220/jmr.v19-i2.10

Enzymes: Actinomycetes produce a wide array of enzymes that prove beneficial to the fields of biotechnology and microbiology such as amylases, xylanases, proteases, and chitinase (Harir et al, 2018). Commercial enzymes like amylase are employed by actinomycetes for extracellular digestion and play a significant role in various biotechnological applications, including the food, textile, and paper industries. The enzyme market demands approximately 25% of amylase production (Rajagopalan et al, 2008). Cellulase are hydrolytic enzyme produced by actinomycetes find applications across industries including paper, pulp, wine, brewing, and other industries. They are also an excellent source of L-asparginase, which is isolated from soil actinomycetes such as *Nocardia sp*, *Streptomyces griseus*, *S, albidoflavus*, *S. Karnataknesis* (Dejong, 1972; Narayana et al, 2008; Mostafa and Salama 1979). Additionally, enzyme inhibitors are also plays a vital role in elucidating enzyme structure and reaction mechanisms within the pharmacological industry (Stutzenberger 1987). Enzyme inhibitors of the alpha-amylase are exhibited by *Streptomyces* sp. and *corchorushii* (Sun et al, 2015).

Pigments : Different hues produced by various species in both synthetic and natural conditions aid in the identification of tiny creatures. Actinomycetes generate pigments such as carotenoids and melanin, varying in hue from yellow to orange to red and employed in the cosmetic and pharmaceutical industries (Klein et al, 2007).

Applications in the realm of agricultural science

The overuse of pesticides has led to considerable decline of soil quality and poses a threat to depriving a large portion of the population of vital food resources. To overcome this problem, natural methods have been implemented in agricultural areas, which have helped in the sustainability and development of agricultural areas. Compared to other microorganisms, actinomycetes help in increasing soil fertility as well as researchers in recent years (Jain et al, 2022) (Fig 2)

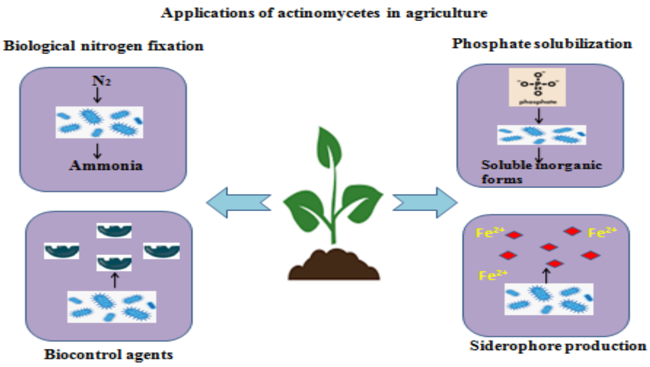

Fig 2. Applications of actinomycetes in agriculture, highlighting their roles in enhancing soil fertility and controlling plant pathogens.

Nitrogen fixation

Nitrogen fixation is a cyclic process in which nitrogen is converted to ammonia. Actinomycetes help in nitrogen fixation either by symbiosis or by free-living conditions, such as *Cornynebacterium* sp. which helps in promoting the growth of maize crops by releasing the level of acetylene and *Micromonospora*, which fix nitrogen symbiotically through actino-nodules of trees and shrubs (Barka et al, 2016). *Frankia* fixes nitrogen by forming symbiosis with

DOI: https://doi.org/10.51220/jmr.v19-i2.10

actinorhizal plants which helps in colonizing nitrogen poor soil and initiation of ecological succession (Normand et al, 2007). Two genes play a major role in nitrogen fixation those are nif and nod genes. Both genes have their own importance; nif genes encode nitrogenase enzymes that help in nitrogen fixing, while nod genes encode Nod factor that helps in nodule formation (Haukka et al, 1998). Example of some nitrogen fixing bacteria are *Herbiconiux*, *Labdella*, *Leucobacter* (Boukhatem et al, 2022).

