

MINI-REVIEW

Uncovering novel species and bioactive compounds from psychrophilic actinobacteria: A concise review

Galana Siro^{1*} , Atanas Pipite² , and Sathiyaraj Srinivasan³ 

¹Department of Biological and Chemical Sciences, School of Agriculture, Geography, Environment, Ocean and Natural Sciences, The University of The South Pacific, Laucala Campus, Suva, Fiji

²School of Natural Sciences, College of Sciences, Massey University, Palmerston North, New Zealand

³Department of Bio and Environmental Technology, College of Natural Science, Seoul Women's University, Hwarangno, Nowon-gu, Seoul, Korea

Abstract

The cold environments serve as life-entrapping reservoirs of diverse life forms, ranging from eukaryotes to diverse microbial inoculi. Actinobacteria are omnipresent in cold environments, and their existence is notably linked to a remarkable potential for producing and harboring unique metabolites. Their ability to survive in such extreme conditions is supported by a range of adaptations tailored to their specific niche, including cold-resistant traits. In this review, we summarize recent advances (2017–2025) regarding psychrophilic actinobacteria, focusing on newly identified species and novel compounds reported in the literature. Notably, we highlight the discovery of 44 new species as well as nine new compounds across various actinobacteria genera. The inventory of abiotic hurdles associated with cold environments positions this field as a potential hotspot and emerging frontier for sourcing pharmaceutical-like compounds of exceptional ingenuity and complexity. By providing an overview of the recent discoveries in psychrophilic actinobacteria and their intriguing metabolites, this review aims to offer valuable insights to facilitate bioprospecting efforts in cold ecosystems.

Keywords: Psychrophilic actinobacteria; Cold environments; Multidrug resistance; Bioactive compounds

*Corresponding author:

Galana Siro
(sirogalana@yahoo.com)

Citation: Siro G, Pipite A, Srinivasan S. Uncovering novel species and bioactive compounds from psychrophilic actinobacteria: A concise review. *Microbes & Immunity*. 2026;3(4):025350087. doi: 10.36922/MI025350087

Received: August 26, 2025

Revised: September 22, 2025

Accepted: October 10, 2025

Published online: November 7, 2025

Copyright: © 2025 Author(s). This is an Open-Access article distributed under the terms of the Creative Commons Attribution License, permitting distribution, and reproduction in any medium, provided the original work is properly cited.

Publisher's Note: AccScience Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. Introduction

The persistent crisis of multidrug-resistant pathogens is following an atypical trajectory and is incompatible with the health sector, resulting in unprecedented mortality rates.^{1,2} To overcome this adversary, many mandatory research explore alternative solutions to this problem. The unquenchable enthusiasm of the scientific community for discovering novel drugs has significantly increased over the years. Extreme habitats, including cold environments, are unusual yet promising sources of new compounds.³⁻⁵ Cold environmental conditions have influenced the adaptations of microbes through a multitude of approaches and mechanisms that help circumvent the severity of icy climatic conditions.^{6,7} Microbes living in cold extremities are referred to as psychrophiles, which thrive at temperatures ranging from –20°C to 20°C. They can be further

categorized into two overlapping groups: Psychrophilic microbes, which preferentially grow at consistently cold temperatures—typically below 15°C but not exceeding 20°C, and psychrotolerant (or psychrotrophs) microbes, which can tolerate cold conditions (below 0°C) while also exhibiting growth at higher temperatures above 15°C.^{8–11} Microorganisms have sophisticated biosynthetic factories,¹² especially those belonging to the phylum Actinomycetota (Actinobacteria),¹ which are the main sources of clinical drugs and the discovery of new antibiotics.^{13,14} Due to this antecedence, actinomycetes living in adverse conditions exhibit remarkable atypical survival strategies.¹⁵ Thus, a continuum of scientific strategies has been encouraged to exploit and exercise their advantageous application characteristics for new pharmaceutical drugs.¹⁶ The reorientation of bioprospecting efforts has been directed towards favorable ecological niches, which tend to favor the novelty of species and compounds.¹⁷ For the purpose of this review, we focus on psychrophilic actinobacteria inhabiting cold environments. Based on the premise that psychrophilic actinobacteria represent a roadmap to biodiscovery, we provide an overview of their bioprospecting aspects, including cultivation techniques. Overall, this review provides a comprehensive synopsis of new compounds and species of psychrophilic actinobacteria from the literature between 2017 and 2025. Prokaryotes active in extremely cold habitats remain underexplored, with limited research data availability.¹⁸

2. The cold environment and biodiversity: A promising frontier of biodiscovery

The Earth's biotopes are mostly frosty, either periodically or permanently, depending on the geographical locations.^{19,20} Cold ecosystems are highly diverse yet extremely inhospitable to most life forms since they possess a pertinent amalgam of low temperature (less thermal energy) and low liquid water availability (higher viscosity).²¹ Despite these hostile conditions, life thrives with remarkable biodiversity and the production of unique natural products.^{22–24} Psychrophiles are cold-tolerant and ubiquitous extremophiles that survive and occupy a larger geographical area, such as deep seas, mountains, and polar regions.²⁵ The cold environment nested a diverse community of microbial life, including those assigned to the phylum Actinobacteria.^{26–28} Molecular characterization of microbes in these habitats uncovered previously unrealized functionalities and provides detailed insights into their evolutionary and taxonomic relationships; this remains an ongoing area of research.^{29,30}

Being part of the cryosphere, psychrophiles played a significant role in the Earth's biogeochemical cycles and are considered indicators of climate change due to their sensitive nature.³¹ These organisms often face perennial physicochemical constraints affecting their cellular architecture and function. Their acclimating capabilities to such distress are governed by a multiplicity of molecular and physical synergetic adaptations.^{22,32–34} Psychrophiles have multifaceted applications, such as their extensive uses in food and textile industries, bioremediation, and pharmaceutical.^{35–37} They express specialized enzymes, osmoprotectants, and metabolites to maintain cellular activity and stability under conditions that typically denature or impair conventional biomolecules.³⁸ These unique features represent broad potential for medical applications, including diagnostics, drug development, therapeutic delivery, and vaccine technology. In summary, psychrophiles are excellent sources of biomolecules; therefore, expertise of extant psychrophiles' biological and physiological adaptation to environmentally challenged regions is important.^{39–41}

3. Diversity and genomic insights of psychrophilic actinobacteria: Being multifarious and overarching

Actinobacteria are primitive lineages among prokaryotes, particularly in the domain Bacteria.⁴² They have a host of beneficial traits that enhance and sustain their ecophysiological profile in hostile environments and during sporadic resource distribution.^{43,44} Actinobacteria are well endowed with various mechanisms and pathways responsible for encoding parvome.⁴⁴ Consequently, their complex biology and versatility translated to heightened tolerance and adaptive responses to environmental adversaries.⁴⁴ These microorganisms made up a significant composition of the microbial community across various cold environments. Notable genera within this group include *Streptomyces*, *Kocuria*, *Rhodococcus*, *Brevibacterium*, *Arthrobacter*, *Lapillicoccus*, *Terrabacter*, *Micromonospora*, *Leifsonia*, *Corynebacterium*, and *Nesterenkonia*.⁴⁵ Representatives of these consortia and their metabolic compounds have certain antibiotic properties. For instance, a study has reported the antifungal properties of actinobacteria derived from Antarctic soils.⁴⁶ A new discovery highlighted *Streptomyces luridus* So3.2 as a novel source of compounds with bioemulsification capabilities.⁴⁷ Isolates of *Streptomyces* spp. from cold sites in the Fez-Meknes region of Morocco demonstrated antimicrobial and antioxidant activities,⁴⁸ whereas *Streptomyces artemisiae* strain MCCB 248 from the Arctic has anticancer effects.⁴⁹ In addition, *Streptomyces fildesensis* So13.3, which was recovered from Antarctica,

