

Bibliometric Insights on Mangrove Actinobacteria's Secondary Metabolites as Antibiotics Using VOSviewer

Rubiyatna Sakaroni^{1*}, Nora Listantia², Dyah Puspitasari Ningthias²

¹Department of Biology Education, Faculty of Teacher Training and Education, Mataram University, Mataram, Indonesia;

²Department of Chemistry Education, Faculty of Teacher Training and Education, Mataram University, Mataram, Indonesia;

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*Corresponding Author:

Rubiyatna Sakaroni,

Department of Biology Education, Faculty of Teacher Training and Education, Mataram University, Mataram City, Indonesia;

Email:

rubysaka7@staff.unram.ac.id

Abstract: Secondary metabolites from actinobacteria have been known to have many potentials as antioxidants, antibiotics, anti-cancer, and others. Various studies have been conducted and published regarding the findings of the potential of actinobacteria. This study aims to determine the development of research related to the potential of actinobacteria originating from mangrove areas and their secondary metabolites as natural antibiotics with bibliometric methods assisted by the VOS Viewer application. The articles used in this study are articles published from 2014 to 2024 and taken from the PubMed database. A total of 78 articles analyzed with VOS Viewer showed that over the past decade, the development of research on this topic still revolves around actinobacteria, microbial sensitivity tests, anti-bacterial agents, and *Streptomyces* as indicated by the high occurrence of these words in the titles and abstracts of the articles analyzed. The potential for research development can be directed at antineoplastic agents, cell proliferation, and mass spectrometry because the use of these terms is still minimal. However, analysis using other databases is needed as a comparison to get clearer results related to the development of research on the potential of actinobacteria derived from mangroves and their secondary metabolites as antibiotics.

Keywords: Actinobacteria, antibiotics, bibliometric analysis, mangrove, secondary metabolites.

Introduction

Bacterial resistance to antibiotics, including the development of cross-resistance to different classes of antibiotics, has become a significant global health threat in the 21st century (MacLean & Millan, 2019; Cândido et al., 2019). This condition reduces the effectiveness of existing antibiotics and increases the risk of difficult-to-treat infections. This issue is particularly of concern in high virulence pathogens such as *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacteriaceae* (Tacconelli et al., 2017). Therefore, the search for new

antibiotics capable of fighting resistant bacteria is an urgent need in global public health management.

According to Haddad et al., (2024), Antibiotics are classified into natural and synthetic, with bactericidal agents that kill or destroy bacteria, and bacteriostatic agents that prevent the proliferation of bacteria. Despite many attempts to chemically synthesis antibiotics, the natural environment remains a major source of discovery for new antibiotic compounds. Actinobacteria, particularly from the genus *Streptomyces* sp, are known to produce about two-thirds of all currently available antibiotics, making them particularly important in fighting multidrug-resistant

pathogens (Barka *et al.*, 2016).

Mangrove forest ecosystems, with their high biodiversity, offer great potential as a source of natural antibiotics that have yet to be fully explored (Medica *et al.*, 2020). The widespread mangroves in tropical and subtropical regions provide a unique habitat for actinobacteria, which produce bioactive compounds including secondary metabolites (Hu *et al.*, 2022). The varied environmental conditions in mangrove forests create a diversity of actinobacteria species that have not been widely studied. Previous studies have shown the great potential of secondary metabolites from mangrove actinobacteria as novel antibiotics, further emphasizing the importance of exploring this ecosystem.

Although research on actinobacteria and their secondary metabolites is growing, some studies focus on different areas. Tacconelli *et al.*, (2017), emphasized the importance of finding new antibiotics to fight resistance of certain pathogens, but without explaining the contribution of mangrove forests as a source. Barka *et al.*, (2016) reviewed the importance of *Streptomyces* sp in producing antibiotics but focused more on terrestrial environments. Meanwhile, Maimunah *et al.*, (2021); Purwanto *et al.*, (2021); and Rahmandhana *et al.*, (2022) only provide a general review of mangrove forest biodiversity without delving into antibiotic potential. There are still rare studies related to the discovery of sources of antibiotic compounds from bacteria isolated in mangrove rhizospheres. Especially there is no research on mangrove rhizosphere in West Nusa Tenggara. However, it is necessary to raise the latest themes related to the discovery of antibiotic compounds from mangrove rhizosphere. Therefore, this research fills the gap by combining bibliometric analysis using VOSviewer to identify the latest research trends related to the potential of actinobacteria from mangroves as a source of natural antibiotics.

This study aims to analyze the development of research related to the potential of actinobacteria from mangrove ecosystems and their secondary metabolites as natural antibiotics through bibliometric analysis. The results of this study are expected to provide an overview of the number of scientific publications in this field, identify the

latest trends and developments, and project the direction of future research. In this way, this research can contribute to the development of new sources of antibiotics that are more effective in combating resistant bacteria.