Solubilization of phosphate

Phosphate is a major growth-macronutrient required for plant growth and development, especially in tropical areas, because of the low availability of soil (Santana et al, 2016). Phosphate has numerous detrimental effects on the environment, yet phosphate-based fertilizers remain costly because of the extraction process from raw materials (Abebe et al, 2022). In the soil, phosphate exists in an insoluble form due to its fixation as insoluble phosphates of iron, calcium, and aluminium. About 75-90% of the agrochemical phosphorous get fixed in the soil by forming metal-cation complexes which led to the deterioration of soil fertility and eutrophication (Sharma et al, 2013). Additionally, they also secrete extracellular enzyme like phytase which aids in the degradation of phytate. Furthermore, they release various acid such as citric, gluconic, malic, oxalic, propionic, and succinic acids, creating an acidic environment that solubilizes potassium (Yadav and Yadav, 2019).

Production of siderophore

Irons are essential nutrient for microorganisms to perform various functions such as growth, repair and nucleic acid synthesis, photosynthetic transport, respiration, nitrate reduction and detoxification of free radical (Hernandez et al, 2018). Siderophores are low molecular weight ligands produced by microorganism that binds to fe^{3+} and transport it in to the cell to fulfil their iron requirement under iron limiting conditions (Gu et al, 2020). Numerous microorganisms are capable of producing siderophores and can also acts as a biocontrol agent. Among them *Streptomyces* strain produced hydroxamate type of siderophore such as deferoxamine (Zhou et al, 2022). Enterobactin is produced by *Enterobactericeae* family. Moreover, Hetrobactins are different type of siderophores found in *Rhodococcus erythropolis*. Desferrioxamine, one of the common class of siderophore that is produced by actinomycete (Wang et al, 2014). When biocontrol agents produced enough amount of siderophores it reduces the availability of Fe^{3+}, which indirectly effects the phytopathogenic fungi because due to lack of iron they would be unable to perform their vital functions.

Biocontrol agent

Globally there has been surge in the discovery of natural compounds as a biocontrol agents. Approximately 60% of insecticides and herbicides derived from *Streptomyces* have been discovered in the last 10 years. Thermophilic actinomycetes increase crop yields as they can supress the plant diseases thus they can be used instead of commercial pesticide (Ngamcharungchit and Chaimusik, 2023). Among all the genera of actinomycete, *Streptomyces* is extensively used as biocontrol due to its easy isolation process (Zou et al, 2021). Marine actinomycetes, like *S. chumphonensis*, effectively decreased green mold syndrome caused by *P. digitatum* in citrus (Hu et al, 2019). The consumption of biostimulants and organic fertilizers such as compost and vermicompost, increase the population of actinomycete. Marine *Streptomyces* sp. showcase improved efficacy in the suppression of *C. fragariae* in strawberry thereby reducing the severity of anthracnose disease. Moreover, they help maintain fruit hardness and color (Cao et al, 2020) (Fig 3).

Table 2. Commercialized biocontrol products based on Actinomycetes

Commercial products	Actinomycetes	Registered countries name	Targeted pathogen/ Disease	References
Actinovate, Novozymes	*S.lydicus*	Canada, USA	*Rhizoctonia*, *Phytophthora Fusarium*, *Pythium*, and *Verticillium*, *Botrytis Alternaria*, *Geotrichum*, and *Sclerotinia* powdery and downy mildew	(Tian and Zheng, 2013)
Polyoxorim	*S. cacaoi var. asoensis*	UE countries	*Sphaerotheca*, powdery mildews, *Sclerotium*, *Alternaria*, *Botrytis*, *Corynespora*, *Cochliobolus*, sheath blight, and *Helminthosporium*	Copping et al. 2007
Mycostop	*S. griseovirids*	Canada, UE countries, and USA	lternaria, *R. solani*, *Phytophthora*, *Fusarium*, *Botrytis* and *Pythium*	(Lahdenpera et al, 1991)
Safegrow KIBC	*S. kasugaensis*	South Korea	Sheath blight and large patch	(Kabaluk et al, 2010)
Bactophil	*Streptomyces albus*	Ukraine	Seed germination diseases	(Nakaew et al, 2009)
Agrimycin, Paushak, Cuprimicin 17, Astrepto 17	*S. griseus*	India, USA, New Zealand, China, Ukraine and Canada	Bacterial rots, *Xanthomona*, and *Pseudomonas*	(Tian and Zheng, 2013