¹ <http://www.bacterio.net/-classifphyla.html#actinobacteria>, accessed on January 7, 2025

shows a high degree of antimicrobial activity.⁵⁰ Evidently, psychrophilic actinobacteria are a tremendous source of active metabolites. There is an increasing use of genome sequencing and genome mining to analyze and delineate the complete biosynthetic potential of microbes.⁵¹ In the present review, we analyzed literature on the genomics of psychrophilic actinobacteria from the cryogenic habitats, and are as follows: The complete genome analysis of *Streptomyces* spp. R527F derived from the Arctic Ocean unveiled at least 30 biosynthetic gene clusters (BGCs) responsible for producing 11 classes of natural metabolites.⁵² Similarly, *Marisediminicola antarctica* ZS314^T was found to harbor five known and four unknown BGCs associated with natural product biosynthesis, despite its relatively small genome of 3,352,609 base pairs compared to other actinomycetes.⁵³ Moreover, Waschulin *et al.*⁵⁴ indicated that Antarctica soil samples featured a large amount of BGCs from uncultivated actinobacteria, particularly within the genus *Streptomyces*, which is notably rich in biosynthetic potential. Indeed, utilizing psychrophilic actinobacteria as a source of novel pharmaceuticals is quite promising, given their vast pool of ancient natural metabolites. This underscores their potential as valuable tools in drug discovery and development.

4. Psychrophilic actinobacteria cultivation principles

Psychrophilic actinobacteria are no different from microbes inhabiting other habitats when it comes to their cultivation specifics under standard laboratory conditions. Different habitats introduce unique growth conditions or geographical characteristics that must be mimicked in a laboratory setting to facilitate proper microbial growth.¹⁷ Numerous factors, such as media composition, culturing conditions, and pre-treatment methods, affect the isolation process. However, temperature is one of the most critical cultivation parameters that has a major influence on psychrophilic actinobacteria survival.⁵⁵ These organisms normally preferred lower cardinal growth temperatures, with optimal isolation temperatures and peak performance observed at or below 4°C and 15°C.^{29,56-58} The actual temperature lower limit for metabolically active psychrophiles is -20°C.¹¹ In most cases, pre-treatments have proven effective in the isolation of psychrophilic actinobacteria. These involve chemical, antibiotic, or heat treatments, which help suppress the growth of undesired microorganisms and also reduce the ratio of certain unarmored actinobacteria species.^{59,60} Actinobacteria spores tend to be more sensitive to moisture than to dry heat, hence frequent applications of heat treatment aid in selective isolation.⁶¹ In total, the functionality of pre-treatments exerts a selection pressure that favors the propagation of

actinobacteria.⁵⁹ Standard dilution plating and plate stamp methods are common isolation approaches that differ in their ability to capture species diversity and population variation across different environmental niches.⁶² For viable bacterial screening purposes, various sophisticated methods are available, including flow cytometry⁶³ and emerging enumeration techniques such as impedance flow cytometry.^{64,65} Notably, lengthy incubation periods promote great opportunities for actinobacteria with slower growth velocity.⁶⁰ A wide range of modified and routine cultivation media enhanced successful isolations and contributed to considerable species divergence.^{56,62,66,67} For isolations targeting temperatures below 0°C, adopting the pragmatics of cryoprotected growth media is a possibility, which will be the subject of subsequent research.⁶⁸

5. Strategies and associated challenges for recovering natural products from actinobacteria

Since the discovery of the first antibiotics, numerous advanced methods and technologies have been developed to facilitate antibiotic discovery.^{69,70} For example, studies have promoted the use of small-molecule inducers to activate secondary metabolite production in actinobacteria.⁷¹ Similarly, metabolic engineering of bacteria has gained recognition for its application in drug science and others.^{70,72,73} Antibiotics, also known as specialized metabolites, natural products, or secondary metabolites, are produced by plants, bacteria, fungi, and many marine organisms.⁷⁴ Unlike primary metabolites essential for growth and maintenance, these specialized metabolites primarily function in defense mechanisms and interspecific interactions.⁷⁵ With the advent of DNA sequencing and bioinformatics, the challenges shifted toward isolating new natural products from uncultured or unidentified genus of bacteria that cannot be cultivated under laboratory conditions. In addition, predicting the nucleotide sequences of biosynthetic pathways and source organisms became feasible.⁶⁹ Today, in the post-genomic era, the focus has shifted to activating cryptic gene clusters that encode a multitude of previously undetected complex secondary metabolites. To achieve this, various innovative strategies have been developed including the “one strain many compounds” approach,⁷⁶ culturing the unculturable, overexpression of pathway-specific regulatory genes,⁷⁷ ribosome or RNA polymerase engineering,⁷⁸ isotope-guided fractionation,⁷⁹ heterologous expression of BGCs,⁸⁰ manipulation of transcriptional activators and repressors,⁸¹ synthetic biology,⁸² functional proteomics,⁸³ combinatorial chemistry,⁸⁴ metabolomics, direct cloning with artificial promoters,⁸⁵ chromatin remodeling,⁸⁶ use of rare earth elements,⁸⁷ high-throughput elicitor screening,⁸⁸

co-cultivation,⁸⁹ environmental signal modulation, small-molecule chemical elicitors⁷¹ and genome mining.^{90,91} These advancements have revitalized the field of natural product research, fostering renewed confidence that many yet-unidentified secondary metabolites with therapeutic and other applications may be identified in the near future.⁹⁰

Furthermore, discovering and producing bioactive secondary metabolites under controlled laboratory conditions remains a significant challenge for researchers, as most bacteria are unculturable with current isolation techniques—<2% of bacteria can be cultured under

standard laboratory conditions.^{92–94} The primary difficulty with traditional methods of isolating secondary metabolites lies in replicating the native environmental conditions required for bacterial strains to produce these compounds, as well as efficiently extracting the bioactive molecules. Research into antibiotic discovery is hindered by limited knowledge of bacterial permeability, reliance on generic *in vitro* methods that overlook the host context, and the intrinsic complexity of bacterial systems.⁹⁵

One important aspect of drug discovery involves extracting bioactive compounds from purified actinomycete

Table 1. New species of actinobacteria from cold habitats reported between 2017 and 2025