Materials and Methods

This research adopts a qualitative approach, utilizing a comprehensive literature review to assess the development of studies on the potential of actinobacteria from mangrove ecosystems and their secondary metabolites as antibiotics. The literature review synthesizes previous research findings, offering a clear and detailed understanding of the topic (Mahanum, 2021). The emphasis on actinobacteria stems from their established ability to produce bioactive compounds, particularly secondary metabolites, which possess significant antimicrobial properties. By examining existing literature, this study seeks to identify trends, gaps, and advancements in this area, thereby enhancing our understanding of its potential applications in antibiotic development.

The literature search was conducted in March 2024 using the PubMed database, employing targeted keywords: actinobacteria, mangrove, and (antimicrobial OR antibiotic). Articles published between 2014 and 2024 were selected to capture a decade's worth of research progress. The selected articles were organized in RIS or BibTeX formats for use in the Mendeley reference manager, while PubMed-compatible formats were utilized for bibliometric analysis via VOSviewer. This software enabled the visualization of networks and relationships between keywords, revealing connections and clusters within the research field (Zakiyyah *et al.*, 2022). The methodological rigor of this approach ensures that the findings not only reflect existing knowledge but also pinpoint future research opportunities in harnessing mangrove-associated actinobacteria for antibiotic discovery.

Results and Discussion

This study identified 78 articles published between 2014 and 2024 that matched the specified keywords. PubMed recorded the highest number of publications in 2019, with 14 articles, reflecting significant interest and research output

during that year. The years 2017 and 2018 also demonstrated substantial contributions, with 9 articles each, indicating consistent scholarly attention to the topic during this period. By contrast, 2024 had the fewest publications, with only 3 articles published at the time of this study, potentially due to delays in research outputs or shifting academic focus. Interestingly, 2015 recorded only 5 articles, yet it produced the most highly cited work, highlighting the potential for high impact even with fewer publications.

Analysing Publication Trends and Citation Impact in Research

According to Table 1, the most cited article, published in 2015, has received 143 citations, underscoring its influence and importance in the field. This finding suggests that the quality and novelty of research may outweigh the quantity of publications in determining scholarly impact. The citation trend also provides insights into the enduring relevance of earlier studies compared to more recent works, which may take time to garner similar attention. Such data reflects the evolving dynamics of research dissemination and influence, emphasizing the need for both quality research and strategic publication timing to maximize impact within the academic community

Table 1. Article Data Sorted by Number of Document Citations or Citations

No	Article Title	Year	Citations	Reference
1	Antimicrobial activities of actinomycetes isolated from unexplored regions of Sundarbans mangrove ecosystem	2015	143	(Sengupta et al., 2015)
2	Bioactive Products From Plant-Endophytic Gram-Positive Bacteria	2019	130	(Ek-ramos et al., 2019)
3	Natural products from mangrove actinomycetes	2014	121	(D. Xu et al., 2014)
4	Mangrove rare actinobacteria: taxonomy, natural compound, and discovery of bioactivity	2015	114	(Azman et al., 2015)
5	Diversity and antimicrobial activities of actinobacteria isolated from tropical mangrove sediments in Malaysia	2014	105	(Lee, Zainal, Azman, Eng, Goh, et al., 2014)
6	Streptomyces as a Prominent Resource of Future Anti-MRSA Drugs	2018	82	(Kemung et al., 2018)
7	Alkaloids from the mangrove-derived actinomycete <i>Jishengella endophytica</i> 161111	2014	70	(P. Wang et al., 2014)
8	Diversity, Novelty, and Antimicrobial Activity of Endophytic Actinobacteria From Mangrove Plants in Beilun Estuary National Nature Reserve of Guangxi, China	2018	67	(Z. Jiang et al., 2018)
9	Penicibrocazines A-E, five new sulfide diketopiperazines from the marine-derived endophytic fungus <i>Penicillium brocae</i>	2015	63	(Meng et al., 2015)
10	<i>Streptomyces pluripotens</i> sp. nov., a bacteriocin-producing streptomycete that inhibits methicillin-resistant <i>Staphylococcus aureus</i>	2014	60	(Lee, Zainal, Azman, Eng, Mutalib, et al., 2014)
11	Cytotoxic Bagremycins from Mangrove-Derived <i>Streptomyces</i> sp. Q22	2017	43	(Chen et al., 2017)
12	Butremycin, the 3-Hydroxyl Derivative of Ikarugamycin and a Protonated Aromatic Tautomer of 5'-Methylthioinosine from a Ghanaian <i>Micromonospora</i> sp. K310	2014	40	(Kyeremeh, Acquah, Sazak, et al., 2014)