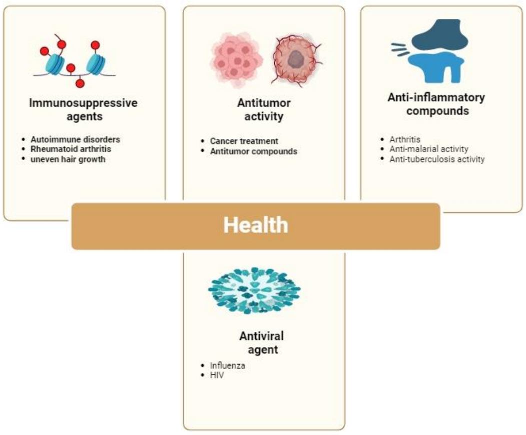

Fig 3. Applications of actinomycetes in the health sector

In health-related area: Actinomycetes have significant importance in the medical field as it produces a wide array of secondary metabolites. These metabolites are used for the treatment of various infection Actinomycetes are particularly noted for synthesizing compounds with potent antitumor,
Antitumor activity: Antinomycin D was the first natural metabolites isolated from *Streptomyces antibioticus*, used for cancer treatment. Due to side effects its applications has been limited but it is

still used for the Wilms tumour in children (Waksman et al, 1941). Marine actinomycetes are the major source for anti-tumour compounds which has vast use in pharamceautical industries. They create strong medications known as secondary metabolites which cannot be produced by terrestrial organisms. The breast cancer cell lines MDA-MB231 and MCF-7 were antagonistic to the actinomycete strains ACT01 and ACTO2 (Ravikumar et al, 2012). Some of the novel bioactive metabolites extracted from marine actinomycetes, such as Streptochlorin, Lynamicins, and marizomib, are anti-tumor compounds (Zuo and Kwok, 2021) (Table 3).

Immunosuppressive agents: Immunosuppresive are the drugs that are used during organ transplantation to decrease the risk of organ rejection. They are employed in managing autoimmune disorders like Crohn`s disease (Persistent inflammation in digestive tract), rheumatoid arthritis, and uneven hair growth. Compounds such as tacrolimus from *Streptomyces tsukubaensis* and ascomycin from *Streptomyces hygroscopicus* have been derived from microorganisms for use as an antifungal-antibiotic agents during organ transplantation (Barreiro et al, 2012)

Anti-inflammatory compounds: Anti-inflammatory compounds are utilized to relief the pain and inflammation related with arthritis and muscle-skelton disorders. Such inflammatory compounds like Saphenic acid and lipomycin is produced by the marine actinomycetes. Also, Cyclomarin A and C are produced by *Streptomyces Arenicola. Cyclomarin A* has both anti-tuberculosis as well as anti-malarial activity. Additionally, it is used to decrease swelling during inflammation (Alenazi et al, 2023)

Table 3. Few examples of antiviral and antitumor metabolites isolated from actinomycete from 2017-2023

Metabolites	Organisms	Compounds names	References
Antiviral	*Actinomadara sp.* 2EPS	Decatromicins	(Euanorasetr et al, 2019)
	Streptomyces Koyangensis SCSIO 5802	Neoabyssomicins F,G	(Keller et al, 2023; Huang et al, 2018)
	Streptomyces bacillaris	Zelkovamycins F,G	(Hao et al, 2022)
	Streptomyces sp. SCSIO 40063	Piericidins A 5, G1	(Peng et al, 2022)
	*Streptomyces kebangsaanensis*WS-68302	Napyradiomycin A4, A80915 H	(Zhang et al, 2023)
	Streptomyces sp. JA74	Dihydromaniwamycin E	(Saito et al, 2022)
	Kibdelosporangium persicum	Persicamidines A–E	(Kimura et al, 2019)
Antitumor	*Streptomyces sp.* N1510.2	Strepantibin D	(Lu et al, 2021)
	Micromonospora aurantiaca 110B	Isoflavonoid glycosides 1-3	(Wang et al, 2014)
	Streptomyces sp. XMA39	Rubiflavin G Photorubiflavin G, E	(Lee et al, 2023)
	Streptomyces sp. shell-016	Shellmycin A–D	(Han et al, 2020)
	Actinomadura sp. K4S16	Nonthmicin, Ecteinamycin	(Igarashi et al, 2017)