Novel species	Family	Source and geographic location	References
<i>Conyzicola nivalis</i>	Microbacteriaceae	Glacial snow; China	106
<i>Cryobacterium aureum</i>	Microbacteriaceae	Glacier; China	107
<i>Amycolatopsis antarctica</i>	Pseudonocardiaceae	Macroalga; Antarctic	108
<i>Subtercola vilae</i>	Microbacteriaceae	Cold volcano lake; Chile	109
<i>Cryobacterium zongtaii</i> , <i>Arthrobacter glacialis</i>	Microbacteriaceae, Micrococcaceae	Glaciers; China	110
<i>Streptomyces polaris</i> , <i>Streptomyces septentrionalis</i>	Streptomycetaceae	Frozen soil; Arctic region	111
<i>Cryobacterium melibiosiphilum</i>	Microbacteriaceae	Glacier; China	112
<i>Haloactinobacterium glaciecola</i>	Ruaniaceae	Ice core from a glacier; China	113
<i>Serinibacter arcticus</i>	Beutenbergiaceae	Ice wedge water; Mammoth Mountain, Russia	114
<i>Pseudarthrobacter psychrotolerans</i>	Micrococcaceae	Soil; Antarctica	115
<i>Lentzea indica</i>	Pseudonocardiaceae	Soil; Kashmir Himalaya, India	116
<i>Cryobacterium ruanii</i> , <i>Cryobacterium breve</i>	Microbacteriaceae	Glacier; China	117
<i>Pengzhenrongella sicca</i>	Not assigned to family (Suborder Micrococcineae)	Soil; High Arctic tundra	118
<i>Gephyromycinifex aptenodytis</i>	Dermatophilaceae	Penguin gut; Antarctica	119
<i>Marisediminicola senii</i>	Microbacteriaceae	Glacier-fed sediment; Antarctica	120
<i>Paeniglutamicibacter terrestris</i>	Micrococcaceae	Phenanthrene-degrading consortium enriched from a soil sample, Antarctica	121
<i>Lacisediminihabitans changchengi</i>	Microbacteriaceae	Swampland mud; Antarctica	122
<i>Arthrobacter terrae</i>	Micrococcaceae	Soil; Antarctica	123
<i>Pseudarthrobacter albicanus</i>	Micrococcaceae	Soil; Antarctica	124
<i>Subtercola endophyticus</i>	Microbacteriaceae	Leaves of an <i>Abies koreana</i> tree; South Korea	125
<i>Arthrobacter vasquezii</i>	Micrococcaceae	Soil; Antarctica	126
<i>Cryobacterium serini</i> , <i>Cryobacterium lactosi</i> , <i>Cryobacterium gelidum</i> , <i>Cryobacterium suzukii</i> , <i>Cryobacterium focusi</i> , <i>Cryobacterium frigophilum</i> , <i>Cryobacterium cryoconiti</i> , <i>Cryobacterium lyxosi</i> , <i>Cryobacterium sinapicolor</i> , <i>Cryobacterium sandaracinum</i> , <i>Cryobacterium cheniae</i> , <i>Cryobacterium shii</i> , <i>Cryobacterium glucosi</i> , <i>Cryobacterium algoritholans</i> , <i>Cryobacterium mannosilyticum</i> , <i>Cryobacterium adonitolivorans</i> , <i>Cryobacterium algoricola</i> , <i>Cryobacterium tagatosivorans</i> , <i>Cryobacterium glaciale</i>	Microbacteriaceae	Ice, cryoconite, and melt water; China	127
<i>Cryobacterium inferilacus</i>	Microbacteriaceae	Water; Antarctica	128

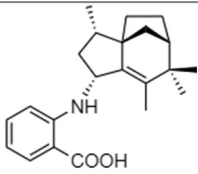
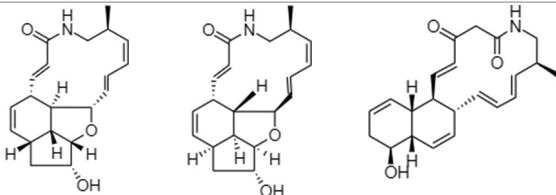
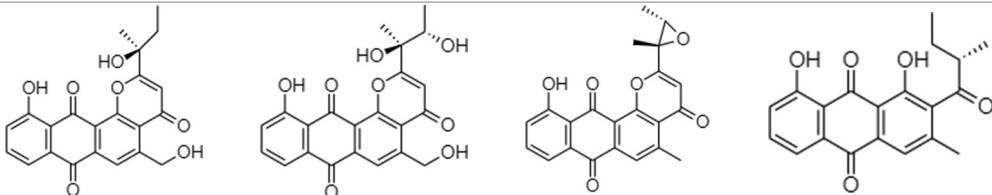
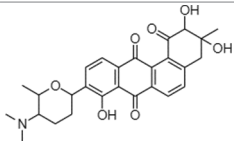
strains. Several strategies and approaches are employed for this purpose. To begin with, the active compound can be extracted either from strain fermentation processes or directly from environmental samples.⁹⁶ The diverse extraction methods include solvent extraction, distillation, pressing, and sublimation, each based on specific principles of extraction. In general, the process of extracting natural products involves the following steps: (i) The solvent penetrates the solid matrix; (ii) Solute dissolves into the solvents; (iii) The dissolved compounds diffuse out of the solid matrix; and (iv) the extracted metabolites are collected.⁹⁷ Chromatographic techniques,⁹⁸ utilizing specific solvents, are commonly used to separate the desired secondary metabolites from bacterial culture medium—whether solid-state fermentation or liquid fermentation (liquid broth cultures).^{99–101} Liquid–liquid extraction, which involves transferring a solute from one immiscible or partially miscible solvent to another, is particularly

favored in actinobacterial studies because bacterial strains are typically cultured in fermentation broth media.^{98,102} Most studies have successfully extracted and purified compounds from actinomycetes using liquid fermentation, employing solvents such as methanol, ethanol, and ethyl acetate. Among these, the latter is frequently used due to its high efficiency in recovering metabolites.^{66,103,104}

6. Novel species and compounds of psychrophilic actinobacteria

Since the cold environment is geographically vast, we focus on psychrophiles mainly from the Antarctica and Arctic regions, sympagic areas, and mountain terrains or plateaus, excluding the deep sea, which was reviewed in a previous article.^{5,105} This review presents 44 new actinobacteria species belonging to five hierarchical families, such as *Microbacteriaceae* (29 species), *Pseudonocardiaceae* (two species), *Micrococcaceae* (seven species), *Streptomycetaceae*

Table 2. New compounds of actinobacteria from cold environments reported between 2017 and 2025

Chemical name and structure	Organism and bioactivity	References
 Antartin	<i>Streptomyces</i> spp. SCO736; Cytotoxic activity	129
 Cyclamenol B Cyclamenol C Cyclamenol D	<i>Streptomyces</i> spp.; Cytotoxic activity	130
 Saliniquinone G Saliniquinone H Saliniquinone I Heraclemycin E	<i>Nocardiopsis aegyptia</i> ; Inhibitory activity against pathogenic bacteria	131
 2-hydroxy-frigocyclinone	<i>Gephyromycinifex aptenodytis</i> ; Cytotoxic activity	132

(two species), *Ruaniaceae* (one species), *Beutenbergiaceae* (one species), *Dermatophilaceae* (one species), and suborder *Micrococcineae* (one species) (Table 1). There are lesser number of novel compounds identified in this review. Nonetheless, the novel compounds summarized belong to different chemical classes and have different strengths of cytotoxic activities against pathogenic microbes. Further, their structural configurations are outlined in Table 2. Discerningly, the structural elucidation of bioactive compounds from the cold habitats is still in its infancy. This field of research is an emerging catalog of interest with diverse potential for drug discovery and development.