13	Evaluation of antibacterial potential of mangrove sediment-derived actinomycetes	2017	34	(Sangkanu et al., 2017)
14	Natural products from mangrove sediments-derived microbes: Structural diversity, bioactivities, biosynthesis, and total synthesis	2022	33	(K. Li et al., 2022)
15	<i>Streptomyces</i> sp. Strain MUSC 125 from Mangrove Soil in Malaysia with Anti-MRSA, Anti-Biofilm and Antioxidant Activities	2020	32	(Kemung et al., 2020)
16	Bioprospecting Red Sea Coastal Ecosystems for Culturable Microorganisms and Their Antimicrobial Potential	2016	29	(Al-amoudi, Essack, et al., 2016)
17	Isolation, diversity, and biotechnological potential of rhizo- and endophytic bacteria associated with mangrove plants from Saudi Arabia	2017	28	(Bibi et al., 2017)
18	Alterporriol-type dimers from the mangrove endophytic fungus, <i>Alternaria</i> sp. (SK11), and their MptpB inhibitions	2014	28	(Xia et al., 2014)
19	Antibacterial anthraquinone derivatives isolated from a mangrove-derived endophytic fungus <i>Aspergillus nidulans</i> by ethanol stress strategy	2018	28	(Yang et al., 2018)
20	Identification of the Actinomycin D Biosynthetic Pathway from Marine-Derived <i>Streptomyces costaricanus</i> SCSIO ZS0073	2019	28	(M. Liu et al., 2019)
21	Butrepyrazinone, a new pyrazinone with an unusual methylation pattern from a Ghanaian <i>Verrucospora</i> sp. K51G	2014	27	(Kyeremeh, Acquah, Camas, et al., 2014)
22	Studies on Antibacterial Activity and Diversity of Cultivable Actinobacteria Isolated from Mangrove Soil in Futian and Maowehai of China	2019	26	(F. Li et al., 2019)
23	Metagenomics as a preliminary screen for antimicrobial bioprospecting	2016	24	(Al-amoudi, Razali, et al., 2016)
24	Isolation, characterization, anti-MRSA evaluation, and in-silico multi-target anti-microbial validations of actinomycin X2 and actinomycin D produced by novel <i>Streptomyces smyrnaeus</i> UKAQ_23	2021	23	(Qureshi et al., 2021)
25	Antimicrobial potential of phylogenetically unique actinomycete, <i>Streptomyces</i> sp. JRG-04 from marine origin	2014	23	(Govindarajan et al., 2014)
26	Secondary metabolites from the mangrove sediment-derived fungus <i>Penicillium pinophilum</i> SCAU037	2019	21	(He et al., 2019)
27	Secondary metabolites from marine-derived <i>Streptomyces antibioticus</i> strain H74-21	2016	20	(Fu et al., 2016)
28	Iakyricidins A–D, Antiproliferative Piericidin Analogues Bearing a Carbonyl Group or Cyclic Skeleton from <i>Streptomyces iakyrus</i> SCSIO NS104	2019	20	(K. Li et al., 2019)
29	Screening of novel actinobacteria and characterization of the potential isolates from mangrove sediment of south coastal India	2017	19	(Arumugam et al., 2017)
30	Novel propanamide analogue and antiproliferative diketopiperazines from mangrove <i>Streptomyces</i> sp. Q24	2017	19	(X. Ye et al., 2016)
31	Isolation, characterization and identification of antibiofouling metabolite from mangrove derived <i>Streptomyces sampsonii</i> PM33	2019	18	(Gopikrishnan et al., 2019)
32	PreQ0 base, an unusual metabolite with anti-cancer activity from <i>Streptomyces qinglanensis</i> 172205	2015	18	(D. Xu et al., 2015)