Conclusion

Actinomycetes, particularly *Streptomyces*, thrive in diverse ecosystems and are crucial for producing bioactive compounds with medical and agricultural applications. In medicine, they combat antibiotic resistance by synthesizing novel antibiotics with unique structures and mechanisms, offering solutions against resistant pathogens. In agriculture, actinomycetes support sustainable practices by fixing nitrogen, producing siderophores, stimulating plant growth, and serving as natural alternatives to synthetic pesticides and fertilizers. These organisms enhance soil health, improve crop yields, and reduce environmental impact. Ongoing research underscores their pivotal role in addressing global health and food security challenges, paving the way for advancements in biotechnology and sustainable agriculture.

Acknowledgments
Authors gratefully acknowledge Dev Bhoomi Uttarakhand University, Dehradun for their necessary support

References

Abebe TG, Tamtam MR, Abebe AA, Abtemariam KA, Shigut TG, Dejen YA. Growing use and impacts of chemical fertilizers and assessing alternative organic fertilizer sources in Ethiopia. *Appl Environ Soil Sci*. 2022;1-14.

Adegboye MF, Babalola OO. Actinomycetes: Source, identification and their applications. *Int J Curr Microbiol Appl Sci*. 2013;3(2):801-832.

Alenazi AB, Anwar Y, et al. A review on Actinomycetes distribution, isolation and their medical application. *Novel Res Microbiol J*. 2023;7(2):1918-1931.

Bano H, Siddiqui S, Amir M, R. House of industrially important bioactive metabolites: a review of actinobacteria. *J Appl Pharm Sci*. 2019;18:293-304.

Barke J, Seipke RF, Grüschow S, Heavens D, Drou N, Bibb MJ, Goss RJM, et al. A mixed community of Actinomycetes produce multiple antibiotics for the fungus farming ant *Acromyrmex octospinosus*. BMC Biol. 2010;8:109.

Barreiro C, Prieto C, Sola-Landa A, Solera E, Martínez-Castro M, Pérez-Redondo R, et al. Draft genome of *Streptomyces tsukubaensis* NRRL 18488, the producer of the clinically important immunosuppressant tacrolimus (FK506). *J Bacteriol*. 2012;194:3756-3757.

Bawazir Ali Mohammad AP, Shantaram M, et al. An implication of actinomycetes in human well being. *Int J Pharm Pharm Sci*. 2019;11:11-18.

Bentley SD, Chater KF, Cerdeno-Tarraga AM, Challis GL, Thomson NR, James KD, et al. Complete genome sequence of the model actinomycete *Streptomyces coelicolor* A3(2). Nature. 2002;417(6885):141-147.

Boukhatem ZF, Merabet C, Tsaki H. Plant growth promoting Actinobacteria, the most promising as bioinoculant? *Front Agron*. 2022;4:1-19

Cao P, Li C, Wang H, Yu Z, Xu X, Wang X, et al. Community structures and antifungal activity of root-associated endophytic actinobacteria in healthy and diseased cucumber plants and *Streptomyces* sp. HAAG3-15 as a promising biocontrol agent. *Microorganisms*. 2020;8:236.

Chaudhary H, et al. Diversity and versatility of actinomycetes and its role in antibiotic production. *J Appl Pharm Sci*. 2013;3:83-94.

Cho Y, Jang G, Hwang CY, Kim EH, Cho BC. *Nocardioides salsibiostraticola* sp. nov., isolated from biofilm formed in coastal seawater. *Int J Syst Evol Microbiol*. 2013;63:3800-3806.

Copping LG, Duke SO. Natural products that have been used commercially as crop protection agents. *Pest Manag Sci*. 2007;63:524-554.

DeJong PJ. L-Asparaginase production by *Streptomyces griseus*. Appl Microbiol. 1972;23(6):1163-1164.