7. Conclusion and future perspectives

Microbes, including actinobacteria, are ubiquitous in nature and form vital components of the Earth's ecosystems. Their ubiquity is attributed to their ability to survive and multiply in diverse habitats such as cold environments. This review offers great insights into the background, cultivation pathways, and techniques, and potential challenges associated with research on psychrophilic actinobacteria—aimed at ambitious researchers eager to explore beyond existing boundaries. Further, we reported the discovery of 44 new species and nine new compounds of psychrophilic actinobacteria between 2017 and 2025. Although most research to date has primarily focused on actinobacteria from environments other than the cold habitats, it is encouraging to observe increasing recognition of cold-region microbiomes as more bioactive compounds are uncovered.¹³³ For future research, more comprehensive and robust studies are recommended to explore pristine cold regions and environments, which harbor untapped psychrophilic actinobacteria, building upon past and current findings.¹³⁴ Metabolites derived from cold-adapted microorganisms exhibit bioactivity against various pathogens, highlighting their potential in pharmaceutical development.¹³³ Overall, the Earth's cold habitats harbor a high degree of microbial endemism, yet their diversity remains largely underexplored. These environments and their microbiomes represent a promising frontier for both pharmaceutical discovery and industrial applications.^{38,135}

Acknowledgments

None.

Funding

None.

Conflict of interest

The authors declare that they have no competing interests.

Author contributions

Conceptualization: Galana Siro, Atanas Pipite

Writing—original draft: Galana Siro

Writing—review & editing: All authors

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Not applicable.

References

1. Foxlee N, Townell N, McIver L, Lau CL. Antibiotic resistance in Pacific Island countries and territories: A systematic scoping review. *Antibiotics (Basel)*. 2019;8(1):29. doi: 10.3390/antibiotics8010029
2. Aslam B, Wang W, Arshad MI, *et al.* Antibiotic resistance: A rundown of a global crisis. *Infect Drug Resist*. 2018;11:1645-1658. doi: 10.2147/IDR.S173867
3. Giordano D. Bioactive molecules from extreme environments. *Mar Drugs*. 2020;18:640. doi: 10.3390/md18120640
4. Soldatou S, Baker BJ. Cold-water marine natural products, 2006 to 2016. *Nat Prod Rep*. 2017;34(6):585-626. doi: 10.1039/c6np00127k
5. Siro G, Donald L, Pipite A. The diversity of deep-sea actinobacteria and their natural products: An epitome of curiosity and drug discovery. *Diversity*. 2023;15(1):30. doi: 10.3390/d15010030
6. Parrilli E, Tedesco P, Fondi M, *et al.* The art of adapting to extreme environments: The model system *Pseudoalteromonas*. *Phys Life Rev*. 2021;36:137-161. doi: 10.1016/j.plrev.2019.04.003
7. Singh M, Jayant K, Singh D, Suyal DC, Mitra A, Bhutani S. Microbial adaptations at higher altitude for sustainable development: A review. *J Appl Pharm Sci*. 2022;12(10):11-19. doi: 10.7324/JAPS.19-1646044973
8. Bölter M. Ecophysiology of psychrophilic and psychrotolerant microorganisms. *Cell Mol Biol*. 2004;50(5):563-573.
9. Helmke E, Weyland H. Psychrophilic versus psychrotolerant bacteria—occurrence and significance in polar and temperate marine habitats. *Cell Mol Biol (Noisy-le-grand)*. 2004;50(5):553-561.

10. Kumar S, Sravani B, Korra T, *et al.* Psychrophilic microbes: biodiversity, beneficial role and improvement of cold stress in crop plants. In: Singh H, Vaishnav A, editors. *New and Future Developments in Microbial Biotechnology and Bioengineering*. Amsterdam: Elsevier; 2022. p. 177-198.
doi: 10.1016/B978-0-323-85163-3.00002-8
11. Sepe F, Costanzo E, Ionata E, Marcolongo L. Biotechnological potential of extremophiles: Environmental solutions, challenges, and advancements. *Biology (Basel)*. 2025;14(7):847.
doi: 10.3390/biology14070847
12. Hussain MH, Mohsin MZ, Zaman WQ, *et al.* Multiscale engineering of microbial cell factories: A step forward towards sustainable natural products industry. *Synth Syst Biotechnol*. 2022;7(1):586-601.
doi: 10.1016/j.synbio.2021.12.012
13. Takahashi Y, Nakashima T. Actinomycetes, an inexhaustible source of naturally occurring antibiotics. *Antibiotics (Basel)*. 2018;7(2):45.
doi: 10.3390/antibiotics7020045
14. Ma R, Karthik L. Pharmacology of FDA-approved medicines from actinobacteria. In: Karthik L, editor. *Actinobacteria: Microbiology to Synthetic Biology*. Singapore: Springer Nature Singapore; 2022. p. 265-276.
doi: 10.1007/978-981-16-5835-8_14
15. Hui MLY, Tan LTH, Letchumanan V, *et al.* The extremophilic actinobacteria: From microbes to medicine. *Antibiotics (Basel)*. 2021;10(6):682.
doi: 10.3390/antibiotics10060682
16. Law JWF, Letchumanan V, Tan LTH, Ser HL, Goh BH, Lee LH. The rising of “modern actinobacteria” era. *Prog Microbes Mol Biol*. 2020;3(1):a0000064.
doi: 10.3687/pmmmb.a0000064
17. Siro G, Pipite A, Christi K, Srinivasan S, Subramani R. Marine actinomycetes associated with stony corals: A potential hotspot for specialized metabolites. *Microorganisms*. 2022;10(7):1349.
doi: 10.3390/microorganisms10071349
18. Zhu C, Miller M, Lusskin N, *et al.* Snow microbiome functional analyses reveal novel aspects of microbial metabolism of complex organic compounds. *Microbiologyopen*. 2020;9(9):e1100.
doi: 10.1002/mbo3.1100
19. De Maayer P, Anderson D, Cary C, Cowan DA. Some like it cold: Understanding the survival strategies of psychrophiles. *EMBO Rep*. 2014;15(5):508-517.
doi: 10.1002/embr.201338170
20. Rodrigues DF, Tiedje JM. Coping with our cold planet. *Appl Environ Microbiol*. 2008;74(6):1677-1686.
doi: 10.1128/AEM.02000-07
21. D'Amico S, Collins T, Marx J, Feller G, Gerday C, Gerday C. Psychrophilic microorganisms: Challenges for life. *EMBO Rep*. 2006;7(4):385-389.
doi: 10.1038/sj.embor.7400662
22. Tendulkar S, Hattiholi A, Chavadar M, Dodamani S. Psychrophiles: A journey of hope. *J Biosci*. 2021;46(3):64.
doi: 10.1007/s12038-021-00180-4
23. Tian Y, Li YL, Zhao FC. Secondary metabolites from polar organisms. *Mar Drugs*. 2017;15(3):28.
doi: 10.3390/md15030028
24. Rizzo C, Lo Giudice A. Life from a snowflake: Diversity and adaptation of cold-loving bacteria among ice crystals. *Crystals*. 2022;12(3):312.
doi: 10.3390/cryst12030312
25. Hamdan A. Psychrophiles: Ecological significance and potential industrial application. *S Afr J Sci*. 2018;114(5):1-6.
doi: 10.17159/sajs.2018/20170254
26. Anesio AM, Laybourn-Parry J. Glaciers and ice sheets as a biome. *Trends Ecol Evol*. 2012;27(4):219-225.
doi: 10.1016/j.tree.2011.09.012
27. Belov AA, Cheptsov VS, Manucharova NA, Ezhelev ZS. Bacterial communities of novaya zemlya archipelago ice and permafrost. *Geosciences*. 2020;10(2):67.
doi: 10.3390/geosciences10020067
28. Margesin R, Collins T. Microbial ecology of the cryosphere (glacial and permafrost habitats): Current knowledge. *Appl Microbiol Biotechnol*. 2019;103(6):2537-2549.
doi: 10.1007/s00253-019-09631-3
29. Moyer CL, Morita RY. Psychrophiles and psychrotrophs. In: *Encyclopedia of Life Sciences*. Chichester: John Wiley & Sons Ltd.; 2007. p. 1-5.
doi: 10.1016/B978-0-12-809633-8.02282-2
30. Bowman JP. Genomics of psychrophilic bacteria and archaea. In: Margesin R, editor. *Psychrophiles: From Biodiversity to Biotechnology*. Cham: Springer International Publishing; 2017. p. 345-387.
doi: 10.1007/978-3-319-57057-0_15
31. Dhakar K, Pandey A. Microbial ecology from the himalayan cryosphere perspective. *Microorganisms*. 2020;8(2):257.
doi: 10.3390/microorganisms8020257
32. Collins T, Margesin R. Psychrophilic lifestyles: Mechanisms of adaptation and biotechnological tools. *Appl Microbiol Biotechnol*. 2019;103(7):2857-2871.
doi: 10.1007/s00253-019-09659-5