33	Pentamycin Biosynthesis in Philippine Streptomyces sp. S816: Cytochrome P450-Catalyzed Installation of the C-14 Hydroxyl Group	2019	18	(Zhou et al., 2019)
34	Deciphering the streamlined genome of Streptomyces xiamenensis 318 as the producer of the anti-fibrotic drug candidate xiamenmycin	2016	18	(M. Xu et al., 2016)
35	Diversity of Streptomyces spp. from mangrove forest of Sarawak (Malaysia) and screening of their antioxidant and cytotoxic activities	2019	17	(Law et al., 2019)
36	Ergosterols from the Culture Broth of Marine Streptomyces anandii H41-59	2016	16	(Zhang et al., 2016)
37	Antifungal activity and molecular docking of phenol, 2,4-bis(1,1-dimethylethyl) produced by plant growth-promoting actinobacterium Kutzneria sp. strain TSII from mangrove sediments	2021	15	(Suganya et al., 2021)
38	Antimicrobial Activity and Phylogenetic Analysis of Streptomyces Parvulus Dosmb-D105 Isolated from the Mangrove Sediments of Andaman Islands	2016	14	(Baskaran et al., 2016)
39	Exploring the Potential of Antibiotic Production From Rare Actinobacteria by Whole-Genome Sequencing and Guided MS/MS Analysis	2020	13	(Hu et al., 2020)
40	Bioactivity Assessment of Indian Origin-Mangrove Actinobacteria against <i>Candida albicans</i>	2018	13	(J. G. S. P. Kumar et al., 2018)
41	Exploitation of Potentially New Antibiotics from Mangrove Actinobacteria in Maowei Sea by Combination of Multiple Discovery Strategies	2019	13	(Lu et al., 2019)
42	Cure of tuberculosis using nanotechnology: An overview	2018	12	(Kerry et al., 2018)
43	Ikarugamycin inhibits pancreatic cancer cell glycolysis by targeting hexokinase 2	2022	12	(S. Jiang et al., 2020)
44	Exploration of Anti-infectives From Mangrove-Derived Micromonospora sp. RMA46 to Combat <i>Vibrio cholerae</i> Pathogenesis	2020	11	(Sarveswari et al., 2020)
45	Angucycline Glycosides from Mangrove-Derived Streptomycesdiastaticus subsp. SCSIO GJ056	2018	11	(Huang & Ju, 2018)
46	Metabolomics Tools Assisting Classic Screening Methods in Discovering New Antibiotics from Mangrove Actinomycetia in Leizhou Peninsula	2021	11	(Peninsula et al., 2021)
47	Genome guided investigation of antibiotics producing actinomycetales strain isolated from a Macau mangrove ecosystem	2018	11	(Hu et al., 2018)
48	Antiamoebic Activities of Indolocarbazole Metabolites Isolated from Streptomyces sanyensis Cultures	2019	9	(Cartuche et al., 2019)
49	Bioactive Molecules from Mangrove Streptomyces qinglanensis 172205	2020	8	(D. Xu et al., 2020)
50	Optimization of media components for production of antimicrobial compound by Brevibacillus brevis EGS9 isolated from mangrove ecosystem	2017	8	(Arumugam & Senthil Kumar, 2017)
51	Bioactive Metabolites Produced by Pseudonocardia endophytica VUK-10 from Mangrove Sediments: Isolation, Chemical Structure Determination and Bioactivity	2015	8	(Mangamuri et al., 2015)
52	Screening, partial purification of antivibriosis metabolite sterol-glycosides from Rhodococcus sp. against aquaculture associated pathogens	2019	7	(Bodhaguru et al., 2019)

53	Metagenomic insights into surface water microbial communities of a South Asian mangrove ecosystem	2022	7	(Ghosh <i>et al.</i> , 2022)
54	Screening and identification of novel isolate <i>Streptomyces</i> sp., NLKPB45 from Nellore coastal region for its biomedical applications	2019	7	(Kalyani <i>et al.</i> , 2019)
55	Genome-guided and mass spectrometry investigation of natural products produced by a potential new actinobacterial strain isolated from a mangrove ecosystem in Futian, Shenzhen, China	2019	7	(Hu <i>et al.</i> , 2019)
56	<i>Schumannella soli</i> sp. nov., a novel actinomycete isolated from mangrove soil by in situ cultivation	2021	7	(F. Li <i>et al.</i> , 2021)
57	Isolation, structure elucidation and anticancer activity from <i>Brevibacillus brevis</i> EGS 9 that combats Multi Drug Resistant actinobacteria	2018	6	(Arumugam <i>et al.</i> , 2018)
58	Characterization of Bioactive Actinomycetes Isolated from Kadolkele Mangrove Sediments, Sri Lanka	2022	5	(Naligama <i>et al.</i> , 2022)
59	Evaluation of antimicrobial activity of the extract of <i>Streptomyces euryhalinus</i> isolated from the Indian Sundarbans	2021	4	(Biswas <i>et al.</i> , 2021)
60	A Meta-Omics Analysis Unveils the Shift in Microbial Community Structures and Metabolomics Profiles in Mangrove Sediments Treated with a Selective Actinobacterial Isolation Procedure	2021	4	(Marfil-santana <i>et al.</i> , 2021)
61	Biosynthesis of silver nanoparticles using actinomycetes, phytotoxicity on rice seeds, and potential application in the biocontrol of phytopathogens	2023	4	(Zwar <i>et al.</i> , 2023)
62	Susceptibility pattern of methicillin resistance <i>Staphylococcus aureus</i> (MRSA) by flow cytometry analysis and characterization of novel lead drug molecule from <i>Streptomyces</i> species	2021	4	(Govindarajan <i>et al.</i> , 2021)
63	In-vitro assessment of antimicrobial properties and lymphocytotoxicity assay of benzoisochromanequinones polyketide from <i>Streptomyces</i> sp JRG-04	2017	4	(Govindarajan <i>et al.</i> , 2017)
64	Larvicidal potency of marine actinobacteria isolated from mangrove environment against <i>Aedes aegypti</i> and <i>Anopheles stephensi</i>	2017	3	(Balakrishnan <i>et al.</i> , 2016)
65	Diketopiperazine and enterotoxin analogues from the mangrove derived-soil <i>Streptomyces</i> sp. SCSIO 41400 and their biological evaluation	2022	3	(Song <i>et al.</i> , 2020)
66	Insights into the phylogenetic diversity, biological activities, and biosynthetic potential of mangrove rhizosphere Actinobacteria from Hainan Island	2023	2	(J. Ye <i>et al.</i> , 2023)
67	Beilunmycin, a new virginiamycins antibiotic from mangrove-derived <i>Streptomyces</i> sp. 2BBP-J2 and the antibacterial activity by inhibiting protein translation	2020	2	(Z. Jiang <i>et al.</i> , 2020)
68	Secondary Metabolite Production Potential of Mangrove-Derived <i>Streptomyces olivaceus</i>	2021	2	(Hu <i>et al.</i> , 2021)
69	Genome-Guided Investigation Provides New Insights into Secondary Metabolites of <i>Streptomyces parvulus</i> SX6 from <i>Aegiceras corniculatum</i>	2022	2	(Quach <i>et al.</i> , 2022)
70	Antibacterial and Anti-HIV Metabolites from Marine <i>Streptomyces albus</i> MAB56 Isolated from Andaman and Nicobar Islands, India	2023	1	(Manikkan <i>et al.</i> , 2023)