Elmallah MIY, Cogo S, Constantinescu A, Esposito SE, Abdelfattah MS, Micheau O. Marine actinomycetes-derived secondary metabolites overcome TRAIL-resistance via the intrinsic pathway through down regulation of survivin and XIAP. *Cells.* 2020;9(8):1760-1778.

Euanorasetr J, Intra B, Thunmrongsiri N, Limthongkul J, Ubol S, Anuegoonpipat A, et al. In vitro antiviral activity of spirotetronate compounds against dengue virus serotype 2. *J Gen Appl Microbiol*. 2019;65:197-203.

Ezeobiora CE, et al. Uncovering the biodiversity and biosynthetic potential of rare actinomycetes. *Future J Pharm Sci*. 2022;1-19.

Farda B. Actinomycetes from caves: An overview of their diversity, biotechnological properties and insights for their use in soil environments. Microorganisms. 2023;10(2):1-19.

Gu S, Yang T, Shao Z, Wang T, Cao K, Jousset A, et al. Siderophore-mediated interactions determine the disease suppressiveness of microbial consortia. *mSystems.* 2020.

Han Y, Wang Y, Yang Y, Chen H. Shellmycin A-D, novel bioactive tetrahydroanthra-γ-pyrone antibiotics from marine *Streptomyces* sp. Shell-016. *Mar Drugs*. 2020;18:58.

Hao X, Li S, Wang G, Li J, Peng Z, Zhang Y, Zelkovamycins F and G, Cyclopeptides with Cα-Methyl-threonine Residues, from an Endophytic *Kitasatospora* sp. *J Nat Prod.* 2022;85:1715-22.

Harir M, et al. *Streptomyces* secondary metabolites. 2018. p. 99-122.

Hasani A, Kariminik A, Issazadeh K. *Streptomycetes*: characteristics and their antimicrobial activities. *Int J Adv Biol Biomed Res*. 2014;2:63-75.

Haukka K, Lindström K, Young JP. Three phylogenetic groups of nodA and nifH genes in *Sinorhizobium* and *Mesorhizobium* isolates from leguminous trees growing in Africa and Latin America. *Appl Environ Microbiol*. 1998;64(2):419-26.

Helmke E, Weyland H. *Rhodococcus marinonascens* sp. nov., an actinomycete from the sea. *Int J Syst Bacteriol*. 1984;34:127-38.

Hernández-Montiel LG, Rivas-García T, Romero-Bastidas M, Chiquito-Contreras CJ, Ruiz-Espinoza FH, Chiquito Contreras RG. Antagonistic potential of bacteria and marine yeasts for the control of phytopathogenic fungi. *Rev Mex Cienc Agríc*. 2018;9:4311-21.

Huang H, Song Y, Li X, Wang X, Ling C, Qin X, et al. Abyssomicin Monomers and Dimers from the Marine-Derived *Streptomyces koyangensis* SCSIO 5802. *J Nat Prod.* 2018;81:1892-8.

Hussain AA, Mostafa SA, Ghazal SA, Ibrahim SY. Studies on antifungal antibiotic and bioinsecticidal activities of some actinomycete isolates. *Afr J Mycol Biotechnol*. 2002;10:63-80.

Igarashi Y, Matsuoka N, In Y, Kataura T, Tashiro E, Saiki I, et al. Nonthmicin, a polyether polyketide bearing a halogen-modified tetronate with neuroprotective and antiinvasive activity from *Actinomadura* sp. *Org Lett.* 2017;19:1406-9.

Infanta AKT, Santhi N. A review on applications of actinomycetes. *J Crit Rev.* 2021;8:566-74.

Jain S, et al. Applications of actinobacteria in agriculture, nanotechnology and bioremediation. In: Intechopen; 2022.

Jiang Y, Li Q, Chen X, Jiang C. Isolation and cultivation methods of Actinobacteria. In: Dhanasekaran D, Jiang Y, editors. Actinobacteria-basics and biotechnological applications. London: InTech; 2016:39–57.