33. Siddiqui KS, Williams TJ, Wilkins D, *et al.* Psychrophiles. *Annu Rev Earth Planet Sci.* 2013;41:87-115.
doi: 10.1146/annurev-earth-040610-133514
34. Alblooshi AS, Nasar MI, Rehman SSU, Alam MT. Genomic and metabolic network properties in thermophiles and psychrophiles compared to mesophiles. *Sci Rep.* 2025;15(1):19757.
doi: 10.1038/s41598-025-05030-z
35. Banerjee R, Halder A, Natta A. Psychrophilic microorganisms: habitats and exploitation potentials. *Eur J Biotechnol Biosci.* 2016;4(3):16-24.
36. Parvizpour S, Hussin N, Shamsir MS, Razmara J. Psychrophilic enzymes: Structural adaptation, pharmaceutical and industrial applications. *Appl Microbiol Biotechnol.* 2021;105(3):899-907.
doi: 10.1007/s00253-020-11074-0
37. Sharma S, Chaturvedi U, Sharma K, Vaishnav A, Singh HB. An overview of survival strategies of psychrophiles and their applications. In: Goel R, Soni R, Suyal DC, Khan M, editors. *Survival Strategies in Cold-Adapted Microorganisms.* Singapore: Springer Singapore; 2022. p. 133-151.
doi: 10.1007/978-981-16-2625-8_6
38. Gallo G, Aulitto M. Advances in extremophile research: Biotechnological applications through isolation and identification techniques. *Life (Basel).* 2024;14(9):1205.
doi: 10.3390/life14091205
39. Garcia-Lopez E, Alcazar P, Cid C. Identification of biomolecules involved in the adaptation to the environment of cold-Loving microorganisms and metabolic pathways for their production. *Biomolecules.* 2021;11(8):1155.
doi: 10.3390/biom11081155
40. Borchert E, Jackson SA, O'Gara F, Dobson ADW. Psychrophiles as a source of novel antimicrobials. In: Margesin R, editor. *Psychrophiles: From Biodiversity to Biotechnology.* Cham: Springer International Publishing; 2017. p. 527-540.
doi: 10.1007/978-3-319-57057-0_22
41. Núñez-Montero K, Quezada-Solís D, Khalil ZG, Capon RJ, Andreote FD, Barrientos L. Genomic and metabolomic analysis of antarctic bacteria revealed culture and elicitation conditions for the production of antimicrobial compounds. *Biomolecules.* 2020;10(5):673.
doi: 10.3390/biom10050673
42. Salam N, Jiao JY, Zhang XT, Li WJ. Update on the classification of higher ranks in the phylum Actinobacteria. *Int J Syst Evol Microbiol.* 2020;70(2):1331-1355.
doi: 10.1099/ijsem.0.003920
43. Rui S, Fengrui G, Yining Z, *et al.* Biological activity of secondary metabolites of actinomycetes and their potential sources as antineoplastic drugs: A review. *Front Microbiol.* 2025;16:1550516.
doi: 10.3389/fmicb.2025.1550516
44. Jose PA, Maharshi A, Jha B. Actinobacteria in natural products research: Progress and prospects. *Microbiol Res.* 2021;246:126708.
doi: 10.1016/j.micres.2021.126708
45. Rizzo C, Lo Giudice A. The Variety and inscrutability of polar environments as a resource of biotechnologically relevant molecules. *Microorganisms.* 2020;8(9):1422.
doi: 10.3390/microorganisms8091422
46. Santos A, Núñez-Montero K, Lamilla C, Pavez M, Quezada-Solís D, Barrientos L. Antifungal activity screening of antarctic actinobacteria against phytopathogenic fungi. *Acta Biol Colomb.* 2020;25(2):353-358.
doi: 10.15446/abc.v25n2.76405
47. Lamilla C, Braga D, Castro R, *et al.* *Streptomyces luridus* So3.2 from antarctic soil as a novel producer of compounds with bioemulsification potential. *PLoS One.* 2018;13(4):e0196054.
doi: 10.1371/journal.pone.0196054
48. Rammali S, Hilali L, Dari K, *et al.* Antimicrobial and antioxidant activities of *Streptomyces* species from soils of three different cold sites in the Fez-Meknes region Morocco. *Sci Rep.* 2022;12(1):17233.
doi: 10.1038/s41598-022-21644-z
49. Dhaneesha M, Benjamin Naman C, Krishnan KP, *et al.* *Streptomyces artemisiae* MCCB 248 isolated from arctic fjord sediments has unique PKS and NRPS biosynthetic genes and produces potential new anticancer natural products. *3 Biotech.* 2017;7(1):32.
doi: 10.1007/s13205-017-0610-3
50. Núñez-Montero K, Lamilla C, Abanto M, *et al.* Antarctic *Streptomyces fildesensis* So13.3 strain as a promising source for antimicrobials discovery. *Sci Rep.* 2019;9(1):7488.
doi: 10.1038/s41598-019-43960-7
51. Ziemert N, Alanjary M, Weber T. The evolution of genome mining in microbes-a review. *Nat Prod Rep.* 2016;33(8):988-1005.
doi: 10.1039/C6NP00025H
52. Duan Z, Liao L, Chen B. Complete genome analysis reveals secondary metabolite biosynthetic capabilities of *Streptomyces* sp. R527F isolated from the Arctic Ocean. *Mar Genomics.* 2022;63:100949.
doi: 10.1016/j.margen.2022.100949
53. Liao L, Su S, Zhao B, *et al.* Biosynthetic potential of a novel antarctic actinobacterium *Marisedimicola antarctica* ZS314T revealed by genomic data mining and pigment