71	Occurrence of <i>Streptomyces tauricus</i> in mangrove soil of Mangalore region in Dakshina Kannada as a source for antimicrobial peptide	2023	1	(Karthilk & Kalyani, 2023)
72	Aromatic Polyketides from the Mangrove-Derived <i>Streptomyces</i> sp. SCSIO 40069	2023	0	(Sun et al., 2023)a
73	<i>Protactiibacter mangrovi</i> sp. nov., isolated from mangrove soil	2023	0	(F. Li et al., 2023)
74	Isolation, Structure Elucidation, and First Total Synthesis of Quinomycins K and L, Two New Octadepsipeptides from the Maowei Sea Mangrove-Derived <i>Streptomyces</i> sp. B475	2023	0	(Sea et al., 2023)
75	Development of Integrated Vectors with Strong Constitutive Promoters for High-Yield Antibiotic Production in Mangrove-Derived <i>Streptomyces</i>	2024	0	(Zhao et al., 2024)
76	Carbazole and Quinazolinone Derivatives from a Fluoride-Tolerant <i>Streptomyces</i> Strain OUCMDZ-5511	2024	0	(Y. Liu et al., 2024)
77	New Polyene Macrolide Compounds from Mangrove-Derived Strain <i>Streptomyces hirosimensis</i> GXIMD 06359: Isolation, Antifungal Activity, and Mechanism against <i>Talaromyces marneffe</i>	2024	0	(Z. Wang et al., 2024)

Network visualization between keywords on the topic

The VOS Viewer application is used to visually explore relationships and networks among topics in 78 articles obtained from the PubMed database using bibliometric methods. A bibliometric network consists of nodes and edges. Nodes, represented as circles, can represent publications, journals, researchers, or keywords. Edges depict the relationships between nodes, with the

strength of the relationship reflected by the distance between them. The closer the nodes are, the stronger the relationship. Image mapping is used to generate a detailed bibliometric network, while clustering provides insight and description of the bibliometric clustering (Aribowo, 2019). Figure 1 shows the visualization of the network between articles on the potential of mangrove actinobacteria and their secondary metabolites as antibiotics.