Kabaluk JT, Svircev AM, Goettel MS, Woo SG. The use and regulation of microbial pesticides in representative jurisdiction worldwide. Hong Kong, China: IOBC Global; 2010.

Kimura T, Suga T, Kameoka M, Ueno M, Inahashi Y, Matsuo H, et al. New

 DOI: https://doi.org/10.51220/jmr.v19-i2.10

tetrahydroquinoline and indoline compounds containing a hydroxy cyclopentenone, virantmycin B and C, produced by *Streptomyces* sp. AM-2504. *J Antibiot*. 2019;72:169-73.

Klein Marcuschamer D, Ajikumar PK, Stephanopoulos G. Engineering microbial cell factories for biosynthesis of isoprenoid molecules: beyond lycopene. *Trends Biotechnol*. 2007;25:417-24.

Lahdenperä ML, Simon E, Uoti J. Mycostop-a novel biofungicide based on *Streptomyces* bacteria. In: Beemster ABR, Bollen GJ, Gerlagh M, Ruissen MA, Schippers B, Tempel A, editors. Developments in agricultural and managed forest ecology. *Amsterdam: Elsevier*; 1991:258-63.

Lee B, Lee GE, Hwang GJ, Heo KT, Lee JK, Jang JP, et al. Rubiflavin G, photorubiflavin G, and photorubiflavin E: Novel pluramycin derivatives from *Streptomyces* sp. W2061 and their anticancer activity against breast cancer cells. *J Antibiot* (Tokyo). 2023;76:1-7.

Macelroy RD. Some comments on the evolution of extremophiles. *Biosystem*. 1974;6:74-5.

Masand M, Jose PA, Menghani E, Jebakumar SRD. Continuing hunt for endophytic actinomycetes as a source of novel biologically active metabolites. *World J Microbiol Biotechnol*. 2015;31:1863-75.

McCarthy AJ, Williams ST. Methods for studying the ecology of actinomycetes. *Methods Microbiol*. 1990;22:534-62.

Meena M, Swapnil P, Zehra A, Aamir M, Dubey M, Goutam J, et al. Beneficial microbes for disease suppression and plant growth promotion. In: Singh DP, Singh HB, Prabha R, editors. Plant-Microbe Interactions in Agro-Ecological Perspectives. *Singapore: Springer*; 2017:395-432.

Meklat A, Sabaou N, Zitouni A, Mathieu F, Lebrihi A. Isolation, taxonomy, and antagonistic properties of halophilic Actinomycetes in Saharan soils of Algeria. *Appl Environ Microbiol*. 2011;77:6710-4.

Mohan KD, Rajamanickam U. Biodiversity of actinomycetes and secondary metabolites. *Inn Orig Inter J Sci*. 2018;5(1):21–7.

Mostafa SA, Salama MS. L-asparaginase producing *Streptomyces* from soil of Kuwait. *Zentralbl Bakteriol Naturwiss*. 1979;134(4):325-34.

Narayana KJP, Prabhakar T, Vijayalakshmi M, Venkat Rao T. L-asparaginase production by *Streptomyces albidoflavus*. *Indian J Microbiol*. 2008;48(3):331-6.

Ngamcharungchit C, Chaimusik N. Bioactive metabolites from terrestrial and marine actinomycetes. *Molecules*. 2023;26(23):1-33.

Normand P, Queiroux C, Tisa LS, Benson DR, Rouy Z, Cruveiller S, et al. Exploring the genomes of Frankia. *Physiol Plantarum*. 2007;130:331-43.

Peng J, Zhang Q, Jiang X, Ma L, Long T, Cheng Z, et al. New piericidin derivatives from the marine-derived *Streptomyces* sp. SCSIO 40063 with cytotoxic activity. Nat Prod Res. 2022;36:2458-64.

Prudence SMM, Addington E, Castaño-Espriu L, Mark DR, Pintor-Escobar L, Russell AH, et al. Advances in actinomycete research: An ActinoBase review of 2019. *Microbiology*. 2020;166:683-94.