- characterization. *Mar Drugs*. 2019;17(7):388.
doi: 10.3390/md17070388
54. Waschulin V, Borsetto C, James R, *et al.* Biosynthetic potential of uncultured antarctic soil bacteria revealed through long-read metagenomic sequencing. *ISME J*. 2022;16(1):101-111.
doi: 10.1038/s41396-021-01052-3
 55. 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: InTechOpen; 2016. p. 39-50.
doi: 10.5772/61457
 56. Lamilla C, Pavez M, Santos A, Hermosilla A, Llanquiao V, Barrientos L. Bioprospecting for extracellular enzymes from culturable actinobacteria from the South Shetland Islands, Antarctica. *Polar Biol*. 2017;40(3):719-726.
doi: 10.1007/s00300-016-1977-z
 57. Margesin R, Moertelmaier C, Mair J. Low-temperature biodegradation of petroleum hydrocarbons (n-alkanes, phenol, anthracene, pyrene) by four actinobacterial strains. *Int Biodeterior Biodegradation*. 2013;84:185-191.
doi: 10.1016/j.ibiod.2012.05.004
 58. Raja A, Prabakaran P, Gajalakshmi P. Isolation and screening of antibiotic producing psychrophilic actinomycetes and its nature from rothang hill soil against viridans *Streptococcus* sp. *Res J Microbiol*. 2010;5(1):44-49.
 59. Gromyko O, Tistechok S, Roman I, *et al.* Isolation and characterization of culturable actinobacteria associated with *Polytrichum strictum* (galindez island, the maritime antarctic). *Ukr Antarct J*. 2021;1:82-97.
doi: 10.33275/1727-7485.1.2021.668
 60. Benaud N, Chelliah DS, Wong SY, Ferrari BC. Soil substrate culturing approaches recover diverse members of actinomycetota from desert soils of herring Island, East Antarctica. *Extremophiles*. 2022;26(2):24.
doi: 10.1007/s00792-022-01271-2
 61. Williams ST, Shameemullah M, Watson ET, Mayfield CI. Studies on the ecology of actinomycetes in soil. The influence of moisture tension on growth and survival. *Soil Biol Biochem*. 1972;4(2):215-225.
doi: 10.1016/0038-0717(72)90014-4
 62. Kamjam M, Xie Q, Deng Z, Hong K. Isolation and diversity of actinomycetes from sediments of different depths between 34 m and 3,235 m in south china sea. *Chiang Mai J Sci*. 2018;45(4):1595-1609.
 63. Marutescu LG. Current and future flow cytometry applications contributing to antimicrobial resistance control. *Microorganisms*. 2023;11(5):1300.
doi: 10.3390/microorganisms11051300
 64. Bertelsen CV. *Screening of Bacteria Using Impedance Flow Cytometry*. Denmark: DTU Bioengineering; 2021.
 65. Parratt K, Newton D, Dunkers J, *et al.* Measurement quality metrics to improve absolute microbial cell counting. *Front Microbiol*. 2025;16:1631377.
doi: 10.3389/fmicb.2025.1631377
 66. Silva LJ, Crevelin EJ, Souza DT, *et al.* Actinobacteria from antarctica as a source for anticancer discovery. *Sci Rep*. 2020;10(1):13870.
doi: 10.1038/s41598-020-69786-2
 67. Lee LH, Cheah YK, Mohd Sidik S, *et al.* Molecular characterization of antarctic actinobacteria and screening for antimicrobial metabolite production. *World J Microbiol Biotechnol*. 2012;28(5):2125-2137.
doi: 10.1007/s11274-012-1018-1
 68. Madigan MT, Kempfer ML, Bender KS, *et al.* Characterization of a cold-active bacterium isolated from the south pole "ice tunnel." *Extremophiles*. 2017;21(5):891-901.
doi: 10.1007/s00792-017-0950-2
 69. Davies J. How to discover new antibiotics: Harvesting the parvome. *Curr Opin Chem Biol*. 2011;15(1):5-10.
doi: 10.1016/j.cbpa.2010.11.001
 70. Yook G, Nam J, Jo Y, Yoon H, Yang D. Metabolic engineering approaches for the biosynthesis of antibiotics. *Microb Cell Fact*. 2025;24(1):35.
doi: 10.1186/s12934-024-02628-2
 71. Alwali AY, Parkinson EI. Small molecule inducers of actinobacteria natural product biosynthesis. *J Ind Microbiol Biotechnol*. 2023;50(1):019.
doi: 10.1093/jimb/kuad019
 72. Green CA, Kamble NS, Court EK, *et al.* Engineering the flagellar type III secretion system: Improving capacity for secretion of recombinant protein. *Microb Cell Fact*. 2019;18(1):10.
doi: 10.1186/s12934-019-1058-4
 73. Kamble NS, Thomas S, Madaan T, *et al.* Engineered bacteria as an orally administered anti-viral treatment and immunization system. *Gut Microbes*. 2025;17(1):2500056.
doi: 10.1080/19490976.2025.2500056
 74. Thirumurugan D, Cholarajan A, Raja SS, Vijayakumar R. An introductory chapter: secondary metabolites. In: Vijayakumar R, Suresh R, editors. *Secondary Metabolites-Sources and Application*. London: IntechOpen; 2018. p. 3-22.
doi: 10.5772/intechopen.79766
 75. Medema MH. Computational genomics of specialized metabolism: From natural product discovery to microbiome