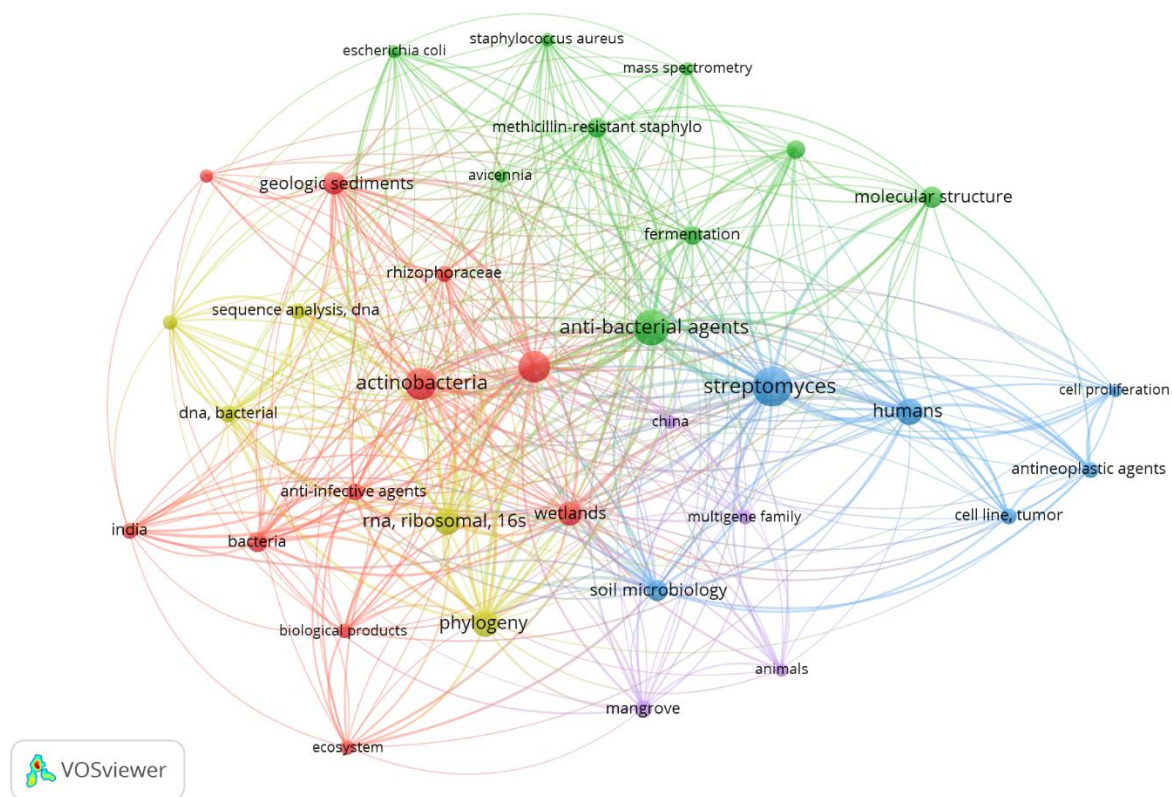


Figure 1. Network visualization between keywords on the topic of potential mangrove actinobacteria and secondary metabolites as antibiotics

The labels in the circles indicate keywords or terms that appear frequently, the size of the circle indicates the number of publications related to the term in the article title, and the color indicates the cluster. According to (Aribowo, 2019), each circle represents a keyword or term that appears in the title and abstract of the article, while the size of the circle indicates the number of publications relevant to that keyword or term. The network visualization in Figure 1 shows a complex relationship between the main keywords, where actinobacteria, microbial sensitivity test, anti-bacterial agents, and streptomyces dominate (marked by the largest circle). These keywords dominate the network, indicating that they are the main topics frequently discussed in the literature regarding the potential of actinobacteria as antibiotics. In addition, other keywords related to these three keywords are humans, fermentation, anti-infective agents, and so on. This relationship

indicates that research on actinobacteria not only focuses on their biological properties but also on the clinical applications and fermentation processes involved in antibiotic development (Kirby, 2023).

The different colors of the connecting lines between the circles indicate cluster relationship (van Eck & Waltman, 2017). The keywords can be further subdivided into 5 different clusters based on the network (indicated by the color difference in the network). This division of clusters within the network provides additional insights. The largest clusters (those marked with a particular color) indicate that the keywords not only appear frequently but also have strong relationships with other keywords, reflecting the high research interest in the area (R. Kumar *et al.*, 2023). A description of the clusters is shown in Table 2, where cluster 1 is the cluster with the most frequent keywords.

Table 2. Keyword grouping based on clusters

Cluster	Keyword
Cluster 1	Actinobacteria, anti-infective agents, antifungal agents, bacteria, biological products, ecosystem, geologic sediments, india, microbial sensitivity test, rhizophoraceae, wetlands
Cluster 2	Anti-bacterial agents, avicennia, Escherichia coli, fermentation, magnetic resonance spectroscopy, mass spectrometry, methicillin-resistant staphylococcus aureus, molecular structure, staphylococcus aureus
Cluster 3	Antineoplastic agents, cell line, tumor, cell proliferation, humans, soil microbiology, streptomyces
Cluster 4	Bacterial typing techniques, dna, bacterial, phylogeny, rna, ribosomal, 16s, sequence analysis, dna
Cluster 5	Animals, china, mangrove, multigene family

Overlay and Density visualization of keywords

In addition to network visualization, overlay visualization is also shown. The overlay visualization shows the development of keywords and terms used over time (van Eck &

Waltman, 2017). Figure 2 provides a view of the temporal progression of keywords and terms that emerged over the last 10-year period (2014 - 2024) related to the potential of mangrove actinobacteria and their secondary metabolites as antibiotics.