Qin S, Li J, Chen HH, Zhao GZ, Zhu WY, Jiang CL, et al. Isolation, diversity, and antimicrobial activity of rare Actinobacteria from medicinal plants of tropical rain forests in Xishuangbanna, China. *Appl Environ Microbiol*. 2009;75:6176-86.

Rajagopalan G, Krishnan C. Alpha-amylase production from catabolite derepressed *Bacillus subtilis* KCC103 utilizing sugarcane bagasse hydrolysate. *Bioresour Technol*. 2008;99:3044-50.

Saito S, Funayama K, Kato W, Okuda M, Kawamoto M, Matsubara T, et al. Dihydromaniwamycin E, a Heat-shock metabolite from thermotolerant *Streptomyces* sp. JA74, exhibiting antiviral activity against Influenza and SARS-CoV-2 viruses. *J Nat Prod*. 2022;85:2583-9.

Santana EB, Marques ELS, Dias JCT. Effects of phosphate-solubilizing bacteria, native microorganisms and rock dust on *Jatropha curcas* L. growth. *Genet Mol Res*. 2016;15(4).

Sarkar G, Suthindhiran K. Diversity and biotechnological potential of marine actinomycetes. *Indian J Microbiol*. 2022;62(4):475-93.

Sen R, Ishak HD, Estrada D, Dowd SE, Hong E, Mueller UG. Generalized antifungal activity and 454-screening of *Pseudonocardia* and *Amycolatopsis* bacteria in nests of fungus-growing ants. *Proc Natl Acad Sci*. 2009;106:17805-10.

Sharma SB, Sayyed RZ, Trivedi MH, Gobi TA. Phosphate solubilizing microbes: sustainable approach for managing phosphorus deficiency in agricultural soils. *SpringerPlus*. 2013;2:587.

Sun Z, Lu W, Liu P, Wang H, Huang Y, Zhao Y. Isolation and characterization of a proteinaceous α-amylase inhibitor AAI-CC5 from *Streptomyces* sp. CC5, and its gene cloning and expression. *Antonie Van Leeuwenhoek*. 2015;107(2):345-53.

Sutaria D, Shah KR, Arora S, Saxena S. Actinomycetes as an environmental scrubber. In: Crude oil-New technologies and recent approaches. 2021.

Tian X, Zheng Y. Evaluation of biological control agents for Fusarium wilt in *Hiemalis begonia*. *Can J Plant Pathol*. 2013;35:363-70.

Wang RJ, Zhang SY, Ye YH, Yu Z, Qi H, Zhang H, et al. Three new isoflavonoid glycosides from the mangrove-derived actinomycete *Micromonospora aurantiaca* 110B. *Mar Drugs*. 2019;17:294.

Wang W, Qiu Z, Tan H, Cao L. Siderophore production by actinobacteria. *Biometals*. 2014;27:623-31.

Xu LH, Li WJ, Liu ZH, Jiang CL. Actinomycete taxonomy. Beijing: Academic Press; 2007. pp. 202-8.

Yadav N, Yadav AN. Actinobacteria for sustainable agriculture. *J Appl Biotechnol Bioeng*. 2019;6:38-41.

Zenova GM, Manucharova NA, Zvyagintsev DG. Extremophilic and extremotolerant actinomycetes in different soil types. *Eurasian Soil Sci*. 2011;44:417-36.

Zhang Y, Fang W, Wang K, Zhang Z, Wu Z, Shi L, et al. Napyradiomycin A4 and its related compounds, a new anti-PRV agent and their antibacterial activities, from *Streptomyces kebangsaanensis* WS-68302. *Molecules*. 2023;28(2):640.

Zhou D, Jing T, Chen Y, Yun T, Qi D, Zang X, et al. Biocontrol potential of a newly isolated *Streptomyces* sp. HSL-9B from mangrove forest on postharvest anthracnose of mango fruit caused by *Colletotrichum gloeosporioides*. *Food Control*. 2022;135:108836.

Zou N, Zhou D, Chen Y, Lin P, Chen Y, Wang W, et al. A novel antifungal actinomycete *Streptomyces sp*. strain H3-2 effectively controls banana Fusarium wilt. *Front Microbiol*. 2021;12:706647.