- ecology. *Msystems*. 2018;3(2):e00182-17.
doi: 10.1128/mSystems.00182-17
76. Zahroh EW, Ningsih F, Sjamsuridzal W. Detection of antimicrobial compounds from thermophilic actinomycetes using one strain many compounds (OSMAC) approach. *J Biol Lingkung*. 2022;9(1):76-94.
doi: 10.31289/biolink.v9i1.6438
77. Xiao X, Fu Y, Zhang D, Gao S. Enhancement of FK520 production in streptomyces hygrosopicus var. ascomyceticus ATCC 14891 by overexpressing the regulatory gene flbR2. *Bioprocess Biosyst Eng*. 2025;48(3):493-507.
doi: 10.1007/s00449-024-03124-y
78. Zhu S, Duan Y, Huang Y. The application of ribosome engineering to natural product discovery and yield improvement in *Streptomyces*. *Antibiotics (Basel)*. 2019;8(3):133.
doi: 10.3390/antibiotics8030133
79. Asamizu S, Ijichi S, Hoshino S, et al. Stable isotope-guided metabolomics reveals polar-functionalized fatty-acylated RiPPs from streptomyces. *ACS Chem Biol*. 2022;17(10):2936-2944.
doi: 10.1021/acscchembio.2c00601
80. Kang HS, Kim ES. Recent advances in heterologous expression of natural product biosynthetic gene clusters in *Streptomyces* hosts. *Curr Opin Biotechnol*. 2021;69:118-127.
doi: 10.1016/j.copbio.2020.12.016
81. Augustijn HE, Roseboom AM, Medema MH, van Wezel GP. Harnessing regulatory networks in Actinobacteria for natural product discovery. *J Ind Microbiol Biotechnol*. 2024;51:kuae011.
doi: 10.1093/jimb/kuae011
82. Wang Q, Zhao J, Liu Z, Ding S, Huang Z, Chen J. Genomic insights and synthetic biology applications of marine actinomycete *Streptomyces griseoincarnatus* HNS054. *Int J Mol Sci*. 2024;25(6):3127.
doi: 10.3390/ijms25063127
83. Gobena S, Admassu B, Kinde MZ, Gessese AT. Proteomics and its current application in biomedical area: Concise review. *ScientificWorldJournal*. 2024;2024(1):4454744.
doi: 10.1155/2024/4454744
84. Talreja S, Tiwari S. From one to millions: The revolution of combinatorial chemistry. *J Anal Tech Res*. 2024;6(2):37-42.
doi: 10.26502/jatr.43
85. Ji CH, Je HW, Kim H, Kang HS. Promoter engineering of natural product biosynthetic gene clusters in actinomycetes: Concepts and applications. *Nat Prod Rep*. 2024;41(4):672-699.
doi: 10.1039/D3NP00049D
86. Bind S, Bind S, Sharma AK, Chaturvedi P. Epigenetic modification: A key tool for secondary metabolite production in microorganisms. *Front Microbiol*. 2022;13:784109.
doi: 10.3389/fmicb.2022.784109
87. Tanaka Y, Hosaka T, Ochi K. Rare earth elements activate the secondary metabolite-biosynthetic gene clusters in *Streptomyces coelicolor* A3 (2). *J Antibiot (Tokyo)*. 2010;63(8):477-481.
doi: 10.1038/ja.2010.53
88. Lee SR, Gallant É, Seyedsayamdost MR. Discovery of cryptic natural products using high-throughput elicitor screening on agar media. *Biochemistry*. 2024;64(1):20-25.
doi: 10.1021/acs.biochem.4c00659
89. Asamizu S. Co-cultivation strategies for natural product discovery from actinomycetes: Unlocking silent secondary metabolism with mycolic acid-containing bacteria. *World J Microbiol Biotechnol*. 2025;41(7):217.
doi: 10.1007/s11274-025-04406-7
90. Begani J, Lakhani J, Harwani D. Current strategies to induce secondary metabolites from microbial biosynthetic cryptic gene clusters. *Ann Microbiol*. 2018;68(7):419-432.
doi: 10.1007/s13213-018-1351-1
91. Wang S, Zeng X, Jiang Y, et al. Unleashing the potential: Type I CRISPR-Cas systems in actinomycetes for genome editing. *Nat Prod Rep*. 2024;41(9):1441-1455.
doi: 10.1039/D4NP00010B
92. Aslam Z, Yasir M, Khaliq A, Matsui K, Ryun Y. Mini review too much bacteria still unculturable. *Crop Environ*. 2010;1(1):59-60.
93. Wade W. Unculturable bacteria-the uncharacterized organisms that cause oral infections. *J R Soc Med*. 2002;95(2):81-83.
doi: 10.1177/014107680209500207
94. Bodor A, Bounedjoum N, Vincze GE, et al. Challenges of unculturable bacteria: Environmental perspectives. *Rev Environ Sci Bio/Technology*. 2020;19(1):1-22.
doi: 10.1007/s11157-020-09522-4
95. Farha MA, Tu MM, Brown ED. Important challenges to finding new leads for new antibiotics. *Curr Opin Microbiol*. 2025;83:102562.
doi: 10.1016/j.mib.2024.102562
96. Gottlieb D. The production and role of antibiotics in soil. *J Antibiot (Tokyo)*. 1976;29(10):987-1000.
doi: 10.7164/antibiotics.29.987
97. Zhang QW, Lin LG, Ye WC. Techniques for extraction and isolation of natural products: A comprehensive review. *Chin Med*. 2018;13(1):20.

- doi: 10.1186/s13020-018-0177-x
98. Balagurunathan R, Radhakrishnan M, Shanmugasundaram T, Gopikrishnan V, Jerrine J. Bioassay-guided isolation and characterization of metabolites from actinobacteria. In: *Protocols in Actinobacterial Research*. Berlin: Springer; 2020. p. 147-163.
doi: 10.1007/978-1-0716-0728-2_8
99. Waithaka PN, Mwaura FB, Wagacha JM, Gathuru EM, Githaiga BM. Purification and cytotoxic assays of four antimicrobial metabolites extracted from actinomycetes of the soils of menengai crater, kenya. *Nov Res Microbiol J*. 2019;3(3):351-365.
doi: 10.21608/nrmj.2019.37208
100. Jiang L, Pu H, Qin X, et al. Syn-2, 3-diols and anti-inflammatory indole derivatives from *Streptomyces* sp. CB09001. *Nat Prod Res*. 2019;35(1):144-151.
doi: 10.1080/14786419.2019.1611812
101. Jiang L, Xiang J, Zhu S, et al. Undescribed benzophenone and xanthenes from cave-derived *Streptomyces* sp. CB09001. *Nat Prod Res*. 2020;36(7):1725-1733.
doi: 10.1080/14786419.2020.1813134
102. Balagurunathan R, Radhakrishnan M, Shanmugasundaram T, Gopikrishnan V, Jerrine J. Production of bioproducts from actinobacteria. In: *Protocols in Actinobacterial Research*. Berlin: Springer; 2020. p. 113-128.
doi: 10.1007/978-1-0716-0728-2_5
103. Stankovic N, Radulovic V, Petkovic M, et al. *Streptomyces* sp. JS520 produces exceptionally high quantities of undecylprodigiosin with antibacterial, antioxidative, and UV-protective properties. *Appl Microbiol Biotechnol*. 2012;96(5):1217-1231.
doi: 10.1007/s00253-012-4237-3
104. Soldatou S, Eldjárn GH, Ramsay A, et al. Comparative metabologenomics analysis of polar actinomycetes. *Mar Drugs*. 2021;19(2):103.
doi: 10.3390/md19020103
105. Kamjam M, Sivalingam P, Deng Z, Hong K. Deep sea actinomycetes and their secondary metabolites. *Front Microbiol*. 2017;8:760.
doi: 10.3389/fmicb.2017.00760
106. Gu Z, Liu Y, Xu B, et al. Description of *Conyzicola nivalis* sp. nov., isolated from glacial snow, and emended description of the genus *Conyzicola* and *Conyzicola lurida*. *Int J Syst Evol Microbiol*. 2017;67(8):2818-2822.
doi: 10.1099/ijsem.0.002027
107. Liu Q, Xin YH, Chen XL, Liu HC, Zhou YG, Chen WX. *Cryobacterium aureum* sp. nov., a Psychrophilic bacterium isolated from glacier ice collected from the ice tongue surface. *Int J Syst Evol Microbiol*. 2018;68(4):1173-1176.
doi: 10.1099/ijsem.0.002647
108. Wang J, Leiva S, Huang J, Huang Y. *Amycolatopsis antarctica* sp. nov., isolated from the surface of an Antarctic brown macroalga. *Int J Syst Evol Microbiol*. 2018;68(7):2348-2356.
doi: 10.1099/ijsem.0.002844
109. Villalobos AS, Wiese J, Aguilar P, Dorador C, Imhoff JF. *Subtercola vilae* sp. nov., a novel actinobacterium from an extremely high-altitude cold volcano lake in Chile. *Antonie Van Leeuwenhoek*. 2018;111(6):955-963.
doi: 10.1007/s10482-017-0994-4
110. Liu Q, Liu HC, Zhou YG, Xin YH. Genetic diversity of glacier-inhabiting *Cryobacterium* bacteria in china and description of *Cryobacterium zongtaii* sp. nov. and *Arthrobacter glacialis* sp. nov. *Syst Appl Microbiol*. 2019;42(2):168-177.
doi: 10.1016/j.syapm.2018.10.005
111. Kamjam M, Nopnakorn P, Zhang L, Peng F, Deng Z, Hong K. *Streptomyces polaris* sp. nov. and *Streptomyces septentrionalis* sp. nov., isolated from frozen soil. *Antonie Van Leeuwenhoek*. 2019;112(3):375-387.
doi: 10.1007/s10482-018-1166-x
112. Liu Q, Tian JH, Liu HC, Zhou YG, Xin YH. *Cryobacterium melibiosiphilum* sp. nov., a Psychrophilic bacterium isolated from glacier ice. *Int J Syst Evol Microbiol*. 2019;69(10):3276-3280.
doi: 10.1099/ijsem.0.003620
113. Wang F, Liu Y, Wang N, et al. *Haloactinobacterium glaciecola* sp. nov., isolated from an ice core. *Int J Syst Evol Microbiol*. 2019;69(11):3519-3523.
doi: 10.1099/ijsem.0.003653
114. Filippova SN, Surgucheva NA, Detkova EN, et al. *Serinibacter arcticus* sp. nov., isolated from a thawing ancient ice wedge. *Int J Syst Evol Microbiol*. 2020;70(2):929-934.
doi: 10.1099/ijsem.0.003848
115. Shin Y, Lee BH, Lee KE, Park W. *Pseudarthrobacter psychrotolerans* sp. nov., a cold-adapted bacterium isolated from Antarctic soil. *Int J Syst Evol Microbiol*. 2020;70(12):6106-6114.
doi: 10.1099/ijsem.0.004505
116. Maiti PK, Mandal S. *Lentzea indica* sp. nov., a novel actinobacteria isolated from Indian Himalayan-soil. *Antonie Van Leeuwenhoek*. 2020;113(10):1411-1423.
doi: 10.1007/s10482-020-01449-8
117. Liu Q, Tian JH, Liu HC, Zhou YG, Xin YH. *Cryobacterium ruanii* sp. nov. and *Cryobacterium breve* sp. nov., isolated from glaciers. *Int J Syst Evol Microbiol*. 2020;70(3):1918-1923.
doi: 10.1099/ijsem.0.003994
118. Kim MC, Ju YH, Hwang UA, Liu P, Pak SH, Peng F.