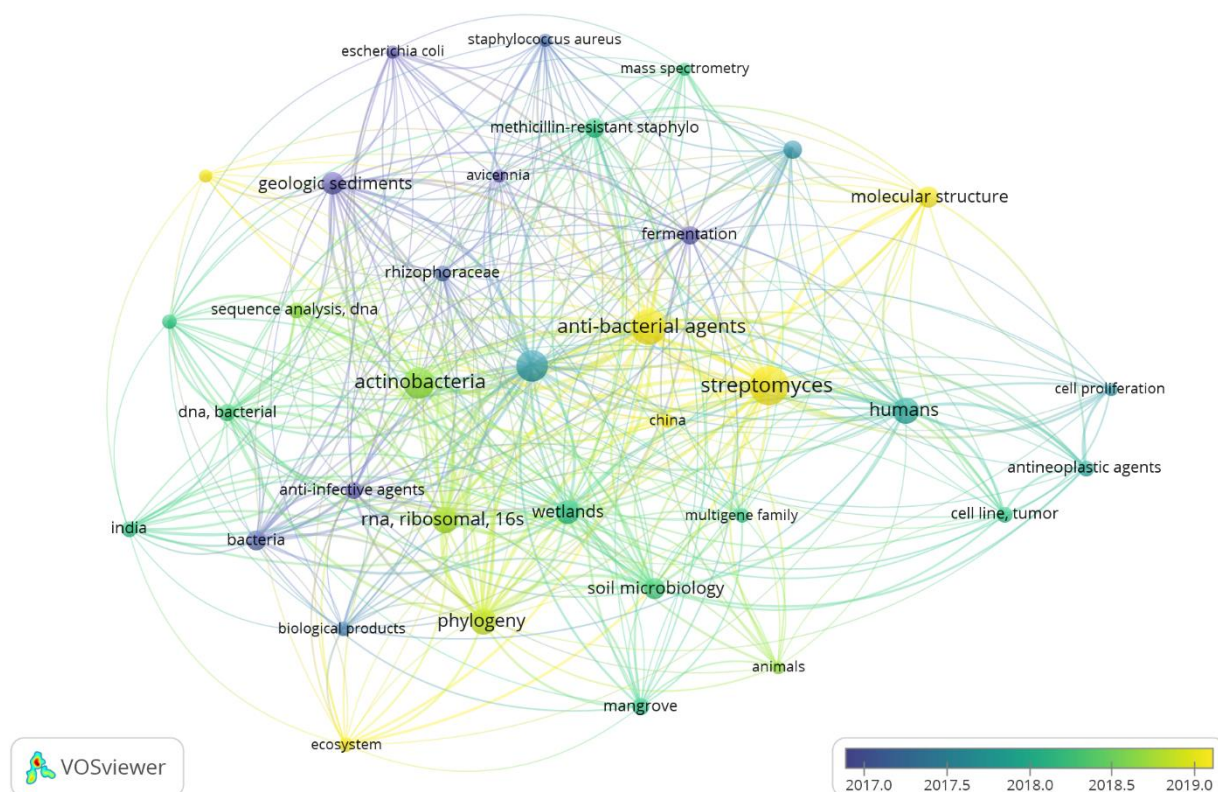


Figure 2. Overlay visualization between keywords on the topic of potential mangrove actinobacteria and secondary metabolites as antibiotics

The color change from blue to yellow in this visualization indicates that some new terms are beginning to emerge and become the focus of newer research. The newly emerging keywords reflect current research trends, such as the development of new methods for the isolation

and characterization of actinobacteria or more in-depth studies of the mechanisms of their secondary metabolites as anti-bacterial agents. This visualization helps identify changes in direction in research and topics that are likely to become more important in the future.

In contrast to network and overlay visualization, density visualization provides a snapshot of the main areas in a topic's bibliometric network (van Eck & Waltman, 2017). The RGB (red-green-blue) saturation levels in Figure 3 indicate the density or frequency of use of keywords and terms in the analyzed articles. The more frequently the word or term is used, the more yellow the area will be. Conversely, if the word or term rarely appears, the color density will be closer to green. Based on the visualization, actinobacteria, anti-bacterial agents, and *Streptomyces* are the most frequently

occurring keywords in the 78 articles analyzed, which means that research on this topic is very active and has a strong literature base. In contrast, the keywords antineoplastic agents, cell proliferation, and mass spectrometry are examples of infrequent words. These keywords and terms that rarely appear in the future can be considered as novel research topics to support the development of the potential of actinobacteria as natural antibiotics.