- Pengzhenrongella sicca* gen. nov., sp. nov., a new member of suborder Micrococccineae isolated from High Arctic tundra soil. *Int J Syst Evol Microbiol*. 2021;71(9):4988.
doi: 10.1099/ijsem.0.004988
119. Zhu WZ, Ge YM, Gao HM, Dai J, Zhang XL, Yang Q. *Gephyromycinifex aptenodytis* gen. nov., sp. nov., isolated from gut of antarctic emperor penguin *Aptenodytes forsteri*. *Antonie Van Leeuwenhoek*. 2021;114(12):2003-2017.
doi: 10.1007/s10482-021-01657-w
120. Jani K, Kajale S, Shetye M, Palkar S, Sharma A. *Marisediminicola senii* sp. nov. isolated from queen maud land, antarctica. *Int J Syst Evol Microbiol*. 2021;71(2):4641.
doi: 10.1099/ijsem.0.004641
121. Sakdapetsiri C, Kuntaveesuk A, Ngaemthao W, et al. *Paeniglutamicibacter terrestris* sp. nov., isolated from phenanthrene-degrading consortium enriched from Antarctic soil. *Int J Syst Evol Microbiol*. 2021;71(3):4689.
doi: 10.1099/ijsem.0.004689
122. Liang Y, Jiang P, Yao B, Jiao Y, Li J. *Lacisediminihabitans changchengi* sp. nov., an actinobacterium isolated from Antarctic swamplands mud. *Arch Microbiol*. 2021;203(9):5519-5524.
doi: 10.1007/s00203-021-02531-z
123. Jiang P, Ren X, Wang W, Niu G, Li J. *Arthrobacter terrae* sp. nov., a psychrophilic actinobacterium with multi copies of capA gene isolated from Antarctic soil. *Antonie Van Leeuwenhoek*. 2022;115(5):635-644.
doi: 10.1007/s10482-022-01727-7
124. Chen Y, Zhang H, Ping W, Zhu L, Xin Y, Zhang J. *Pseudarthrobacter albicanus* sp. nov., isolated from antarctic soil. *Int J Syst Evol Microbiol*. 2022;72(1):5182.
doi: 10.1099/ijsem.0.005182
125. Jiang L, Peng Y, Seo J, et al. *Subtercola endophyticus* sp. nov., a cold-adapted bacterium isolated from *Abies koreana*. *Sci Rep*. 2022;12(1):1-13.
doi: 10.21203/rs.3.rs-1458414/v1
126. Valenzuela-Ibaceta F, Carrasco V, Lagos-Moraga S, Dietz-Vargas C, Navarro CA, Pérez-Donoso JM. *Arthrobacter vasquezii* sp. nov., isolated from a soil sample from union glacier, antarctica. *Int J Syst Evol Microbiol*. 2023;73(10):6095.
doi: 10.1099/ijsem.0.006095
127. Liu Q, Yang LL, Xin YH. Diversity of the genus *Cryobacterium* and proposal of 19 novel species isolated from glaciers. *Front Microbiol*. 2023;14:1115168.
doi: 10.3389/fmicb.2023.1115168
128. Berestovskaya YY, Tourova TP, Grouzdev DS, et al. *Cryobacterium inferilacus* sp. nov., a psychrophilic ureolytic bacterium from lake untersee in antarctica. *Microorganisms*. 2025;13(5):990.
doi: 10.3390/microorganisms13050990
129. Kim D, Lee EJ, Lee J, et al. Antartarin, a cytotoxic zizaane-type sesquiterpenoid from a *Streptomyces* sp. isolated from an antarctic marine sediment. *Mar Drugs*. 2018;16(4):130.
doi: 10.3390/md16040130
130. Shen J, Fan Y, Zhu G, Chen H, Zhu W, Fu P. Polycyclic macrolactams generated via intramolecular diels-alder reactions from an antarctic *Streptomyces* species. *Org Lett*. 2019;21(12):4816-4820.
doi: 10.1021/acs.orglett.9b01710
131. Zhou L, Chen X, Sun C, et al. Saliniquinone derivatives, saliniquinones G-I and heraclemycin E, from the marine animal-derived *Nocardiopsis aegyptia* HDN19-252. *Mar Drugs*. 2021;19(10):575.
doi: 10.3390/md19100575
132. Zhu WZ, Wang SH, Gao HM, et al. Characterization of bioactivities and biosynthesis of angucycline/angucyclinone derivatives derived from *Gephyromycinifex aptenodytis* gen. nov., sp. nov. *Mar Drugs*. 2022;20(1):34.
doi: 10.3390/md20010034
133. Quinn GA, Dyson PJ. Going to extremes: Progress in exploring new environments for novel antibiotics. *NPJ Antimicrob Resist*. 2024;2(1):8.
doi: 10.1038/s44259-024-00025-8
134. Medeiros W, Kralova S, Oliveira V, Ziemert N, Sehnal L. Antarctic bacterial natural products: from genomic insights to drug discovery. *Nat Prod Rep*. 2025;42(5):774-787.
doi: 10.1039/D4NP00045E
135. Hwengwere K, January GG, Howell KL, Peck LS, Upton M, Clark MS. Psychrotrophic antarctic marine bacteria as potential reservoirs for novel antimicrobial genes. *FEMS Microbes*. 2025;6:xtaf004.
doi: 10.1093/femsmc/xtaf004