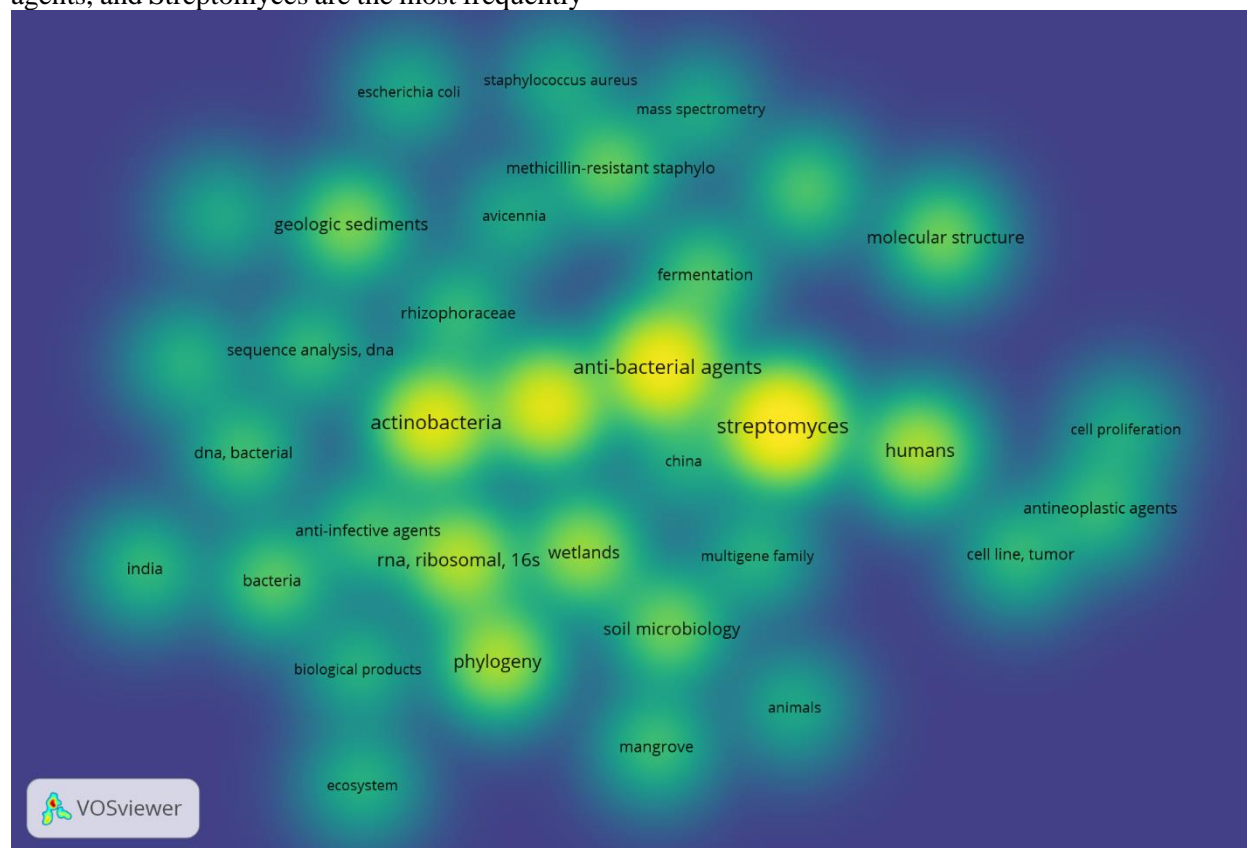


Figure 3. Density visualization of keywords and terms that appear in articles related to the potential of mangrove actinobacteria and their secondary metabolites as antibiotics

The results of this analysis show that research on the potential of actinobacteria from mangroves as a source of natural antibiotics has significant attention among researchers, especially in relation to microbial sensitivity and anti-bacterial agents. However, there are also less explored areas, such as the use of actinobacteria in the context of anti-neoplastic agents or cell proliferation analysis. Going forward, further

research could be focused on exploring these under-addressed topics, such as the use of actinobacteria in cancer therapy or the development of new analytical techniques using mass spectrometry. In addition, given the emerging trends in overlay visualization, efforts should be made to keep up with the latest methodological developments in the isolation and characterization of actinobacteria, as well as exploring their

potential applications in the pharmaceutical industry.

Conclusion

This study aims to examine the evolution of research concerning the potential of actinobacteria derived from mangrove regions and their secondary metabolites as natural antibiotics. This study analyzed 78 articles published between 2014 and 2024 from the PubMed database. The article entitled "Antimicrobial activities of actinomycetes isolated from unexplored regions of Sundarbans mangrove ecosystem," published in 2015, was the most frequently cited article, with 143 citations. Moreover, the VOS Viewer analysis indicates that the keywords "actinobacteria," "microbial sensitivity test," "antibacterial agents," and "streptomyces" have the highest frequency of occurrence in the title, abstract, and relevance to the subject matter under investigation. The terms "antineoplastic agents," "cell proliferation," and "mass spectrometry" may be regarded as promising avenues for further investigation, particularly in light of their limited prevalence in existing research on the potential of actinobacteria as antibiotics. Nevertheless, this research employs a single database, necessitating further investigation using additional databases for comparative purposes.

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